ADVANCES IN SCIENCE AND TECHNOLOGY

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Dr. Mujeeb Shaikh

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Advances in
Science and Technology

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PREFACE

Science and technology are at the forefront of human progress, driving innovation, transforming societies, and shaping the world we live in. Over the years, we have witnessed remarkable advancements in various scientific disciplines, as well as ground breaking technological breakthroughs that have revolutionized our lives in countless ways.

In this edited book, entitled "Advances in Science and Technology," we bring together a collection of cutting-edge research and developments from diverse fields, highlighting the incredible progress made in recent years. The book serves as a testament to the collective efforts of brilliant minds, researchers, and scientists who have tirelessly worked towards unravelling the mysteries of the universe and harnessing the potential of technology for the betterment of humanity.

The chapters within this volume cover a broad spectrum of topics, encompassing fields such as physics, chemistry, biology, computer science, engineering, medicine, and more. Each chapter delves into specific areas of research and presents the latest advancements, novel methodologies, and thought-provoking discoveries that have pushed the boundaries of scientific knowledge and technological capabilities.

As we explore the pages of this book, we embark on a journey through the realms of science and technology, witnessing breakthroughs that have the potential to reshape our world. From quantum computing and artificial intelligence to genetic engineering and renewable energy, the chapters provide a comprehensive overview of the remarkable progress being made across disciplines.

This book also serves as a platform for interdisciplinary exchange, fostering collaboration and stimulating new avenues of research. By bringing together experts from various scientific domains, we aim to encourage cross-pollination of ideas and facilitate a holistic understanding of the interconnected nature of scientific advancements and technological innovations.

We extend our heartfelt gratitude to all the authors who have contributed their valuable insights and expertise to this volume. Their dedication, passion, and commitment to advancing knowledge have made this book possible. We also express our appreciation to the reviewers and editors who meticulously reviewed the chapters, ensuring the highest quality of content.

It gives us immense pleasure to express our heartfelt thanks to Hon. Nisar I. Patel, Chairman, Y and M Anjuman Khairul Islam Trust, Hon. Hani Ahmed Farid, General Secretary, Y and M Anjuman Khairul Islam Trust and Hon. Dr. Hanif Lakdawala, Trustee of Y and M Anjuman Khairul Islam Trust, Mumbai for their valuable help and

excellent support. We are very much thankful to our Principal Professor Dr. Aftab Anwar Shaikh, for his valuable guidance, advice and help rendered to us.

Lastly, we extend our gratitude to the readers of this book, as it is through your curiosity and thirst for knowledge that the impact of these advancements will be realized. We hope that this collection of chapters inspires, enlightens, and sparks further exploration into the vast realm of science and technology.

Together, let us celebrate the remarkable achievements chronicled within these pages and embrace the infinite possibilities that lie ahead as we continue to advance in science and technology.

Dr. Iqbal N. Shaikh

Dr. Mujeeb Shaikh

ACKNOWLEDGEMENT

We would like to express our sincere gratitude and appreciation to all those who have contributed to the creation and completion of this edited book, "Advances in Science and Technology." It is through the collaborative efforts of numerous individuals that this comprehensive collection of ground breaking research and innovative ideas has come to fruition.

First and foremost, we extend our heartfelt thanks to the authors who have generously shared their expertise, insights, and discoveries in their respective fields. Your dedication to advancing scientific knowledge and technological progress has made this book a valuable resource for researchers, scholars, and enthusiasts alike.

We would also like to acknowledge the invaluable support provided by the peer reviewers, whose meticulous evaluation and constructive feedback have helped ensure the quality and rigor of the included chapters. Your expertise and commitment to maintaining scholarly standards have greatly enhanced the credibility and reliability of this publication.

Furthermore, we are grateful to the editorial team who worked diligently to coordinate and manage the editing process. Your meticulous attention to detail, organizational skills, and editorial expertise have played a vital role in shaping the content and structure of this book.

We would like to express our appreciation to the publishers and production team for their dedication and commitment to producing a high-quality publication. Your expertise in the publishing industry and your tireless efforts in bringing this book to life are commendable.

It gives us immense pleasure to express our heartfelt thanks to Hon. Nisar I. Patel, Chairman and Hon. Hani Ahmed Farid, General Secretary and Hon. Dr. Hanif Lakdawala Trustee of Y and M Anjuman Khairul Islam Trust, Mumbai for their valuable help and excellent support. We are very much thankful to our Principal Professor Dr. Aftab Anwar Shaikh, for his valuable guidance, advice and help rendered to us.

Lastly, we would like to thank our families, friends, and colleagues for their unwavering support, encouragement, and understanding throughout this endeavour. Your patience, understanding, and belief in our work have been a source of motivation and inspiration.

This book is a testament to the collaborative spirit and collective effort of all those involved. We hope that it serves as a catalyst for further advancements in science and technology, inspiring future generations of researchers and innovators to push the boundaries of knowledge.

Thank you all for your invaluable contributions.

Sincerely,

Dr. Iqbal N. Shaikh

Dr. Mujeeb Shaikh

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ANALYSIS OF SEASONAL VARIATIONS IN OXYGEN DEMANDING PARAMETERS (DO, BOD, COD) OF RIVER GANGA IN KANPUR

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Sunrise University, Alwar, Rajasthan

INTRODUCTION

River Ganga is the best example of fresh water ecosystem originates from Gangotri (Uttranchal) and offer traversing a distance of 2525 km falls into Ganga Sagar (W.B.). Ganga along with its tributaries in the largest and very important river basin the country. It has been a symbol of purity but today, it is grossly polluted and in utters, disregard to its sanctity. Ganga is getting increasingly polluted in highly congested areas of U.P.

The population in Kanpur is increasing resulting in the increase in development in areas adjoining the river; this has put tremendous pressure on the limited fresh water resources. The increasing silt and nutrient load further deteriorate the water bodies.

The River Ganga (2,525 km long) is the largest river basin in India, covering 26.2 percent of India's total geographical area. The plankton in a reservoir is an important biological indicator for evaluating the water quality of a reservoir. While phytoplankton are important primary producers and the basis of the food chain in open water some species on the other hand can be harmful to human and other vertebrates by releasing toxic substances into the water, Ariyadej et al. (2004). Phytoplankton studies and monitoring are useful for control of the physico-chemical and biological conditions of the water in any irrigation project. Phytoplankton is increasingly being used to monitor the ecological quality and health of the water environment and also to measure the effectiveness of management or restoration programmers or regulatory actions. In India the fresh water constitutes rivers, streams, lake, wetlands, ponds and reservoirs. These freshwater bodies directly help in the growth of human civilization. The freshwater resource is becoming day by day at the faster rate of deterioration of the water quality is now a global problem. The fresh water communities i.e., phytoplankton, zooplankton, macrophytes and macro invertebrates are sensitive to environmental factors. Different species of plankton vary in different seasons due to the changes in physico chemical nature of water. The phytoplankton community shows high diversity with the seasonal fluctuation, which indicates the diversity in ecological niches. The zooplankton occupying the secondary level in the food chain play a key role in the transformation of food energy synthesized by the phytoplankton to the higher trophic level. Both phytoplankton and zooplankton supports the economically important fish populations, Joshep et al. (2011).

Of all the Earth's ecosystems, rivers are the most dynamic having as their primary functions the transportation of water. Rivers and their landscapes are complex ecosystems that can be seen as an interaction between five main components: physical habitat, flow regime, the energy or food base of the system, biological interactions and water quality. All contribute to the maintenance of the biological or ecological integrity of the system which refers to the capacity to support and maintain a balanced, integrated, and adaptive biological system having the full range of elements and processes expected in a region's natural habitat. River pollution becomes apparent at times during accidents through horrifying scenes of dead fish floating on the surface of water.

But more often, it exists as chronic and insidious pollution originating from different human activities. Pollution causes a general deterioration in the state of health of rivers across the entire planet. The growing problem of river pollution has necessitated the monitoring of the Water quality of the river in different states of our country to restore the waste quality.

A review of literature reveals that various studies have already been carried out by different workers in studying the various physio-chemical and biological parameters of Indian rivers and this work is briefly reviewed here.

Three season studied 1. Winter, 2. Summer, 3. Monsoon

The river basin is one of the most thickly populated areas of the world. It sustains thousands of aquatic species of flora and fauna including many endemic and charismatic mega-fauna like the Ganges dolphin, (Matta, G. and Kumar, A. (2017)) (Matta, G.; Laura, G.; Kumar, A. and Machel, J. (2018)) Gavials etc. However, since 1950s the river is facing threats of erosion of its ecological integrity due to anthropogenic pressures in the form of construction of dams, barrages and embankments; loss of forest cover in its catchment area leading to heavy siltation, pollution from industrial effluents and domestic sewage degrading the water quality to the extent that the river water is not fit for even bathing purpose. Nevertheless, the river harbors rich and abundant aquatic biodiversity. The ecological changes cannot be attributed entirely to GAP but definitely it played an important role (Matta, G.; Kumar, A.; Naik, P. K.; Tiwari, A. K. and Berndtsson, R.

(2018) (Matta, G.; Kumar, A.; Walia, A.; Kumar, S.; Mishra, H. K.; Dhingra, G. K.; Pokhriyal, P. and Watts, M. (2016)

MATERIAL AND METHODS

For Plankton study samples were collected from Ganga River from March 2018 to April 2019 from six sampling sites. The samples were taken in a borosil glass bottle of 300 ml capacity and in plastic container. For qualitative analysis the plankton samples were collected with the help of standard plankton net with uniform speed. Identification of plankton was made with the help of available literature. (APHA, 1998; Edmondson, 1992 and Khanna and Bhutiani, 2004).

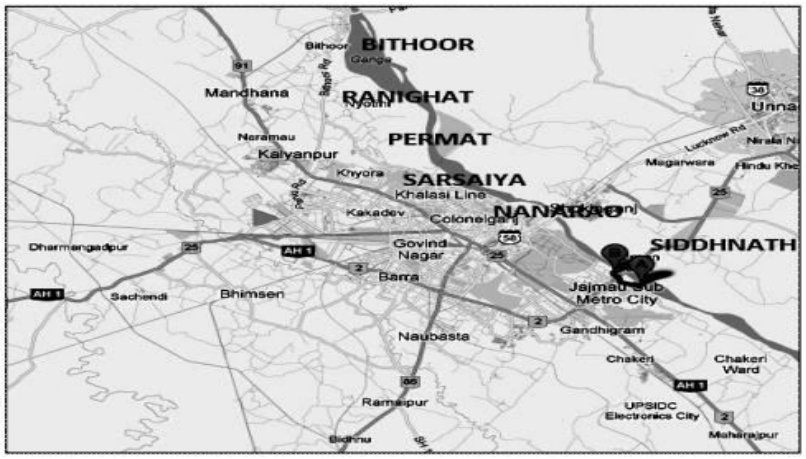
Sampling was done at five different sampling sites i.e.-

The investigators on the river Ganga were conducted fortnightly at six sampling stations (A to F) within a stretch of nearly 25 km. at Kanpur. All samples were sampled from July 2018 to June 2019 for three seasons i.e. summer, winter & monsoon season. Polyethylene bottles were used to collect the water samples. The purpose of sampling was to handle the water sample very carefully in such a way that no significant changes occur in composition before the tests are made. The bottles were properly labeled with the sample number and date of sampling and were put in the bag to carry them to the area of testing. The bottles were tightly closed after being filled & stored at room temperature.

Table 1: Methods used during these investigations

Parameters	Method used for estimation/Instrument
Dissolved Oxygen	Winkler's method
Biological Demand Oxygen	Winkler's method
Chemical Demand Oxygen	Reflux Titration method

The standard methods were adopted for these parameters. Data was statistically analyzed by using One Way ANOVA at 5% level of significance among various spot and different seasons.



Kanpur is known as Manchester of the East, the largest industrial hub of Uttar Pradesh State. It is bounded by 26.28degrees North latitude and 80.21degrees East longitude. Kanpur is situated on the western bank of the river Ganga. In Kanpur River Ganga takes entry at Bithoor and passing along several ghats, takes exit at Jajmau, total covering a distance of 24 kms. Six sampling stations (A to F) within a stretch of nearly 24 Kms at Kanpur city.

Bithoor Ghat, Bhairav Ghat, Permut Ghat, Sarsaiya Ghat, Bhagwat Das Ghat, Jajmau Bridge/Siddhnath Ghat

Ghat-1 BITHOOR GHAT (A)

Bithoor ghat is historical place. It is believe that this is center place of the earth. There is a small pillar of God Brahma named Brahma Ki Khuti due to this is known as Brahma Varth ghat. There many fishes.

This ghat is situated at 26.61 degrees North latitude and 80.27degrees East longitude of river Ganga in Kanpur. Bithoor is on the upstream of the river Ganga at a place, where it enters Kanpur city. No tanneries are located on Upstream of this point in Kanpur district. The sampling point is being applied/utilized as bathing Ghats by little population inhabited around it. It receives moderate amount of household pollution from nearby residential habitation.

Ghat-2 BHAIRAV GHAT (B)

Bhairav ghat is located on the Company Bagh area of Kanpur. This ghat is famous for worship as the temple of "God Bhairav" is situated in this ghat. This ghat is used for the cremation purpose as dead bodies are used to burn and thrown in the Ganga. It is situated at 26.29 degrees North latitude and 80.19 degrees East longitude of river Ganga in Kanpur. The upstream of this sampling site receives organic load from different sources. The river is subjected to various types of human activities like washing clothes by laundries, bathing and disposal of sewage alongside the bank of river.

Ghat-3 PERMUT GHAT (C)

Permut ghat is located on the VIP road of Kanpur. This ghat is famous for the temple Anadeshwar Mandir, (God Shankar). The temple attracts many people; the devoters perform

"Puja" after taking a dip in the river Ganga. The biggest leather factory named Flux India (Previous Cooper Allen) is situated at permut. It is situated at 26.29 degrees North latitude and 80.20degrees East longitude of river Ganga in Kanpur. This ghat is in the middle of the stream, where an estimated 600 bodies per month are cremated or burned and unburned ashes are thrown into the river. This causes river water unfit for use. It is situated in the middle of city and receives household sewage as well as industrial effluents due to which it is highly polluted and completely filled with dirt and filth along its side.

Ghat-4 SARSAIYA GHAT (D)

Sarsaiya ghat is located near the Central Jail and Police Line Kanpur. The name Sarsaiya has come from the tree Sarsai. As this place was covered by the tree of sarsai before many years ago. In this ghat many temples are situated. This ghat is famous for monkeys also. It is situated at 26.28 degrees North latitude and 80.21degrees East longitude of river Ganga in Kanpur. This ghat is situated adjacent to the Kanpur Jail. All the small drains carrying sewage through Jail premises find its way to Ganga. Beside these drains, also the sewer lines of this locality that remain choked most of the time, as a result of which the sewage overflows and by passes into Ganga. Downstream to this location Ganga receives huge amount of household sewage, because of dense population in this area.

Ghat-5 Bhagwat Das Ghat (E)

Bhagwat Das/Guptar Ghat Nala starting point coordinates is Latitude: 26028' 27.49" N & Longitude: 800 21' 42.88" E. end point coordinates of the end point of the drains is Latitude: 260 28' 28.10" N & Longitude: 800 21' 56.26" E Length covered distance of Bhagwat Das/Guptar Ghat Nala to meeting Point of Ganga River is approx. 1.3 Km. Details of discharge of the drain Bhagwat Das/Guptar Ghat Nala is a major drain this is directly meets into River Ganga at the time of inspection, its flow was measured 11.05 MLD. It contains Sewage water of civil line area, Bhagwatdas ghat, mall road.

Ghat-6 Siddhnath Ghat /JAJMAU BRIDGE (F)

Jajmau Bridge in located on the Jajmau area of Kanpur. It said that Jajmau was the capital of King Yayati. There is temple of Siddhnath God. This location is famous for the leather and bones. Many leather industries are situated. In this ghat the crimination happened, and many unburned dead bodies use to throw in the river Ganga. The industrial effluent and other waste come in the river Ganga. Due to this it is the most polluted ghat. The animals collected from the river were classified under the following heads.

OBERSEVATION

Table 2: Fluctuation in Dissolved Oxygen (DO) (mg/lit) at various sampling stations of river Ganga during the study period

	Sampling Station					
	A	B	C	D	E	F
July 18	6.1	6.0	6.4	6.0	5.7	5.0
Aug 18	6.4	6.2	6.3	6.0	5.2	5.1
Sep 18	6.2	6.3	6.2	5.8	5.4	5.2
Oct 18	6.5	6.9	6.1	5.9	5.5	5.3
Nov 18	6.6	7.2	6.4	5.7	5.6	5.2

Dec 18	6.8	8.1	6.2	6.1	5.9	5.5
Jan 19	7.2	7.8	6.7	6.0	6.3	5.2
Feb 19	6.9	7.1	6.4	5.9	5.1	5.1
Mar 19	6.1	6.4	6.3	5.8	5.4	4.4
Apr 19	6.3	6.5	6.2	5.6	5.0	4.5
May 19	7.2	6.9	5.9	5.1	5.7	4.7
June 19	7.1	6.1	6.5	6.3	6.0	4.4

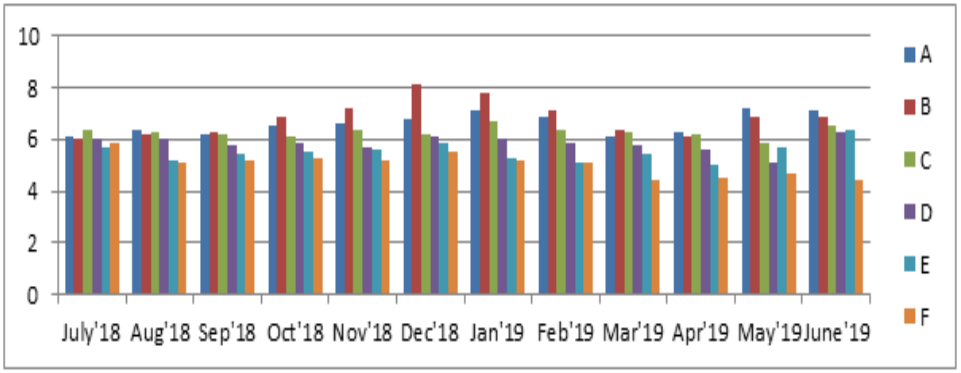
Table 3: Fluctuation in BOD (mg/lit) at various sampling stations of river Ganga during the study period

Month 2018-19	**Sampling Station**					
	A	B	C	D	E	F
July 18	2.6	2.7	3.2	4.8	4.1	6.9
Aug 18	2.8	2.9	3.4	4.6	4.2	7
Sep 18	2.7	2.8	3.5	4.2	4.5	10
Oct 18	2.9	3	4.1	4.5	4.8	8
Nov 18	3.1	3.4	3.7	4.7	4.9	12
Dec 18	2.9	3.2	3.1	4.1	4.7	7.9
Jan 19	2.5	2.4	3.1	4.2	4.0	7.1
Feb 19	3.1	3.4	3.5	4.5	4.9	8.9
Mar 19	3.4	3.5	3.9	5.0	5.5	12
Apr 19	3.9	4.1	4.4	5.1	6.4	13.5
May 19	4.2	4.5	4.7	5.4	6.9	14
June 19	4.1	4.3	4.8	5.2	7.1	15

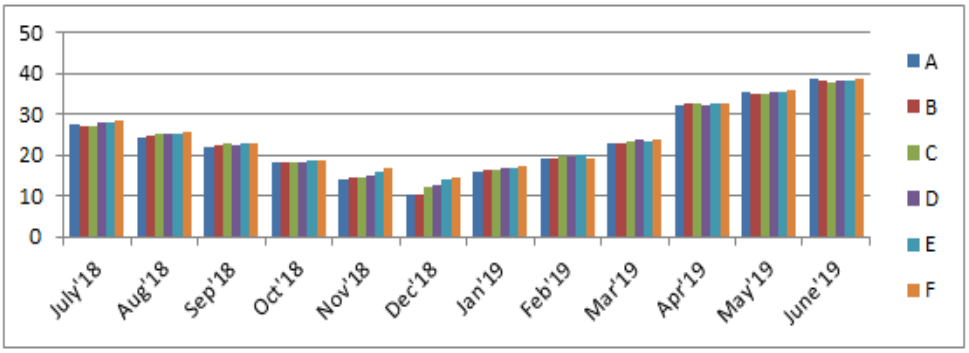
Table 4: Fluctuation in COD (mg/lit) at various sampling stations of river Ganga during the study period

Month 2018-19	Sampling Station					
	A	B	C	D	E	F
July 18	28	29	32	34	37	60
Aug 18	24	26	29	32	34	57
Sep 18	23	30	33	38	39	61
Oct 18	20	22	28	30	33	55
Nov 18	18	20	24	32	29	48
Dec 18	20	22	27	36	35	50
Jan 19	14	16	18	20	22	30
Feb 19	15	18	22	27	28	34
Mar 19	19	20	32	39	40	59
Apr 19	26	28	30	38	39	45
May 19	27	28	34	34	35	49
June 19	27	29	31	34	35	62

Graph 1: Fluctuation in Dissolved Oxygen (DO) (mg/lit) at various sampling stations of river Ganga during the study period



Graph 2: Fluctuation in Dissolved Oxygen (BOD) (mg/lit) at various sampling stations of river Ganga during the study period



Graph 3: Fluctuation in Dissolved Oxygen (COD) (mg/lit) at various sampling stations of river Ganga during the study period

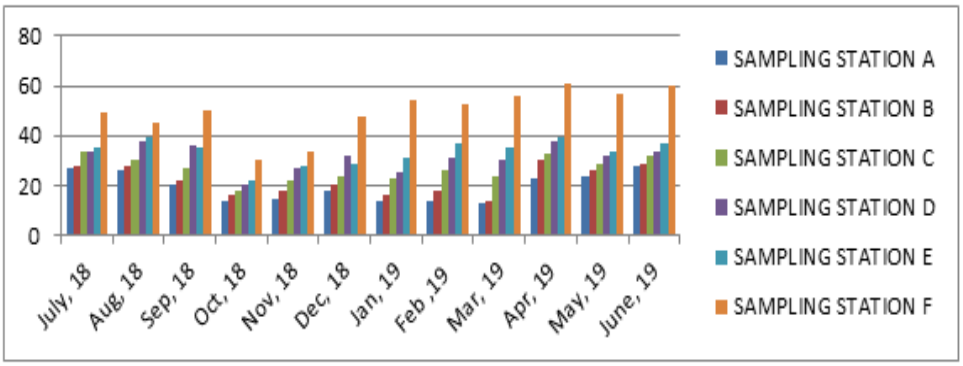


Table 5: Seasonal values of physico-chemical parameters in river Ganga during at Ghat1 (Bithoor Ghat)

Physico-chemical parameters	**Seasons (2018-19)**			**WHO Standards**
	Summer ± Sd	Monsoon ± Sd	Winter ± Sd	
Dissolve Oxygen (mg/l)	6.67±0.556	6.23±0.1527	6.78±0.23	2-6
BOD (mg/l)	4.06±0.152	2.66±0.152	2.9±0.244	Central Pollution

				Control Board, permissible value of BOD is 30 mg/l.
COD (mg/l)	25±3.162	22.25±3.59	15.66±2.08	Central Pollution Control Board, permissible value of COD is 250 mg/l.

Table 6: Seasonal values of physico-chemical parameters in river Ganga during at Ghat2 (Bhairav Ghat)

Physico-Chemical parameters	**Seasons (2018-19)**			**WHO Standards**
	Summer ± Sd	Monsoon ± Sd	Winter ± Sd	
Dissolve Oxygen (mg/l)	6.57±0.39	6.16±0.1527	7.42±0.50	2-6
BOD (mg/l)	4.3±0.2	2.8±0.1	3.08±0.414	Central Pollution Control Board, permissible value of BOD is 30 mg/l.
COD (mg/l)	25.25±4.99	26.6±2.79	18±2	Central Pollution Control Board, permissible value of COD is 250 mg/l.

Table 7: Seasonal values of physico-chemical parameters in river Ganga during at Ghat3 (Permut Ghat)

Physico-chemical parameters	Seasons (2018-19)			WHO Standards
	Summer ± Sd	Monsoon ± Sd	Winter ± Sd	
Dissolve Oxygen (mg/l)	6.225±0.25	6.3±0.1	6.36±0.23	2-6
BOD (mg/l)	4.63±0.208	3.26±0.321	3.5±0.42	Central Pollution Control Board, permissible value of BOD is 30 mg/l.
COD (mg/l)	31±2.160	30.4±2.70	21.33±3.055	Central Pollution Control Board, permissible value of COD is 250 mg/l.

Table 8: Seasonal values of physico-chemical parameters in river Ganga during at Ghat4 (Sarsaiya Ghat)

Physcio-Chemical Parameters	**Seasons (2018-19)**			**WHO Standards**
	Summer ± Sd	Monsoon ± Sd	Winter ± Sd	
Dissolve Oxygen(mg/l)	5.7±0.49	5.93±0.115	5.92±0.0663	2-6
BOD (mg/l)	5.23±0.152	4.2±0.4	4.4±0.2449	Central Pollution Control Board, permissible value

				of BOD is 30 mg/l.
COD (mg/l)	35.25±4.11	34.8±2.28	26.33±6.027	Central Pollution Control Board, permissible value of COD is 250 mg/l.

Table 9: Seasonal values of physico-chemical parameters in river Ganga during at Ghat5 (Bhagwat Das Ghat)

Physcio-Chemical Parameters	**Seasons (2018-19)**			**WHO Standards**
	Summer ± Sd	Monsoon ± Sd	Winter ± Sd	
Dissolve Oxygen (mg/l)	5.62±0.59	5.43±0.251	5.48±0.30	2-6
BOD (mg/l)	6.8±0.36	4.2±0.3	4.66±0.378	Central Pollution Control Board, permissible value of BOD is 30 mg/l.
COD (mg/l)	36.75±3.304	36±2	26.33±3.785	Central Pollution Control Board, permissible value of COD is 250 mg/l.

Table 10: Seasonal values of physico-chemical parameters in river Ganga during at Ghat6 (Jajmu Bridge Ghat)

Physcio-Chemical Parameters	**Seasons (2018-19)**			**WHO Standards**
	Summer ± Sd	Monsoon ± Sd	Winter ± Sd	
Dissolve Oxygen (mg/l)	4.5±0.141	5.4±0.43	5.26±0.151	2-6
BOD (mg/l)	14.16±0.763	7.96±1.76	8.78±1.909	Central Pollution Control Board, permissible value of BOD is 30 mg/l.
COD (mg/l)	59.25±3.095	52.2±6.14	37.33±9.45	Central Pollution Control Board, permissible value of COD is 250 mg/l.

A. DISSOLVED OXYGEN

At station 'A' dissolved oxygen recorded a minimum in March and July (6.1 mg\it) and maximum (7.2 mg/lit.) in January in 2018-2019 (Table 2). At station 'B' dissolved oxygen recorded was minimum 6.1 mg/lit. In June and maximum 8.1 mg/lit. In December 2018-2019 (Table 2). At station 'C' the dissolved oxygen was minimum (5.9 mg/lit.) in May and maximum (6.7mg/lit.) during January in 2018-2019(Table 2).At station 'D' minimum dissolved oxygen recorded was (5.1 mg/lit.) in May and maximum (6.8 mg/lit.) in January in 2018-2019 (Table 2).At station 'E' in 2018-2019, the minimum dissolved oxygen recorded was (4.4 mg/lit) in March and June and maximum (6.3 mg/lit.) in December which ranged from (5.0 mg. /lit.) which ranged from (5.0 mg/lit. to 7.2 mg/lit) (Table 2).Station 'F' in 2018-2019showed the minimum dissolved oxygen (4.4 mg/lit.) in June and maximum (5.5 mg/lit.) in December (Table 2).

B. BIO-CHEMICAL OXYGEN DEMAND

At station 'A' BOD recorded a minimum in January (2.5 mg\lit) and maximum (4.2 mg/lit.) in May in 2018-2019 (Table 3).At station 'B' BOD recorded was minimum (2.4 mg/lit.) in January and maximum (4.5 mg/lit.) in May 2018-2019 (Table 3).At station 'C' the BOD was minimum (3.1 mg/lit.) in January and maximum (4.8 mg/lit.)during June in 2018-2019 (Table 3).At station 'D' minimum BOD recorded was (4.1 mg/lit.) in December maximum (5.4 mg/lit.) in May in 2018-2019 (Table 3).At station 'E' in 2018-2019, the minimum BOD recorded was (4.0 mg/lit) in January and maximum (7.1mg/lit.) in June (Table 3).Station 'F' in 2018-2019showed the minimum BOD as (7 mg/lit.) in August and maximum (15 mg/lit.) in June (Table 3).

C. CHEMICAL OXYGEN DEMAND

At station 'A' COD recorded a minimum in March (13.0 mg\lit) and maximum (28 mg/lit.) in June in 2018-2019 (Table-4).At station 'B' COD recorded was minimum (16.0 mg/lit.) in October, January and maximum (30 mg/lit.) in April 2018-2019 (Table-4). At station 'C' the COD was minimum (18 mg/lit.) in October and maximum (34 mg/lit.) during July in 2018-2019 (Table-4). At station 'D' minimum COD recorded was (20 mg/lit.) in October and maximum (38 mg/lit.) in August, April in 2018-2019 (Table-4). At station 'E' in 2018-2019, the minimum COD recorded was (22 mg/lit) in October and maximum (39 mg/lit.) in August, April (Table-4). Station 'F' in 2018-2019showed the minimum COD as (30 mg/lit.) in October and maximum (61 mg/lit.) in April (Table-3).

Dissolve Oxygen (mg/l)

The DO in the surface water is important parameter because it indicates the status of biological degradation of sewage by aerobic and anaerobic microorganisms while the former require free oxygen, the latter can react with the chemically bound oxygen from nitrates & sulphates etc. DO levels of 6 mg/l are considered optimal for proper growth of fish and other aquatic life. As dissolved oxygen levels in water drop below 5.0 mg/l, aquatic life is put under stress. Most fishes cannot survive for prolonged periods at DO levels below 3mg/l. Oxygen-demanding organic matter particularly requires the oxygen from water for the process of decomposition. More organic waste in water results into decrease in average DO concentrations. However, in water bodies where a large proportion of the organic matter is brought in from outside the water bodies, the oxygen production and consumption are not balanced and DO may decrease.

The Dissolve Oxygen are was observed in season (2018-19) 6.78±0.23 in winter season, 6.67±0.556 in summer season and 6.23±0.1527 in monsoon at Bithoor ghat (Table 5).In Bhairav Ghat Dissolve Oxygen was observed in season (2018-19) 7.42±0.50 in winter season, 6.57±0.39 in summer season and 6.16±0.1527 in monsoon(Table 6). In Permut Ghat Dissolve Oxygen was observed in season (2018-19) 6.36±0.23 in winter season, 6.225±0.25 in summer season and 6.3±0.1 in monsoon. (Table7) In Sarsaiya Ghat Dissolve Oxygen was observed in season (2018-19) 5.92±0.0663 in winter season, 5.7±0.49 in summer season and 5.93±0.115 in monsoon.(Table 8) In Bhagwat Das Ghat Dissolve Oxygen was observed in season (2018-19) 5.48±0.30 in winter season, 5.62±0.59 in summer season and 5.43±0.251 in monsoon(Table 9).

In Jajmu Ghat Dissolve Oxygen e was observed in season (2018-19) 5.26±0.151 in winter season, 4.5±0.141 in summer season and 5.4±0.43 in monsoon (Table10)

BOD (mg/l)

BOD is the amount of the oxygen required by microorganisms for the decomposition of the organic matter present in water. Therefore, it reflects the amount of organic pollutants in water. A high BOD value indicates the presence of a large number of microorganisms, which shows a high level of pollution.

The BOD are was observed in season (2018-19) 2.9±0.244 in winter season, 4.06±0.152 in summer season and 2.66±0.152 in monsoon at Bithoor ghat (Table 5). In Bhairav Ghat BOD was observed in season (2018-19) 3.08±0.414 in winter season, 4.3±0.2 in summer season and 2.8±0.1 in monsoon (Table 6). In Permut Ghat BOD was observed in season (2018-19) 3.5±0.42in winter season, 4.63±0.208 in summer season and 3.26±0.321in monsoon. (Table7) In Sarsaiya Ghat BOD was observed in season (2018-19) 4.4±0.2449 in winter season, 5.23±0.152 in summer season and 4.2±0.4 in monsoon. (Table 8) In Bhagwat Das Ghat BOD was observed in season (2018-19) 4.66±0.378 in winter season, 6.8±0.36 in summer season and 4.2±0.3 in monsoon (Table 9). In Jajmu Ghat BOD was observed in season (2018-19) 8.78±1.909 in winter season, 14.16±0.763 in summer season and 7.96±1.76 in monsoon (Table10)

COD (mg/l)

COD is the measure of pollution in aquatic system. High COD may cause oxygen depletion on account of decomposition of microbes to a level detrimental to aquatic life. It is the amount of oxygen present in the water that is required or used in various chemical reactions (mainly oxidation) occurring in the water. Chemical oxygen demand (COD) is used as a measure of oxygen requirement of a sample that is susceptible to oxidation by strong chemical oxidant.

The COD are was observed in season (2018-19) 15.66±2.08 in winter season, 25±3.162 in summer season and 22.25±3.59 in monsoon at Bithoor ghat (Table 5). In Bhairav Ghat COD was observed in season (2018-19) 18±2 in winter season, 25.25±4.99 in summer season and 26.6±2.79 in monsoon (Table 6). In Permut Ghat COD was observed in season (2018-19) 21.33±3.055 in winter season, 31±2.160in summer season and 30.4±2.7 in monsoon (Table 7) In Sarsaiya Ghat COD was observed in season (2018-19) 26.33±6.027 in winter season, 35.25±4.11 in summer season and 34.8±2.28 in monsoon (Table 8) In Bhagwat Das Ghat COD was observed in season (2018-19) 26.33±3.785 in winter season, 36.75±3.304 in summer season and 36±2 in monsoon (Table 9). In Jajmu Ghat COD was observed in season (2018-19) 37.33±9.45 in winter season, 59.25±3.095 in summer season and 52.2±6.14 in monsoon (Table 10) According to Table 2-10 DO recoded minimum 4.4 in March & June and maximum 8.1 in December. It was low particularly in summer.

BOD recoded minimum 2.4 mg/lit in January and maximum 15 in June. Seasonally the BOD was minimum in winter in other hand maximum in summer.

COD recoded a minimum of 14 mg/lit in January and maximum 62 mg/lit in June. The COD was minimum in winter in other hand maximum in summer.

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ANGIOGENESIS CAM ASSAY

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INTRODUCTION

The process of creating new capillary blood vessels, or angiogenesis, involves a dynamic interaction between cells and soluble substances. Endothelial cells that have been triggered move and multiply to create new blood vessels. Small blood vessels are bordered by pericytes, small blood vessels are surrounded by layers of peri-endothelial cells, and large blood vessels are surrounded by smooth muscle cells.

This process, which involves the creation of new blood vessels from pre-existing ones, is crucial in both the healthy and pathological states. A precise balance of positive and negative regulation, encompassing both stimulating and inhibiting elements, is thought to be necessary for blood vessel development.

Normal angiogenesis takes place during wound healing, cyclical embryonic development, and in some reproductive tissues of adult females. Additionally, it happens in conditions like inflammation, psoriasis, and diabetic retinopathy, and tumors need angiogenesis to continue growing. There is currently interest in figuring out the variables that control or influence angiogenesis because of its significant involvement in both healthy and pathological processes.

Disrupted angiogenesis, or an excessive or insufficient number of new blood vessels, is the cause of angiogenesis-dependent diseases. Numerous diseases and conditions, including von Hippel-Lindau syndrome, diabetes, hereditary hemorrhagic telangiectasia, arteriosclerosis, delayed wound healing, delayed ulcer healing, reproduction-associated disorders, myocardial ischemia, peripheral ischemia, cerebral ischemia, retinopathy, remodeling disorder, and others are linked to insufficient angiogenesis. On the other hand, malignant cells and cancer metastasis are characterized by an excess of angiogenesis.

It is still in the early stages of research to determine the effects of various chemical, pharmacological, and endogenous plants on angiogenesis in vivo and in vitro studies using model animals. Since many growth factors have been shown to exert chemotactic, mitogenic, modulatory, or inhibitory activities on endothelial cells, smooth muscle cells, and fibroblasts, it is reasonable to assume that these growth factors will contribute to angiogenic processes in one way or another by decreasing their levels.

Recently, attempts have been made to use this knowledge in developing of novel treatments because angiogenesis appears to play a major role in the pathophysiology of numerous disease states. Testing is done to determine how different pharmacological substances and natural plant extracts affect angiogenesis and its suppression, which is helpful in managing different illness stages.

Research on angiogenesis is underway in order to create a variety of medications that will be effective at different stages of sickness. However, different angiogenic factors have been employed therapeutically in various vasculatures stages as an effect to diverse vasculatures, and more research has been done on the role of angiogenic in hypertension. Thus, it is evident that

the topic is currently receiving significant research efforts as methods are developing to evaluate potential therapeutic alternatives.

Although different pharmacological substances and natural plant extracts have been examined for angiogenesis and antiangiogenesis activities, the information is limited due to these substances' opposing effects on angiogenesis, which alternately stimulate and inhibit angiogenesis. Similar but distinct substances that act in opposition to each other include proliferin and proliferin-related protein, which respectively stimulate and inhibit angiogenesis.

Studies on the angiogenesis and antiangiogenesis of herbal extract-based medications suggested that the relationship between them was significant for their screening in in vitro angiogenesis studies. Different types of plant extract, such as aqueous extract, alcoholic extract, and whole plant extract, produce different effects on the activity of angiogenesis. It shows that plant extracts are intricate and produce various types of fractional extraction using various solvents. The outcome of an herbal extract therefore varies.

There are many known variables that control angiogenesis. These include tissue oxygen and soluble components. There are numerous elements that may control angiogenesis. The cell specificity of these substances and factors as well as the methods by which they stimulate the development of new blood vessels vary. Not all substances that are active in vivo exhibit the same range of endothelial cell activities in vitro. Numerous of these substances have pleiotropic effects and, among other things, may cause endothelial cells to migrate and proliferate as well as produce collagenase and plasminogen activator.

However, several of these substances are neither chemotactic nor mitogenic for endothelial cells. They most likely produce their effects by luring in additional cells, activating existing cells, and then triggering the release of angiogenic factors from these activated cells. By assessing the induced migration of endothelial cells or the impact of these factors on cell proliferation in vitro, one can ascertain the biological activities of angiogenic factors since many of them are mitogenic and chemotactic endothelial cells.

The physiological characterization of angiogenic vessels, the direct determination of angiogenic activities, and the inhibition of vessel formation in response to tissue, cells, or soluble factors are all made possible by several bioassays.

The chicken chorioallantoic membrane assay (CAM assay) is one of the most widely used angiogenesis assays. The fusing of the chorion and the allantois results in the formation of the chorioallantoic membrane in extra-embryonic chicken embryos. It has a massive capillary network and is in direct contact with the shell. With the aid of a sealed window carved out of the shell, the membrane can be utilized in living organisms. The angiogenesis assay uses chicken chorioallantoic membrane, which is cheap but straightforward and simple to evaluate surfactant.

A popular in vivo method for studying angiogenesis and anti-angiogenesis is CAM. The very few restrictions on its use are mainly caused by nonspecific inflammatory reactions and the presence of pre-existing vessels, which make it difficult to determine the true extent of angiogenesis and anti-angiogenesis. CAM, however, has the advantage of being relatively.

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CLIMATE CHANGE: A WAKEUP CALL!

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INTRODUCTION

The history of Earth shows eight cycles of Ice Age and warm periods in the last 800,000 years. The last Ice Age 11,700 years ago, marked the beginning of "Modern Climate Era- and human civilization. Small variations in the earth's orbit were the main cause of climate changes. But, the current trend is due to human activities since mid-1800 and is proceeding at an alarming rate almost 250 times faster! Evidence from long-term monitoring studies is now accumulating and suggests that the climate of the past few decades is anomalous compared with past climate variation. Climate change is considered to be the foremost environmental hazard in the world (Olausson, 2011).

Combustion of coal, oil, and natural gas, and to a lesser extent deforestation, land-cover change, and emissions of halocarbons and other greenhouse gases, are rapidly increasing the atmospheric concentrations of climate-warming gases (MacCracken MC., 2008). These gases are leading to climate change. The evidences of rapid change are:

- Rising global temperature
- Oceans getting warmer
- Shrinking ice sheets
- Retreating glaciers
- Decreasing snow cover
- Rising sea level
- Declining Arctic Sea ice
- Increase in frequency of extreme events
- Increase in ocean acidification.

The latest report by Intergovernmental Panel on Climate Change (IPCC) says that extreme heat waves that would usually happen every 50 years are already happening every 10 years. These might occur every 5 years, if global warming continues.

Climate change and Biodiversity

Climate change is a major threat to biodiversity. The climate crisis is dismantling ecosystems. Extreme events such as heatwaves, storms, wildfires, droughts, flooding are destroying habitats. Increasing temperatures are changing the timing of natural phenomenon such as when birds hatch eggs, turtles lay eggs, speeding up of life cycle of plant thus reducing productivity, increase in pests, weeds, plant diseases, shifting of plant communities, and many more. Recent climatic and atmospheric trends are already affecting species physiology, distribution and phenology (Hughes, L, 2000).

Over the past 100 years, species have responded to climatic changes throughout their evolutionary history2, but, a primary concern for wild species and their ecosystems is the rapid rate of change3. Analyses revealed a consistent temperature-related shift, or 'fingerprint', in species ranging from molluscs to mammals and from grasses to trees. Evidence from studies strongly suggests that a significant impact of global warming is already evident in animal and plant populations. It could easily disrupt the connectedness among species and lead to a reformulation of species communities, reflecting differential changes in species, and to numerous extirpations and possibly extinctions (Root TL, et al., 2003).

Climate change and Man

The common man thinks, "Is this change going to affect me? Why care?" The reality is that each one of us is already affected! The unseasonal rains alternating with extremely hot days, cloudy days in April, aren't these affecting us today? One can't turn a blind eye to these happenings around us, can we? Every individual should be aware of these abnormal phenomena and the causes behind them. They must know ways of dealing with it.

The WAKEUP CALL lies in the statement by WHO, which states: "Climate change affects social and environmental determinants of health – safe drinking water, clean air, sufficient food and secure shelter. Between 2030 and 2050, climate change is expected to cause approximately 250000 additional deaths per year from malnutrition, malaria, diarrhea and heat stress." This should be an eye opener and a warning to all mankind. The interconnections between climate change and its impact on biodiversity, including man, cannot be underestimated or ignored!

Mitigation

Time is running. Socioeconomic conditions have deteriorated in most countries of the world. This year's 16th edition of the Climate Risk Index states: Less developed countries are generally more affected than industrialised countries.

Immediate mitigation and solutions to reduce impact of climate change are a MUST. It is never too late to take action. Our survival depends on how we handle our environment and save the planet and ourselves! We need to anticipate, adapt and become resilient to current and future impacts of climate change.

How can we fight climate change?

The basis for all mitigation strategies at governmental, economic, scientific, or personal levels is: reliable estimation of the extent of these impacts.

a. Role of Government

Governments and funders need to support scientists in efforts to understand the safety and efficacy of various innovative technologies. In Glasgow, 22 countries, as well as the European Commission (EC), announced plans to cooperate on innovation focused on greening cities, curbing industrial emissions, promoting CO_2 capture and developing renewable fuels, chemicals and materials.

Prakash Javadekar, Minister for Environment, Forests and Climate Change of India, called for building of robust governance structures at local, national and regional levels to address climate- and fragility-related risks, pressing donor countries to provide greater financial, technological and capacity-building assistance to help fragile States enact adaption and

mitigation strategies. These strategies should be explained to the common man. Media can play a vital role in educating common man towards obtaining Sustainable Development Goals (SDP).

b. Role of researchers and scientists

IPCC states: "Scientific evidence for warning of the climate system is unequivocal." A sound research database is essential for sustainable approaches for assessing and mitigating climate change impacts. If left unchecked, climate change will undo a lot of the progress man has made over the past years in development. For this, experts from all areas of climate change need to collaborate. These areas range from ecology, life sciences, meteorology, health care, social, and economic sciences, mathematics and computer science to energy, food, and transport. Interdisciplinary approaches surely deliver huge amounts of reliable data. These studies can provide a comprehensive understanding of the problem and possible measures at all levels.

Innovations will be most instrumental — for example, in the form of technologies that can pull carbon dioxide out of the atmosphere. In addition to enabling green innovation, scientists have an important part to play in evaluating climate policies and tracking commitments made by governments and businesses (Nature **601**, 7; 2022).

b. Role of every person, especially youth:

The measure of human demands on Earth's natural resources is known as our ecological footprint. Currently, we use the equivalent of 1.5 Earths to produce all the renewable resources we use. As the human population grows, the challenge of reducing our footprint becomes more urgent. The more developed a country is, the larger the footprint. But, we can make smart choices and reduce our footprint. Small changes in our everyday activities such as: walking, cycling instead of driving, turning off the air conditioning or reducing its use, replacing dryer with a clothesline can reduce our footprints to a satisfactory level.

The youth should follow a healthy and sustainable way of living based on traditions, values of conservation and moderation. With the use of social media, they need to propagate for 'LIFE'– 'Lifestyle for Environment' as a key to combating climate change; increase the green cover or carbon sink by planting trees. Reduction of emissions plays a key role in reduction of GHG.

DISCUSSION

Today, each one need to recognize that global warming will have economic, as well as health and environmental impacts all over the world. Each country should ensure that it uses the best and most effective renewable energy technology under the Kyoto Protocol. To implement SDG, the government, scientists, business tycoons, politicians, educational institutions, media and citizens need to come together. Scientific institutions should generate detailed studies listing these impacts, and make sure this information is made available to the people. The goal is that everyone lives within the Earth's capacity to sustain people and nature—and has equitable access to, and use of, natural resources.

CONCLUSION

Every individual needs to be sensitized on the issue, taught to take up responsibility and make sure that the choice one makes is actually helping to reduce the burdens of climate change. By addressing climate change, we can build a sustainable world for everyone. But, we need to act now to help create a world where humans and nature thrive together!

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DIVERSITY OF ROTIFER COMMUNITIES IN KAL RIVER AT MAHAD TALUKA DIST RAIGAD

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INTRODUCTION

Diversity of rotifera communities in Kal River at Mahad, Raigad India is a subject of great interest of study aquatic ecology. The Kal River is an important water resource in Mahad region and the Rotifera communities play an important role in its exploitation and utilization. Rotifera are small aquatic animals that live in the Kal River and elsewhere in Mahad, Raigad. The rotifera communities in kalriver are diverse species. They consume and recycle nutrients and help reduce algae growth and turbidity of the water. They are a major source of food for fish, other aquatic animals and other organisms. Rotifera are also important for the deposition of fine sediments, which protects the river from floods and erosion of its banks. Rotifers are a major component of the aquatic food web and generally feed on unicellular and some minute multicellular organisms. While one group of rotifers known as the non-selective filter-feeders prefer to feed on suspended microorganisms, such as diatoms and chironomids, another group termed the selective filter-feeders feed on microalgae, such as diatoms. (Dodson and Frey, 1991). Higher water temperatures favor the growth of large colonies of rotifers, while colder temperatures favor small colonies. Higher pH levels favor larger rotifers and a higher abundance of smaller ones. Availability of food also plays an important role in the growth of the rotifers, with a high abundance of available food resulting in higher numbers of rotifers. The rotifers can recycle nutrients, help reduce algae growth and turbidity, and provide a rich source of food for fish and other organisms.

Roifers are one of the major groups of freshwater zooplankton and make up a vital part of aquatic food webs worldwide by linking the lower (phytoplankton, bacteria, fungi) and higher trophic levels (fish, macro-invertebrates) The non-pelagic rotifers, of which the majority consists of the specious family brachinus, thrive in littoral areas of freshwater habitats and in shallow freshwater lakes, where aquatic macrophytes dominate (Whiteside and Harmsworth, 1967).. The littoral provides shelter against predators for pelagic as well as non-pelagic species. (Fryer, 1968). Often, the littoral is understood as a single habitat. It is clear that under this general term, high diversity in micro-habitats is present among small aquatic invertebrates such as rotiferns (e.g., Whiteside et al., 1978).The aim of the present study was to explore the seasonal variation of rotifer of two points in river kal atmahad.

MATERIALS AND METHODS

The rotifers (Zooplankton) were collected from July 2018 to June 2019 from two points of river by filtering 40 liters of water through the plankton net. The plankton was preserved in 5 % formalin at the sites and then brought to the laboratory for qualitative and quantitative analysis. Now, the volume of same was made to 10 ml and it is thoroughly shaken. 1ml of material was taken from the sample and placed in a Sedgwick rafter Plankton Counting chamber. For counting lower power of the compound microscope was used. The planktons were identified up

to species level. Wherever possible, with the help of Needham and Needham (1962), ward and whipple (1960) & Michael and Sharma (1973).

The quantities estimation of Zooplankton was made by the following formula

N = (A x 1000) C/L Where,

N = No. of Plankton / liter of water,

A = Average no. of Plankton in 1 ml sub Sample

C = ml of Plankton concentrates.

1= liter 1000000UL

The present contribution of the in dividable species in respect to the class and group was collected individually.

Table 1: Monthly Variations of Rotifers Population (in dv/L) at Point I (From Jul 2019 to June 2020)

Month /	**J**	**Au**	**Se**	**Oc**	**No**	**De**	**Ja**	**Fe**	**Ma**	**Ap**	**Ma**	**Jun**
Rotifers												
B. caudatus	2	4	4	1	7	5	2	4	4	2	20	22
B. falcatus	-	14	10	-	7	14	-	4	10	12	18	7
B. Calyciflorus	10	5	4	10	17	15	7	1	-	9	15	15
Filinialogistea	2	4	-	8	3	-	4	-	6	12	10	13
B. rubens	12	15	4	6	13	18	7	14	10	9	15	15
Total	**18**	**42**	**22**	**25**	**47**	**54**	**20**	**23**	**30**	**44**	**78**	**72**

Table 2: Monthly Variations of Rotifers Population (in V/ L) at Point II (From Jul 2019 to June 2020)

Month /	**J**	**Au**	**Se**	**Oc**	**No**	**De**	**Ja**	**Fe**	**Ma**	**Apr**	**Ma**	**Ju**
B. falcatus	5	4	9	15	8	3	12	4	2	-	12	10
B. caudatus	7	1	-	1	7	5	7	-	-	4	6	19
B. forficula	13	1	4	6	-	8	8	8	3	12	2	4
B. Calyciflorus	-	5	14	16	7	3	-	4	5	8	17	11
Filinialogistea	4	8	-	3	12	4	8	3	12	4	8	17
Keratellatropica	2	1	3	5	1	6	6	9	4	2	2	1
Total	**31**	**20**	**30**	**46**	**35**	**29**	**41**	**28**	**26**	**28**	**47**	**62**

Table3: Diel Variations in Rotifers Population (in dv/L) at Point I during winter (04-01-2019to 05-01 2020).

	Time Periods in Hours(24 hrs)							
Organisms	70	900	1200	1400	1700	2000	2000	400
Rotifers								
Monostyle species	3	4	-	8	7	1	4	1
Filinialogistea	6	9	7	4	2	2	8	5
Keratellatropica	-	2	2	7	7	3	3	3
B. caudatus	5	9	8	4	12	4	3	6
B. falcatus	9	14	10	1	17	4	9	8
Total	**23**	**38**	**27**	**22**	**45**	**14**	**27**	**23**

RESULTS

During the study of diel variation a total number of 5 species were collected at Point I and 7 species in Point II. The Rotifers populations were dense during the night hour.

The maximum number (45 U/L) of total Rotifers was recorded at 1700 hours in Point I and at 400 hours (41 U/L) in Point II. Whereas minimum (14 U/L) and (7 U/L) at 2000 hours in both station during winter seasons. In summer, the highest number (36U/L and 32 U/L) of total Rotifers were recorded at 200 hours in Point I and 400 hours in Point II, while the lowest (7U/L and 10 U/L) at 400 hours in both points. In monsoon the maximum density of rotifers was recorded at 700 hours (28 U/L and 36 U/L) in Point I & II respectively. Whereas, the minimum density (6 U/L) and (4 U/L) at 1200 hours in point I & II respectively.

In Point I, during the winter Monostyle species, Filinialogistea, Keratellatropica, B. caudatus, & B. falcatus were several as most abundant species. The highest number (17 U/L) of B. falcatus was recorded at 1700 hours and the lowest (22 U/L) at 1400 hours. The maximum density (12 U/L) of B. falcatus was noticed at 400 hours and minimum (1U/L) at 1200 hours. B. caudatus minimum shows their maximum density (3 U/L and 2 U/L) at 200 hours.

In Point II, B. Monostyle species, Filinialogistea, Keratellatropica, B. caudatus and B. falcatus were recorded as the most abundant species during the study of winter dial variation.

The highest density (6 U/L) of B. falcatus was recorded at 400 hours and lowest density (2 U/L) at 2000 hours. B. caudatus was observed as the most dominant species during dial study. It shows their highest abundance (13 U/L) at 400 hours and the lowest (2 U/L) at 2000 hours. Filiniaterminalis was found only at point II. The maximum density (8 U/L) of this was observed at 2000 hours and minimum (1 U/L) at 1400 hours.

In Point I, during summer Filinia terminalis and B. falcatus were the most dominant species. The maximum density (8 U/L) of B. forficula was observed at 700 hours and the minimum (1 U/L) at 1700hours B. falcatus shows their maximum density (4 U/L) and (1 U/L) at 1700 hours and minimum (1 U/L) at 400 hours. Filinia terminalis where recorded as most abundant cladocers in point II during the investigation of summer diel variations. The maximum density (5 U/L) of B. forficula was recorded at 200 hours and the minimum (1 U/L) at 900 hours respectively.

B. caudatus shows their highest (9 U/L) at 700 hours and lowest density (4 U/L) at 400 hours. The maximum abundance (4 U/L) of Polyarthra Sp. was observed at 700 hours and minimum (6 U/L) respectively. Polyarthra Sp. was the most dominant species in point II during monsoon. Its maximum and minimum density was (12 U/L) and (1 U/L) at 700 hours and 1200 hours respectively.

DISCUSSION

The overall Rotifersdensity was significantly lower in the open water habitat than in more littoral areas. Relatively lower density of Rotifers in the pelagic zone (with less vegetation cover on the bottom) in river has been recorded before with different sampling methods (Inpang, 2008). However, most comparisons in Rotifers density between littoral and pelagic zones in lakes are based on limited sampling and ignore bottom-inhabiting species. The density of

floating vegetation in open water is also very low as a result of wind and wave action (Inpang, 2008).

Zooplankton plays important role between the autotrophs and heterotrophs and form an important link in the food web of fresh water ecosystem. It is good indicator of change in water quality because it is strongly affected by environmental condition and responds quickly to change in environmental quality (Shivakami et.al., 2007).The distribution of B. Calyciflorus species was different in different in two points under study were only Monostyle species was found in point I. The second point showed the presence of four species of this genus. Though at one time maximum of 2 species of Monostyle speciesa was collected. This species is also regarded as indicator of pollution on the basis of its higher presence in polluted point II can be explained.

The study of diel cycle shows that Rotifers dominating the Zooplankton population showing migration on towards surface culminating in its maximum at 800 hours on both the points. Such observation was reported by (Vaisali, G, Madhuri, P. (2012). B. caudatus was dominant species in both the points throughout the year round. The B. forficulas hows a well mark diurnal migration, aggregating the surface during night hours and sink at day time. The seasonal variation of cladocera, (Nasar S.A.K (1997), reported that fluctuation is controlled by abiotic and biotic factor. In the present investigation the maximum rotifers were found in winter season and the diel variation was maximum at night hours. The higher quality of rotifers in winter season may be due to favorable condition of artistic factor like temperature pH and abiotic factors. Such observation was also reported by Shivakami et. al. (2011)

CONCLUSION

Population density increases due lack of pollution in covid 19 during industrial effluent stop because favorable climatic condition for zooplankton growth. Rotifers are one of the major zooplankton groups in various freshwater habitats, where few other species have managed to penetrate. Conclusion we studied the community composition, density and species richness of Rotifers species abundance in Poladpur River over 1 year using activity traps. The main conclusions are:

1) The dominant Rotifers species include the Monostyle species, Filinialogistea, Keratellatropica, B. caudatus & B. falcatus Its play a dominant role in over brachinus and these groups may enter into direct competition with one another. 2) The fluctuation of Rotifers species by responsible for climatic conditions influenced by pH and depth. 3) We noticed a temporal variation (between months over a single year) in Rotifers species richness and density, yet a similar maximum richness of species coexisting at any given time for each habitat (max. 5species). There could be a seasonal pattern in species density and richness, with strong density peaks during the dry and wet seasons.

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ETHNOBOTANY OF LICHENS AND THEIR ANTIOXIDANT PROPERTIES

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INTRODUCTION

Lichens are alliances made up of the consociation of a fungus and an alga(green or blue-green) whose dual nature was first reported by Schwendener in 1869 (Gökalsın et al., 2020; Stocker-Wörgötter, 2001). Some lichens show the presence of members of Chlorophyceae as primary photobiont and members of cyanophycaeae as secondary photobiont (Awasthi, 2000). Algal partners common to this association are Trebouxia, Trentepohlia and Nostoc (Awasthi, 2000). The fungus obtains food from algal partner as algal cells become porous to this export by the fungus and this process is called lichenization. They grow at slow rate and are unique organisms which colonise almost 8% of the land surface (Panta, 2022; Purvis & Pawlik-Skowrońska, 2008; Yusuf, 2020).

Some lichens show presence of three or more partners (Awasthi, 2000). Ancient Chinese and Egyptian civilizations boast the usage of lichens for various ethnobotanical purposes, namely medicine, dyes, cuisine, and perfumeries(Singh et al., 2015; Yang et al., 2021). Along with using it as food, people in temperate regions like the arctic, usually employ lichens in pharmaceutical products, and for different traditional uses(Crawford, 2019).The occurrence of unique secondary metabolites in lichens facilitates their medicinal properties (Ranković & Kosanić, 2015). Around 800 secondary metabolites have been recognized to date and are still being reported (Nayaka et al., 2013). Lichen metabolites are employed in a number of organic activities like antibiotic, anti-inflammatory, anti-oxidant, antiproliferative and anti-tumorous effects (Malhotra et al., 2008).

In recent times the edible and traditionally used lichens are getting acknowledged by researchers due to their various uses and these may prove useful in various commercial purposes which may lead to the exploration of potent active compounds (Bharucha & Pretty, 2010).

Heterodermia diademata is lichen of which a plaster is made and applied on cuts and injuries to defend from effect of water and infection. Extract of Artemisia vulgarisis combined with Heterodermia diademata and used to treat fresh injuries in Uttarakhand (Devkota et al., 2017). Parmotrema reticulatum is used for preparing a tea that provides ease from nephrological disorder or venereal disease. This tea is made during late afternoon and kept aside on previous night before consumption. Parmotrema austrosinense, Parmotrema tinctorum and Parmotrema hababianum are used as a spice or flavoring agent for meat and vegetables.

Lichen Antioxidants

Phytochemicals are plant metabolites which play major role in sustaining plants against external environmental threats, and also control growth and reproduction in plants (Molyneux et al.,

2007). Compounds acquired from original edible sources such as grains, pulses, lichens, spices, vegetables are being explored (Chen et al., 1996). Lichens are rich source of different biologically active substances possessing antibiotic, anti-microbial, anti-oxidant properties and thus need further investigation (Huneck, 1999).

Free radicals are molecular entities with one or more uncoupled electrons, which give them their reactive properties. The hydroxyl free radical (OH), nitric oxide (NO), peroxyl radical (ROO) and superoxide radical anion (O_2) are among the most important ROS (Firuzi et al., 2011).To some extent, free radicals are advantageous in a variety of physiological tasks and cellular signalling pathways. When these radicals exceed their limits, they detoxify or damage the cells, resulting in all inflammatory, ischemic, hemochromatosis, and neurologic diseases and disorders (McCord, 2000).

The reactive oxygen species serve important roles in plant signalling, growth, and development, but they are also damaging because they produce oxidative damage under stress conditions, which can lead to cell death (Das & Roychoudhury, 2014).Oxidative stress is a result of misbalance between ROS manufacturing and ROS scavenging. The imbalance between ROS production and quenching causes oxidative stress (Amo de Paz et al., 2010).Oxidative stress due to free radical damage causes many degenerative diseases, like cancer, cardiovascular disease, aging and cataracts (Poljsak et al., 2013). Antioxidants have the property of preventing unwanted oxidation by reacting with the ROS, quenching free catalytic metals and work as oxygen scavengers (Behera et al., 2004; Gülçin et al., 2003).

Antioxidants belong to two major categories: natural and synthetic (artificial) antioxidants. With time natural antioxidants have been replaced by artificial antioxidants due to their cost effectiveness but have been proved harmful to human beings. Therefore, natural antioxidants are in trend again and new, novel antioxidants that are non-toxic, cheap and stable are being worked upon. Considerable amount of research has explored high number of edible and medicinal lichens rich in antioxidant compounds. The presence of these compounds makes it indispensable for researchers to further investigate this field.

Though there are enormous numbers of original products currently used as antioxidants, the hunt for novel chemical entities with antioxidant properties is still a growing field. Lichens play essential role as they produce novel antioxidant compounds. The pharmaceutical value of lichens stems from their ability to create a wide range of secondary metabolites, majority of which are uniquely found in the lichenised fungus. The most important specialized metabolites of lichen are phenolic chemicals, and the most studied metabolites are depsides, depsidones, dibenzofurans (Huneck, 1999).

Lichen phenolic chemicals differ significantly from vascular plant phenolics. Depsides, depsidones, and dibenzenofurans are the most common phenols in lichens(Gaucher & Shepherd, 1968). Phenols in lichens are often released by the mycobiont and form crystals on the surface of hyphal cell wall (Hyvärinen et al., 2003). Except pulvinic acid derivatives, which are synthesised through the shikimic acid route, lichen phenols are mostly acetate-polymalonate-derived (Mosbach, 1969).

METHODS OF DETERMINING ANTIOXIDANT POTENTIAL:

DPPH radical scavenging method

The DPPH radical is a compound with an absorbance maximum at 515 nanometer. Antioxidants get reduced to DPPH-H on reaction with DPPH or hydrazine (DPPH-R).

Superoxide anion radical scavenging

In a PMS-NADH system, superoxide radicals are produced by the oxidizing NADH and measured by the reducing NBT. The extent of nitro blue tetrazolium NBT reduction, as assessed by reaction mixture absorbance, correlates with the lichen extract's superoxide radical scavenging activity.

Major antioxidants from lichen with their class:

Compound class	Examples of some compounds	Lichens whih show their presence
Depside	Atranorin, lecanoric acid	Hypotrachyna revoluta and Usnea articulata
Dibenzofuran	Evernic acid, usnic acid	Usnea articulate, Usnea longissima, U. complanata
Depsidone	Condidymic acid, lobaric acid	Usnea subvacata, Parmotrema stuppuem, Parmotrema tinctorum
Diphenyl ethers	Praesorethers E, F and G	Parmotrema praesorediosum

(Paudel et al., 2011) demonstrated that ramalin extracted from Ramalina terebrata has a high potency of about five times than synthetic butylated hydroxyl anisole (BHA) in scavenging DPPH, 27 times active in quenching ABTS•+ than the vitamin E similar compounds. (Kosanić & Ranković, 2011) reported that Lecanora atra showed high DPPH radical scavenging activities.

Antioxidants work by following ways: i) by stopping the formation of primary and secondary dicals ii) converting toxic free radicals to less toxic ones iii) quelling the primary antioxidants iv) increasing the activity of original antioxidant systems (Kozarski et al., 2015).

CONCLUSION AND FUTURE PERSPECTIVES

In recent times, the search for new and novel antioxidants is appealing for the curing a wide range of human disorders, with a particular focus on substances with neuroprotective potential and oxidative stress regression(González-Burgos et al., 2013). Though an enormous amount of natural compounds are in use nowadays as antioxidant agents, the quest for novel chemical substances with antioxidant potential is still a developing subject. Lichens are a source of novel antioxidant compounds and thus, need further exploration.

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DIVERSITY OF FISH PARASITES FROM MARINE FISH

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INTRODUCTION

India is one of the largest producer countries of fish in the world. Fisheries are important for the Indian economy. Fish farming remains a high-risk investment mainly due to disease problems caused by parasitic infection. Fish parasitic studies are important for obtaining the fish parasite relationships, host selectivity and geographical distribution of fish parasites. Mumbai region as a distinct part of coastline is familiar with the diversity of marine organisms including marine fish. In this study parasite species richness from marine fish is observed.

MATERIALS AND METHODS

A total number of 235 fish was collected from Mumbai from June 2022 to March 2023. The collected fish were brought to the laboratory for detailed investigation. The experimental fishes were measured and examined by standard parasitology examination. The external examination was observed to identify the pathological damage caused by parasites. The body, skin, fins, gill were thoroughly examined as well as intestine for external parasites and endoparasites infestation. The surface of body and fins were scrapped, and intestines were cut to observe parasites infestation. The parasites examination and identification were done by using the microscopic examination.

RESULTS AND DISCUSSION

Parasites rarely regulate their host population or influence either natural or sexual selection of host. It is obvious from the present study that the distribution of fish populations in Mumbai fishing site, coastal zone near is changing due to the period, place, and way of fishing, besides the physical and chemical characters of the marine water.

A total of 235 fish were examined of which 40 fish were infected and a few Protozoan (zooflagellates, dinoflagellates) Helminths (nematode, cestode) and Flukes (dactylgyrus) were found.

CONCLUSION

Parasites should not be neglected as they may have various effects on host behavior, growth, and mortality. Parasite scan provide information on population structure evolutionary hypothesis, environmental stressors, biodiversity and climate conditions. The information about advance research in parasite diversity of marine fish is needed along with economic value and the burden that caused by it. The routine monitoring in parasitic diversity could prevent the huge economic losses caused by parasitic diseases. These results also provide relevant “base-line” data for assessing the effectiveness of future control strategies against parasites in marine fish.

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HISTOPATHOLOGICAL CHANGES IN THE INTESTINE OF DASYATIS BLEEKERI (Blyth, 1860) WITH SPECIAL REFERENCE TO HELMINTHIC INFECTION

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INTRODUCTION

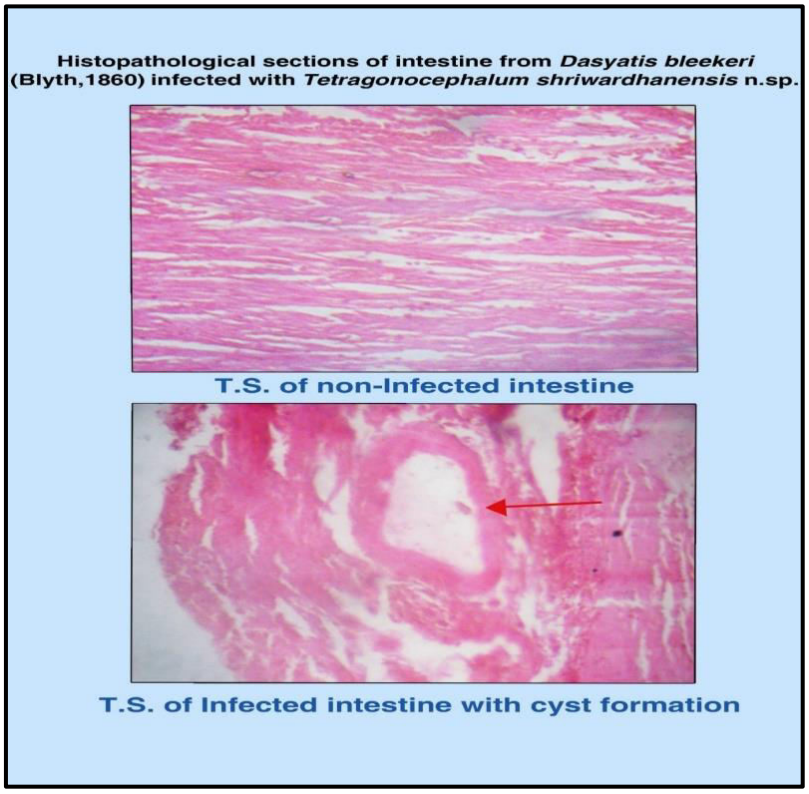
Parasite is an important group of pathogen causes infection and diseases of fish both in marine and fresh water with increasing interest in aquaculture parasitic infections are becoming threats for fish health management and aquatic crops production throughout the world. Parasites can be deleterious to their fish hosts, leading to reduction of growth and reproduction capacity, mortalities and increased vulnerability to predation (Bakke & Mackenzie, 1993; Longsiiaw, M., 1996; Kritsky, & II Eckman, 33 2002). The histopathological effects on the host can estimate the impact of the parasites on the fish hosts, by reduction of the commercial value of the fish.

The host-parasite relationship results in the gain of one organism and the loss of another and leads to various diseases and disorders. Naturally, it is important to study this relationship, not because of their parasitological value but for the relative existence of humankind. These studies may have considerable intrinsic interest and raise fundamental question, common to other areas of biology, at a molecular, cellular, tissue and whole organism level. Several studies on the effect of intestinal parasites have shown that the main detrimental consequences for the host species are localised at the site of infection (Hoste, 2001).

MATERIAL AND METHODS

Marine fish intestine Dasyatis bleekeri (Blyth, 1860) were brought to the local laboratory alive and sacrificed just before examination. In order to see the degree of infection, the intestines were cut open and examined under a stereomicroscope during the parasitological examination. The tapeworms were collected, placed in saline solution, freed from the adhering mucus by gentle shaking, they were flattened, processed and stained for morphological studies and were identified as Tetragonocephalum shriwardhanensis n. sp. Within short time 2 to 3 cm long pieces of proximal intestinal segments containing tapeworms were fixing in Bouin's solution for 24 hrs, as the tissue undergoes autolysis rapidly after death and rapid fixation is essential. The fixed content was transported and extracted by increasing alcohol scales, dried in a miscible wax agent and impregnated in wax (M.P. 58o-60oC). Sectioning was carried out on a rotary microtome at 6µm. Sections were floating at 48^0C on warm water and placed on chemically polished, egg albumin-coated slides. The mounted, unstained sections were dewaxed in three stages of xylene at 1 minute each and stained with most widely used standard haematoxylin and eosin stain, staining was carried out using haematoxylin and eosin staining technique (Bullock, 1978). This stained is often sufficient for identification of larger parasites such as helminthes, in this method the nuclei of cells are stained by the haematoxylin; the cytoplasm is coloured by the eosin. Stained mounted sections were examined for successful ones chosen for photomicrography under a light microscope. Stained mounted sections were examined under light microscope for good ones chosen for photomicrography.

RESULT &DISCUSSION



Histopathological changes associated with the infection are of a localized nature. Essentially, it is more or less, a typical connective cyst, which is seen to project from the outer wall of the intestine, connected to a typical cyst, and seems apparently to be formed of the fibrous connective tissue. There is slight infiltration of plasmacytes at around the site of infection.

The selected slides were observed under microscope and reveal that it causes much damage to the host intestine by invading in the mucosa layer.

The worm Tetragonocephalum shriwardhanensis n. sp. is having non- penetrative type of scolex, further it was observed those cysts are easily floating near the villi in lumen of intestine. The cyst is able to reach the intestine and are adhered to it. Due to favourable condition for the parasites in the lumen of intestinal is freely floating to cause a disturbance in the absorption of food by piercing the intestinal tissue. Thus, it can be concluded that the worm could be able to take nourishment from the host and maintain good histopathology relationship with its host.

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HORMONAL REGULATIONDURING PHASES OF FEMALE REPRODUCTIVE CYCLE

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INTRODUCTION

During the menstrual phase female usually exhibit cyclic changes in both ovaries and the uterus. The cycle involves mainly oogenesis and preparatory phase of the uterus to receive a fertilized ovum. The main hormones responsible for control the events are mainly secreted by the hypothalamus, anterior pituitary, and ovaries. If fertilization does not occur the endometrium lining is removed. The menstruation period is a series of events in the endometrium of the uterus to prepare it for the fertilized ovum until birth.

Hormonal Regulation

Hypothalamus secretes the most important hormone, i.e., GnRH (Gonadotropin-releasing hormone which chiefly controls the ovarian and uterine cycles. GnRH in turn stimulates the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior

pituitary. LH stimulates further development of the ovarian follicles while FSH initiates follicular growth. FSH and LH stimulate the ovarian follicles to secrete estrogens. LH stimulates the theca cells of a developing follicle to produce androgens. Under the influence of FSH, androgens are taken up by the granulosa cells of the follicle and then those are converted into estrogens. At mid phase of the cycle, LH triggers ovulation and then promotes formation of the corpus luteum, hence it is named as luteinizing hormone. After the Stimulation by LH, the corpus luteum secretes estrogens, progesterone, relaxin, and inhibin. As per recent studies, at least six different estrogens have been isolated from the plasma of human females, but only three are present in significant quantities: beta-estradiol, estrone and estriol. In a woman, who is not pregnant the most abundant estrogen isbeta-estradiol, which is synthesized from cholesterol in the ovaries.

Estrogens which are secreted by ovarian follicles have various important functions which are given as follows:

It promotes the development and maintenance of female reproductive structures, secondary sex characteristics, and the breasts. The secondary sex characters include enlargement of the breasts, abdomen, monspubis, and hips, voice pitch, a broad pelvis, and hair growth on the head and body. Estrogens help in increase protein anabolism, which includes the building of strong bones in the body. Estrogens are symbiotic with human growth hormone (HGH). Estrogens help in lowering blood cholesterol level, which is the main reason that women under age 50 have a lower risk of coronary artery disease than men.

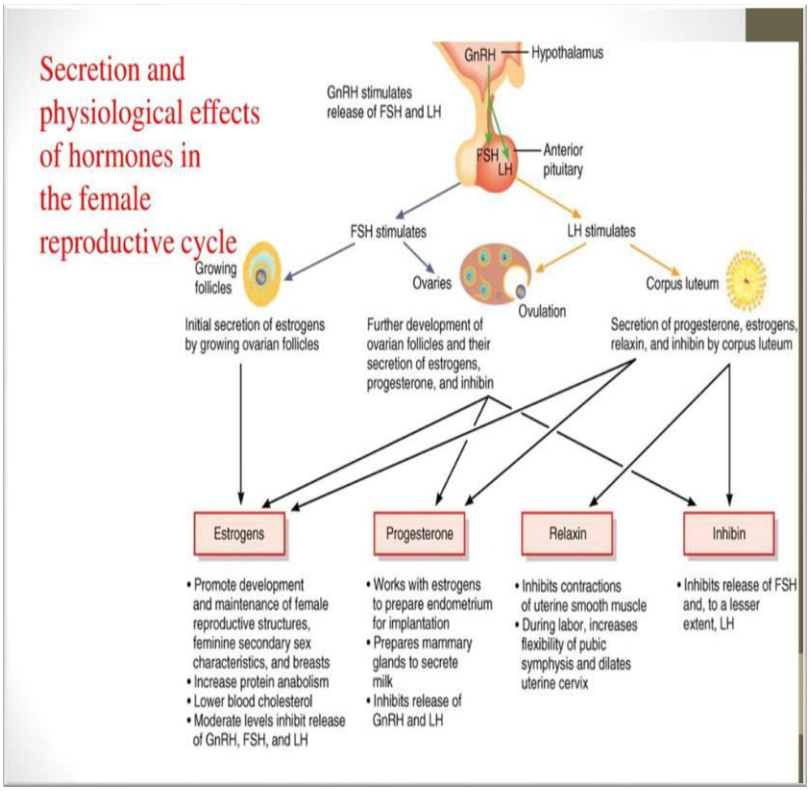
Moderate levels of estrogens in the blood inhibit secretion of LH and FSH by the anterior pituitary and also release of GnRH by the hypothalamus cells of the corpus luteum, which is mainly secreted by Progesterone in coordination with estrogens helps in preparing and maintaining the endometrium for implantation of a fertilized ovum and also to prepare the

mammary glands for milk secretion. If there are high levels of progesterone in the blood it inhibits the secretion of GnRH and LH. Relax in which is produced in small quantity by the corpus luteum during each monthly cycle relaxes the uterus by inhibiting contractions of the myometrium. Implantation only takes places in the relaxed uterus. During the pregnancy, the placenta produces more relaxin so that the relaxin continues to relax the uterine smooth muscle. At the conclusion of pregnancy, relaxin helps in increasing the flexibility of the pubic symphysis and helps in the dilation of the uterine cervix which will make the delivery easy for the mother.

Granulosa cells of growing follicles secretes Inhibin which inhibits secretion FSH and LH.

Phases of the Female Reproductive Cycle

The time period of the female reproductive cycle ranges from 24 to 35 days. Duration of 28 days and divide it into four phases: the menstrual phase, the preovulatory phase, ovulation, and the postovulatory phase.



Menstrual Phase

The word "menstruation" is etymologically related to "moon". The terms "menstruation" and "menses" are derived from the Latin mensis (month), which in turn relates to the Greek mene (moon). Women were thought to be at the height of their spiritual and mental power at this time.

It lasts for roughly the first 5 days of the cycle.

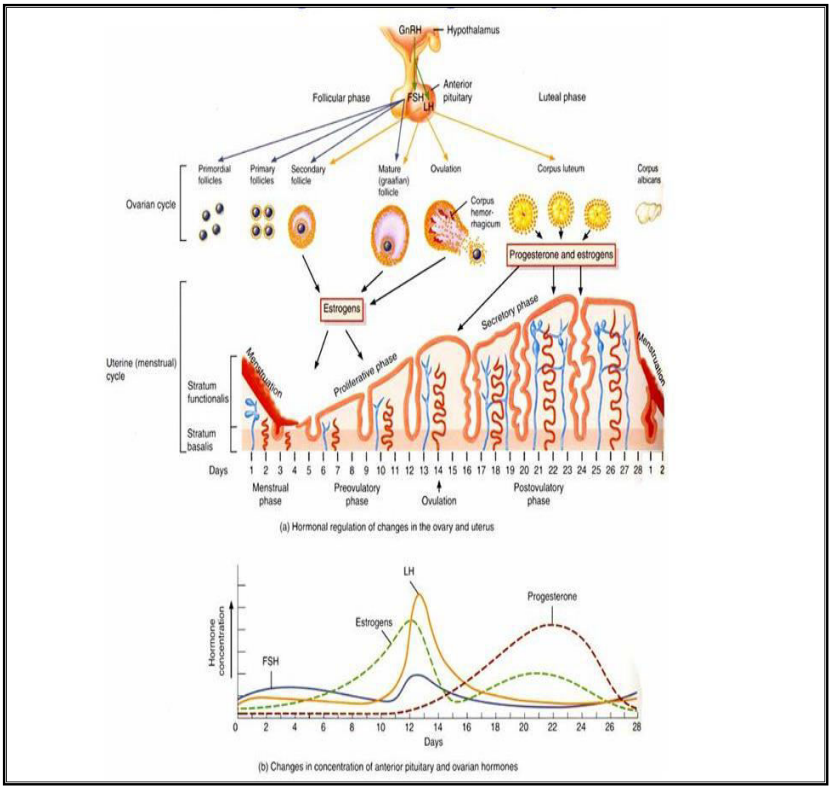
Events that occur in the ovaries

Under the influence of FSH, primordial follicles development results into primary follicles and then into secondary follicles. This process may take several months to occur. Therefore, a

follicle that begins to develop at the initial stage of a particular menstrual cycle may not reach maturity and ovulate until several menstrual cycles later.

Events that occur in the uterus

Menstrual flow includes 50–150 mL of blood, tissue fluid, mucus, and epithelial cells which are shed off from the endometrium. This discharge occurs because of the lower levels of progesterone and estrogens which stimulate release of prostaglandins that causes the constriction of uterine spiral arterioles which results, in the cells they supply become oxygen-deprived and start to die. Finally, the entire stratum functionalis sloughs off the endometrium is very thin, about2–5 mm, because the one which is remaining is the stratum basalis.



Changes occurring during the menstrual phase

Preovulatory Phase

The period between the end of menstruation and ovulation is called the **preovulatory phase.** It lasts from days6 to 13 in a 28-day cycle.

Changes taking place in the Ovaries

Secretion of estrogens and inhibin by some of the secondary follicles in the ovaries begin. At day 6, a single secondary follicle in one of the two ovaries has outgrown all the others to become the dominant follicle**.** Estrogens and inhibin secretion by the dominant follicle decrease the secretion of FSH, which causes less well-developed follicles to stop growing and undergo atresia, when two or three secondary follicles become codominant and later are ovulated and fertilized at about the same time, non identical twins or triplets are formed. Usually, the one dominant secondary follicle becomes the mature (graafian) follicle, whose enlargement takes place until it is more than 20 mm in diameter, and which is ready for ovulation. This follicle

forms a blister like bulge due to the swelling antrum on the surface of the ovary. The mature follicle continues to increase its production of estrogens when it is finally matured. The ovarian cycle, the menstrual and preovulatory phases together are termed the follicular phase because there is growth and development of ovarian follicles.

Changes in the uterus

Estrogens which are liberated into the blood by growing ovarian follicles stimulates the repair of the endometrium; mitosis occurs in the cells of stratum functionalis which produce new stratum functionalis. The thickness of the endometrium approximately doubles, to about4–10 mm. Endometrium is proliferating hence the it is termed as proliferative phase.

Ovulation

At this stage, the rupture of the mature graafian follicle and the release of the secondary oocyte into the pelvic cavity, usually occurs on day 14 of the 28-day cycle. The secondary oocyte remains surrounded by its zona pellucida and corona radiata, during ovulation.

At the last part of the preovulatory phase there are high levels of estrogens which exert a positive feedback effect on the cells that secrete LH and gonadotropin-releasing hormone (GnRH) which then causes ovulation. There is high concentration of estrogens which stimulates more frequent release of GnRH from the hypothalamus. It also directly stimulates gonadotrophs in the anterior pituitary to secrete LH. GnRH promotes the release of FSH and additional LH by the anterior pituitary. LH causes rupture of the mature (graafian) follicle and expulsion of a secondary oocyte about 9 hours after the peak of the LH surge. Home test that detects a rising level of LH can be used to predict ovulation a day in advance.

Postovulatory Phase

The time between ovulation and onset of the next menses is called as postovulatory phase The time duration is of 14 days in a 28-day cycle.

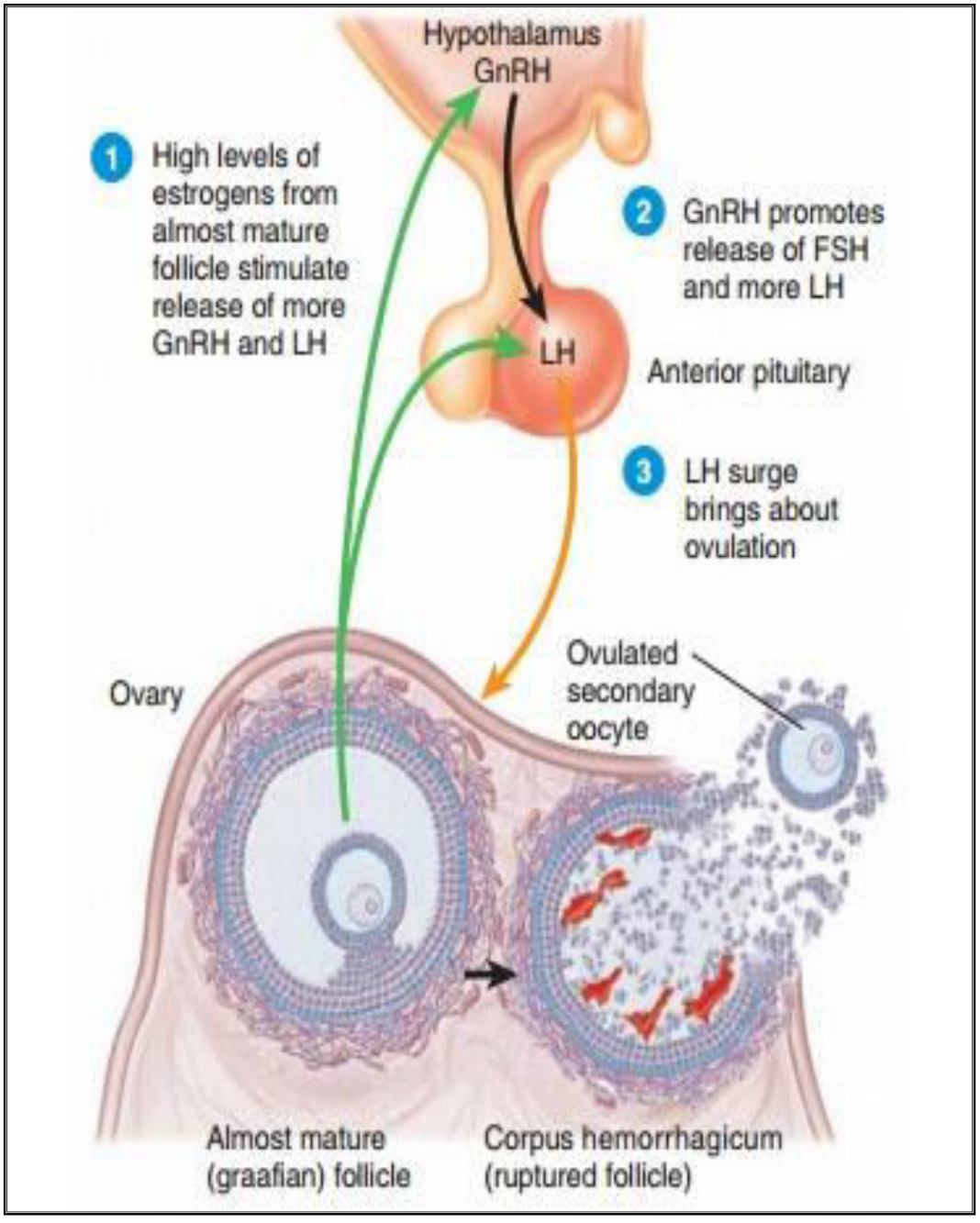
Events observed in one ovary

After ovulation, the mature follicle collapses, and the basement membrane between the granulosa cells and theca interna break down. Once a blood clot forms from minor bleeding of the ruptured follicle, the follicle becomes the corpus hemorrhagicum. Then the Theca interna cells mix with the granulosa cells and they all become transformed into corpusluteum cells under the influence of LH. Stimulated by LH, the corpus luteum secretes progesterone, estrogen, relaxin, and inhibin. The luteal cells also absorb the blood clot. Now this phase is called as luteal phase**.** In an ovary that has ovulated an oocyte depend**,** on whether the oocyte is fertilized. If the oocyte is not fertilized, the corpus luteum has a lifespan of only 2 weeks. Then, its secretory activity declines, and it degenerates into a corpus albicans. As the levels of progesterone, estrogens and inhibin decrease, release of GnRH, FSH, and LH rises due to, loss of negative feedback suppression by the ovarian hormones. Follicular growth resumes and a new ovarian cycle begins.

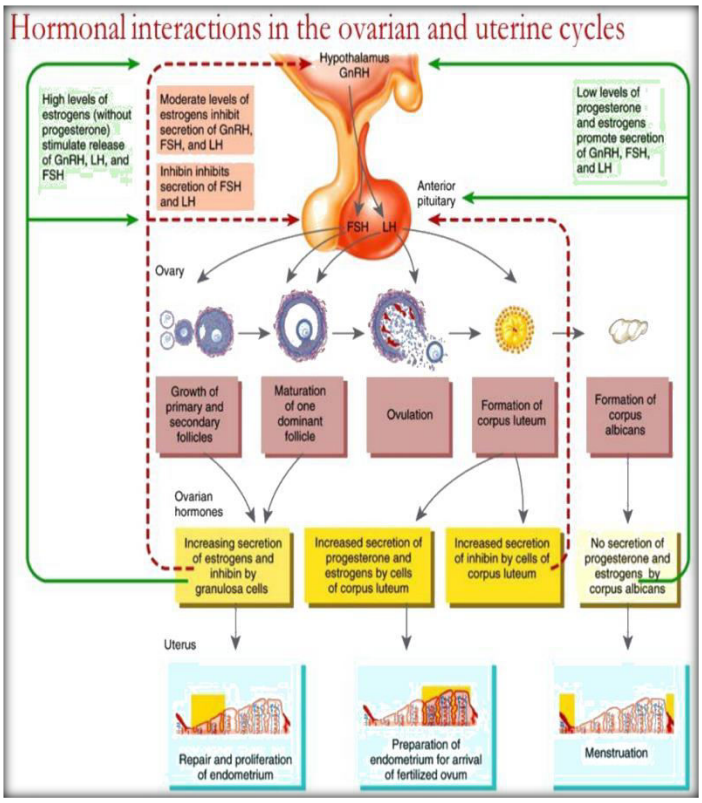
High levels of estrogens exert a positive feedback, effect on the hypothalamus and anterior pituitary, thereby increasing secretion of GnRH and LH.

Events taking place in the uterus

Hormones like Progesterone and estrogens which are produced, by the corpus luteum promote growth and coiling of the endometrial, glands, vascularization of the superficial endometrium, and thickening of the endometrium to 12–18 mm (0.48–0.72 in.). This period is called the secretory phase of the uterine cycle because of the secretory activity of the endometrial glands, which begin to secrete glycogen. These preparatory changes, peak about one week after ovulation, at the time a fertilized, ovum might arrive in the uterus. If fertilization does not occur, the levels of progesterone and estrogens decline due to degeneration, of the corpus luteum. Withdrawal of progesterone and estrogens causes menstruation.



The LH mainly triggers the process of ovulation as shown in the above diagram.



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HUMAN ORIGIN AND DIFFERENT STEPS IN ITS EVOLUTION

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INTRODUCTION

There are many opinions regarding the origin of man. The origin of the earth is believed to be approximately four billion years ago. Animal life is believed to have originated much later and humans may have originated on Earth 20 million years ago. The life of the earth is considered to be more than four hundred million years. With the passage of time, the earth got colder and an atmosphere and water cover was formed on the earth and an environment favorable for the formation of living organisms was created. Human history is also ancient. Humans originated millions of years ago. Since then, the development of human life has continued continuously. English scientist Charles Darwin in AD. In 1859, the scientific theory of the evolution of living organisms was presented. According to that, about fifty million years ago, Amoeba, a single-celled living organism, was formed from the algae on the reservoir. As time passed, various aquatic, amphibian and terrestrial animals appeared on earth. About six million years ago, birds and mammals arose. Among these, humans are the advanced stage in the evolution of ape, a mammal. The history of how the advanced humans who ride on the moon today reached this stage is very interesting.

METHODOLOGY

Very simple methodology is used in this article hence in this article try to highlight the main Human origin and different steps in its Evolution. In this article used secondary data source of human Origin and different steps in evolution required data have been collected from various reports, journals & reference, books, web site etc. The origin and evolution of man is explained as follows.

Origin of Man

In fact, the question of how humans originated has influenced human thought for thousands of years. The origin of man on the back of the world has been envisaged in different ways. According to the Christian scripture 'Bible', the earth and human beings were created in just six days. James Curr, Archbishop of Ireland, based on the Bible's calculation, the date of origin of earth and man is 23rd October 4004 AD. S. BC is scheduled at 09.00 am. According to Hindu mythology; man was created from sage Manu after the churning of the sea. Some scholars date Samudramanthana to AD. S. BC 3210 says this. Such fictional stories are also told in China. Carbon deposits from the Archaeozoic period have been found in Ontario, Canada. According to plant scientists, the presence of carbon indicates the presence of life. The Archaeozoic era began about one billion and fifty million years ago. Finally, it has been proven that life had originated by that time. As research progressed, it became clear that single- celled germs were formed in the Eozoic period, even before the Archaeozoic period. The period of which is considered to be approximately 3 billion 50 million years ago. The origin of life on earth was 350 million years ago. Initially life was formed in water. In it we get the remains of marine life and fish. Later, during the middle period of life, insects, amphibians, as well as plants such as algae are found.

Snakes, dinosaurs were born in the last fossil age. The remains of these are also found in abundance. Dinosaurs ruled the earth for almost 10 million years. Hence the Mesozoic period is called the age of reptiles. The late Cenozoic period, the last of the geological period, saw the first appearance of the mammal, the ape or monkey. From that came the origin of primitive man and then today's human.

Field of Origin of Man

The question of where the primitive man originated remains controversial. Human remains have been found in various places in the world. From the study of these fossils, we realize that no remains of male apes from the Pleistocene era (25 million years ago) have been found in the North American continent. Originating in Siberia and Alaska during the Pleistocene, Plesoindians first came to North America. So it can be said that humans did not originate in North America. South America does not contain any fossils of Pletorine monkeys or more advanced male apes. Finally, it can be said that the origin of human beings did not occur in the Americas. The origin of humans is more likely to have occurred in Asia and Africa. Asia is thought to be the place of human origin. Until Davin's study, information about the continent of Africa was very sketchy. Until Darwin's time, scholars believed that humans originated and developed in Asia. It has also been thought that hominids may have evolved in Southeast Asia, based on fossils of Rampithecus from the Miocene age in India's Siwalik Hills, or Pithecanthropus found in Java. Later, in the final years of the nineteenth century, jaws of the Prosomium organism were obtained from the Faym Oligocene basin of Egypt. Which was named Bopliopithecus as well as Para Pithecus? These fossils were approximately 300 million years old. Fossils of the Ramapithecus species were discovered in Africa in the 1930s. Leake later discovered the remains of Australopithecus African's in Africa. Which was approximately 25 years ago? After that, fossils of Neanderthal man such as Gingainthropus, Homo habilis, Pithecanthropus Rhodesian man and Neanderthal man have not been found in all areas in Africa. The discovery of human- like apes, gorillas, orangutans, as well as chipmunks found in Africa changed the previous ideas about the origin of humans. All scholars now openly accept that the place of origin of primitive man was undoubtedly South Africa. From where humans moved to other parts of the world. According to the research done on the basis of this has been proved. That Africa was the area of origin of primitive man. From there, humans reached other parts of the world.

Gradual Development of Man

Approximately 13 million years ago, mammals such as mice, cats, dogs, buffaloes, cows etc. were born. But there was more time for the origin of man. However, humans are also mammals. Male monkeys originated about 6 million years ago. But they evolved 4 crore years ago. Tailed apes evolved and then tailless apes about 2.5 million years ago.

Formation of organisms in aquatic environment

According to scientists, about two and a half thousand million years ago, living organisms were formed from inorganic matter in marine animals. For the first time, formless and colorless living matter was formed in sea water. Initially there was no covering around this material. But later on this formless living matter formed a coating and from it 'single- celled animals' (Protozoa) emerged. From this single- celled organism, living organisms with a very simple structure were created. From this simple organism, various complex or composite organisms were

simultaneously developed gradually and gradually. Scientists believe that the animals and plants in the present state of the earth are the evolved descendants of that simple organism. That is, all living beings are created through successive changes and from a single ancestor.

Creation of Human Beings

When, where and how was human created on earth? This is an unanswered question for scientists. But like other organisms on earth, human beings have also been created through the process of evolution. Everyone has agreed on this. There are many differences of opinion among scientists regarding the exact ancestor of humans. The current concept of human ancestry is based on human fossils in modern times. About 65 to 70 days. L. Eons ago, the giant insectivore on the tree evolved from a reptile. From this ancient prakrishtha arose a group of prakrishthas. It is called Lemuridus. Many of these lemurs did not have special hand and foot grips and their heads were far from each other. Tarzosaurs evolved from these lemurs. These tarsiers had large and close- set eyes. The tail was long and the hind legs were also very long. From these tysirs arose the ancestors of monkeys, apes and humans. Their ancestors are called 'Athropoidus'. Which evolved from tarsiers? These anthropoids were characterized by protruding lips, a well- developed brain, and two serrated teeth on the lower and upper jaws. From this Athropoidus animals evolved in three directions. In the first direction, the New World Monkey, in the second direction, the Old World Monkey, and in the third direction, the Kapi andSubfamily Homininag Homininae, Subfamily Ponginae, Family Hylobatidae, Tribe Panini,Tribe of Man, Tribe Gorillini, Gorillas, Orangutans, Gibbons, Monkeys, Chimpanzees, Hominoidea . AHaplorrhini , Anthropoidea , Strepsirrhini, Bushbabies, lemurs,Tarsiers, Humans evolved. All these ancestors were given the collective name 'Propliopithecus. According to some scholars, Samapithecus (like the early human giant) evolved from Opithecus. According to some scientists, dryopichcs (such as fossil monkeys) evolved and gave rise to modern monkeys and humans. Modern apes (gibbons, orangutans, chimpanzees, gorillas) were included in the super family Hominoidae, while humans were included in the Hominoidae. This contains only one species and one cell. He is the intelligent human (Homo sapiens).

Evolution of Man

Fossils have been found in various parts of the world. From their study, it can be seen that Australopithecus Africans primitive man lived in the continent of Africa during the Lower Pleistocene era, 2.5 million years ago. Australopithecus was a male ape. But he was very close to human. Now he could stand on his feet and walk straight. That's why L. S. B. Leake named it Gynaethropus erectus. This man may have started experimenting with rough tools made of batia stone and hand axes for his hunting. It is thought that modern humans may have evolved from this species, Ginganthropus. At the level where the remains of Ginganthropus are found, another human species is found below it. Of course, fossils of homohablis are also found. Finally, some historians say that the present day human evolved from Homo habilis. But other historians believe that Homo habilis could not survive in the competition of rivals and it died out. Gynoanthropus erectus had to go through many stages to become the present human. which mentions Pithecanthropus erectus from the Middle Pleistocene strata of Java. It originated approximately 5 lakh years ago. It was very close to human. Peking Man of China is mentioned after Pithecanthropus erect. It has been dated to approximately 2 or 3 lakh years ago. whose duration is similar to that of Pithecanthropus erect. Many scholars believe that Pacing Man is a

species of Pithecanthropus. The next name that comes on the evolutionary path is Neanderthal man. This human 1 LakhYears ago was inhabited by the Pleistocene era. But it is believed that the evolution of this human took place during the middle Pleistocene era, 2.5 million years ago. The measurement of this human eye is approximately 1450 C. C. was Fossils of Neanderthal man have been found in every region of the world. About 50,000 years ago this breed became extinct due to interbreeding. The next stage of development refers to Komainan man. Its remains have been found all over the continent of Europe. It is 5 feet 11 inches long and 1666 c. C. The skull was human. It was a human like modern man in its entirety. He was making beautiful tools and murals out of stone. 20,000 years ago, this race was spread across Europe and other continents. This is what today's intelligent humans call Homo sapiens.

Early humans (Homo helibus)

The first stage in human evolution is adihuman. Their existence was around two million years ago. Human remains have not been found in India, but the tracese of their existence can be seen through the ston tools they used. They used rough stone tools. Chiseled or chipped stone tools were used for hunting, cutting tree branches and other work. Except for some areas around the Ganga, Yamuna and Indus rivers, such weapons have been found everywhere else in India. Man- made remains found recently at Bori in Maharashtra date back to fourteen million years ago. This adihuman was hairy, narrow forehead, wide and forward jaw, bigger brain than other animals, standing on two legs, bent back and bent. It was called Homo Helibus. In this phase, their daily routine was to protect themselves from wild animals.

New Man (Homa Erectus)

A new human evolved around four and a half to five lakh years ago after gradual progress in the stage of human beings. He is known as Homo Erectus because he stands erect than other humans. The physical characteristics of this human include increased brain size, large teeth, erect posture, tighter claw grip. It is also known as 'Peking Man' because the remains of this human bone were found in the city of Peking, China. The routine of humans at this stage was to wander in search of food and prey.

Thoughtful human (Homo sapiens)

A rational human being is the next stage in human evolution. The physical characteristics of this human were all the same as the new human. The only difference was that the brain was larger than before. Due to the growth of the brain, this human began to use the intellect to live life. Hence it came to be called Homo sapiens. The remains of this human were found at a 'Neanderthal' site in Germany. Therefore, it had advanced tools and weapons. They should also know the usefulness of fire.

More intelligent humans (Homo sapiens)

The period of more intelligent man should be about twenty eight thousand years ago. This was a very important stage in the evolution of the human body. Humans in this phase were more thoughtful than before. Hence it is called more intelligent human (Homo sapiens). This human is similar to the common human. This man used his intelligence more and more in his daily life. Greater use of firestarted to be done. The stone tools and weapons of these humans were more advanced. The remains of this human were found at Cromanon in France, so it is also known as 'Cram'. 'Chromenon Man'.

Characteristics of Stone Age Man

The Stone Age is regarded as the oldest period in the history of human life. During this period, stone was an important element in the daily use of human beings. Man- made tools and weapons of stone, wood and bone are the hallmark of this age. Since wood and bone are perishable, only stone tools and implements are widely available today. That is why this period is called Stone Age. Most of the daily life of primitive man in this period was spent gathering food. The discovery of Yathavash agriculture brought stability to their life. Tribes came into existence as they started living in groups for hunting and self- defense. Men and women started living together for reproduction and rearing of offspring. The Kutub organization was created out of it. Later, during the Neolithic period, humans became more advanced. Factors like agriculture, animal husbandry, industry, trade, language, art, communication, religious faith etc. were developed. Now man became producer and consumer. His life became stable. Fire also began to be used on a large scale. Over time, copper, bronze, and iron were used to make tools and equipment.

CONCLUSION

In this way, it is clear from the above discussion that how did the human being originate and evolve? After the 18th century, the goddess theory of the origin of man fell away with the advent of scientific theory. According to the modern theory, while the gradual origin of life takes place. Man was born. According to this theory, fish, frogs, reptiles then birds and mammals originated. Among the mammals, the most prominent primate was the male ape. From which humans evolved.

1) All living things on earth have evolved through successive changes and from a common ancestor.
2) Amoeba was the first living organism to be born on earth followed by aquatic, amphibians and terrestrial animals were born in this order.
3) Man is an advanced stage in the evolution of ape, a mammal.
4) Humans have evolved from Ape- like ancestors.
5) The first stage of human evolution is Adiman.
6) There are stages and they are determined by human anatomy and brain (intelligence) development.
7) During these various stages of human evolution, many important inventions (agriculture, fire, wheel etc.) stabilized human life.
8) The history of human progress from Stone Age to Atomic Age is very exciting.

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IMPACT OF PLASTIC POLLUTION ON MARINE LIFE

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INTRODUCTION

Ecosystems are at risk from plastic contamination. Both plant and animal species change in response to their surroundings. Time and again, a new natural equilibrium is established. That balance is disturbed by plastic in the environment. In the last few decades, plastic pollution has emerged and is quickly spreading. Animal species just haven't had the chance to develop the skills necessary to deal with it, such as avoiding plastic or surviving on it. Another factor that can make one species more susceptible to plastic than another is dependency.

As the world's capacity to deal with the rapidly rising production of disposable plastic goods exceeds it, plastic pollution has emerged as one of the most urgent environmental issues. In impoverished Asian and African countries, where rubbish collection services are either ineffective or nonexistent, plastic pollution is most noticeable. However, the developed world also has issues with properly collecting used plastics, particularly in nations with low recycling rates.

A whale shark swims beside a plastic bag in the Gulf of Aden near Yemen. Although whale sharks are the biggest fish in the sea, they're still threatened by ingesting small bits of plastic. (Photograph by Thomas P. Peschak, Nat Geo Image Collection)

A sponge crab wears a clear sheet of plastic over its shell in Edithburgh, Australia. Historically, sponge crabs put sponges over their shells to camouflage themselves from predators. This man-

made covering is not adequate protection. (Photograph by Fred Bavendam, Minden Pictures/Nat Geo Image Collection)

The food chain has already been impacted by plastic. Animals' bodies contain microplastics. These microplastics are consumed along with the food they contain. The 'trophic transfer' of microplastics is what is referred to as in this process. Microplastics can travel up the food chain since animals consume other animals. Microplastics resemble plankton, which is a food source for hundreds of species at the base of the food chain. As a result, plastic is present across entire ecosystems. Researchers have even found evidence of animals as tiny as coral polyps frequently ingesting microplastics.

In addition, plastics themselves contain hazardous compounds in addition to absorbing contaminants that are floating about in the ocean. According to preliminary studies, animals that swallow these toxins-infused particles may suffer organ damage, become more prone to illness, and have different reproductive patterns.

(Image: Mary Flora Hart/China Dialogue Ocean)

Microplastics can be distinguished in the following ways based on their shapes, sizes, and chemical makeup.

Types of Microplastics

Microplastics are divided into primary and secondary categories according to their place of origin (Avio et al., 2017). Primary microplastics are synthetic polymers that are microscopic in size. They are utilised as exfoliates in a number of processes, including chemical synthesis, sandblasting media, maintaining various plastic products, and producing synthetic clothing. Microbeads are a different class of primary plastics (size 2 mm), made of polyethylene (PE), polypropylene (PP), and polystyrene (PS) beads, and they are utilised in cosmetic and healthcare applications.

The fragmented form of macro- or meso-plastics, secondary microplastics are typically produced as a result of a variety of environmental processes, including biodegradation, photodegradation, thermo-oxidative degradation, thermal degradation, and hydrolysis (Sharma and Chatterjee, 2011). Nanoplastics are plastic pieces with a size of less than one micron, and due to their high surface-to-volume ratio, both microplastics and nanoplastics may have ramifications for the bioamplification and bioaccumulation of different chemicals and pollutants (de Costa et al., 2016).

Sources of plastic pollution

These dangerous plastic fragments are present in the terrestrial and aquatic ecosystems because of a variety of anthropogenic activities, such as home, industrial, and coastal ones. Because of residential runoff that contains microbeads and microplastic pieces (used in cosmetic and other consumer products) as well as from the fragmentation of massive plastic garbage, microplastics have mostly entered the aquatic ecosystem (Anthony L. Andrady, 2011). The production of plastics in the form of pellets and resin powders by air-blasting results in the emission of polymers that contaminate the aquatic environment (Michiel et al., 2011). In addition, the marine ecosystem is contaminated by coastal activities such as fishing methods, aquatourism, and marine enterprises.

Microplastics are subject to a variety of physico-chemical reactions once they enter the marine environment, including biofouling, leaching, and incorporation of secondary pollutants. Microplastics come in a variety of sizes, forms, and densities. Because of these characteristics, plastic fragments have been transported throughout the marine ecosystem (eventually settling in the benthos) and are now accessible to marine life (Sharma and Chatterjee, 2011).

While benthic organisms like polychaete and tubifex worms, amphipods, and mollusks are known to come into contact with dense microplastics, the pelagic marine biota, which is made up of planktons and crustaceans, is exposed to low-density microplastics (Luis et al., 2018). The polymer type, biofouling, and surface chemistry of the particles are a few examples of the variables that might affect how quickly microplastics settle through the water column (Turner and Holmes, 2015). In the majority of investigations, sediments and benthic ecosystems have contained microplastics. A variety of marine biota depend on the benthic environment as one of their major food sources. Recent research has demonstrated that microplastics, which are found in the water in the form of microbeads and microfibers, are consumed by marine benthic biota (Courtene et al., 2017).

Impacts of plastic pollution on aquatic environment

According to research from Sweden, fish can develop abnormal behaviour after ingesting nanoplastics in the food chain. Water fleas eat the nanoplastics found in algae, and fish eat the fish that they consume. The food chain is traversed in this manner by plastic debris. With and without nanoplastics, the researchers simulated the food chain. The fish that consumed nanoplastics behaved abnormally, eating more slowly and acting hyperactively, as opposed to the fish who weren't given any. Although the study was conducted in a lab setting, accumulation of plastic in living organs can also occur in the wild, particularly if the animals live for a very long time. Slow-moving fish make for simple prey. Plastic can obstruct the natural environment in this way.

At least 800 species are reportedly impacted by marine waste worldwide, and up to 80% of that trash is plastic, according to the UN. A junk or garbage truck load of plastic is thought to be dumped into the ocean every minute, amounting to up to 13 million metric tonnes of plastic every year. The ingestion of plastic trash by fish, seabirds, sea turtles, and marine animals can result in asphyxia, malnutrition, and drowning. The threat still affects people: While the full decomposition of plastics is thought to take hundreds of years, some of them break down much more quickly into minute particles, which then end up in the seafood we eat.

Studies show that plastic has been consumed by 50% of all sea turtles globally. Some people who do this wrongly think that because their bellies are full, they have eaten enough and then starve. Plastic pollution on many beaches is so ubiquitous that it is reducing turtle reproductive rates by changing the temperature of the sand where incubation takes place.

According to a recent study, marine turtles who consume just 14 bits of plastic are at an elevated risk of dying. The young are particularly vulnerable because they like to consume anything they feel like, unlike their elders, and because they drift with the currents much like plastic.

A sea turtle found in the Pacific Ocean had this debris in its stomach, according to The Ocean Cleanup, a foundation.

Up to a million seabirds per year are killed by plastic garbage. Similar to sea turtles, when seabirds consume plastic, it occupies space in their stomachs and can occasionally result in malnutrition. Numerous seabirds are discovered dead with this waste still in their stomachs. Scientists predict that by 2050, 99 percent of all seabird species would have consumed plastic, up from the current estimate of 60 percent.

A dead albatross chick found on Midway Atoll in the Pacific Ocean with plastic debris in its stomach. U.S. Fish and Wildlife Service

The great intelligence of dolphins makes it unlikely that they would consume plastic, yet they are still vulnerable to contamination by synthetic substances infected by their prey.

A dolphin with a plastic bag trailing from its fin swims in the Fernando de Noronha Archipelago in Brazil. João Vianna

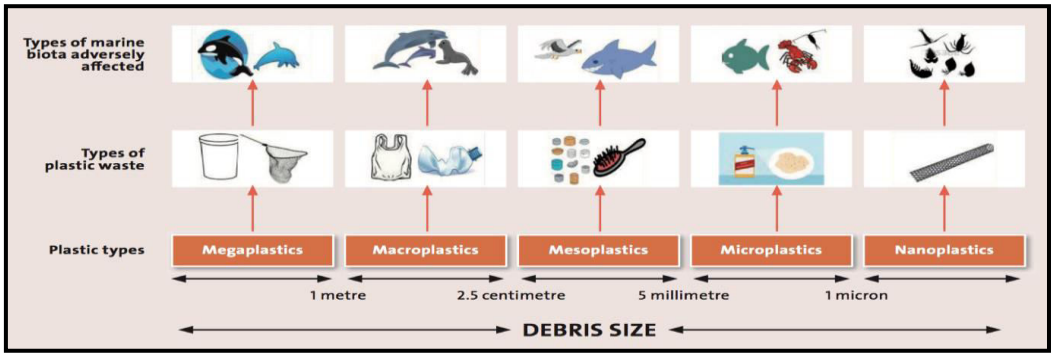
Both large and small oceanic species are impacted by plastic. the small seahorses that live in coral reefs, the whales, and dolphins, to the schools of fish that live in the same reefs and nearby mangroves.

A seahorse wraps its tail around a plastic cotton swab near Sumbawa Island, Indonesia. Courtesy of Justin Hofman

A plastic band restricts the growth of a blue-striped grunt fish in the Caribbean Sea. Karen Doody/Stock trek Images

Pathogens in the ocean may multiply more readily as a result of plastic garbage. A recent study by experts found that corals that come into touch with plastic had an 89 percent probability of being ill, compared to corals that do not have a 4 percent chance.

The weight of ocean plastics is expected to surpass the total weight of all fish in the seas by 2050, according to scientists, unless immediate action is taken to address this pressing issue.



Diagrammatic representation of different types of plastics and their effect on marine organisms

CONCLUSION

Plastic has a significant negative impact on the aquatic ecology and its habitat. Additionally impacted is species interdependence. Microplastics are also subject to the trophic transmission process. The food chain is therefore also disrupted.Plastic pellets and resin powder released by the plastics sector contaminate the aquatic environment. Plastic garbage generated by businesses, households, and other sources can enter the marine ecosystem directly or indirectly. Fishing, fish hatcheries, and offshore drilling are all sources of plastic that directly enter aquatic systems and endanger biota through secondary microplastics that form after long-term degradation.To protect the environment, the government has made steps to ban single-use plastics and introduced biodegradable plastics. Individuals must refrain from using plastic so that the aquatic environment is not abused.There should be awareness-raising campaigns about the correct handling of plastic garbage and the negative effects of plastic use. The most crucial method for reducing the amount of plastic entering the ecosystem is to gather and recycle plastic scraps. The best course of action is to discontinue production altogether and look at plastic products as a replacement in order to eliminate any potential harm.

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INTRODUCTION TO CANCER BIOLOGY

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INTRODUCTION

What is Cancer?

Cancer is a condition in which some cells of the body grow uncontrollably due to multiple changes in gene expression and spread to other bodily regions. Cancer causes significant morbidity and, if left untreated, the death of the host (Ruddon, R. W. 2007). Malignant cancer can penetrate locally, spread to nearby lymph nodes, and metastasis to distant organs in the body, which distinguishes it from benign tumors.

Molecular Basis of Cancer

Cancer is mostly caused by two gene classes, which together make up a very small part of the entire genetic repertoire. These are Proto-oncogenes and tumor suppressor genes. Proto-oncogenes can develop into oncogenes, which are carcinogenic and encourage unchecked cell division, as a result of mutations.The mutations may cause the proto-oncogene that code for the growth-stimulatory protein to create excessive amounts or a hyperactive form of it. On the other side, cancer is brought on by mutations that make tumor suppressor genes inactive.As a result of the absence of functional suppressor proteins, the cell lacks crucial brakes that prevent unrestrained development (Weinberg, R. A. 1996).

The Characteristics of Cancer Cells

Following characteristics are acquired by a normal cell to develop into cancer.

- Independence in Growth Signals
- Lack of sensitivity to antigrowth signals
- Resistance to apoptosis
- Endless Potential for Replication
- Sustained Angiogenesis
- Metastasis

Independence in Growth Signals

Normal cell depends on mitogenic growth signals (GS) to enter into cell division. These signals are transmitted to cells via transmembrane receptors; examples of such signals are growth factors, extracellular matrix components, and cell-to-cell adhesion/interaction molecules. We are aware that no normal cell type that can multiply without such stimulatory signals. In contrast to a normal cell, a cancer cell shows independence for exogenous growth signals because of oncogenes. From this, we conclude that cancer cells generate many of their own growth signals. Cancer cells produce mutant proteins (also known as "oncogenic proteins") that imitate these typical growth signals (also known as "proto-oncogenic proteins"). Proto-oncogenes can become oncogenes due to a variety of processes, including mutations, chromosomal

rearrangements, viral insertion, gene amplification, etc. In any healthy tissue, an oncogenic transformation has the consequence of rendering cancer cells independent of these external growth signaling factors.

Lack of sensitivity to antigrowth signals

Normal cells continuously check their internal and exterior environments before cell division to make sure conditions are favorable for mitosis. Whether a cell should divide, go into quiescence, enter the post-mitotic stage or experience self-destruction is determined by signals from the internal or external environment. For instance, the presence of proteins necessary for DNA replication after the G1 phase causes the cell to enter the S phase, but significant DNA damage can cause the cell to undergo quiescence or self-destruction through apoptosis.

These checks offer a vital homeostatic mechanism that enables the cell to advance to cell division at the appropriate time and under the most favorable growth circumstances. Contrarily, cancer cells bypass or avoid these anti-growth signals to promote their own development and multiplication. For instance, changes to genes that ordinarily prevent cell proliferation would lead to more frequent cell division. These tumor suppressor genes (TSGs) are part of a huge family of genes that encode proteins that normally regulate cell division. Unlike oncogenes, which are gain-of-function mutations, these genes are loss-of-function mutations, and often both copies (alleles) of the gene must be changed to promote tumor growth.

Resistance to apoptosis

Both the rate of cell death and the rate of cell proliferation affect the capacity of tumor cell populations to grow in number. Apoptosis, a form of programmed cell death, is a major contributor to this death. Numerous studies using transgenic models strongly show that altering apoptotic machinery components can significantly alter the dynamics of tumor progression, indicating that the inactivation of this machinery is an important factor during tumor development. There are several strategies for cancer cells to avoid apoptosis. The most typical technique utilizes p53 tumor suppressor gene alterations that lead to the lack of proapoptotic regulators. The p53 protein is inactivated in more than 50% of all human malignancies (and 80% of squamous cell carcinomas). Because of its crucial function in the way cells react to stress, P53 is also known as the "guardian of the cell."

Endless Potential for Replication

Hayflick's early research (reviewed in Hayflick, 1997) showed that cells in culture have a limited capacity for replication. Cultured cancer cells, in contrast to normal cells, have the ability to significantly outperform typical doubling times to practically limitless levels. The HeLa cells are a vivid illustration of this. These cells were initially cultivated in 1951 from a cervical adenocarcinoma from Henrietta Lacks, a cancer patient, and they have since multiplied and grown in thousands of labs all over the world. This demonstrates that these cancer cells have damaged or circumvented the cell's internal senescence regulators, giving them the ability to divide indefinitely.

A normal cell's lifespan is limited by the length of its telomeres. Each time DNA is replicated, a portion of the telomere is lost from the ends of each chromosome. The reason for this continual shortening is because the DNA polymerase, the enzyme in charge of synthesizing new DNA, cannot replicate the ends, the end of the strand. As a result, these sequences degrade and the

length of the chromosomes gets shorter with each DNA replication cycle. Since each chromosome only has a limited number of these telomere repeats, subsequent cycles of replication cause the telomeres to gradually erode, leading to genetic changes, chromosomal end-end fusions, and eventually cell death. Contrarily, cancer maintains the length of its telomeres. Telomerase is an enzyme that is primarily activated by cancer cells as a means of maintaining telomere lengths. An active telomerase is present in almost 85–90% of malignancies. Telomerases thus stop the erosion of DNA ends, maintain the necessary lengths above the critical threshold, and permits infinite replicative capacity.

Sustained Angiogenesis

Incipient tumors require the ability to produce blood (angiogenesis) vessels in order to grow to a greater size (Bouck et al., 1996; Hanahan and Folkman 1996; Folkman, 1997). Most cells are found within 100 μm of a capillary blood vessel because they require oxygen and nutrients to survive and thrive. Angiogenesis is a crucial step in the transformation of a small, benign cluster of mutant cells into a massive, malignant growth that can spread to other places. Normally, this shift might take many months or even years, and without activating angiogenesis, solid tumors won't enlarge exceeding the size of a pea(Hejmadi, M. 2014).

Metastasis

Cancer cells can leave the primary tumor mass and colonize new areas of the body where nutrients and space are not initially scarce thanks to their propensity to invade and metastasize. 90% of people with cancer die from these distant tumor cell colonies, called metastases (Sporn, 1996).

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PROTOPLAST CULTURE: FROM SINGLE CELLS TO WHOLE PLANTS

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INTRODUCTION

One of the main differences which make the plant cell different from animal cell is presence of cell wall. The cell wall is an external protective layer that gives structural stability, support, and controls the movement of chemicals inside the cell. Therefore, all fundamental plant physiology processes depend on cell walls. Protoplast culture is the method used to create whole plants from a culture of cells lacking a cell wall. Since its discovery more than a century ago, this method has been employed extensively in agricultural improvement and plant breeding initiatives.The current chapter describes the techniques for protoplast isolation, purification, culture techniques, protoplast fusion and somatic hybridization techniques.

What is a protoplast?

Term protoplast introduced in 1880 by Hanstein. A protoplast is a live plant cell that does not have a cell wall. Protoplasts are essentially "naked cells" that have had their cell walls mechanically or chemically removed. They are characterized by their peculiar spherical shape and are encased in a plasma membrane, which does not provide the same level of security as the cell wall. Klercker successfully isolated the first protoplast using a mechanical approach in 1892. When Cocking employed an enzymatic approach to remove cell walls in 1960, he made the true breakthrough in protoplast research. In 1971, Rakabe and his collaborators succeeded in regenerating a complete tobacco plant from protoplasts. Due to their totipotency, protoplasts are incredibly interesting. It implies that they are capable of developing into a complete plant when cultured. They are delicate, adaptable, and can be made from any kind of plant, organ, or tissue. The majority of the time, protoplasts are made from leaf tissues, although they can also be made from callus, cell suspension, and pollen grains.

Why are protoplasts needed, exactly?

Protoplasts are a special experimental system for research on the structure and functioning of plant cells because they don't have a cell wall. Additionally, the absence of the cell wall enables the uptake of small and large molecules, viruses, bacteria, and genetic components like DNA and nuclei by plant protoplasts. It is possible to regenerate entire plants from separate protoplasts as well as from the somatic hybrid that results from their fusing. Under particular chemical and physical conditions, plant protoplasts can also absorb foreign DNA through their bare plasma membrane. Additionally, protoplasts offer an experimental platform for a variety of biological and molecular studies, including research into the growth characteristics of particular cells and studies of membrane transport.

Isolation of protoplast

Almost all plant components, including roots, leaves, fruits, tubers, root nodules, endosperm, pollen mother cells, etc., can yield protoplast.

Protoplasts are isolated from cells by two methods-

- Enzymatic Method

- Mechanical Method

Enzymatic Method

It is the protoplast isolation method that is most frequently utilised. Using enzymatic solutions, protoplasts are separated from the source in this procedure. This method is quicker, more effective, and releases more viable protoplasts without causing any harm.

Cellulase, hemicellulase, and pectinase are the enzymes employed for isolating protoplasts because the plant cell wall is made up of cellulose, hemicellulose, and pectin. The type of enzymes used to make the solution affects how long protoplast sources must incubate in enzymes.

There are two ways of isolating protoplasts using the enzymatic technique as follows:

Sequential Method: Cellulase and pectinase are two enzymes that are used in the sequential method. Pectinase first separates cells from the middle lamella, and cellulase subsequently separates the protoplast from the rest of the cell wall.

Simultaneous Method: For comprehensive protoplast isolation, this method uses both cellulase and macerozymes at the same time.

Mechanical Method

In this procedure, a little portion of the plant's epidermis is removed and plasmolyzed, causing protoplasts to separate from the cell wall. The tissue is then cut apart to allow the protoplasts to be released.

This method of isolating protoplasts is laborious and only yields a few number of isolated protoplasts. The limited survivability of the produced protoplasts is one of the other drawbacks. Nevertheless, due to the negative effects of the enzymes used in the enzymatic approach to protoplast isolation, the technique is still preferred by some labs.

Purification of protoplast

There are two methods of protoplast purification:

Sedimentation & washing: This approach involves centrifuging a suspension of crude protoplasts at low speed (50–100g for 5 min). It is possible to pipette off the supernatant containing cell debris once the intact protoplasts have formed a pellet. The pellet is rewashed after being gently resuspended in brand-new culture media with mannitol. To produce a reasonably clean protoplast preparation, this technique is performed two or three times.

Flotation: A concentrated solution of mannitol, Sorbitol and sucrose (0.3-0.6M) is used as a gradient and crude protoplasts suspension are centrifuged in this gradient at an appropriate speed. Since protoplasts have a lower density than other cell debris, they can float while the other cell debris settles. After centrifugation, protoplasts can be removed from the tube's top using a pipette.

After being isolated, plant protoplasts may rebuild the cell wall. They have therefore served as a crucial instrument for examining the process of cell wall development. Additionally, cell organelle separation, cell cloning, and cell fusion can be done using protoplasts. Plant protoplasts' adaptability has tremendously aided the advancement of biotechnology, physiology,

and contemporary botany. Protoplast culture is a useful technique for large scale plant regeneration. The plants generated from protoplast culture show high somaclonal variation.

Methods of protoplast fusion

Protoplast fusion can be broadly classified into two categories-

1. Spontaneous fusion (fuse through their plasmodesmata)

2. Induced fusion (needs a fusion inducing chemicals):

a) Mechanical fusion

b) Chemo fusion

c) Electro fusion

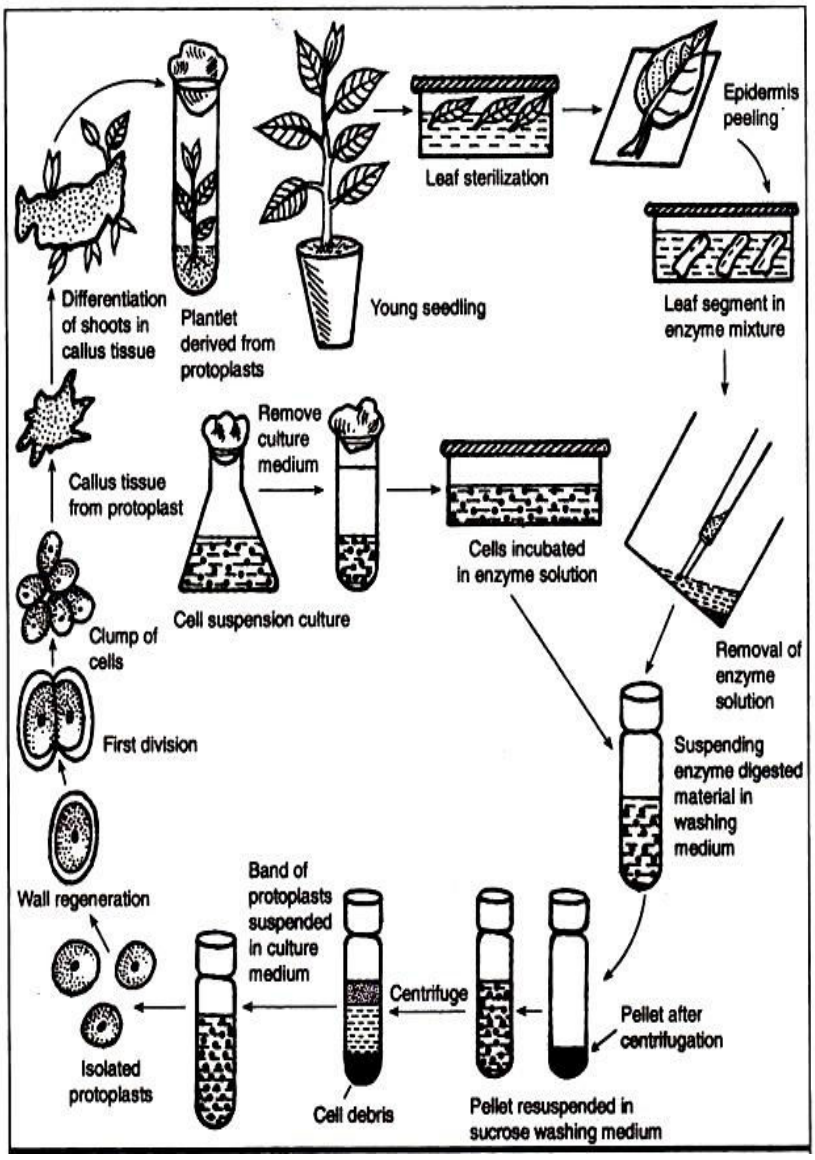

Fig. Steps involved in protoplast isolation, culture and regeneration(Source: Biology Discussion)

1. Spontaneous fusion

The cell walls some of the adjoining protoplasts may fuse to form homokaryons during enzymatic degradation. The number of nuclei infused cells sometimes contain 2-40 because of expansion & subsequent coalescence of plasmodermal connections between cells.

2. INDUCED FUSION

a) Mechanical fusion

The segregated protoplasts are mechanically brought into close physical contact with the help of a perfusion micropipette or micromanipulator under microscope.

b) Chemofusion

$NaNO_3$, polyethylene glycol and Calcium ions are been used to induce protoplast fusion.

NaNO3 treatment – Isolated protoplasts are exposed to 5.5% $NaNO_3$ in 10% sucrose solution and Incubation is carried out for 5 min. at 35^0C followed by centrifugation. The pellet containing chloroplast is kept in water bath at 30^0C for 30 min. which result in protoplast fusion.

Treatment with calcium ions (Ca^{++}) at high pH - In this method, the protoplasts are incubated in a solution of 0.4 M mannitol containing 0.05 M $CaCl_2$ at pH 10.5 (glycine-NaOH buffer) at 37^0C for 30-40 min. Fusion occurs within 10 min.

Polyethylene glycol (PEG) treatment- Theculture medium (1 ml) containing isolated protoplast is mixed with equal volume (1ml) of 28-56% PEG (mol. Wt.- 1500-6000 dalton) in a tube. Tube is shaken and then allowed to settle and settled protoplasts are washed several times with culture medium during which fusion occurs.

c) Electro fusion:

In this method an electric field of low strength (10Kv/m) gives rise to dielectrophoretic dipole generation within the protoplast suspension or a high strength of electric field (100Kv/m) for some micro seconds are applied this lead to fusion.

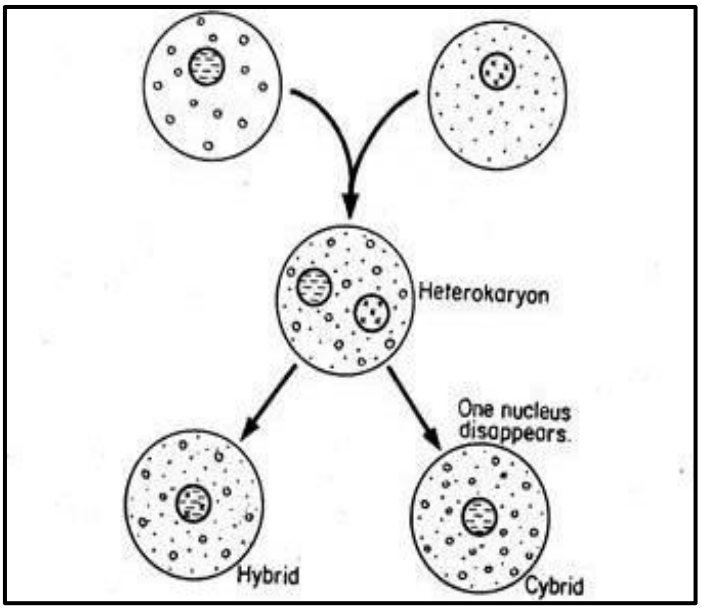

Fig.2: Fusion products (Hybrids and Cybrids) of two different protoplasts

Fusion of cytoplasm of two protoplasts results in union of cytoplasms. The nuclei of two protoplasts may or may not fuse together even after fusion of cytoplasms.

- The binucleatecells are known as heterokaryon.
- When nuclei are fused the cells are known as **hybrid**.
- Only cytoplasms fuse and genetic information from one of the two nuclei is lost is known as cybrid.

The use of protoplast technology extends beyond the regeneration of whole plants and the creation of hybrids between species that are incompatible sexually. The development of fundamental scientific knowledge on cell biology, plant compatibility, membrane functions, cell organelle investigations, and cell wall regeneration, however, has been made possible by these procedures.

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STEM CELL THERAPY: RECENT ADVANCES AND FUTURE STRATEGIES

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INTRODUCTION

The phrase "stem cell" was first used by German scientist and Darwinist Ernst Haeckel to describe the stammzelle, an evolutionary notion for a primordial cell that transforms into all cells and multicellular animals, at the turn of the 20th century. More than 200 different cell types can be found in the adult body, and stem cells are regarded to be the progenitor of these cells. All stem cells are undifferentiated, unspecialized cells that share traits with other members of the same family type (lineage) (Zakrzewski et al., 2019). Throughout their lifespan, they can continue to divide, producing new, highly specialized cells that can replace any lost or dying ones.A stem cell is a young, immature, or unspecialized cell that can divide into other cells of the same kind (self-renewal) and become other, more specialized cells with specific functions (figure 1).

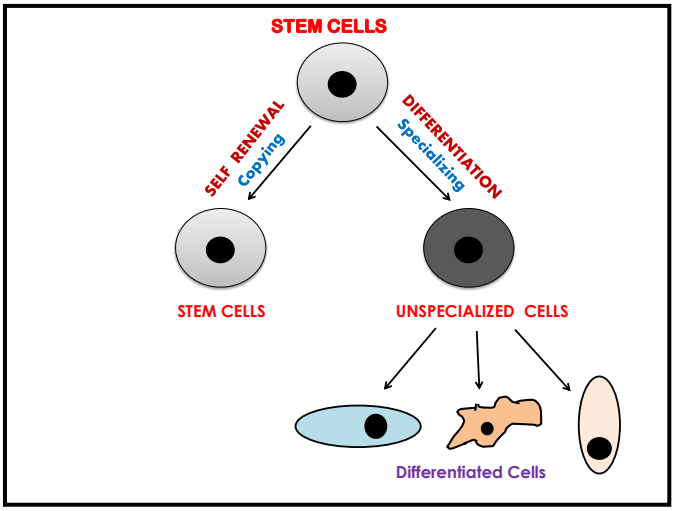

Figure 1: Scheme of stem cell self-renewal and differentiation Stem cells are capable of maintaining the stem cell compartment through self-renewal and can also give rise to progenitor cells that may undergo subsequent differentiation along more than one lineage to generate cell-type-specific derivatives

Historical Background

Though attempts to fertilize mammalian eggs outside of the body were undertaken for the first time in 1878, research on human stem cells didn't begin until the 1960s, thanks to discoveries made by Canadian scientists Ernest A. McCulloch and James E. Till (Charitos et al., 2021). Terato carcinomas in mice were found to develop from embryonic germ cells in the late 1960s, and embryonic carcinoma (EC) cells were recognized as a subtype of stem cells. In 1968, the first human egg was successfully fertilized in a lab, opening the door to the potential use of totipotent stem cells. In the 1970s, models of mouse embryonic development using cultured EC cells were investigated (Ludwig et al., 2006). Scientists discovered mouse embryonic stem cells in the 1980s, which led to the cloning of Dolly the sheep in 1997. Due to the huge demand for

human and medical applications, federal R&D funding was practically stopped in the US in 2001. For the previous discovery of induced pluripotent stem cells (iPS), a Nobel Prize was given in 2012. They essentially make mature non-stem cells function like stem cells once again by restoring their potency and capacity for self-renewal. The initial wave of stem cell start-ups appeared between 2010 and 2019 coupled with R&D initiatives at numerous major pharmaceutical firms, sparking innovation and the first iPS and associated therapy human clinical studies (Moradi et al., 2019).

Cell Potency

Potency describes the stem cells' various potentials. The fusion of an egg and a sperm cell results in totipotent stem cells. The fertilized egg's initial cell divisions also result in totipotent cells (Zhang et al., 2006). These cells are capable of differentiating into both extraembryonic and embryonic cell types. Only morula cells are totipotent, implying they can develop into any type of tissue, including a placenta (Boroviak et al., 2014). The progeny of totipotent cells, pluripotent stem cells can develop into cells from all three germ layers. A blastocyst's inner cell mass, or blastula, is where pluripotent stem cells are first formed. A blastocyst is a hollow, thin-walled sphere formed of an inner mass of pluripotent stem cells, a chamber filled with fluid, and an exterior layer of cells. (Figure 2). After cleavage but before implantation, the blastocyst develops in around 5 days. Except for the placenta, these stem cells can develop into any kind of tissue in the body. Only cells derived from a closely related family of cells can be produced by multipotent stem cells; for instance, hematopoieticstem cells can differentiate into red blood cells, white blood cells, platelets, etcZakrzewski et al., 2019.). Unipotent stem cells are capable of producing only one type of cell, however, they can regenerate on their own, distinguishing them in contrast to non-stem cells.

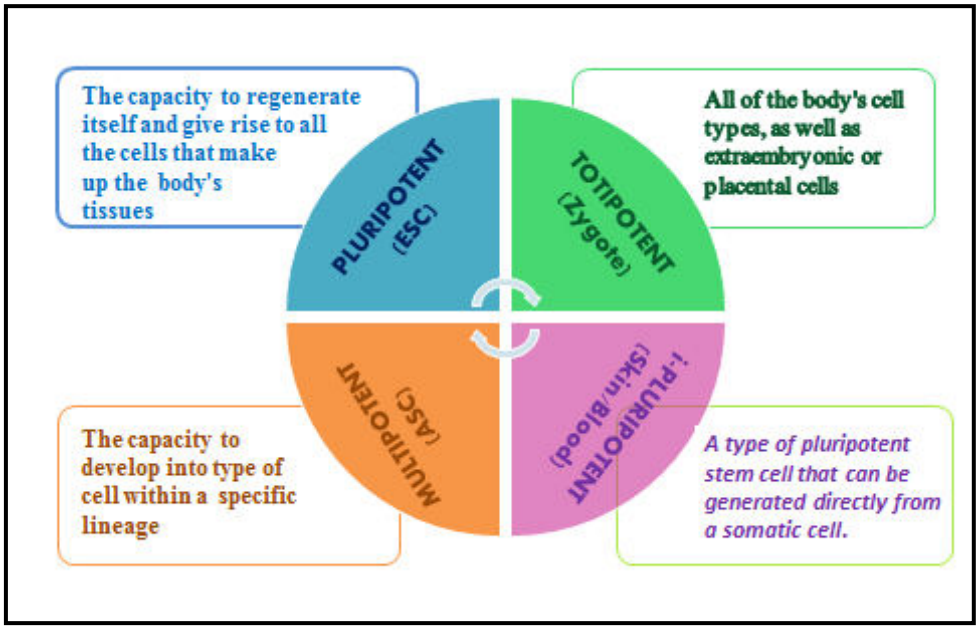

Figure 2: Types of Cell Potency. ESC (Embryonic Stem cells), ASC (Adult Stem cells).

Types of stem cells

Stem cells can originate from many locations inside the body or can arise at various points throughout our lifetimes.

These consist of

Embryonic stem cells (ESC)

Embryonic stem cells are produced from embryos that are still developing before their fate would ordinarily implant in the uterus. These pluripotent cells can be separated from the blastocyst stage of development, which has 32 cells. Different proteins that control ES cells' pluripotency have been described (Takahashi et al., 2006). Among them is an important marker for ES cells and the pluripotent cells of the complete embryo is the Oct. 4 protein. For ES cells to continue to be undifferentiated, their expression needs to be kept at a critical threshold. Nanong protein is necessary for keeping mouse and human cells in their undifferentiated form (Ellerström et al., 2009). Additionally, recent research links the Wnt-b-catenin signaling to the preservation of pluripotency (Rodolfo et al., 2018).

Adult stem cells (ASC)

Adult Stem cells also known as somatic stem cells are cells that grow into various body tissues throughout fetal development and remain there throughout life. Discovering the fundamental molecular mechanisms that govern the self-renewal and differentiation of adult stem cells has been the focus of recent studies. Bmi-1: The polycomb-groupprotein, a transcriptional repressor, was identified as a common oncogene activated in lymphoma and later demonstrated to specifically regulate hematopoietic stem cells. Notch: For many years, developmental scientists have been aware of the Notch pathway. Its function is in regulating the proliferation of several stem cell types, such as hematopoietic, neuronal, and mammary stem cells (Laino G et al., 2005). These developmental pathways, Sonic Hedgehog and Wnt have also been closely linked to the regulation of stem cells. Transdifferentiation (Plasticity) is the term for a change in stem cell differentiation from one cell type to another, and developmental stem cell differentiation refers to the variety of stem cell differentiation options (Prentice DA., 2019).

Induced pluripotent stem cells (iPSC)

Induced pluripotent stem cells (iPSCs) are a subclass of pluripotent stem cells that are derived from adult somatic cells that have undergone genetic reprogramming to resemble embryonic stem cells (ESCs) by being forced to express specific genes and factors that are crucial for maintaining the ES cells' distinctive characteristics. The induction effectiveness of iPS cells has recently been reported to be enhanced by a variety of growth agents and pharmacological substances. Shi et al.'s research (2018) showed that Sox2-compensating small compounds could successfully transform mouse embryonic fibroblasts (MEF) into iPS cells. They converted MEF into iPS cells by combining Oct4/Klf4 transduction with BIX-01294 and BayK8644s. According to Huangfu et al., [2008], the DNA methyltransferase inhibitor 5-azacytidine and the histone deacetylase inhibitor valproic acid significantly enhanced the reprogramming of MEF (Huangfu et al., 2008).

Stem Cell Therapy

Stem cell therapy has developed into a highly promising and sophisticated scientific study area in recent years. Great expectations have been raised by the emergence of therapy options. Controlled stem cell culture and derivation in the lab come after the formation of stem cells. Assays for teratoma formation and quality control are crucial steps in determining the characteristics of the stem cells under test. To create the ideal environment for regulated

differentiation, extraction techniques and the use of culture medium are essential. Studies on the use of stem cell therapies (Larijani et al., 2012) for Crohn's disease, Multiple Sclerosis, Lupus, COPD, Parkinson's, ALS, stroke recovery, and more have been undertaken. Stem cell therapies have also been utilized to treat autoimmune, inflammatory, neurological, orthopedic, and traumatic disorders (Li et al., 2018)

The idea behind novel stem cell therapies is to enable the body to repair itself sufficiently to temporarily lessen the symptoms of various illnesses, even though they may not always cure them. This impact frequently significantly improves patients' quality of life while also delaying the onset of the disease.

Stem cell therapy defined

A type of regenerative medicine called stem cell IV therapy works to restore damaged cells in the body by lowering inflammation and controlling the immune system. Numerous medical conditions, including autoimmune, inflammatory, and neurological disorders, can be treated with it (Christodoulou et al., 2018). There are various stem cell therapies available, such as amniotic fluid stem cell therapy and umbilical cord stem cell therapy. Hematopoietic stem cell transplantation is the most popular FDA-approved stem cell-based therapy and is used to treat blood malignancies like leukemia. In addition, stem cells can be used as a regenerative therapy for corneal injury and severe burns to the skin.

Turning point in stem cell therapy

The discovery that multipotent adult stem cells might be reprogrammed to become pluripotent by scientists Shinya Yamanaka and Kazutoshi Takahashi marked a turning point in the field of stem cell treatment. By using this method, the life of the fetus was not in danger. Four transcription factors that are primarily expressed in embryonic stem cells—Oct-3/4, Sox2, KLF4, and c-Myc—could be retrovirus-mediated transduced into mouse fibroblasts to cause them to become pluripotent iPSCs is the name given to this novel stem cell type (Cantore et a;., 2018). The experiment with human cells was successful a year later as well. Following this success, the technique created a new area of stem cell research by producing iPSC lines that can be tailored to the patient's needs and are biocompatible with them.

Recent Advances in Stem cell therapy

The importance of stem cells in medicine has the potential to grow significantly. They not only contribute significantly to the advancement of restorative medicine, but their research also sheds light on the intricate processes involved in human development. The DNA of the cells reveals the distinction between stem cells and developed cells. The old cell has loosely organized DNA and functional genes. Genes that are no longer required are shut down as signals reach the cell and the differentiation process starts, while genes necessary for the specialized function will stay active. It is recognized that gene sequence interaction can produce such pluripotency and that this process can be reversed. Octamer-binding transcription factors 3 and 4 (Oct3/4), sex-determining region Y (SRY)-box 2, and Nanog genes were found to operate as core transcription factors in sustaining pluripotency by Takahashi and Yamanaka [2006]. Oct3/4 and Sox2 are two of them that are necessary for the production of iPSCs.

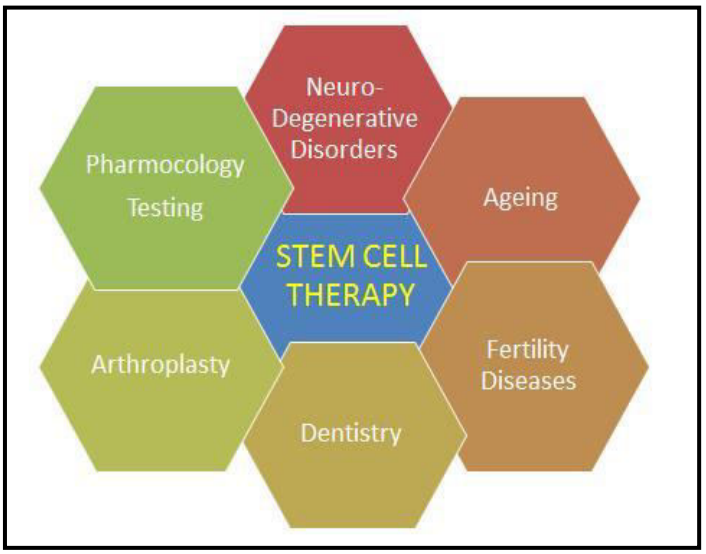

Figure 3: Recent Advances in diseases using Stem cell therapy

Stem cells in Ageing

The slowing of aging can be greatly aided by stem cells. Combining stem cells and anti-aging genes can build a strong barrier that can ward off the consequences of aging. Increased cellular damage, accelerated aging, and increased wear and tear of the body's natural stem cells. Age-related stem cell dysfunction results from altered cell-intrinsic pathways and external environmental factors. Effective regenerative medicine techniques for the elderly are more necessary than ever due to the dramatic increase in disorders related toaging (Ahmed et al., 2018). Fortunately, rapid advancements in stem cell and regenerative medicine technologies continue to give us a better understanding of illnesses, enabling us to create more efficient treatments and diagnostic tools to better treat aged persons.

Stem cells in pharmacological testing

New drug tests can make use of stem cells. Specific differentiated pluripotent cells can be used safely in every experiment on living tissue (Polini et al., 2019). Drug formulations can be altered if any unfavorable effects manifest until they are sufficiently effective. Without endangering any live testers, the medication can be sold on the pharmaceutical market. When comparing the effects of two medications, the conditions must be the same to test the drugs adequately. To produce pure populations of differentiated cells, researchers must fully regulate the differentiation process.

Stem cells in Arthroplasty

Autologous stem cells, sometimes referred to as adult stem cells, have the potential to strengthen or rebuild articular cartilage in arthritic joints by naturally reducing inflammation. This is particularly true for tendon injuries, which frequently result in unsuccessful outcomes because present treatment options tend to focus either on conservative or surgical treatment. The ability of the tendons to regenerate is where problems begin. After an injury, tendons don't functionally regenerate; instead, they merely recover by creating scar tissues that don't function as healthy tissues do. Hyper vascularization, calcific material deposition, discomfort, or edema are some of the factors that can contribute to an ineffective healing response. In addition to tendon issues, a degenerative condition of the joints termed osteoarthritis (OA) is also quite

likely to develop (Hernigou et al., 2021) due to the avascular nature of articular cartilage and its limited capacity for regeneration. Even though arthroplasty is currently a common treatment for OA, it is not recommended for younger patients because they may outlive the implant and require additional surgeries down the road. However, these techniques need more development, and long-term hyaline cartilage maintenance research is needed.

Stem cells in fertility diseases

Stem-cell treatment has given the field of managing reproductive disabilities new hope in recent years. Under appropriate conditions, stem cells, which are undifferentiated, self-renewing cells, can become specialized cells. They are present in an embryo, a fetus, and an adult human, and they can divide to form different types of cells. Even if there are still numerous problems with stem cells, there are undoubtedly new techniques to treat infertility. There are numerous clinical applications for ovarian-derived stem cells (OVSC). The use of stem cells in medicine should adhere to ethical standards, such as informed consent and other ethical guidelines for clinical research. Furthermore, it is still unknown if gametes made from pluripotent stem cells can produce healthy offspring. Currently, gametes derived from stem cells can be used as an in vitro model to assess the effects of medications (Wang et al., 2019). Overall, the study of stem cells has produced significant advances in the management of infertility.

Stem cells in incurable neurodegenerative diseases

Incurable neurodegenerative disorders including Parkinson's disease, Alzheimer's disease (AD), and Huntington's disease can now be treated with stem cell therapy, but more significantly, the root of the problem can be addressed. In the field of neuroscience, the theory that adult central nervous systems are incapable of neurogenesis has been disproved by the identification of neural stem cells (NSCs). Preclinical AD rodent models' cognitive performance can be improved by neural stem cells (Sivandzade et al., 2021) Parkinson's disease (PD) causes localized neuronal degeneration, and hESCs can effectively produce dopaminergic neurons. PD is the perfect condition for iPSC-based cell therapy is still under trial.

Stem cells in Dentistry

Dental stem cells (DSCs), a significant source of mesenchymal stem cells (MSCs), are readily accessible through minimally invasive procedures and have been used to treat several disorders. Modern understanding of the indirect paracrine effect has shed new light on the riddle of their actual low engraftment and differentiation capabilities in vivo. The classic paradigm attributed the mechanism of their therapeutic action to direct cell differentiation following focused migration. DSC-EVs (Extracellular Vesicles) presented exceptional therapeutic potential in several disorders by carrying and transferring particular bioactive contents (such as functional RNAs and proteins) to target cells. However, several significant obstacles limit the potential applications of DSC-EVs. It is necessary to keep working to hasten the clinical translation of DSC-EVs.

Other Aliments

In stem cell transplants, stem cells either replace diseased or chemo-damaged cells or work with the immune system of the donor to combat certain cancers and blood-related illnesses such as leukemia, lymphoma, neuroblastoma, and multiple myeloma. Adult stem cells or umbilical cord blood are used in these transplants.

Challenges concerning stem cell therapy

Innovative scientific and medical developments must constantly be closely regulated to ensure that they are morally and physically secure. Stem cell therapy shouldn't be handled any differently because it already has a significant impact on many facets of life. There are currently several difficulties with stem cells. The first and most crucial one focuses on thoroughly comprehending how stem cells work in animal models first. However, using human embryos raises ethical concerns, and ESC transplants into mouse models can cause cancerous tumors. How to decrease contamination and lower the danger of cancer are further challenges facing research on the use of ESC. There have been reports of human ESC lines produced from a single blastomere (Klimanskaya et al., 2006). This approach could address the ethical challenges and enable the production of matching tissues for children and siblings born from transferred preimplantation genetic diagnostic embryos. It could also develop new stem cell lines and medicines without harming embryos.

The immune system of the recipient rejects the cells adopted in research, which is another ongoing problem. By introducing four factors—Oct3/4, Sox2, c-Myc, and Klf4—to mouse embryonic and adult fibroblast cells, Yamanaka et al. reported the production of iPS (Takahashi and Yamanaka, 2006). Some of the issues with ESC, such as immune rejection issues and ethical concerns, may be resolved by directly inducing pluripotent cells from the patient's cells to produce tissue or cells. But there is still no answer to the low frequency of iPS cell derivation. The infamous function that iPSCs play in tumorigenicity is one of the defenses against their utilization. When cells are reprogrammed, there is a chance that the expression of oncogenes will increase. The tumor suppressor gene p53 may aid reprogramming, but it also functions as a major cancer regulator, making it impossible to remove to prevent further mutations in the reprogrammed cell. The identification of stem cells in adult organs remains a significant challenge for scientists.

Future Strategies of stem cell research

Despite these formidable obstacles, the field of stem cell research is constantly making great strides. There are now many diseases and ailments that can be treated using stem cell treatment. Their effect on future medical technology seems to be significant.

Implementing a self-destruct feature if stem cells become harmful is one of the concepts that could make them a "failsafe" substance. The adaptability and further development of stem cells may result in lower treatment costs for patients with diseases that are currently incurable. The patient would be able to use stem cell therapy instead of extremely expensive medication treatment when suffering certain organ failure. A successful procedure would have an immediate impact and spare the patient from long-term pharmaceutical therapy and its unavoidable negative effects.

- Bone regeneration: Mesenchymal stem cells from both humans and animals can be grown and pumped, and they have been demonstrated to rebuild functional tissue when administered to the site of musculoskeletal abnormalities in test animals. In a clinically significant osseous defect, mesenchymal stem cells can regenerate bone, which makes them a potential replacement for autogenous bone grafts.

- Low blood supply: A technique has been discovered to manufacture a lot of red blood cells. With the help of stromal cells, precursors of red blood cells, or hematopoietic stem cells, are cultivated in a manner that closely resembles the conditions found in bone marrow, where red blood cell development occurs naturally. A growth agent called erythropoietin is administered to encourage the stem cells to finish final differentiation into red blood cells.
- Baldness: Hair follicles also contain stem cells, and some researchers anticipate conducting a study on these follicles. As early as 2019, "hair cloning" (also known as "hair multi-placation"), a technique that uses stem cells, may be successful in treating baldness. This procedure is anticipated to operate by harvesting stem cells from mature follicles, growing them in vitro, and then implanting them into newly formed follicle cells that have shrunk due to aging. The newly formed follicle cells then react to these signals by repairing and producing healthy air once more
- Diabetes Type I: In persons with type I diabetes, the patient's immune system kills the pancreatic cells that typically create insulin. According to recent studies, human embryonic stem cells may be able to be differentiated in cell culture in a way that results in the production of insulin-producing cells that could one day be employed in transplantation therapy for diabetics.
- Deafness: Stem cell therapy is being used to regrow cochlear hair cells.
- Blindness and vision enhancement: Since 2003, retinal stem cells have been successfully implanted into injured eyes to restore eyesight. Scientists can now generate a sheet of the most potent stem cells in the lab using embryonic stem cells. The stem cells induce neuronal healing when these sheets are implanted over the injured retina, eventually restoring eyesight.
- Missing teeth: The development of new teeth has advanced to the point where they will be accessible to the general public. In the lab, patient stem cells might be stimulated to develop into a tooth bud that, when implanted in the gums, would give rise to a new tooth, the growth of which is anticipated to take two months. When it fuses with the jawbones, it will release chemicals that will encourage blood vessels and nerves to grow close to it.

CONCLUSION

Stem cell therapy is becoming a major game changer for medicine after decades of research. The potential of stem cells is expanding with every experiment, but there are still numerous challenges to be solved. Regardless, stem cells have a significant impact on transplantology and regenerative medicine. With stem cell therapy, neurodegenerative diseases that are currently incurable may one day be cured. Further studies and trials are needed to improve conditioning regimens and supportive care modalities due to the high pre and post-transplant morbidity and mortality. The use of a patient's cells is made possible through induced pluripotency. We are now better able to extend human life than ever before thanks to stem cell therapy and all its restorative effects.

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STUDY OF EFFECT OF LEAD ACETATE ON DROSOPHILA MELANOGASTER

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INTRODUCTION

Lead being the heavy metal of the carbon family is most concerned because of its nature to show toxic effects when once present at specific concentrations. Lead is found in various forms like lead nitrate, lead chloride, lead phosphate, and lead acetate. Lead is already in the list of hazardous material. There have been many studies carried out earlier on various organisms. Evidence suggests that developmental lead acetate exposure causes embryonic toxicity and memory deficits in adult Zebrafish [1]. It induced malformations such as single swim bladder inflation, change in spine curvature, and yolk sac oedema. Lead has been found to negatively affect the embryo implantation and defective organ development in swiss albino mice [2]. Lead has been shown to induce micro-nuclei formation in chick embryo [3]. All these studies indicate the toxic nature of lead in various forms/ salts.

In the present study we have assessed effects of lead acetate using Drosophila melanogaster as model system. Drosophila has been used as model system in various conventional fields such as genetics, developmental biology, Neurology etc. Apart from this, Drosophila has been proved to be a promising translational model system in the field of toxicology, physiology, behaviour etc. short life cycle, availability of various mutants, homology between metabolic pathways of vertebrates and Drosophila makes it a very good model system for Toxicological studies. In the present study toxic effects of Lead acetate with respect to the development, life history traits were assessed.

MATERIALS AND METHODS

Drosophila wild type strain Oregon- K (ORK) was reared and maintained on standard corn meal agar food medium in BOD.

Study of biocompatibility of lead acetate on Drosophila melanogaster and find out mortality rate or survival rate

Treated culture medium with various concentrations of lead acetate was made and eggs were transferred to it. After every 24 hours number of larvae dead or alive was counted to understand the mortality rate in response to increasing concentrations of lead acetate.

Study of larval behavioural response towards lead acetate

Ability of lead acetate to act as attractant or repellent was studied by transferring 3rd instar larvae to a clean petri-plate containing paper disc soaked in lead acetate solution. Time spent by larvae near to the paper disc or away from paper discs was recorded.

Effect on Life cycle

The study also confirmed some changes in the duration of life cycle of Drosophila melanogaster when exposed to different chemical concentration of lead acetate. It was found that the total period of life cycle was prolonged on exposure to different concentration as compared to the control flies

The changes were prominently observed in the larval period and also in the pupal period. The following graphs depict the changes observed in the various concentrations.

Effect on phenotype

The phenotypes of adults grown in various concentrations were examined microscopically and photo- documented to determine morphological changes if any. Phenotype of F1, F2 generations were also recorded.

RESULT

Keeping in the view that lead is environmental pollutant and exists in various compound it was the need of the hour to study the effects of lead compounds hence the lead acetate chemical was selected and the effects of lead acetate was studied. The present study has confirmed the following results.

Larval response to the chemical lead acetate

Lead acetate was found to be an attractant for Drosophila larvae. The chemical lead acetate also showed toxic effects on the survival of the flies, there was altered mortality rates on considering different stages of life cycle, also the mortalities were found to be more when the concentration of the chemical was subsequently increased.

The study also confirmed some changes in the duration of life cycle of Drosophila melanogaster when exposed to different chemical concentration of lead acetate. It was found that the total period of life cycle was prolonged on exposure to different concentration as compared to the control flies**.** The changes were prominently observed in the larval period and also in the pupal period.

Effect on phenotype

The phenotypes of adults of various concentrations were examined and it was found that the concentration of 50 ppm had shown malformations in wings of adults of F_2 and F_3 generations skipping the F_1 generation. Further the affected wing of these generations showed the inability to fold the wings on the back which would lead to their minimal flight or difficulties in taking flight in the concentration bottles.

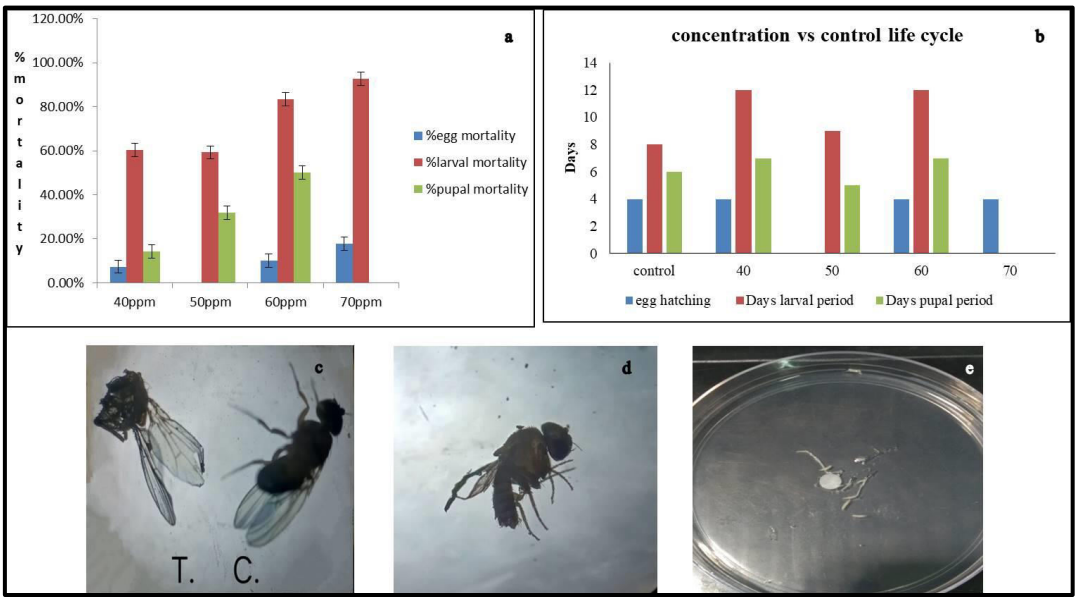

Figure 1: a, Lead acetate mediated Mortality of Drosophila larvae; **b,** effect of lead acetate on life cycle; **c-d,** lead acetate mediated defect in Drosophila wings; **e,** larval behaviour towards lead acetate.

DISCUSSION

Lead ion exists in various compounds notably lead sulphate, lead nitrate, lead acetate etc. and is also known to show adverse effects when exposed to the organism in varied concentrations. Studying the toxicity of the lead in its varies compound forms becomes all the more important because in the current status lead ion is considered as potent environmental pollutant. The concerned compound of lead in the present study is lead acetate.

The findings of the present study revealed that the chemical lead acetate has potential to cause toxic effects on Drosophila melanogaster. There was delay in the life cycle at 40, 50, 60 ppm concentration of lead acetate as seen in the fig 3 , 4, 5 ,6, similar delay results in the larval and pupal periods were suggested by Safaee et al 2014 [4]. In their study of effect of lead ion on D.melanogasterindicating lead ion interferences with enzymes in the mitochondrial functions leading to less production of energy required in the transition process also the interference of lead ion in the growth hormones.

The study also concluded that the death rates increased as the concentration of lead acetate was increased, similarly experiments conducted by Joanna Burger 2010 on the hatchling slider turtles had suggested that lead ion when given in the increasing concentrations from 0 to 2.5mg/g showed increasing in the mortality

The chemical lead acetate has also shown effect on the morphology of wings of adults flies, as their wings had difficulty in folding [5]. (Rizwanual Haq et al 2011)

The study revealed one peculiar result that the first filial generations obtained by transferring of 3rdinstar larvae in the concentration of 50ppm lead acetate appeared to be normal without any morphological changes in the adults but self-cross obtained progeny and further examining for 2 generations it was seen that the adults obtained from F_2 and F_3 generations had altered in the morphology of their wings i.e. the wings of the adults obtained were unable to fold on their back

and were resting at 45 to 80 degrees with respect to the back also there was a fly which had one wing twisted by many folds.

CONCLUSION

Considering the aspects studied in the present study it is very clear that the chemical lead acetate can cause its toxic effects on various parameters, be it the effect on life cycle i.e. increase in the length of life cycle, its effect on morphology of the adult flies examining even after two generations, its effect on polytene chromosomes i.e. altering various segments in the chromosomes, and also its effect on survival of the egg, larvae, pupa and adults of the flies is detrimental. Thus by looking carefully in the observations it can be concluded that the chemical lead acetate has great potential to cause toxic effects in the organism Drosophila melanogaster.

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TREATING PCOS: DIET, NUTRITION, MEDICATION AND LIFESTYLE CHANGES

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INTRODUCTION

While we become knowledgeable about polycystic ovary syndrome, we may be inclined to search for a medication that can easily cure it. However, this is not the case. After determining the extent to which lifestyle and dietary adjustments can manage the condition, medications may aid in achieving weight loss, reducing the risk of diabetes, controlling symptoms, and enhancing fertility for those who seek it. Nevertheless, medicines are not a complete solution. Similar to managing other chronic health problems, a natural approach is often beneficial. Medications cannot substitute for an unhealthy diet or lack of physical activity and may have side effects and be costly (Bhalerao and Aranha, 2021, 2023).

Women with PCOS often struggle to receive a proper diagnosis and treatment for their various symptoms. They may have received fragmented care, including birth control pills for irregular periods, electrolysis for facial hair, and therapy for depression. While some of these treatments may have helped, others may have been temporary fixes or dead ends. Accompanying diet and lifestyle changes could have improved the effectiveness of some treatments. Despite feeling overwhelmed by the prospect of making lifestyle changes, it is important to understand that PCOS is treatable, and women can gain control over their health through manageable lifestyle adjustments.

CAUSES OF PCOS

PCOS is a hormonal disorder that affects women of reproductive age. The exact cause of PCOS is not known, but several factors may contribute to its development.

Insulin Resistance

Insulin is a hormone that helps regulate blood sugar levels. Insulin resistance is a condition in which cells become resistant to the effects of insulin, leading to high blood sugar levels. Insulin resistance can cause the ovaries to produce more androgens (male hormones) than normal, which can lead to PCOS.

Hormonal Imbalances

PCOS is often associated with hormonal imbalances, particularly an excess of androgens such as testosterone. The exact cause of hormonal imbalances is not clear, but it is thought that genetics and environmental factors may play a role.

Genetics

PCOS tends to run in families, suggesting that there may be a genetic component to the disorder. Several genes have been associated with PCOS, but more research is needed to understand how these genes contribute to the development of the condition.

Inflammation

Chronic inflammation may contribute to the development of PCOS. Inflammation can cause insulin resistance and hormonal imbalances, both of which are associated with PCOS.

Lifestyle Factors

Obesity and a sedentary lifestyle have been linked to PCOS. Excess weight can cause insulin resistance and hormonal imbalances, while physical inactivity can lead to weight gain and exacerbate other PCOS symptoms.

Overall, the causes of PCOS are complex and multifactorial as shown in Figure 1. While some risk factors are out of a person's control, such as genetics, others, like lifestyle factors, can be modified to reduce the risk of developing PCOS or manage symptoms. It is important for women to talk to their healthcare provider if they suspect they may have PCOS or if they have concerns about their reproductive health.

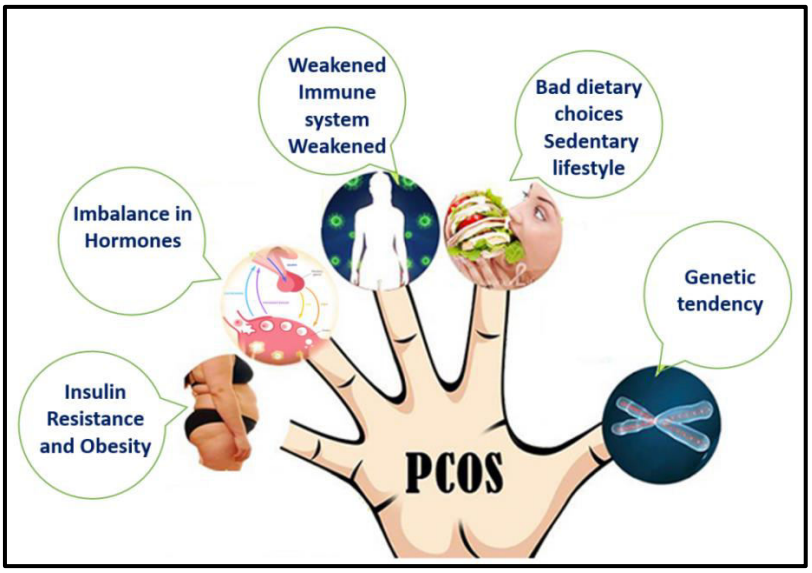

Figure 1. Major causes of polycystic ovary syndrome (PCOS)

Making a Difference with Diet and Lifestyle

Lifestyle modification is widely considered to be the cornerstone of PCOS treatment (Aly and Decherney, 2021).There is ongoing research to determine the best diet and lifestyle strategies for women with PCOS, but large-scale studies are still needed to provide definitive answers. However, research and clinical experience suggest that weight loss, improved cholesterol levels, blood pressure control, exercise, and specific dietary changes can help manage symptoms and improve metabolic health in women with PCOS. Even a 5% weight loss can make a significant difference. Scientific research has mainly focused on carbohydrates and protein as dietary factors that may benefit women with PCOS. The studies discussed to explore the relationship between nutrition and PCOS. High insulin levels, which can lead to obesity, exacerbate PCOS symptoms. Studies suggest that including a higher proportion of protein in the diet and limiting simple sugars can help with weight loss, reducing body fat, and improving cholesterol levels. While the studies are limited by their small sample sizes and the use of supplements rather than whole foods, the findings suggest that reducing overall carbohydrate intake and increasing protein may be beneficial for women with PCOS.

Research suggests that a reduced-calorie diet with low glycemic load (GL) carbohydrates and higher protein can lead to weight loss and improvements in insulin sensitivity and inflammatory markers in women with PCOS (Patel, 2018). However, many women with PCOS are not paying

enough attention to the overall quality of their diet and tend to consume a higher GI diet, aggravating PCOS symptoms and promoting weight gain. Overweight women with PCOS tend to have lower-quality diets and report a greater tendency to overeat when exposed to highly palatable food and when feeling stressed. Weight loss is the cornerstone of treatment for any woman with PCOS who is overweight, and low GI/GL diets can be helpful. The best approach is the one that will consistently help you eat less in a sustainable way, with a focus on whole foods and protein.

Weight Loss and Fertility

PCOS is a common hormonal disorder that affects many women of reproductive age. One of the major symptoms is problems with fertility, and seeking treatment for infertility often leads to a diagnosis. Research has analyzed the connections between diet, exercise, weight loss, and fertility. Studies have found that even modest weight loss can improve the health and fertility of women with PCOS. Lifestyle interventions that include calorie restriction, weight loss meds, and physical activity can lead to weight loss, improved ovulation rates, and live birth rates. Overweight women with PCOS have a higher risk of prenatal complications, such as a longer time to pregnancy, more preterm births, and higher birth weight. While there is no optimal dietary treatment for PCOS, managing its symptoms through diet, nutrition, medication, and lifestyle changes can be effective.

Diet and Nutrition

Managing PCOS involves maintaining a healthy weight through a balanced diet. Women with PCOS should consume a diet that is high in fiber, protein, and healthy fats while avoiding processed and sugary foods. It is beneficial for women with PCOS to follow a low glycemic index (GI) diet, which focuses on carbohydrates that do not cause a spike in blood sugar (Frias-Toral et al., 2021). To reduce inflammation and improve insulin resistance, which is a key feature of PCOS, women should consume foods that are high in antioxidants such as berries, spinach, and kale. Taking supplements like magnesium, zinc, and vitamin D may also help to regulate hormone levels and improve symptoms.

PCOS is closely linked to diet since most patients with PCOS are overweight or obese, have abdominal obesity, and experience insulin resistance. To design a diet plan for PCOS, the following general points should be kept in mind:

Reduce simple carbohydrates and consume low GI carbohydrates, which can improve menstrual cycle regularity, ovulation, and hunger stimulation. Increase fiber intake, especially from whole grains, green leafy vegetables, beans, peas, and sprouts. Consume low-fat dairy products, such as milk, cottage cheese, and curd. If lactose intolerant, curd and soya milk can be included in the diet. Distribute calorie intake among several meals per day with low intake from snacks and drinks. Drink plenty of liquids with less sugar, salt, and no caffeine. Include lemon water, buttermilk, tender coconut water, green tea, soup, etc. Consume foods low in fat, especially saturated fats. Increase the use of foods rich in antioxidants, such as tomatoes, berries, citrus fruits, green leafy vegetables, green tea, etc., to reduce oxidative stress. Reduce salt intake and avoid caffeine, especially in fizzy drinks. Avoid pre-prepared packaged foods and spreads, such as cheese spread, ketchup, mayonnaise, and flavoured sauces. Moderate physical activity of about 30-40 minutes/per day should be the goal. Diet and exercise should be customized

according to individual needs and preferences. Even a small weight loss can have better hormonal results, especially the resumption of menses.

Medications

There are various medications available to manage PCOS symptoms. Birth control pills can regulate menstrual cycles and minimize acne and excess hair growth. Metformin, typically used for type 2 diabetes, can enhance insulin sensitivity and regulate menstrual cycles. Clomiphene citrate is a medication that can stimulate ovulation and improve fertility in women with PCOS (Bhalerao and Aranha, 2023).

Lifestyle Changes

Lifestyle modification is the key fertility fitness programme suggested by researchers (Norman et al., 2002). Maintaining a regular exercise routine is crucial for managing PCOS. Exercise aids in weight management reduce insulin resistance and enhance overall well-being. A combination of aerobic and strength training exercises is recommended, with at least 150 minutes of moderate-intensity exercise each week.

Managing stress is equally important since it can exacerbate PCOS symptoms. Activities like yoga, meditation, and deep breathing can help to lower stress levels. While PCOS cannot be cured, managing its symptoms through dietary adjustments, medication, and lifestyle changes can greatly enhance the quality of life for women with this condition. It is recommended that those with PCOS collaborate with a healthcare provider to create a personalized treatment plan.

CONCLUSIONS

The most common cause of menstrual irregularities and hyperandrogenism is polycystic ovary syndrome (PCOS). It is the most common cause of female infertility. Several risk factors for PCOS have been studied, including glucose intolerance, obesity, and dyslipidemia. Many treatments are currently available, but they are associated with moderate to serious side effects. Several herbs can be used individually or in combination to relieve risk factors associated with PCOS. It is observed that a few herbs given in combination produce a synergistic effect. The pharmacological action is seen more in combination than as a single entity. Several market preparations use a combination of several herbs and, each herb potentiates the pharmacological action of the other. Lifestyle changes are the most recommended treatment for PCOS. Eating a PCOS-friendly diet and making some lifestyle changes may help to reduce some of the associated symptoms of PCOS. Weight loss through a low-calorie diet combined with moderate exercise activities should be the daily regime. Losing weight may increase the effectiveness of medications and it can help with infertility.

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THE ROLL OF WAREHOUSE IN SUPPLY CHAIN MANAGEMENT AND OPERATION RESEARCH

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INTRODUCTION

A warehouse is a building for storing goods. Warehouses are used by manufacturers, importers, exporters, wholesalers, transport businesses, customs, etc. They are usually large plain buildings in industrial parks on the outskirts of cities, towns, or villages. The warehouse's original function was purely for storage. One of the key part of any supply chain are Warehouses. They play a key role: tamping the material flows in the supply chain to accommodate the variability of variables, including seasonality and/or batching, in manufacturing and transport. They are consolidating goods from different suppliers for joint distribution to the consumers and while modern warehouses serve many more purposes, storing goods remains a primary function. This is where organizations can store their goods, equipment, inventory, and other items.

In this competition market requires continuous improvement of production-distribution network design and operation, requiring increased warehouse performance [2]. New management approaches, including tight inventory control, shorter response time and a more comprehensive range of products, are also being introduced in warehouse production systems, for example, Just-in-Time (JIT) or Lean production. Instead, the widespread application of modern IT (Bar Coding and Warehouse Management Systems (WMS) offers new warehouse operation opportunities. The supply and distribution networks can also be so complex that goods must be consolidated at stock holding points so that Multiproduct Orders for consumers, i.e., in break-bulk or make-bulk consolidation centres, may be supplied together. The operations of these warehouses are essential for high levels of service to customers [8]. Many warehouses provide inventory customers with a single or next day lead time, and they need to do this confidently at a high pace, precision and lack of damage tolerances [6].

This paper aims to classify and summarise the previous research findings and the identification of potential research opportunities. The desired result guides the analyst's methodologies and tools to facilitate effective operational planning in the warehouse and a roadmap for academic researchers for future research opportunities [7].

OBJECT

The objective of effective warehouse design is to ensure each function is optimized and that material handling, which is the movement of goods between each function, is as efficient and has as few touch points as possible. Receiving raw materials inventory and storing it appropriately. Ensuring temperature-controlled products are maintained. Picking, packing, and shipping products efficiently. Monitoring warehouse operations to address errors and inconsistencies. Warehouse design is the process of defining the optimal warehouse size, layout and technology for a facility or operation. It looks at the processes to determine the requirements of a new facility (i.e. footprint, clear height, floor strength, power, yard size etc.) based on the preferred handling technology. Warehouse design must include the organization

and distribution of space into different operational zones and storage rack areas. Generally, a central warehouse must consist of six sections: reception, quality control, adaptation of unit loads, storage, order preparation and dispatches. One of the most important first steps in designing a warehouse layout is to determine space and other requirements for warehouse automation solutions and other equipment.

Receiving and shipping

Goods are brought into a factory and unloaded at the receiving docks. They are subsequently loaded into a carrier, leaving it through the shipping docks. The goods obtained are sent directly to the shipping docks for docking warehouses. For conventional inventory warehouses, goods obtained are stored and then selected and delivered through shipping docks. In this case, the reception and delivery operations are more complex to administer as they are linked to the storage and picking function [4]. For example, shipping trucks can be planned depending on how orders are loaded and allocated to wave collection and the opposite.

The fundamental decisions for shipping can be defined as -

Given:

(1) Input information such as time of arrival and contents of incoming shipments.

(2) Customer request information, such as orders and their estimated delivery time.

(3) Configuration of the warehouse dock and available tools for material handling.

Determine:

(1) the assignment to the docks of incoming and outgoing carriers determining the aggregate internal flows.

(2) Timetable of the carriers' operation at each port. Assumption of the assignment of a group of carriers to a shipyard is analogous to a planning issue for the machine, where the incoming companies are planning the work.

(3) Distribution and dispatch of services of material handling, such as labour and equipment for material handling.

Subject to performance criteria and constraints such as:

(1) Resources needed to complete all operations of shipping and receiving.

(2) Service levels, including overall cycle time and carriers load/unload time.

(3) Layout or arrangement of docks and warehouse facilities for the relative location.

(4) Policies of management, e.g., one shipping customer by dock.

(5) All docks' performance criteria.

Storage

The warehousing role is important. Three essential decisions form the storage role, i.e., how much inventory the SKU should be stored at the warehouse, how often and when the SKU stock should be filled up and where the SKU should be stored in the warehouse, distributed and transferred between various warehouse areas. The first two questions refer to the issue of lot

size and staggering which are in the conventional field of inventory management, respectively and are not addressed further here. For comprehensive reviews, readers can consult Gallego et al. (1996), Hariga and Jackson (1996). This section focuses on the issue of the allocation of SKUs in different departments and the planning of stock transfers from one department to another, the allocation of SKUs in different zoning zones and the storage location assignment in each department. The storage efficiency corresponding to holding capacity and access effectiveness corresponding to resources consumed through insert (store) and mining (order pick) processes are two main criteria for making such decisions. The givenTable provides a literature review on different problem areas of dynamic storage.

Table: Dynamic storage location assignment problem

Citation	Problem statement	Method
Christofides and Colloff (1972)	The set of items to be relocated and their destinations are given, and the problem is to route the relocation tour to minimize the total relocation cost.	Two-stage heuristics that is optimal in a restricted case
Muralidharan et al. (1995)	The set of high-demand items to be relocated and their destinations are given, and the problem is to route the relocation tour to minimize the total relocation cost	A nearest-neighbor heuristic and an insertion heuristic
Jaikumar and Solomon (1990)	Determine the items to be relocated and their destinations with the objective to find the minimum number of relocations that results in a throughput satisfying the throughput requirement in the following busy periods	Optimal ranking algorithm
Sadiq et al. (1996)	Determine the relocation schedule in face of the dynamically changing order structure, i.e., relocate items that are more likely to appear in the same order in clusters	Rule of thumb procedure based on cluster techniques
Roll and Rosenblatt (1987)	Using zone storage without splitting, it might happen that none of the zones has sufficient space to accommodate an incoming shipment. The problem is how to shift some stored products in a certain zone to other zones in order to free space for the incoming shipment	Rule of thumb procedure

Order picking

For example, in a warehouse, single-order picking, batching, sorting, batching and sorting, zoning, and batching with zoning can be employed with different order picking procedures. The following basic steps are used for each pickup procedure: batching, routing, sequencing and sorting [3].

Batching: The problem with batching is part of the order picking schedule. Orders are received and released for completion after that. The problem with a set of released orders is to divide up the loads, where each load is chosen and collected for packaging and shipping during a given

time or "pick-wave" window. The time needed to choose the items in any lot shall not exceed the time window or the duration of the wave. If zone picking is used, the lots should balance pick effort across the zones to achieve high use of pickers, while reducing the time required for picking.

Sequencing and routing:The decision to sequence and to route for selection decides the best sequence and route of the places where such elements can be selected and/or stored. Usually, the goal is to reduce the overall cost of handling materials. This problem is a travelling salesman (TSP) problem specifically for warehouses, where an object is collected/stored. The problem with multiple candidate locations for retrieval or storage of an item, which often is encountered in practise, is more complicated and few research findings are available [4]. Due to the aisle arrangement of potential routes, the TSP in the warehouse is special. The research published covers four categories of warehouse systems - traditional multi-parallel alignment systems, AS/RS man-on-board systems, AS/RS unit charge systems and carousel systems.

Sorting:When several orders are collected together, sorting is essential. This can be done either during picking (sort-and-select) or after picking (sort-after-pick). The selection is very easy and is usually modelled by inflating the extraction time of products. For sort-after selection, the sorting feature is carried over with a separate downstream sorting method. A variety of issues concern the functioning of the method of sorting.

Picking productivity and e-fulfilment

To produce the customer order accurately in a certain period of time, a good information and communication system is required. The pick-up information required of the picker essentially consists of the pick-up points and their series, the order quantities and the selecting SKUs and their destination. In order to enhance picking processes, numbers of information systems and methods can be implemented [1].

Online ordering now requires more responsive supply chains via Internet technologies and e-commerce businesses. In e-fulfillment systems in which a huge number of small customer orders are required for a wide array, low pricing and good quality products in a short time, pickup workloads are improved according to Rushton et al. (2006). In order to respond more to demand, companies follow "Pull" supply chain models, where the demand of customers drives production. Online shopping leads to all product varieties being held in sufficient amount by retailers and distributors, a failure that reduces service levels and increases opportunities to lose costs. Time, cost and operational efficiency are being combined. Therefore, research should focus on such products (perishable/food) and warehouses (department/distribution), in order to ensure customer satisfaction and shorter response times [6]. This requires appropriate inventories. High service standards and shorter response times could save costs on the downstream supply network, but they press for lean or JIT philosophy in companies.

Importance and Benefits of Warehousing

- Centralized Storage Location.
- Enhanced Inventory Management.
- Better Order Processing.
- Additional Storage.

- Price Stabilization.
- Excellent Customer Service.
- Better Risk Management.

CONCLUSIONS

Warehouse examples include retail stores, distribution centers, cold storage facilities, and manufacturing plants. In retail stores, items are stored and organized in a warehouse and shipped to customers or other stores.Regardless of the product, every warehouse moves things, stores them, keeps track of them, and sends them out. Those four functions result in our four essential categories of equipment: storage, material handling, packing and shipping, and barcode equipment.

In contrast, research development is not well-balanced. Some issues received much greater attention than others from the research community. For instance, 32 percent of all surveyed literature is covered by SLAP and routing problems, while less than 6 percent is accounted for by zoning. There is also little direct evidence of the academic research community's cooperation with industry. Many of the results of research in warehouse practises are not adequately communicated to industry to have a significant impact. Further communication between the two sides could help identify the real challenges in warehouse operations better and appreciate the possibilities for better operation by working closely with researchers and practitioners.

The issues discussed in this paper are operational, so decisions must be taken quite often and the effects of these decisions are usually short-lived and localised. Usually such decisions must be taken quickly without comprehensive computational tools. This encourages the use of heuristic methods, which are reliable in reasonable time to find a good solution. Furthermore, from an organizational perspective, a simple, intuitive and reliable solution method should be used in order to minimise warehouse training costs.

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EMERGING COPPER SULFIDE NANOSTRUCTURES FOR DIVERSIFIED APPLICATIONS

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INTRODUCTION

Transition metal chalcogenides (CuS, CdS, ZnS, HgS, and PbS) at the nano-scale are becoming particularly attractive among other types of nanomaterials because of their vast use in many applications. Because of its fascinating shape and varied stoichiometric compositions with changing crystalline phases, copper sulfide is an important p-type semiconductor. CuS is favored over other metal sulfides such as Co_9S_8, Ni_3S_2, $NiCo_2S_4$, and MoS_2 due to its metal-like conductivity (10^3 S/cm), low toxicity, and inexpensive cost [1, 2].

CuS, as a p-type semiconductor, has potential applications in photothermal conversion [3], capacitors [4], sensors [5], batteries [6], and solar cell devices [7], and exhibits superconductivity at 1.6 K [8], among other things, due to variations in stoichiometric compositions, complex structures, nanocrystalline morphology, nonlinear optical properties, increased conductivity at high temperatures, excellent solar radiation absorbing properties and cathode material with a high capacity in lithium secondary batteries [9].

Copper sulfide is a binary inorganic material having the general formula Cu_xS_y. It exists in both synthetic and minerals form as CuS (covellite) and Cu_2S (chalcocite). Several meta-stable and stable phases of different stoichiometries exist between covellite and chalcocite. Copper sulfide forms five stable phases at room temperature, which vary according to values of x ($1 \leq x \leq 2$): covellite (CuS), anilite ($Cu_{1.75}S$), digenite ($Cu_{1.8S}S$), djurleite ($Cu_{1.95S}$) and chalcocite (Cu_2S) [10, 11].

Structure

At normal temperature, CuS occurs as a copper-poor phase and others as copper-rich phases. Furthermore, CuS is known to exist in two forms: brown CuS and green CuS. Green CuS is a true crystalline form consisting up of one-third Cu (II) and two-thirds Cu (I). Brown CuS has been discovered to exist in poor crystalline or amorphous form and to be made only of Cu(I)S, which is not stoichiometrically balanced. Cu(I)S possessed a complicated type of hexagonal structure with space group P63/mmc and lattice constants: a=b=0.3784 nm and c=1.633 nm. Furthermore, one-third of the metal ions in CuS are surrounded by three neighboring S atoms at the corners of a triangle, and two-thirds are surrounded by four S neighbors in a tetrahedral arrangement [12] [13].

Diversified applications

Due to variations in stoichiometric compositions, complex structures, nanocrystalline morphology, nonlinear optical properties, increased conductivity at high temperature, excellent solar radiation absorbing properties, and high capacity cathode material in lithium secondary batteries, CuS, as a p-type semiconductor, has potential applications.

ENERGY STORAGE DEVICES

Supercapacitance

CuS-based nanomaterials have grown in prominence due to their potential applications in energy storage devices such as supercapacitors, LIBs, and solar cells. Because of its higher electronic conductivity and large energy capacity, CuS has lately become a popular electrode material. CuS nanomaterial supercapacitor applications were studied using cyclic voltammetry (CV) at various scan rates ranging from 5 mV to 100 mV. It is generally known that the shape of CV curves in a double layer capacitor should be an ideal rectangle, however Faradaic reactions can modify the shape of CV curves in pseudocapacitive materials. The CV curves revealed the presence of redox pairs corresponding to Faradaic reactions occurring at the electrode surface, indicating the CuS's pseudo capacitive nature. Because the CV curves are non-rectangular and have a few strong redox peaks, the capacitance is dominated by the Faradaic redox reaction. Aside from that, the planar supercapacitor had 94% cyclic stability and better capacitance retention after 5000 charge/discharge cycles [14, 15].

Lithium Ion Batteries (LIBs)

LIBs are dominant and growing technology utilized for energy storage in electric vehicles as portable electronic gadgets. The electrode materials are principally responsible for determining the battery's energy and power density, its specific capacity and rate capability. Due to its high electronic conductivity (10^3 Scm^{-1}), high energy capacity (560 $mAh^{-1}g$), and flat discharge curves, CuS is frequently employed as a high capacity cathode material in lithium secondary batteries [16].

Photocatalysis

Because most synthetic dyes are toxic, non-biodegradable, and resistant to direct degradation by sunlight, they are classified as persistent pollutants. CuS nanoparticles are less hazardous, less expensive, and more stable under ambient settings, making them an attractive material for application in clean technology to solve environmental challenges. CuS nanotubes' improved photocatalytic activity may be ascribed to their unusual structure, which has a smooth inside and a coarse outer made up of nanoparticles positioned on the nanotubes' surface. Nanoparticles contain a greater number of photocatalytic active sites, which may account for increased photocatalytic degradation. The as-prepared flower-like CuS microsphere exhibited improved photocatalytic activity due to its low band gap energy (1.45 eV), high specific surface area, and unusual hierarchical structure within the interconnected nanosheets (very active photocatalytic sites) [17].

A sequence of chemical reactions (1-6) can be used to understand the response of CuS with oxidants and reductants. Finally, the superoxide ions ($\dot{O}^{2-}$) and OH• radicals decompose the organic pollutants into harmless products [18].

$$CuS + h\nu \rightarrow h^+ (CuS) + e^- (CuS) \quad (1)$$

$$H_2O \rightarrow H^+ + OH^- \quad (2)$$

$$e^- (CuS) + O_2 \rightarrow \dot{O}_2^- \quad (3)$$

$$e^- (CuS) + H_2O_2 \rightarrow \dot{O}H + OH^- \quad (4)$$

$h^+ (CuS) + OH^- \rightarrow {}^{\cdot}OH$ (5)

Organic pollutant + ${}^{\cdot}OH$ + ${}^{\cdot}O_2^-$ →harmless degradation products (6)

The dye molecule is initially adsorbed on the surface of the catalyst. When a CuS photocatalyst absorbs visible light, one electron that comes from the valence band is excited to the conduction band, where it forms electron-hole pairs. The electrons from the conduction band are transferred to the catalyst surface reducing O_2 to ${}^{\cdot}O_2^-$. While, the holes in the valence band react with H_2O_2 on the surface of the catalyst to form $OH^{\cdot}$. These radicals (${}^{\cdot}O_2^-$ & $OH^{\cdot}$) show high oxidizing ability reacting with organic dyes to oxidize it [19].

Electrochemical bio-sensing

CuS nanoparticles with nanotube morphology have demonstrated remarkable electrocatalytic activities, which may provide a low-cost, high-sensitivity, stable, and dependable alternative nanomaterial to Au and Ag-based glucose biosensors. Because of its inexpensive cost and excellent electron transfer capabilities, CuS has recently been used as a sensing material for hydrogen peroxide reduction or glucose oxidation [20]. However, the applications of CuS in the field of non-enzymatic sensing require further investigation, and only a few studies on the electrocatalytic oxidation of N_2H_4 using CuS as an electro-catalyst have been reported. Morphology, in addition to the inherent properties of the sensing material, was critical in adjusting the electro catalytic performance. CuS of various forms were thus tested for electrocatalytic activity. It has been found that a flower-like CuS with a 3-D porous structure could provide a larger surface area and more active sites for the N_2H_4 reaction, as well as reduce the diffusion resistance of N_2H_4 molecules with greater contact with more active surfaces [21, 22].

Drug delivery

The porosity and hollowness of nanoparticles were crucial in drug loading and drug release with targeted delivery. Because of their mesoporous and hollow form, hollow CuS nanoparticles have benefits in drug delivery capabilities and sustained drug-release features [22]. Hollow CuS nanoparticles (d ~55 nm) were used as a vehicle for improved transdermal drug delivery employing a nanosecond-pulsed laser and a localized heat effect of the skin. Because hollow CuS nanoparticles have a high specific surface/volume ratio and a large number of mesoporous pores, they can be loaded with hydrophobic drug molecules [23].

DNA detection

CuS nanoparticles' sensing capacity is principally based on their metal-like electrical conductivity and ability to induce electron transfer interactions with bio-molecules. Many applications require sequence specific detection of DNA, such as in various laboratory procedures (e.g., gene analysis), pathological tests for disease diagnosis, drug screening, forensic sciences, and so on. A variety of ways for detecting DNA hybridization have been investigated, with nanomaterial-based chemiluminescence detection holding the most promise [24].

Thermal Ablation

CuS nanostructures have various advantages over gold nanostructures, including a substantially lower cost of manufacture. Furthermore, NIR absorption in CuS was caused by the d-d transition of Cu^{+2} ions, whereas NIR absorption in gold nanostructures was caused by the

localized surface plasmon resonance (LSPR) [25]. CuS 's NIR absorption is comparable to trapped excitons in doped nanoparticles. As a result of quantum size confinement, absorption intensity is greatly dependent on particle size. In other words, their absorption can be controlled by modifying particle size, but post-synthesis treatments and the surrounding environment have only a minor impact. The d-d transition peaks at 900 nm are in the near-infrared spectrum, making them appropriate for in vivo applications. As a result, no complicated processes are required to induce NIR absorption in CuS nanoparticles, which is then followed by the formation of certain gold textures such as hollow nanospheres, nanoshells, or nanorods [26]. hydrophilic CuS superstructures was also proposed to improve NIR light absorption and photothermal conversion efficiency [25].

CONCLUSION

CuS (Covellite) nanostructures are effective and versatile nanomaterials for a variety of applications. The performance is determined by the size, shape, and other factors. CuS nanostructures can thus be used as a versatile nanomaterial in a variety of possible applications such as photocatalysis, electrocatalysis, sensing, energy storage, and so on. CuS (Covellite) nanostructures will pave the way for new research in future applications.

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A NEW APPROACH TO A PHYSICAL SYSTEM PROBLEMS USING SOME INTEGRAL TRANSFORMS

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INTRODUCTION

From last few decades considerable efforts have been made using some techniques towards the development of computational methods to solve different methods for given linear differential equations in various fields of science and engineering. The analysis was made in applied physical sciences. Some methods are applied to find the best solution of such problems related to science and engineering. Now a days Laplace transform methods (LTM) and Differential Transform method (DTM) have been attracted the great interest towards researchers of physical and mathematical sciences and many research papers were published in these fields.

Undamped force of vibrations

Forced undamped vibration is described as the kind of vibration in which a particular system encounters an outside force that makes the system vibrate. Examples of undamped forced vibration are: Movement of laundry machine due to asymmetry. The vibration of a moving transport due to its engine. Movements of strings in guitar.

Consider the undamped forced vibrations of spring given by the differential equation is**.**

Undamped force vibration of spring:

Consider the undamped force vibrations of spring given by the differential equation is,

$$m\frac{d^2y}{dt^2}+k\,y(t)=f(t) \quad \text{.....(1)}$$

In this paper we take the special choice of f(t)=(1-sint), m=1kg, k=1N/m, with initial conditions $y(0)=y'(0)=0$ then equation (1) gives us,

$$\frac{d^2y}{dt^2}+y(t)=(1-\sin t) \text{.....(2)}$$

Main results

Applying both sides Laplace transform method (LTM)

Consider the equation (2) applying both the sides Laplace Transform

$$L\left[y''(t)\right]+L\left[y(t)\right]=L[1]-L[\sin t]$$

$$\left[s^2\,L[y(t)]\right]-s\,y(0)-y'(0)]=\frac{1}{s}-\frac{1}{s^2+1}$$

Since y (0) =y$'$ (0) =0. And applying both sides inverse transform.

We get

$$y(t) = 1 - \cos t - \frac{1}{2}[\sin\ t - t\cos t] \ldots\ldots\ldots\ldots\ldots\ldots (4)$$

Applying the Differential transform method (DTM) both the side for equation (2)

$$(k+1)((k+2)y(k+2) + y(k) = 1 - \sin\left(\frac{k\pi}{2}\right)$$

$$y(k+2) = \frac{1 - \sin\left(\frac{k\pi}{2}\right) - y(k)}{(k+1)(k+2)} \ldots\ldots\ldots\ldots\ldots\ldots (5)$$

Put k=0 $y(2) = \frac{1 - \sin(0) - y(0)}{(1)(2)} = \frac{1}{2} = 0.5$

Put k=1 $y(3) = \frac{1 - \sin(\pi/2) - y(1)}{(2)(3)} = \frac{1}{6} = 0.16666$

Put k=2 $y(4) = \frac{1 - \sin(\pi) - y(2)}{(3)(4)} = 0.0416\,6$

Put k=3 $y(5) = \frac{1 - \sin(\frac{3\pi}{2}) - y(3)}{(4)(5)} = 0.08166$

Put k=4 $y(6) = \frac{1 - \sin\left(\frac{4\pi}{2}\right) - y(4)}{(5)(6)} = 0.0306$

Let us consider the solution is of the form

$$y(t) = \sum_{k=0}^{\infty} y(k)\,t^k$$

$$y(t) = y(0)t^0 + y(1)t + y(2)t^2 + y(3)t^3 + y(4)t^4 + y(5)t^5 + \ldots\ldots (6)$$

Substituting the different values of y we get

$$y(t) = t + (0.5)t^2 + (0.0416)t^3 + (0.08166)t^4 + (0.0306)t^5 + \ldots.. (7)$$

Table 1: Absolute errors for undamped force for different mesh points.

t	DTM	LTM	Absolute error
0.1	0.105050066	0.105051311	-0.045472165
0.2	0.220472333	0.235271251	-0.014798918
0.3	0.346858555	0.346857222	1.328×10^{-6}
0.4	0.485064252	0.494952121	-9.887869×10^{-3}
0.5	0.636262622	0.636258121	4.502×10^{-6}

0.6	0.795172512	0.805125812	$-9.9952668 \times 10^{-3}$
0.7	0.984000000	0.984014000	-1.4×10^{-5}
0.8	1.190074015	1.200012000	-9.937985×10^{-3}
0.9	1.406933332	1.367458121	0.04242122
1	1.653858522	1.653458212	4.0031×10^{-4}

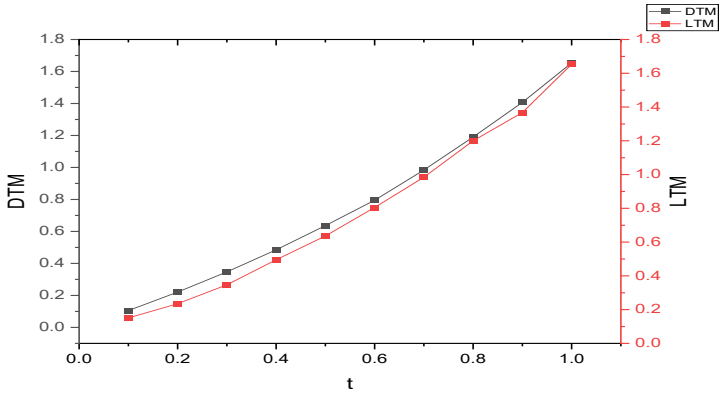

Figure 1: Comparisons for DTM, and LTM for different mesh points for undamped force of vibration problem

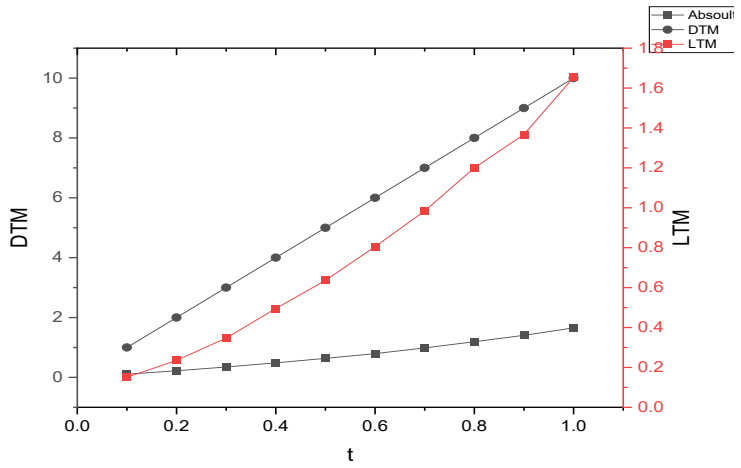

Figure 2: Comparisons for DTM, and LTM for different mesh points with respect to absolute error for undamped force of vibration problem

CONCLUSION

The main basic objective of this work is to implement the given transformations to linear non homogeneous differential equations which are occurring in the field of engineering, applied sciences and other physical systems The methods which are proposed here are two transformations LTM and DTM and shown graphically.

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EVALUATION ON SUBSTANCE ABUSE & CHEMICAL CHANGES IN HUMAN BODY

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INTRODUCTION

Over the various decades humans has engaging themselves into various chemical and substance usage. Various pre-occupied notions have been identified on the using pattern of the chemical substances. Although, sample amount of substance usages, led to serious physical turbulences [3]. However, human have gained enormous amount of benefits from the prescription based substance usage. For instance, alcoholics, maniacs have to take substance on the basis of their doctors' opinion on a regular basis. This helps them to reduce undesirable thoughts such as willing to consume alcohols in an excessive manner. Moreover, various life problems such as depression, psychosocial dysfunctions, apathy and various developmental lags- this reasons could be treated by adequate substance usages under the medication of medical treatment. [6].

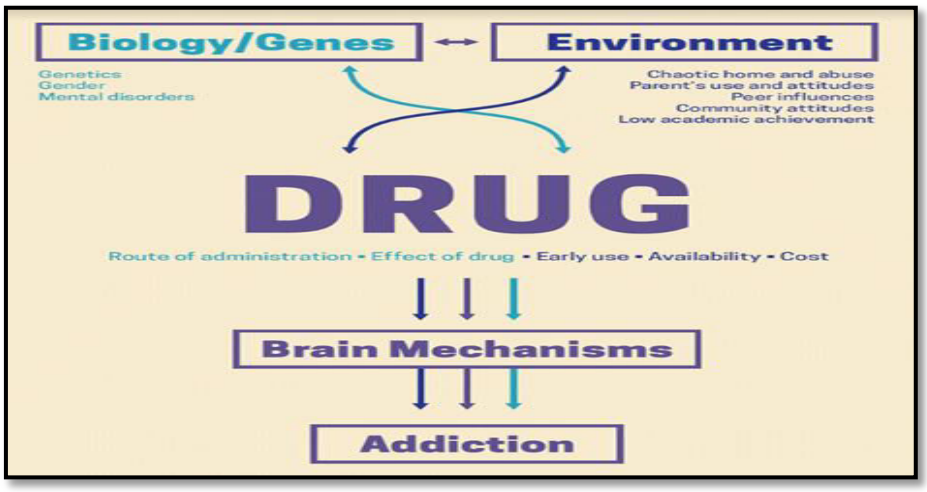

Figure 1: Factors influencing brain mechanism

Past studies have shown significant impacts on the substance abuse that it is highly influenced by the familial drug records, coexistence of an individual in intimate circles [2]. Various detrimental effects of the chemical substance have been identified. As the over usage of drug substances could gradually destroy the immune system of an individual. It also effects in the conviction of the dehydration-induced seizures for the alcoholic patients. It has been from the previous studies, there are several stages of the changing pattern in the drug usage [8]. In addition, drug usage leads to abusive behavior that causes emotional pain. Moreover, Drug abuse encompasses wide range of stages such as action pre-contemplation, maintenance, contemplation and preparation. Various studies have shown the significance of chemical reactions occurring continuously on the human body due to use of substances. Moreover, these chemicals drive the procedure of the life circle [11]. It can be said eloquently, that this chemicals can take the control of all over the human organs. As an example, secretion of the dopamine on the happy occasions triggers the changes in the human body.

OBJECTIVES

- To investigate the evaluation on substance abuse
- To understand the impact of changes of chemicals in Human Body
- To evaluate neurobiological effects of substance usage
- To examine various dimension of substance usage
- To demonstrate the effects of drug abuse in the brain function
- To analyze the cause and effects of prescription drugs

METHODOLOGY

Various studies have found, a significant amount of populations have suffered from the illicit drug usage. For instance, 7 million people have been reported that 7 million people have faced the usage disorder of the illicit drug abuses [5]. Moreover, one in four deaths has been reported for the reason of the alcohol, prescription drug use and tobacco usage. Several scientists have mentioned, mixing the substances is never safe. It has been shown effects of the compounded drugs are more impact full and more unpredictable. This can lead to damage of nerve system and resulting the deadly consciences.

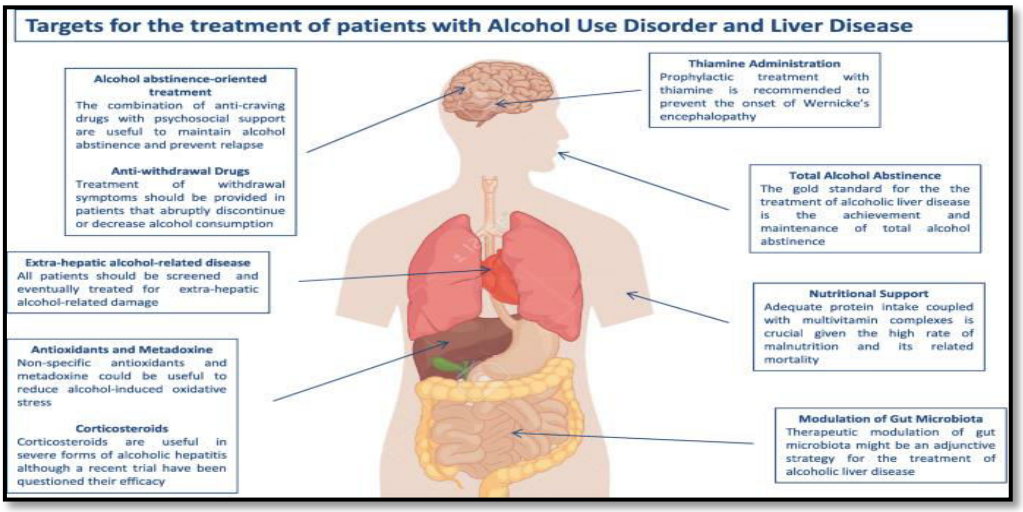

Figure 1: effected areas of human bodies on the usage of the alcohol abuse

Various detrimental effects of the chemical substance have been identified. As the over usage of drug substances could gradually destroy the immune system of an individual [9]. As illustrated on the above picture, excessive usage of alcohol usage could impact several parts of the body.

E-PHARMACY

Virtualization of every resources of human society has become significant in the modern time. Over the last few decades availing internet services has become integral part of the life. Especially, after the COVID-19 pandemic human race have become heavily dependent on the internet [5]. The E-pharmacy is an emerging notion that indicates the changing pattern of pharmaceutical services. This phenomenon signifies trading the medicines according to requirements to the consumer within stipulated time. Therefore, the process of drug purchasing

has become more convenient and effortless. Moreover, E-Pharmacy model distributed and strategically organized each and every essential medical product as per the different medical segment. Various advantages and disadvantages of E-pharmacy have been identified [3]. One of the importance's of E- Pharmacy application is it take very less time to order. Besides that, one can take benefits of this application to save money. Moreover, this application maintains privacy and confidentiality of every penitent.

NEUROBIOLOGY

Several scientists have concluded their research on the substantial study of the body [12]. Neurobiology refers an Intellectual basis which is interested with the crucial facts of the biological mechanisms which is closely related to the mediate behavior of the neuro system [4]. Past studies have shown, any addiction cycle can be explained by the mechanisms of the neurobiology. The domain of this study includes the functions of the particular brain circuits. Moreover, various advantages and disadvantages of neurobiology have been identified [5]. Through the neurobiological process molecular and neurochemical interchange in between different brain circuits can be examined efficiently. Thus, neurobiological methods can significantly analyze the effects of the chemical in the brain.

DIFFERENT DIMENSION OF SUBSTANCE

Table 1: Different dimension of substance

Dimension	**Description**
Physical	Significant among teenagers
Psychosocial	Identified among psychological patients
Environmental	Usage of magic mushroom

Various dimension of substances usage has been found by eminent scientist. Dimension of drug substance encompasses wide range of stages including emotional dimension, Environmental dimension, financial dimension, Physical dimension, Social dimension and spiritual dimensions [6]. Moreover, various life problems such as depression, psychosocial dysfunctions, apathy and various developmental lags- this reasons could be treated by adequate substance usages under the medication of medical treatment.

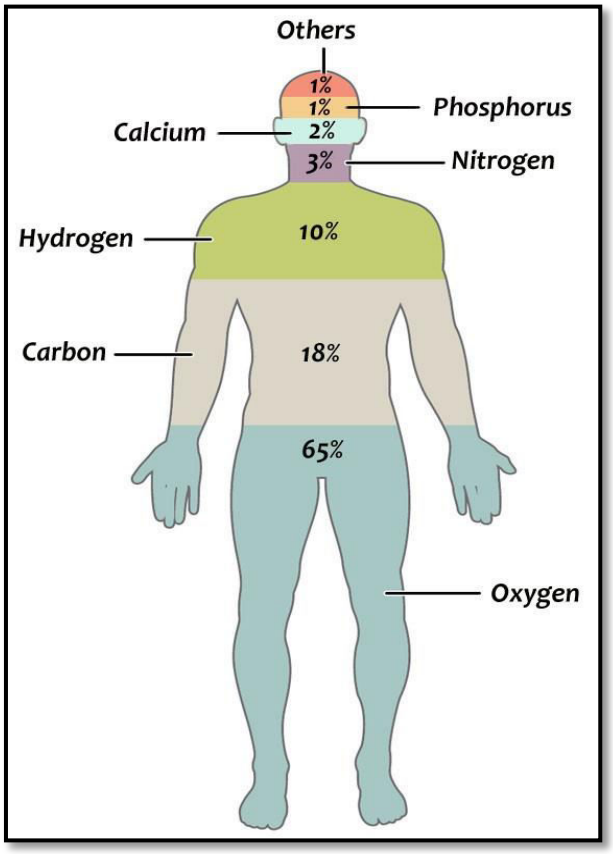

Figure 3: Chemicals in human body

Although, it has been seen many teenagers are using drugs because of their facial problem. Past studies have found in modern times women are talking more drugs than the men. Besides that, several life factors have influenced the people to taking drug substances such as poor academic performance, toxic friends group [10]. Various studies have shown the significance of chemical drugs among the patients for the betterment of their physical as well as mental health [4]. Furthermore, it has been found that the several patient's from all over the world taking prescription based substance to avoid painful psychological syndrome. Moreover, various psychological problems have been cured by the usage of chemical substances. Moreover, the different chemical substances such as LSD, magic mushrooms are harmful for the immune system [9]. These are considered as psychedelic drugs and depict the state of spiritual imaginations. Several studies have shown detrimental effects of these drugs in case of extensive psychedelic drug use [14]. An eminent scientist is well known for the research on this domain, named Terence Makena.

SIGNIFICANCE OF BLOCKCHAIN SYSTEM:

The healthcare industry is regarded as the backbone of any nation as it has a significant impact on the welfare of the people [7]. Healthcare services can be categorized into four following sub-sections as Pharmaceuticals and connected sections, Health care amenities and facilities, Medical insurance and assistance, Medical gadgets, instruments, and hospital supplies constructors. Technological advancement is shaping the dimensions of the healthcare industry over the last few decades [6]. Health technology assessment (HTA) have developed for

evaluating patient data systematically, block chain system is one of them. This study has explored the indications of a block chain-based record system in improving patient disease evaluation. This research has examined the importance and principles of the block chain system in the healthcare industry.

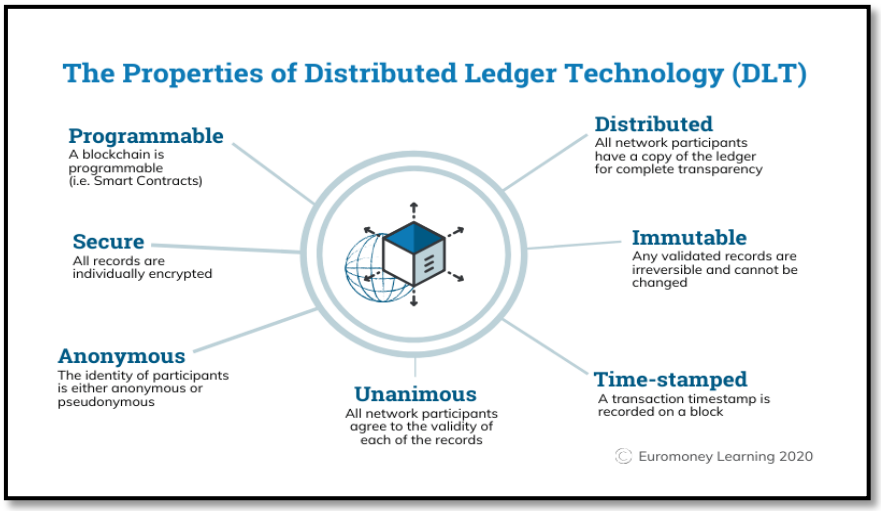

Figure 4: properties of block chain record system in healthcare

In this research, it has been shown that the blockchain system provides a proper structure for impersonal issues and helps to sustain the economic structure of the organizations by reducing the uncertainty of clinical delivery [13]. Various studies show quality record tracking can be done by the proper implication of blockchain management in the healthcare industry. Thus, the systematization of data and structured management of patients' issues can be done accordingly through this advanced system.

PROBLEM STAMENT

In this study, several detrimental issues have been identified for the expanding amount of the drug usage. In order to reducing the alcoholic addictions, medical assistances and reputed doctors suggested various prescription drugs [8]. It can be concluded that some appropriate drug substances helps to mitigate the risks of the patient even in critical health issues and provide impersonal clinical trials. Moreover, medical executives are suggested to use various tools such as the TAM model to escalate the productivity of the healthcare system along with a blockchain-based record system. Furthermore, this system is created to secure the data of every individual and provide a structured medical record of the patients.

CONCLUSION

It has been found in this study, various adequate and inadequate effects has been found for the usage of substance and along with that various types of drug usage has been explored in this study.

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MEDIATED GREEN SYNTHESIS: CHALCONES AND ITS HETEROCYCLIC REACTION

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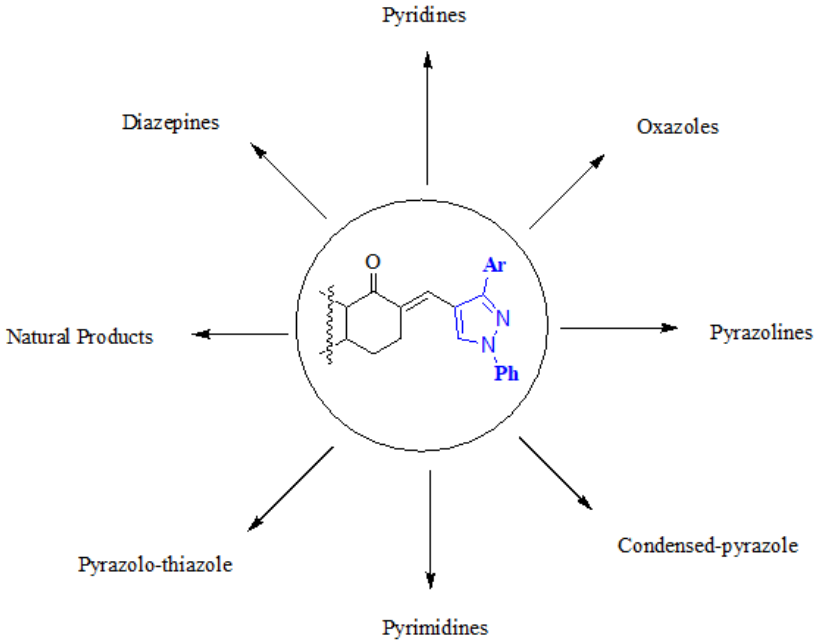
[2]Assistant Professor, Organic Chemistry Research Laboratory, Poona College of Arts, Science and Commerce Pune -411001,Maharashtra,India

ABSTRACT
Chalcones are of a high interest due to their use as starting materials in the synthesis of a series of various heterocyclic compounds. Thus the synthesis of chalcones has generated vast interest to organic as well as for medicinal chemists and polyethylene glycol (PEG-400) as an efficient and green reaction medium for the synthesis of α, β-unsaturated carbonyl compounds (Chalcones) by Claisen-Schmidt condensation method.

***Keywords**: polyethylene glycol (PEG-400), α, β-unsaturated carbonyl compounds (Chalcones) & Heterocycles.*

INTRODUCTION
Solvents are widely used in organic synthesis and have been a cause of major concern due to their associated environmental hazards. The major disadvantages are their pyrophoric nature, volatility, and poor recovery. To address some of these issues, attempts have been made to develop solvent-free chemistry, which to some extent has been successful for a few transformations. However, in performing the majority of organic transformations; solvents play a critical role in making the reaction homogeneous and allowing molecular interactions to be more efficient. To address the concerns raised by volatile organic solvents, we initiated a new to identify whether any available liquid polymers or low melting polymers can be used as solvents. Recently, polyethylene glycol (PEG) has been found to be an interesting green solvent system. The use of PEG as an environmentally benign protocol has proved to have many applications particularly, in substitution, oxidation and reduction reactions. A number of recent reviews have also covered PEG chemistry and its applications in biotechnology and medicine. Chalcones (1,3-diaryl-2-propen-1-ones) constitute an important class of natural products belonging to the flavonoid family, which have reported to possess a wide spectrum of biological activities. The presence of (functional group) in chalcones confers antibiotics activity, i.e. bacteriostatic/ bactericidal activity. Some newly synthesized chalcones and their analogues as potential therapeutic agents for diseases of the cardiovascular system. Some newly synthesized 4-(alkoxy) substituted chalcones reported as antiproliferative agents.In vivo for diagnosis treatment, e.g. proliferative conditions, such as cancer, and inflammatory conditions. Also reported that the 2', 5'-dihydroxy- chalcones have anti-inflammatory effects. 5-Lipoxygenase chalcone inhibitors are of current interest for asthma therapy, inflammatory diseases. Some chalcones derivatives also showed a profound influence on the cardiovascular, cerebrovascular and neuromuscular systems including the vital organs of the experimental animals. Newly synthesized chalcones (1,3-diarylpropen-1-ones) and their analogs as potential therapeutic agents for diseases of the cardiovascular system. Some new chalcones reported on CYPIA inhibitory action. Some newly synthesized 4-(alkoxy) substituted chalcones reported as antiproliferative agents. In vivo for diagnosis and treatment, e.g. proliferative conditions such as cancer and inflammatory conditions. Additionally some of chalcone derivatives have been found to inhibit several important enzymes in cellular systems, such as xanthenes oxidase and protein tyrosine kinase. Some newly synthesized chalcones and their analogues as potential therapeutic agents for diseases of the cardiovascular system. Curcumin, a natural product

isolated from the spice turmeric, has been shown to exhibit a wide range of pharmacological activities including certain anti-cancer, anti-oxidant, anti-inflammatory, and anti-HIV properties. Perhaps most importantly, it has also exhibited significant anti-tumor activity.(1-10)



MATERIAL AND METHOD:

Solvents are widely used in organic synthesis and have been a cause of major concern due to their associated environmental hazards. The major disadvantages are their pyrophoric nature, volatility, and poor recovery. To address some of these issues, attempts have been made to develop solvent-free chemistry, which to some extent has been successful for a few transformations. However, in performing the majority of organic transformations, solvents play a critical role in making the reaction homogeneous and allowing molecular interactions to be more efficient.

Following are the merits of this green reactions method.

i] This reaction is more versatile, efficient and convenient.

ii] Short reaction time as compared to the reported method.

iii] It gives excellent yield and purity of the product.

iv] Work-up and isolation is easier.

v] PEG is a benign reaction medium than ethanol or other solvents.

vi] PEG is potentially recyclable reaction medium.

vii] PEG is nontoxic, being used in food products and cosmetics.

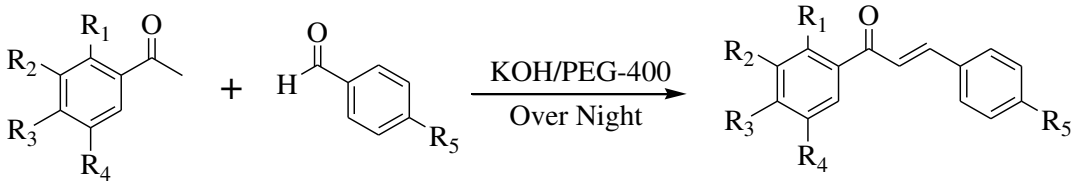
viii] Procedure is green and environmentally benign.

The use of PEG as a recyclable solvent system for the metal mediated radical polymerization of methyl methacrylate and styrene has also been reported (11-15)

RESULT AND DISCUSSION:

The substituted chalcone derivatives were prepared by stirring a solution of substituted acetophenone (1 mmol), KOH (2.0 mmol, with a minimum of H_2O) and an appropriate

aldehyde (1 mmol) in ethanol as a solvent at 50-60^{0}C temperature for one hour. All the products were isolated by acidification of the cool diluted acid solution and washed with ice cold water and recrystallized by aqueous acetic acid to give pure product. A mixture of substituted acetophenone (1 mmol), substituted aldehyde (1 mmol) and KOH (2. mmol, with a minimum of H_2O) were taken in ethanol and stirred at 50-60^0 C temperature for one hour. The reaction went to completion within determined by TLC. The products were isolated by acidification of the cool diluted acid solution and obtained solid product was filtered and washed with 2x5 mL water and recrystallized by aqueous acetic acid to give pure product. All the starting materials were synthesized in laboratory except p-chloro acetophenone.



Acetophenones Aldehydes Chalcones **1(a-h)**

Wilson Test for performing Wilson Test, the reagent used was prepared freshly by mixing two solutions A and B in equal volumes. 'A' solution was absolute acetone saturated with boric acid and 'B' solution was absolute acetone containing 10% anhydrous citric acid. About 0.001 g chalcone was dissolved in about 1mL dry acetone, it was then divided in two equal portions. Nearly 2mL of boric acid-citric acid in acetone (Wilson reagent) was added to one portion and the other portion was diluted to an equal volume using 'B' solution only. The colors of the two solutions were compared at the end of few minutes. It was observed that chalcone containing solution gave strong coloration as compared to the other. This is positive test

CONCLUSION

In summary, synthesized and characterized some new aryl substituted chalcones and its cyclisation reaction developed and study with simple and efficient system. Synthesized compounds showed antibacterial and antifungal activity.

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THE SYNTHESIS OF NANOPARTICLES VIA PHYSICAL METHODS

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1.1. INTRODUCTION

The term "nanotechnology" is a portmanteau of the words "nano" and "technology." Particles less than 100 nm in size are the focus here. Because of their versatility, nanoparticles are increasingly important in cutting-edge industries like medicine, energy, the environment, textiles, etc. Recent research has made it abundantly clear that at the nano-level, the behavior of different substances radically changes. Nanotechnology techniques allowed scientists to go beyond the bounds of more conventional approaches. For instance, in quantum mechanics, subatomic particles like neutrons, protons, and electrons are studied at the nanoscale. Because of their large, exposed surface area, nanoparticles can serve as an effective catalyst in chemical reactions. Atoms can change their chemical properties by establishing a chemical zone, which occurs when atoms are free to move within or around one another. Researchers in the medical field are interested in nanoparticles because of the many ways they could improve patient care, such as in the treatment of cancer and the development of improved imaging and diagnostic tools. Since both radiotherapy and chemotherapy can harm healthy cells, researchers are trying to devise ways to deliver nanoparticles specifically to the cancer cells that need them. Physical, chemical, biological, electrical, and optical properties all contributed to the development of better tools. Nanoparticles surface properties and small dimensions are responsible for its wide range of usefulness. Bottom-up and top-down methods have formed the basis for the synthesis of nanoparticles. Nanoparticles are typically prepared using a bottom-up method. In bottom-up, the fundamental components of nanoparticles are mobilized into a more complex structure through the application of both physical and chemical effort. This bottom-up strategy is put into action by starting with the biological world, where all necessary structures for life were originally constructed by chemical force. Condensation of atomic vapors and coalescence of liquid atoms are just two examples of the bottom-up methods that have been developed for making nanoparticles. The objective of this method involves synthesizing nanoparticles in uniform nanosized without compromising their individual properties. Drug discovery, Biosensor, Biology Imaging, Food science and technology, Textile Industry and many more field. The second approach is top-down, or big for its own good. Chemical processes could be used in the procedure. Acids were used in a chemical process to etch the metal to obtain the required particles. Synthesis of nanoparticles via physical methods is one of the popular options.

1.2. PHYSICAL METHODS:

Here, we'll look at some physical approaches to nanoparticle synthesis, including those that make use of high-energy radiation, condensation, and thermal energy. High-energy ball milling, laser ablation, electro spraying, inert gas condensation, physical vapour deposition, laser pyrolysis, and flash spray pyrolysis are all examples of physical synthesis methods for nanoparticles. show in **figure 1.**

A) High Energy Ball Milling:

At room temperature, structural changes and chemical reactions can take place thanks to the kinetic energy of the moving balls in the high energy ball milling process, which is used to

break chemical bonds [1-2]. Nitrogen doped carbon particles can be synthesized using ball milling technology, making this process environmentally friendly. These particles have potential applications in electrochemical catalysis [3]. More than a thousand times the local temperature and pressure are used in the high energy ball milling process, making it a mechano-chemical synthesis [4].

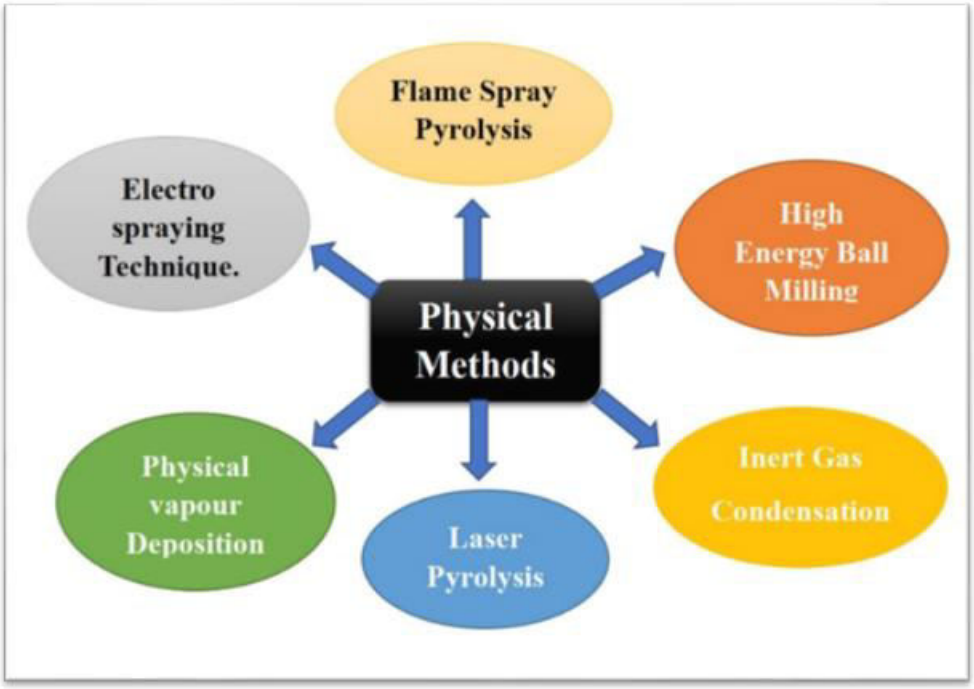

Figure 1. Types of Physical Methods

Biosurfactants are essential in nanoparticle synthesis because of their hydrophobic and hydrophilic properties. In recent years, ball milling with the aid of surfactants has emerged as a promising technique for nanoparticle synthesis. Surfactants significantly increase particle size by preventing agglomeration due to electrostatic forces. Vibratory mills, planetary ball mills, attritors, and even tumbler ball mills were modified for use in high-throughput synthesis using ball milling [5]. There are two types of ball milling, the high energy ball milling, and the tumbler type [6]. Small quantities of nanoparticles, typically less than 100 g, can be quickly and cheaply produced using either a vibratory or planetary mill [7].

B) Inert Gas Condensation:

The substrate holder in the inert gas condensation method is liquid nitrogen, and the inert gases involved are helium or argon. Manganese nanoparticles synthesized by using this method successfully [8]. Inert gas condensation is widely regarded as the most effective method for synthesizing silver and platinum nanoparticles [9]. Inert gas condensation is accomplished using a combination of plasma-gas-condensation-type cluster deposition equipment [10]. Inert gas condensation method was used to carry out metallic dielectric multicore-shell synthesis of nanoparticles [11]. To keep the nanoparticles from oxidizing and to keep them in an aggregated state, they were deposited in a silicon shell.

C) Physical Vapour Deposition:

There are three primary steps involved in the physical vapour deposition process, which is a collective synthesis of nanoparticles using the vacuum deposition technique. In the first case, a solid metal particle is vaporized. The next step involves sending the vaporized particle

somewhere else. The final process is nucleation and the development of nanoparticles thin films [12].

i. Sputtering:

Sputtering Depositing films and nanoparticles is a common application of sputtering, a vacuum-based technology that works on the momentum transfer principle. Multiple processes contribute to the technique's fundamental mechanism. The neutral gas plasma within the electrodes is generated via collision techniques. The energy gap between the electrodes propelled the plasma's ions upwards, towards the target. The impact of this energy causes the target to eject matter, which is then carried to the substrate and deposited there. Magnetron sputtering is an improved version of this technique that outperforms the traditional method by preserving its two advantages, a greater deposition rate and protection against target overheating and damage. The magnetic field produced by magnetron sputtering is responsible for the increased deposition rate. As a result of the electron's deviated path, more gas was ionized, leading to more heated ions that could be deposited on the target.With simple support materials like WO_3 and a carbon surface [13] were able to produce Gold nanoparticles deposition. Titanium dioxide ,silver ,gold ,yttrium ,carbon ,cobalt ,and iron have all been synthesized using magnetron sputtering, as has titanium Fe oxide [14-15].

ii. Electron Beam Evaporation:

The physical vapor deposition process in a vacuum is a viable option for making thin layers and nanoparticles. The electron filament at the heart of an evaporation by electron beam system needs a steady flow of current to maintain its operational state and produce electron beams. Materials can be targeted using electron beams and magnets. To advance 2D and 3D metal patterning, the evaporation by electron beam method has been incorporated [16-17]. Synthesis of gold nanoparticles and Platinum nanoparticles on multiwall carbon nanotubes was also carried out to create composite electrodes for sensors and energy storage applications [18-19]. Antibacterial silver nanoparticles were fabricated on TiO2 nanotubes with tunable diameters using a simple evaporation by electron beam process [20-21]. It has been reported that 3D graphene scaffolds were decorated with artificial silver nanoparticles for electrochemical use [22].

iii. Pulsed Laser Deposition and Laser Ablation:

Pulsed laser deposition Particles in a solid are evaporated using a high-powered laser beam in this laser ablation technique [23]. laser ablation can be either a continuous laser or a pulsed laser, depending on the application. laser ablation generates a practical method that can aid in the manufacturing of polymeric materials. Micro lens assemblies using the laser ablation method and polymer surface scanning to achieve the best possible focal distance and diameter have been reported [24-25]. The synthesis of iron-cobalt nanoparticles in an inert gas atmosphere using Pulsed laser deposition, which is relevant to the field of nanoparticles production [26]. Properties of synthesized iron-cobalt nanoparticles, such as their morphology and size, have been highlighted [27]. Once again, the average particle size is larger where there is more argon gas pressure. However, as the number of pulses has increased, some morphological shifts have been seen. Fibrous was created from the intertwined chains. Similarly, significant shifts have been noted with respect to pressure. Nanoparticles exhibit a floccules-like Nano-network at low pressure and a chain-like network at high pressure. Nanostructured silver thin films, made up of arrays of nanoparticles, were deposited using Pulsed laser deposition in an argon atmosphere, as was also mentioned [28]. Optimizing the argon pressure and number of pulses allows for precise manipulation of silver nanoparticles size and shape.

iv. Vacuum Arc:
Arc of Vacuum using an electric arc to vaporize the material, the vacuum arc physical vapor deposition process can be used to create metallic, ceramic, and composite nanoparticles and films in a vacuum environment. Magnesium-Aluminum alloy was created using a plasma arc process [29]. The synthesis of inter-metallic iron-tin nanoparticles using a vacuum arc has also been reported [26]. The high-pressure arc discharge process to investigate the beneficial properties of thin film carbon nanoparticles [30].

D) Laser Pyrolysis:
Vapor phage synthesis is the foundation of the CO_2 laser pyrolysis method [31]. This method can be used to create a wide variety of oxide nanoparticles, including TiO_2, SiO_2, Al_2, and O_3. Some non-oxide compounds, such as Si, Si_3N_3, and MoS_2, and ternary composites, such as Si, C, and N, are also synthesized using the laser pyrolysis technique[32].

E) Flame Spray Pyrolysis:
Flame spray pyrolysis is the most cutting-edge of the flame aerosol technologies [33]. The precursor was discovered in a liquid state, so this is a high-combustion technique. High combustion enthalpy, defined as more than half of the total energy of combustion, is typically observed in an organic solvent. Both droplet and gas-to-particle pathways can be taken by the liquid precursor, with the latter yielding more uniform morphologies and sizes[34-35].

F) Electro spraying Technique:
The only real difference between electro spraying and electrospinning is in the product[36]. The syringe is an electrochemical device for combining the polymer of choice with the solvent. The capillary tip is then shocked with a high voltage, creating charged droplets. Particles make it to the counter electrode, where the solvent evaporates, and are eventually collected. This method's famed adaptability and command over surface parameters contributed to its widespread adoption [37] investigated the use of electro spraying to deposit various nanoparticles and to create gold nanoparticles. In his extensive review of the electro spraying technique, a lipid-based delivery system [38]. Nanoparticle synthesis also involves the use of various physical techniques..

1.3. CONCLUSION:
Researchers are always looking into new and improved the physical methods for producing nanoparticles in the lab. Selecting the right nanoparticles for a given application relies heavily on factors like optimal size and morphology. The ideal size and shape of nanoparticles are two of the parameters that must be maintained during the development process. In this chapter, we show a clear big-picture perspective on the physical methodological approaches to nanoparticles synthesis. This chapter has the potential to supply researchers with detailed information about the different physical methods to synthesis of nanoparticles.

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HEAT TRANSFER NANOFLUIDS

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INTRODUCTION

Nanofluids are a new class of fluids engineered by dispersing nanometer-sized materials (nanoparticles, nanofibers, nanotubes, nanowires, nanorods, nanosheet, or droplets) in base fluids. In other words, nanofluids are nanoscale colloidal suspensions containing condensed nanomaterials. They are two-phase systems with one phase (solid phase) in another (liquid phase). [1]

Nanofluids have been found to possess enhanced thermophysical properties such as thermal conductivity, thermal diffusivity, viscosity, and convective heat transfer coefficients compared to those of base fluids like oil or water. It was introduced by Choi on Argonne National Laboratory at 1995. [2]

PROPERTIES

Heat transfer fluids provide the conditions for the exchange of energy in a system and their effects depend on the physical properties such as thermal conductivity, viscosity, density, and heat capacity. Commonly used heat transfer fluids such as water, ethylene glycol, and engine oil have relatively low thermal conductivities. Solids have high thermal conductivity and can be used to increase the thermal conductivity of a fluid by adding small solid particles to that fluid. The usage of such solid–liquid suspensions of solid particles with sizes on the order of 2 millimeters or micrometers for heat transfer was found to have significant drawbacks as follows: [3]

1. The particles settle rapidly, forming a layer on the surface and reducing the heat transfer capacity of the fluid.
2. If the circulation rate of the fluid is increased, sedimentation is reduced, but the erosion of the heat transfer devices, pipelines, etc., increases rapidly.
3. The large size of the particles tends to clog the flow channels, particularly if the cooling channels are narrow.
4. The pressure drop in the fluid increases considerably.
5. Finally, conductivity enhancement based on particle concentration is achieved (i.e., thegreater the particle volume fraction is, the greater the enhancement—and greater the problems, as indicated above).

Nanofluids having properly dispersed nanoparticles possess the following advantages compared to conventional solid–liquid suspensions for heat transfer intensifications:[4]

1. High specific surface area and therefore more heat transfer surface between particles and fluids.
2. High dispersion stability with predominant Brownian motion of particles.
3. Reduced pumping power as compared to pure liquid to achieve equivalent heat transfer intensification.
4. Reduced particle clogging as compared to conventional slurries, thus promoting system miniaturization.
5. Adjustable properties, including thermal conductivity and surface wettability, by varying particle concentrations to suit different applications.

Nanofluids provide higher thermal conductivity compared to base fluids. Its value increases with particles concentration. Temperature, particles size, dispersion and stability do play important role in determining thermal conductivity of nanofluids.

Synthesis of Nanofluids

Nanofluids are not just dispersion of solid particles in a fluid. The essential requirements that a nanofluid must fulfill are even and stable suspension, adequate durability, negligible agglomeration of particles, no chemical change of the particles or fluid, etc. Nanofluids are produced by dispersing nanometer scale solid particles into base liquids such as water, ethylene glycol, oil, etc. In the synthesis of nanofluids, agglomeration is a major problem. There are mainly two techniques used to produce nanofluids: the single-step and the two-step method.[5]

The Single-step Process

The one-step process consists of simultaneously making and dispersing the particles in the fluid. In this method, the processes of drying, storage, transportation, and dispersion of nanoparticles are avoided, so the agglomeration of nanoparticles is minimized, and the stability of fluids is increased. The one-step processes can prepare uniformly dispersed nanoparticles, and the particles can be stably suspended in the base fluid. One-step physical method cannot synthesize nanofluids in large scale, and the cost is also high, so the one-step chemical method is developing rapidly. However, there are some disadvantages for one-step method. The most important one is that the residual reactants are left in the nanofluids due to incomplete reaction or stabilization. It is difficult to elucidate the nanoparticle effect without eliminating this impurity effect.

The Two Step Process

Two-step method is the most widely used method for preparing nanofluids. Nanoparticles, nanofibers, nanotubes, or other nanomaterials used in this method are first produced as dry powders by chemical or physical methods. Then, the nanosized powder will be dispersed into a fluid in the second processing step with the help of intensive magnetic force agitation, ultrasonic agitation, high-shear mixing, homogenizing, and ball milling. Two-step method is the most economic method to produce nanofluids in large scale, because nanopowder synthesis techniques have already been scaled up to industrial production levels. Due to the high surface area and surface activity, nanoparticles have the tendency to aggregate. The important technique to enhance the stability of nanoparticles in fluids is the use of surfactants. However, the functionality of the surfactants under high temperature is also a big concern, especially for high-temperature applications.

Applications:

Nanofluids can be used in various engineering applications. These are following application of nanofluids.[6]

A. Heat Transfer Applications

1. Industrial Cooling Applications:

The application of nanofluids in industrial cooling will result in great energy savings and emissions reductions. It is predicted that electric power industry, using nanofluids in closed loop cooling cycles could save large economy.

2. Extraction of Geothermal Power and Other Energy Sources:

When extracting energy from the earth's crust that varies in length between 5 to 10 km and temperature between 5000C and 10000C, nanofluids can be employed to cool the pipes exposed to such high temperatures.

B. Automotive Applications

1. Nanofluid Coolant:
The use of nanofluids as coolants would allow for smaller size and better positioning of the radiators. Owing to the fact that there would be less fluid due to the higher efficiency, coolant pumps could be shrunk and truck engines could be operated at higher temperatures allowing for more horsepower while still meeting stringent emission standards.

2. Lubricants:
In automotive lubrication applications, surface-modified nanoparticles stably dispersed in mineral oils are effective in reducing wear and enhancing load-carrying capacity.

C. Electronic Applications
A principal limitation on developing smaller microchips is the rapid heat dissipation. However, nanofluids can be used for liquid cooling of computer processors due to their high thermal conductivity.

D. Nuclear Systems Cooling:
The researchers are exploring the applications of nanofluids in nuclear reactors, specifically as main reactor coolant to enable significant power uprates/generation, thus enhancing their economic performance.

Challenges of Nanofluids:
Although nanofluids exhibits enormous exciting potential applications, some vital hinders pose challenges before commercialization of nanofluids. [6]

1. **Higher viscosity:** The viscosity of nanoparticle–water suspensions increases in accordance with increasing particle concentration in the suspension. So, the particle mass fraction cannot be increased unlimitedly.
2. **Lower specific heat:** specific heat of nanofluids is lower than basefluid. CuO/ethylene glycol nanofluids, SiO2/ethylene glycol nanofluids and Al2O3/ethylene glycol nanofluids exhibit lower specific heat compared to basefluids. An ideal coolant should possess higher value of specific heat which enable the coolant to remove more heat.
3. **Thermal conductivity:** The existing models for predicting thermal conductivities of CNT nanofluids, including Hamilton–Crosser model, Yu–Choi model and Xue model, cannot predict the thermal conductivities of CNT nanorefrigerants within a mean deviation of less than 15%.
4. **High cost of nanofluids:** Higher production cost of nanofluids is among the reasons that may hinder the application of nanofluids in industry. Nanofluids can be produced by either one step or two steps methods. However both methods require advanced and sophisticated equipments.
5. **Difficulties in production process:** Nanoparticles are inherently produced from processes that involve reduction reactions or ion exchange. Furthermore, the base fluids contain other ions and reaction products that are difficult or impossible to separate from the fluids. Nanoparticles' tendency to agglomerate into larger particles, which limits the benefits of the high surface area nanoparticles. To counter this tendency, particle dispersion additives are often added to the base fluid with the nanoparticles. Unfortunately, this practice can change the surface properties of the particles, and nanofluids prepared in this way may contain unacceptable levels of impurities [7].

CONCLUSION

Nanofluids are important because they can be used in numerous applications involving heat transfer, and other applications such as in automotive, electronics etc. Problems of nano particle agglomeration, higher viscosity, lower specific heat, difficulties in production process, all need to be addressed before its applications on commercial scale.

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DFT, CRYSTALLOGRAPHY AND CHEMOINFORMATIC IN CHEMISTRY AND VALIDATION OF EMERGING DRUG TARGETS: STREAMLINING DRUG DISCOVERY

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INTRODUCTION

Discovering drugs to a disease is still a challenging task for medical researchers due to the complex structures of biomolecules which are responsible for disease such as AIDS, Cancer, Autism, Alzheimer etc. Design and development of new efficient anti-drugs for the disease without any side effects are becoming mandatory in the recent history of human life cycle due to changes in various factors which includes food habit, environmental and migration in human life style. Cheminformatics deals with discovering drugs based in modern drug discovery techniques which in turn rectifies complex issues in traditional drug discovery system. Cheminformatics tools, helps medical chemist for better understanding of complex structures of chemical compounds. Cheminformatics is a new emerging interdisciplinary field which primarily aims to discover Novel Chemical Entities [NCE] which ultimately results in design of new molecule [chemical data]. It also plays an important role for collecting, storing and analysing the chemical data. Recent chemical developments for drug discovery are generating a lot of chemical data which is referred as information explosion. This has created a demand to effectively collect, organize, analyse and apply the chemical information in the process of modern drug discovery and development. The drug discovery process is aimed at discovering molecules that can be very rapidly developed for effective treatments to meet medical needs.

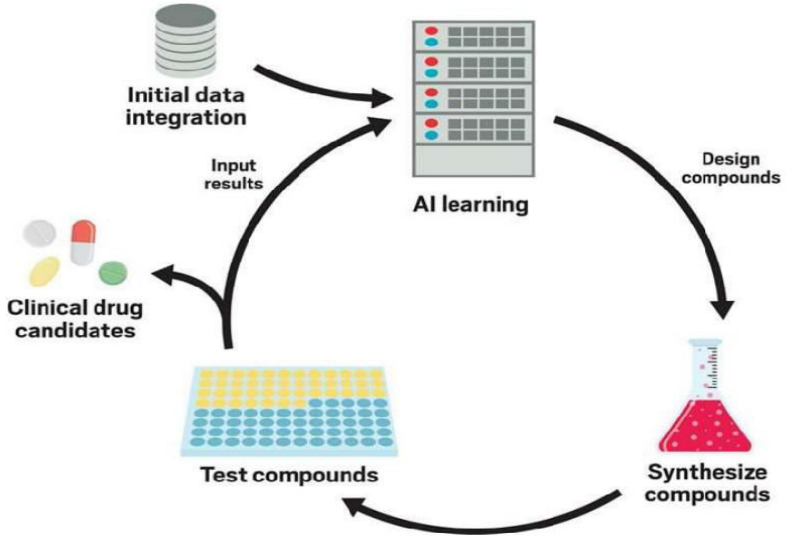


Fig. 01. AI learning in drug design identification of target drug, optimization and clinical integration

The challenges of Modelling Drug Discovery Data

The modern applications of deep learning in drug discovery are exploring new areas such as compound generation 16–18 and compound synthesis. Meanwhile, realizing the goal of a fully generalized deep learning quantitative structure-activity relationship (QSAR) model that can be applied to general pharmaceutical project data, on both large and small scales, with minimal human intervention, has not received the same degree of attention. There are many pre-deep learning QSAR methods including decision trees and random forests radial basis functions,

support vector machines 25,26 and Gaussian processes. Intermediate neural network methods. So far, despite all this effort, attempts to apply traditional deep learning methods such as deep neural networks 9,10 and deep belief networks to prediction of experimental drug discovery endpoints, in a practical way that helps a project progress, have resulted in only small improvement over traditional QSAR modelling methods 33 such as random forests, with an average increase in coefficient of determination. Significant improvements over 'conventional' machine learning is generally only seen in large datasets, or in the case of multitask learning where there are strong correlations between the endpoints. The reason this increase is not larger is likely due to challenges that arise when using pharmaceutical data in conventional approaches. These are problems arising from sparse, noisy, heterogenous and dynamic data, that prohibit deep methods from adding their full value. In this paper, we describe an application of a deep learning method for data imputation, Alchemite™, to an ongoing drug discovery project. While originally developed and proved in the context of materials discovery 36–39, success has been seen in an example application of this method to a challenging, public domain benchmark data set of kinase activity data. In late December 2019 at Wuhan (China), an unknown acute respiratory disease was reported. At the first week of January 2020, a new virus called the severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) was identified as the etiological agent of the related cases, which would be later named as the coronavirus disease 2019. Rapidly progressing from a local outbreak to a pandemic scenario, by the end of November 2020, the SARS-CoV-2 infection had been diagnosed in more than 57.8 million people, with almost 50% of cases in the Americas and over 11,789,000 of them in the United States of America (U.S.A.). Until 24 November 2020, over 1,377,000 deaths happened worldwide, with 252,460 (18.3%) in the U.S.A., due to the rapid SARS-CoV-2 spread and the severity of COVID-19. Figure 1 presents an overview of the main events occurring during the year of 2020 and related to SARS-CoV-2, until the submission of this document. It comprises several key events, especially the number of deaths and the efforts made by the World Health Organization. Many physical, chemical and biological data have been predicted from structural data. For the early phases of drug design, methods have been developed that are used in all major pharmaceutical companies. However, all domains of chemistry can benefit from chemoinformatics methods; many areas that are not yet well developed, but could substantially gain from the use of chemoinformatics methods. The quality of data is of crucial importance for successful results. Computer-assisted structure elucidation and computer-assisted synthesis design have been attempted. Because of the importance of these fields to the chemist, new approaches should be made with better hardware and software techniques. Society's concern about the impact of chemicals on human health and the environment could be met by the development of methods for toxicity prediction and risk assessment. In conjunction with bioinformatics, our understanding of the events in living organisms could be deepened and, thus, novel strategies for curing diseases developed. With so many challenging tasks awaiting solutions, the future is bright for cheminformatics.

Achievements

Databases: Clearly, the most widely-accepted achievement of cheminformatics is that it provides access to chemical information in databases on a scale unattainable by working through the chemical literature. With presently 90 million known compounds, it would just be impossible to obtain an overview of the known chemistry without databases. Just to put the massive increase in chemical information in recent decades into perspective: when the present author obtained his PhD in chemistry, only 1.5 million compounds were known. Most chemical researchers take access to chemical information through databases so much for granted that they do not appreciate that databases on chemical information would not exist without research in cheminformatics that laid the foundation for such databases. Furthermore, chemists can communicate with databases in their international language, the graphical language of structure

diagrams and reaction equations. Many methods had to be developed for allowing the construction of databases on chemical information: , graphical input of chemical structures , graphical output of chemical structures , unique and unambiguous representation of chemical structures Molecules , conversion of names to structures and vice versa , ring perception , aromaticity perception , full-structure search , sub-structure search , similarity search , development of file formats for information exchange.

Different tools To investigate the arrangements of intra and intermolecular interactions in the crystal and H-bond interactions, Hirshfeld surface analysis is done. Hirshfeld surface analysis is an effective tool to study unit cell packing in crystals. Analysis is based upon 3D representation in the space region where the molecules come in contact with neighboring molecules and the 2D fingerprint plot summarizes the type of interactions between atoms. Hirshfield surface and finger print were plotted using Crystal Explorer 17. The CIF file downloaded from ccdc. Mapping of normalized contact (d_{norm}), can be expressed by the equation

$$d_{norm} = \frac{d_i - r_i^{vdw}}{r_i^{vdw}} + \frac{d_e - r_e^{vdw}}{r_e^{vdw}}$$

where r_i^{vdw} and r_e^{vdw} represent the van der Waals radii of atoms. The interactions involved in analyzed with the distance from the surface to nearest nuclei internal d_i and external to the atom

The red region in a Hirshfield surface plot represents a negative value of d_{norm} and close intermolecular interaction whereas blue region corresponds to positive value of d_{norm} and longer intermolecular interactions while the white portion depicts a zero d_{norm} value. The d_i and d_e in 2D fingerprint plot tells about type of intermolecular interactions within the molecules in crysta Density functional theory (DFT) approach B3LYP method and 6-311++G(d,p) basis set. Gaussian 03W used to perform all the calculations in this research. While some of calculations such as thermochemistry parameters at different temperatures, obtained by ORCA 4.0.1. VEDA4 software learned thoroughly used to carry out the vibrational assignments in the form of potential energy distribution. Using the optimized structure, the geometrical parameters, vibrational wavenumbers and other molecular properties like HOMO-LUMO, NBO, and MEP analyzed. Atoms in molecules theory (AIM) learned in the Multiwfn software to find the topological parameters, electron density ellipticity and electron localization function. Swiss ADME to obtain the drug-likeness nature and ADME properties of the titled molecule. Origin8.0 and Multiwfn software used to draw all the graphs in this research. Ionization potential (IP) and electron affinity (EA) have been taken according to the Koopman's theorem i.e EA= - E_{LUMO} and IP= -E_{HOMO} and with help of IP and EA the chemical reactivity descriptors are obtained by applying the following formulas:

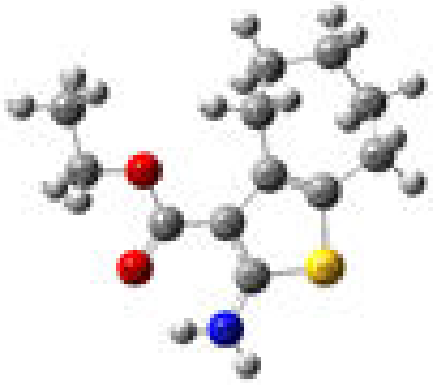
Electronegativity (χ) = $\frac{IA+EA}{2}$ Chemical potential (μ) = $\frac{-(IA+EA)}{2}$

Chemical hardness (η) = $\frac{-IA-EA}{2}$ Chemical softness (σ) = $\frac{1}{2\eta}$Electrophilicity index (ω) = $\frac{\mu*\mu}{2\eta}$

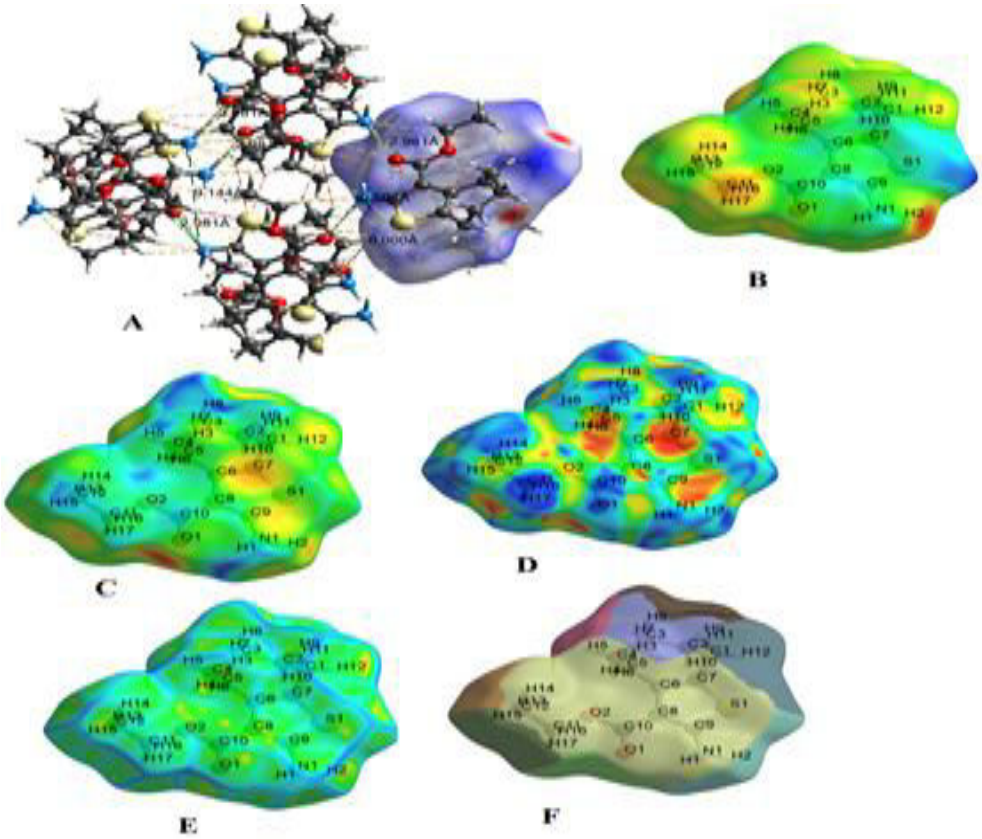
Electron density distribution (ρ^{ele}(r)) and hole density distribution (ρ^{hole}(r)) maps drawn at DFT/6-311G(d,p) with IEPCM in MeOH and DMSO solvents, at two wavelengths with high oscillatory strength, and Multiwfn, these maps show the characteristic zone that belongs to photoexcited state in comparison to ground state molecular orbital. Lu and Chen have described EDD and HDD with regards to orbital wave function (ϕ) corresponding to transition of electrons from occupied molecular orbital to (i) to a virtual molecular orbital (l) on electron excitation shown by below equations.

$$\rho^{ele}(r)=\sum_{i\to j}\left(w_i^l\right)^2\phi_l(r)\,\phi_l(r)+\sum_{i\to j}\sum_{i\to m\neq l}w_i^l\,w_i^{m2}\phi_l(r)\,\phi_l(r)$$

$$\rho^{hole}(r)=\sum_{i\to j}\left(w_i^l\right)^2\phi_l(r)\,\phi_l(r)+\sum_{i\to j}\sum_{j\neq i\to l}w_i^l\,w_i^{m2}\phi_l(r)\,\phi_l(r)$$

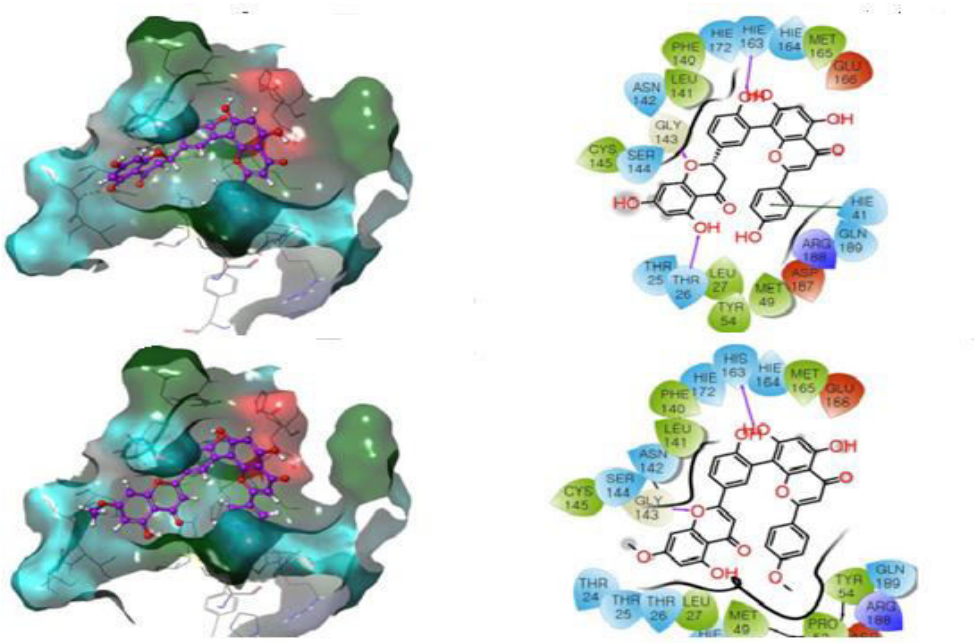


General Optimized molecular geometrical structure with atom numbering



Representation Of Hirshfeld surface mapped with d_{norm}(A), di (B), de (C), shape index (D) curvedness (E), Fragment patch (F)

Molecular docking One of the most widely used techniques for studying the structrue–activity relationship and in drug discovery is molecular docking as it gives the result with a high degree of accuracy. There is information about the strength of the low molecular weight ligand with the macromolecular targets (receptor) i.e. the binding energy and the binding site of the ligand and the macromolecule. It is very important in pharmaceutical research and development.



3D and 2D interactions of protein with ligands.

MD simulation analysis In computational drug discovery, MD simulation is used to predict the docked complexes stability and formation of intermolecular interaction in reference to time. Herein, docked complexes of respective natural compounds analyzed via MD simulation to establish the respective complexes stability and intermolecular interactions between receptor and ligand against 100 ns interval. Protein-ligand interaction mapping As hydrogen bonding properties in drug design are well known to exert strong influence on drug specificity, metabolism and adsorption; hence, intermolecular interactions, such as hydrogen bond formation, hydrophobic interactions, ionic interactions and water bridge formation information.

CONCLUSIONS

It is imperative to note that this addressed the molecular understanding of ligands thereby providing a dual target approach towards drug discovery. his computational investigation has enabled us to estimate arrays of energy components that are indeed difficult to estimate through experimental protocol. Recognition and assessment of morphological and functional interactions of chemical compounds and biological molecules is one of the most important requirements for medical research which is made easier with the advent of Cheminformatics. A developing field which is progressing rapidly in the biochemical world.

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MULTICOMPONENT REACTIONS: PERCEPTION OF GREEN SYNTHESIS IN MEDICINAL CHEMISTRY

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INTRODUCTION

Multicomponent reactions (MCRs) are one-pot, convergent chemical processes that use more than two starting components and retain a sizable amount of each starting material in the final product. This cutting-edge method has become a more effective, affordable, and environmentally friendly alternative to the traditional sequential multi-step synthesis of a variety of biologically active pharmacophores..

A product produced by multicomponent reactions contains the majority (ideally all) of the atoms of the reactants, which are at least three reactants[1] together in one vessel.[2] Their atom economy, efficiency, moderate circumstances, high convergence, concurrent step economy, and overall compatibility with green solvents would warrant a key position in the arsenal of sustainable synthesis techniques. Despite the fact that there are more and more reports of MCR applications in medicinal chemistry and drug discovery programs,[3] combinatorial chemistry,[4] natural product synthesis,[5] agro-chemistry,[6] and polymer chemistry,[7] organic chemists are still unaware of the fact that MCRs can actually solve complex chemical issues in an environmentally friendly way. Because of this, the sustainability element of this chemistry is only sporadically acknowledged and discussed in literature, despite the widespread understanding and dissemination of the chemical benefits of MCRs (convergence/divergence, diversity-oriented synthesis, library generation).[8] Thus, the purpose of this review is to highlight the advantages and disadvantages that the use of MCRs for green synthesis and process design entails.

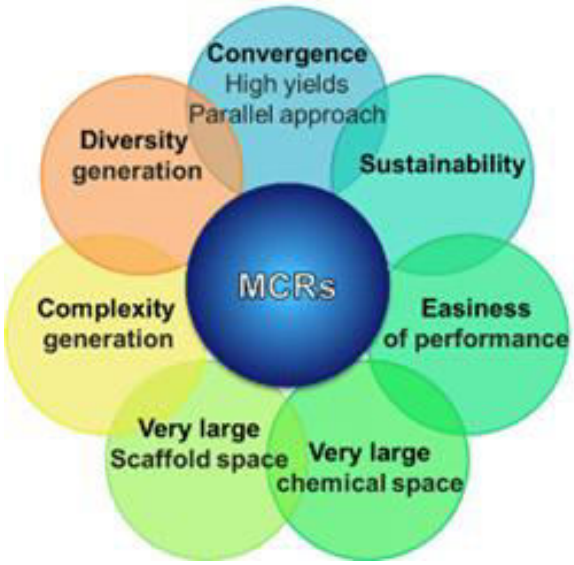


Fig-1 Basic Characteristics of Modern Multicomponent Reactions (MCRs)

Efficiency is typically thought of by synthetic chemists in terms of yield, selectivity, and number of steps. However, the green chemistry approach is much broader and takes into account standards for waste production, reagent and solvent consumption, use of potentially harmful compounds, energy intensity, and general safety. All of these requirements are compiled in the 12 principles that Anastas and Warner gives in 1998 (Fig. 2).[9]

Fig-2 General Representation of Twelve Principles of Green Chemistry

"Green chemistry is the synthesis of chemical products or processes that minimize or stop the generation of harmful compounds." Green chemistry covers all aspects of a chemical product's life cycle, including its generation, use, and final disposal.

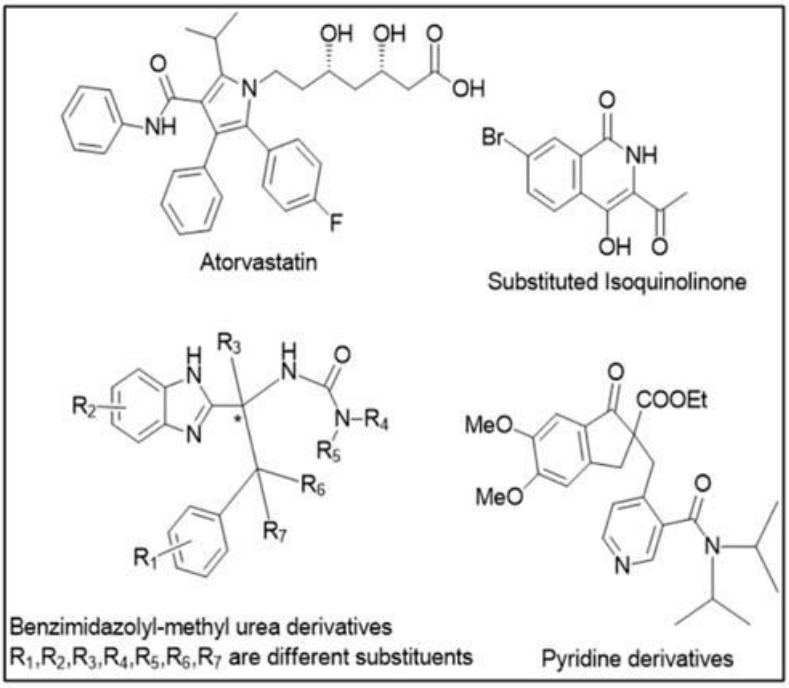
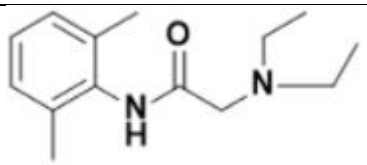
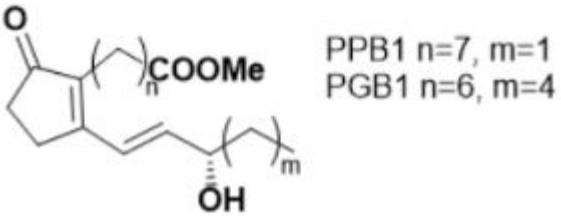
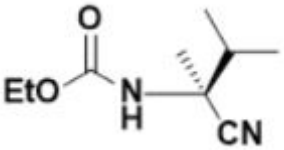
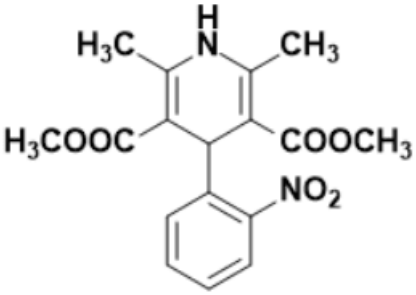
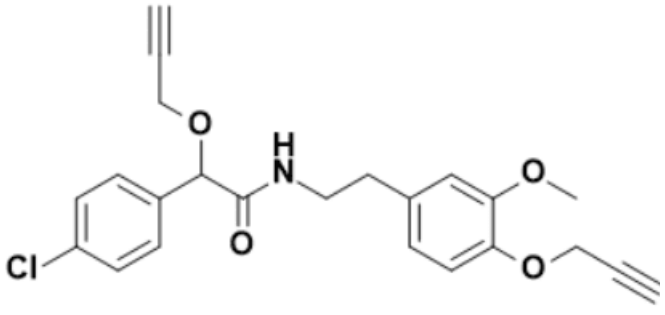


Fig-3 Structures of some scaffolds of medicinal importance [14-19]

MCRs have proven to be the best strategy for the construction of large and complex, heterocyclic structures with easy and comparatively simple steps. Numerous MCRs are well reported for the synthesis of phosphonates[10], pyrimidines[11], pyridopyrimidines [12], pyridines [13-14], pyridazines [15], quinazolinones[16] and substituted isoquinolinone and other various related derivatives[17], imidazolines[18], benzimidazolyl-methyl urea[19] and their derivatives are considered to be very important heterocycles thereby find applications in medicinal, pharmaceutical chemistry, and materials science (Fig-3).

MCRs have a vast area of applications since almost 150 years and are mostly named reactions. MCRs have proven their wide applicability in the field of chemistry with multiple commercial products in the market (Table-1) [20].

Table-1 Some Named Multicomponent Reactions (MCRs)

Named MCRs	Structure	Activity
Ugi 3CR	 Lidocaine	Local anaesthetic[20]
Pauson-Khand 3CR	 Prostaglandin B1	Antioxidant and ionophoric activities[21]
Strecker 3CR	 (S)-N-Ethoxycarbonyl-a-methylvaline	Applications in peptide-mimetics and in the de novo design of protein[22]
Hantzsch 3CR	 Nifedipine	Calcium channel blocker[24]
Passerini 3CR	 Micora	Fungicidal compound[25]

1. Waste minimization

At the single-reaction level, a typical analysis of multicomponent chemistry indicates strong conversions, outstanding selectivity (especially chemo- and regioselectivity; stereoselectivity is more difficult to achieve[26]), and nearly stoichiometric utilisation of reactants without the addition of any additives. So there is less waste in the form of unreacted raw materials and byproducts. Next, the lack of large molecular weight by-products is another inherent trait of many MCRs.

2. Atom economy

The (near-)perfect atom economy that multicomponent reactions typically exhibit makes them appropriate synthetic tools for addressing this green chemistry requirement.[27] Quantification shows that the majority of MCRs have at least 80% atom economy.

3. Less hazardous synthesis

MCRs use relatively straightforward and low-hazard reactants:

4. Safe chemicals design

The most significant use of MCRs is library generation for drug discovery and design, where the toxicity component is implicitly incorporated into the optimisation of the target molecule's function. Because of the nature of their intended use, these MCR goods are therefore secure by definition.

5. Benign solvents and auxiliaries

In 2012, a thorough analysis of the scientific community's efforts to apply MCRs in environmentally friendly solvents was conducted.[28] It is interesting to see the list of novel MCRs or improved variations that operate in fluids like water, ionic liquids, polyethylene glycol polymers (PEGs), scCO2, bio-derived solvents, and clean systems.

6. Energy efficiency

Many MCRs are enhanced by ultrasound[29] or, more recently, microwave[30] irradiations, which are energy sources that are preferable to thermal heating.[25] additionally, the successful demonstration of multicomponent chemistry's compatibility with continuous operation in microreactors brings up new possibilities for process energy intensity optimisation.

7. Renewable feedstocks

The majority of the building blocks offered are very simple, but they do show the responsiveness handles needed to allow for the construction of more sophisticated products (Fig. 4).These components are useful building blocks for molecular complexity in multicomponent processes.

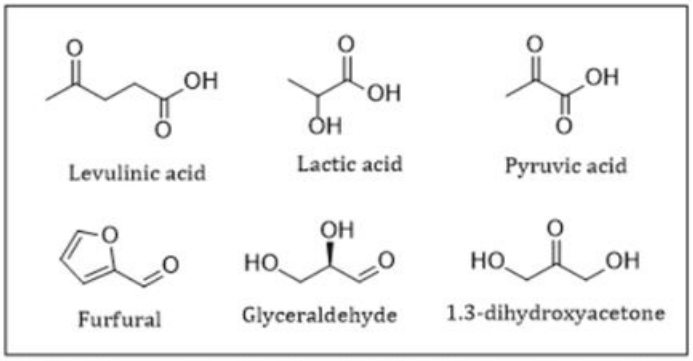


Fig-4 Renewable building blocks for multicomponent chemistry.

8. Reduced use of derivatives

It is still very difficult to completely exclude protective groups, particularly when MCR sequences are used to access high complexity products. The reaction-deprotection-cyclization (or, for Ugi-type condensations, Ugi-deprotection-cycliza- tion, UDC) strategy is a frequently employed technique in which the conflicting reactivity of a functional group in one of the MCR inputs is concealed by protection and released following the MCR as the foundation for the creation of an incredibly wide variety of useful scaffolds[28].

9. Catalysis

Some MCR classes, such as Ugi-type MCRs, can operate profitably under benign conditions without the need of a catalyst, catalysis has often proven favourable and even necessary for other reaction types. One of the most active areas of green multicomponent chemistry research is the creation of effective catalytic systems. Bronsted and Lewis acids, organocatalysts, metal complexes, heterogeneous catalysts, biocatalysts, and (magnetically recoverable) nanoparticles[116] have all been used in the catalysis of MCRs[30].

10. Design for degradation

A quick examination of common MCR products highlights their high concentration of carbon-heteroatom linkages, particularly amide and ester bonds, which are vulnerable to microbial oxidation. On the other hand, a large number of structures are (aromatic) heterocycles, which are likely troublesome for the environment in terms of biodegradability.

11. Real-time analysis for pollution control

The last two green chemistry principles are more process-focused and have the most utility in industrial settings. Real-time reactor monitoring is essential for accident avoidance and pollution control since it allows for quick response to anomalies that are detected.

12. Inherently safe chemistry for accident prevention

It is a difficult undertaking to examine every aspect of safety in a field as broad as multi-component chemistry. The use of highly toxic or corrosive reagents is only occasionally employed, automation in flow reactors with in situ monitoring is applicable, and high temperatures or pressures are not necessary. Nevertheless, reviewing the application of the previous green chemistry principles to MCRs highlights their good overall behaviour when it comes to safety.

CONCLUSION

Multicomponent reactions (MCRs) have gained renewed attention in modern organic synthesis as convergent, atom-efficient, and environmentally friendly chemical processes that allow for the quick and effective production of medicinally applicable chemical libraries made up of a variety of biologically relevant templates. In the recent years, a variety of diverse classes of compounds have been produced using this cutting-edge and practical one-pot synthesis approach in high yields for evaluation and identification as lead molecules against various biological targets and the development of novel therapeutic medicines. A variety of heterocyclic compounds with biological potential are prepared using a multicomponent reaction method. In organic synthesis, MCR has gained a lot of interest for producing highly functionalized compounds that may be tested against a variety of biological targets to identify potential therapeutic leads. In-depth research has been done on the three or four multicomponent processes to synthesis various heterocyclic compounds, examine their biological potential, and identify them as new or novel therapeutic medicines.

To provide eco-friendly chemistry, the majority of MCR reactions can be performed in a single pot without the need for a typical volatile solvent. The MCR can create libraries of compounds with a variety of functional groups for use in screening against potential biological targets with great versatility. Diversity-focused synthesis is becoming more popular.

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DESIGN, SYNTHESIS AND CHARACTERIZATION OF 3-AMINO-2H-BENZO[4,5]IMIDAZO [1,2-A]PYRAZOLO[3,4-D]PYRIMIDIN-4(10H)-ONE AND ITS N-SUBSTITUTED DERIVATIVES

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ABSTRACT
The synthesis of pyrazolo-pyrimido-benzimidazole derivatives is challenging due to the complex structure and the need for a multi-step synthetic route. However, several synthetic strategies have been reported, including the use of multi-component reactions and cyclization reactions of appropriately substituted precursors. 2-(methylthio)-4-oxo-4,10-dihydrobenzo[4,

5]imidazo[1,2-a]pyrimidine-3-carbonitrile(1) condensed with differently substituted hydrazine compounds (2) in presence of ethyl alcohol containing triethylamine to afford the corresponding 3-amino-2H-benzo[4,5]imidazo[1,2-a]pyrazolo[3,4-d]pyrimidin-4(10H)-one and its N-substituted derivatives(3a-d). The structure of compounds was confirmed by IR, ^{1}H NMR and Mass spectroscopic techniques.

Keywords: *ethyl alcohol, triethylamine, hydrazine, spectroscopic techniques.*

INTRODUCTION:
The unique structure of pyrazolo-pyrimido-benzimidazoles, which contains fused rings of pyrazole, pyrimidine, and benzimidazole, provides a rich platform for the design and synthesis of novel compounds with enhanced biological activity reported in the literature, including their anticancer, anti-inflammatory, and antimicrobial properties. The synthesis of benzimidazole derivatives has been the focus of several research studies. Various synthetic strategies have been developed to access these compounds, ranging from traditional organic synthesis methods to more advanced techniques such as microwave-assisted synthesis and green chemistry approaches. These synthetic methods have enabled the preparation of a diverse array of pyrazolo-pyrimido-benzimidazole derivatives, which have been tested for their biological activities.

MATERIAL AND METHODS
All the chemicals used in the present works are from SD-fine and Spectrochem. Melting Points of the products are determined in open capillary tubes on melting point equipment and are uncorrected. All the reactions were monitored by TLC. IR, ^{1}H-NMR and Mass spectra were recorded on Shimadzu FT-IR spectrophotometer, Bruker Avance spectrophotometer 500 MHz in DMSO-d_6 using tetramethylsilane as an internal standard and GC-MS spectrometer using the ESI technique respectively.

GENERAL PROCEDURE:
An equimolar mixture of 2-(methylthio)-4-oxo-4,10-dihydrobenzo[4,5]imidazo[1,2-a]Pyrimi

dine-3-carbonitrile **1** (0.01 mole) and substituted hydrazino compounds **2a-d** (0.01 mole) was stirred with gentle heating at 70 °C in ethyl alcohol (20 ml) containing 1 ml triethylamine till consummation of starting materials. The reaction mixture was cooled to room temperature and poured into ice cold water. After completion of the reaction, the separated solid product was filtered and then washed with water and recrystallized from Toluene/EtOAc (10:1) to get corresponding 3-amino-2H-benzo[4,5]imidazo[1,2-a] pyrazolo[3,4-d]pyrimidin-4(10H)-one and its N-substituted derivatives **3a-d.**(Scheme-I).

RESULT AND DISCUSSION

In the present work, Compound **(1)** contain bis electrophilic center which will give nucleophilic substitution with -SCH_3 group followed by nucleophilic attack of –NH- of hydrazine on the nucleophilic center of –CN to form new five-membered cyclic fused pyrazolo heterocycles (**scheme-I).** The structures of newly synthesized compounds were proved on the basis of spectral analysis such as IR, ^{1}H NMR & mass spectral data. Compounds 5a-g show the absence of IR peak in the range of 2200-2270 cm^{-1} of cyanide stretching. Carbonyl stretch occurs between 1600 cm^{-1} to 1670 cm^{-1}. ^{1}H NMR is one of the very important tools for the verification of organic molecules in that we observed the characteristic peaks from δ 6.50 to 8.70 ppm due to aromatic =C-H proton in all the structures. Similarly, -NH and -NH_2 protons show singlet between δ 3.8 to 4.2 ppm. Molecular ion peaks of mass spectra are also in good agreement with the molecular weight of structures.

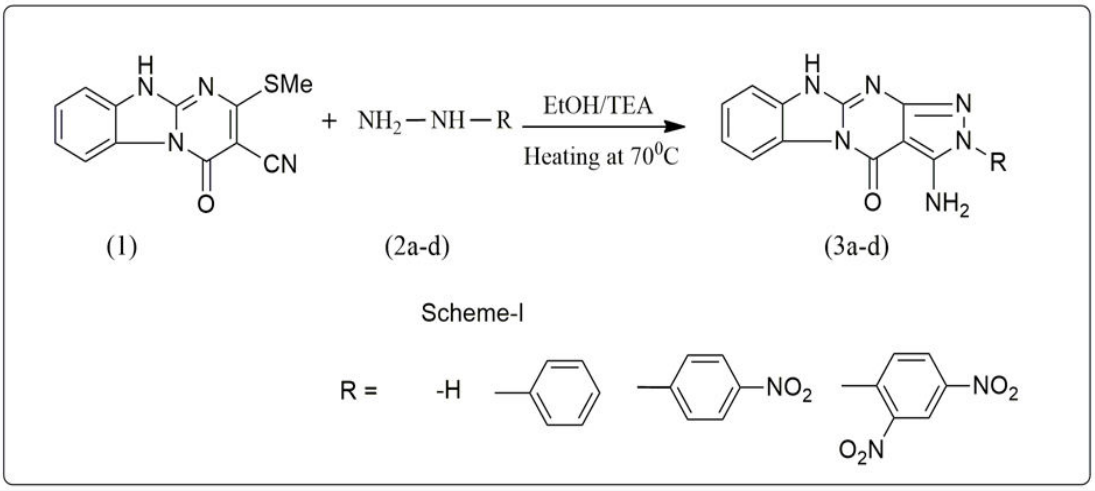
3-amino-2H-benzo[4,5]imidazo[1,2-a]pyrazolo[3,4-d]pyrimidin-4(10H)-one (3a)

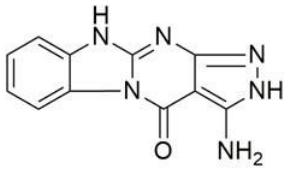
M.F C11H8N6O, IR: 3305, 3460 cm^{-1} (aromatic -NH, -NH2), 1640 cm^{-1} (-CO), 1458-1650, (aromatic C=C stretch); ^{1}H NMR : (500 MHz, DMSO) δ : 3.81 (s, 1H, aromatic -NH), 4.5 (s, 2H, -NH_2), 7.2-8.4 (m, 8H, Ar-H) ppm; Mass: m/z = 241 (M+1).

3-amino-2-phenyl-2H-benzo[4,5]imidazo[1,2-a]pyrazolo[3,4-d]pyrimidin-4(10H)-one (3b) M.F C17H12N6O, IR: 3310, 3450 cm^{-1} (aromatic -NH, -NH2), 1660 cm^{-1} (-CO), 1450-1650, (aromatic C=C stretch); ^{1}H NMR : (500 MHz, DMSO) δ : 4.0 (s, 1H, aromatic -NH), 4.5 (s, 2H, -NH_2), 7.5-8.5 (m, 8H, Ar-H) ppm; Mass: m/z = 317 (M+1).

3-amino-2-(4-nitrophenyl)-2H-benzo[4,5]imidazo[1,2-a]pyrazolo[3,4-d]pyrimidin-4(10H)-one (3c) M.F. C17H11N7O3, IR: 3330, 3470 cm^{-1} (aromatic -NH, -NH2), 1680 cm^{-1} (-CO), 1450-1600, (aromatic C=C stretch); ^{1}H NMR : (500 MHz, DMSO) δ : 3.9 (s, 1H, aromatic -NH), 4.3 (s, 2H, -NH_2), 7.0-8.5 (m, 8H, Ar-H) ppm; Mass: m/z = 362 (M+1).

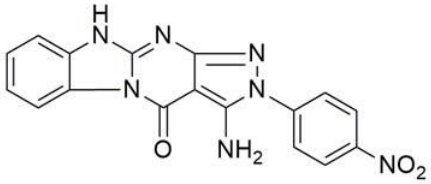
3-amino-2-(2,4-dinitrophenyl)-2H-benzo[4,5]imidazo[1,2-a]pyrazolo[3,4-d]pyrimidin-4 (10H)-one (3d) M.F. C17H10N8O5, IR: 3350, 3490 cm^{-1} (aromatic -NH, -NH2), 1670 cm^{-1} (-CO), 1470-1650, (aromatic C=C stretch); ^{1}H NMR : (500 MHz, DMSO) δ : 3.7 (s, 1H, aromatic -NH), 4.1 (s, 2H, -NH_2), 7.2-8.2 (m, 8H, Ar-H) ppm; Mass: m/z = 407 (M+1).





3a

3b



3c

3d

CONCLUSION:

Pyrazolo-pyrimido-benzimidazole derivatives are a class of heterocyclic compounds that have gained significant attention due to their diverse biological activities. A review of the literature suggests that these types of compounds have shown promising results as potential therapeutic agents for the treatment of various diseases, including cancer, inflammation, and infectious diseases. In this chapter, we have provided a one-pot synthetic transformation of such pharmacologically important compounds having pyrazolo-pyrimido-benzimidazole nucleus.

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Nrf2 AND HO-1: KEY REGULATORS OF OXIDATIVE STRESS AND CELLULAR HOMEOSTASIS

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INTRODUCTION

Oxidative stress is a natural process that occurs in the body due to normal metabolism and exposure to environmental stressors, such as radiation, pollution, and toxins. During oxidative stress, reactive oxygen species (ROS) are generated, which can damage cellular components such as lipids, proteins, and DNA, leading to cellular dysfunction, inflammation, and disease.

Antioxidant defense mechanisms are essential for maintaining cellular homeostasis and preventing the harmful effects of oxidative stress. Antioxidants are molecules that can neutralize ROS and prevent them from causing damage. The body produces its antioxidants, such as Heme oxygenase (HO-1), glutathione and superoxide dismutase, and obtains them from the diet, such as vitamins C and E, and plant-derived compounds like flavonoids.

The importance of oxidative stress and antioxidant defense mechanisms lies in the balance between their effects. While some ROS are necessary for normal cellular signaling and immune function, excessive amounts can lead to cellular damage and disease. Therefore, maintaining a proper balance between ROS and antioxidants is essential for maintaining cellular health and preventing disease. Nuclear factor erythroid 2-related factor 2 (Nrf2) and HO-1 are key players in regulating oxidative stress and maintaining cellular homeostasis.

Nrf2 activates genes (such as HO-1) involved in antioxidant defense, while HO-1 protects against oxidative stress through its antioxidant, anti-inflammatory, and anti-cell death effects. Dysregulation of Nrf2 and HO-1 has been implicated in various diseases, and ongoing research is focused on developing therapies that target these factors.

Nrf2 TRANSCRIPTION FACTOR

Nrf2 is a transcription factor critical in regulating the expression of antioxidant response genes. It is a member of the basic leucine zipper (bZIP) family of transcription factors and consists of several functional domains that contribute to its structure and function.

The Nrf2 protein contains a basic region, which binds to DNA, and a leucine zipper domain, which mediates dimerization with other bZIP transcription factors. The Neh1 domain is a transactivation domain that interacts with coactivator proteins, such as CBP/p300, to activate transcription. The Neh2 domain is a regulatory domain that interacts with the cytoplasmic inhibitor protein Kelch-like ECH-associated protein 1 (Keap1). Keap1 acts as a negative regulator of Nrf2 by promoting its ubiquitination and subsequent degradation by the proteasome. The Neh3 domain is a negative regulatory domain that interacts with the transcriptional repressor protein Bach1, which competes with Nrf2 for binding to antioxidant response elements (AREs).

Under normal conditions, Nrf2 is maintained at low levels in the cytoplasm through its interaction with Keap1. Keap1 acts as a sensor for oxidative stress and electrophiles, which can

modify critical cysteine residues on Keap1, releasing Nrf2. This results in the translocation of Nrf2 to the nucleus, where it binds to AREs in the promoter region of target antioxidant genes such as HO-1, leading to their upregulation.

In addition to Keap1, other proteins can also regulate Nrf2 activity. For example, the protein p62 can interact with Keap1 and compete with Nrf2 for binding, activating Nrf2. Additionally, the protein DJ-1 has been shown to stabilize Nrf2 and enhance its activity.

Multiple mechanisms, including post-translational modifications, protein-protein interactions, and protein turnover, regulate the activation of Nrf2 and subsequent binding to AREs.

One mechanism by which Nrf2 activates gene expression is through its interaction with coactivator proteins, such as CBP/p300. These coactivators interact with Nrf2 through the transactivation domain, Neh1, and help to recruit other proteins involved in transcriptional activation, such as RNA polymerase II. This interaction is critical for the upregulation of Nrf2 target genes.

Another mechanism by which Nrf2 activates gene expression is through its interaction with histone acetyltransferases (HATs) and histone deacetylases (HDACs). Nrf2 has been shown to interact with HATs, such as p300/CBP, which acetylate histones, leading to a more relaxed chromatin structure that facilitates transcription. On the other hand, Nrf2 has also been shown to interact with HDACs, such as HDAC3, which deacetylate histones, leading to a more condensed chromatin structure that represses transcription. These interactions with HATs and HDACs play a critical role in regulating Nrf2 target gene expression.

Post-translational modifications, including phosphorylation, acetylation, and ubiquitination, also regulate nrf2 activation. These modifications can affect the stability, localization, and activity of Nrf2. For example, phosphorylation of Nrf2 at specific sites by protein kinases, such as PKC and ERK, has enhanced Nrf2 activity by promoting its nuclear localization and preventing its degradation by the proteasome. Similarly, acetylation of Nrf2 by HATs, such as p300/CBP, has enhanced Nrf2 activity by promoting its binding to AREs and increasing its stability. Conversely, ubiquitination of Nrf2 by Keap1 and subsequent degradation by the proteasome leads to the downregulation of Nrf2 target genes.

Dysregulation of Nrf2 can lead to serious consequences for cellular function and various diseases, including cancer, neurodegenerative diseases, cardiovascular disease, and liver disease. Mutations in the Keap1 gene can increase Nrf2 stability, resulting in upregulated cell proliferation and resistance to chemotherapy in some cancers. Nrf2 also plays a crucial role in maintaining neuronal function and protecting against oxidative damage in neurodegenerative diseases. Nrf2 protects against oxidative stress and inflammation in cardiovascular disease and liver disease. Novel therapies targeting the Nrf2 pathway could be developed for treating these conditions.

HO-1 ANTIOXIDANT

Heme oxygenase-1 (HO-1) is an enzyme critical in cellular defense against oxidative stress. HO-1 is a member of the heme oxygenase family of enzymes, which catalyzes heme degradation to biliverdin, carbon monoxide (CO), and free iron. Biliverdin is rapidly converted to bilirubin, a potent antioxidant, by biliverdin reductase.

The structure of HO-1 is composed of a catalytic domain containing a heme-binding pocket, which is critical for the protein's enzymatic activity. The protein also contains several regulatory domains, including a basic helix-loop-helix (bHLH) domain, a leucine zipper (LZ) domain, and a nuclear localization signal (NLS) sequence, which play important roles in the regulation of HO-1 expression.

Several factors, including oxidative stress, inflammation, and growth factors, regulate HO-1 expression. The transcriptional regulation of HO-1 is primarily controlled by the transcription factor Nrf2, which binds to the antioxidant response element (ARE) in the promoter region of the HO-1 gene.

In addition to Nrf2, several other factors, including mitogen-activated protein kinases (MAPKs), hypoxia-inducible factor 1 (HIF-1), and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), can also regulate the expression of HO-1 in response to various stimuli.

HO-1 is a critical component of the cellular antioxidant defense system and protects against oxidative stress through several mechanisms:

Bilirubin production: The primary product of HO-1 activity is biliverdin, rapidly converted to bilirubin by biliverdin reductase. Bilirubin is a potent antioxidant that can scavenge reactive oxygen species (ROS) and protect against oxidative stress.

CO production: HO-1 activity also produces carbon monoxide (CO), which has been shown to have cytoprotective effects through several mechanisms, including the activation of guanylate cyclase, the inhibition of apoptosis, and the suppression of inflammation.

Iron regulation: HO-1 activity releases free iron from heme, which can be beneficial and detrimental to cells. Iron can participate in Fenton reactions, leading to the generation of ROS and oxidative damage. However, iron can also be sequestered by ferritin, which can protect against oxidative stress.

Anti-inflammatory effects: HO-1 can also have anti-inflammatory effects by suppressing pro-inflammatory cytokine production and modulating immune cell function.

Autophagy Regulation: Recent studies have suggested that HO-1 can regulate autophagy, a cellular process that plays an important role in maintaining cellular homeostasis and eliminating damaged organelles and proteins. HO-1 can modulate autophagy by regulating key signaling pathways, including AMP-activated protein kinase (AMPK) and the mammalian target of rapamycin (mTOR).

Given the cytoprotective effects of HO-1 against oxidative stress and inflammation, there is growing interest in exploring its potential therapeutic applications in various diseases. In cardiovascular disease, HO-1 can protect against oxidative stress, inflammation, and improve cardiac function. HO-1 is also implicated in regulating tumor growth in cancer, with complex effects depending on the specific type and stage of cancer. In neurodegenerative diseases, HO-1 may protect against neuronal damage through modulation of oxidative stress, inflammation, and protein aggregation. HO-1 is also protective in organ transplantation by reducing ischemia-reperfusion injury, inflammation, and oxidative stress. Finally, HO-1 may have therapeutic potential in autoimmune diseases by reducing inflammation and promoting immune tolerance.

Nrf2 and HO-1 in Disease:

Nrf2 and HO-1 play critical roles in various disease states through their ability to modulate oxidative stress, inflammation, and cellular homeostasis. Here is an overview of their roles in some specific diseases:

Diabetes: Oxidative stress is a key contributor to the pathogenesis of diabetes, and both Nrf2 and HO-1 have been shown to play important roles in protecting against diabetic complications. Nrf2 activation has been shown to reduce diabetic nephropathy, neuropathy, and retinopathy. HO-1 overexpression has also improved glucose homeostasis and reduced diabetic complications in animal models.

Cancer: Dysregulation of Nrf2 and HO-1 has been implicated in cancer development and progression. Nrf2 activation has been shown to promote tumor cell survival and resistance to chemotherapy and radiation therapy in some cancer types. However, Nrf2 activation may also have anti-tumor effects by reducing oxidative stress and inflammation. HO-1 has been shown to have complex effects on cancer development, with some studies suggesting that it may promote tumor growth and others suggesting that it may have anti-tumor effects.

Neurodegenerative diseases: Oxidative stress and inflammation are key contributors to the pathogenesis of neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, and Huntington's disease. Nrf2 activation and HO-1 overexpression have both been shown to have neuroprotective effects in these diseases by reducing oxidative stress, inflammation, and protein aggregation.

Cardiovascular disease: Oxidative stress and inflammation play critical roles in the development of cardiovascular disease. Nrf2 and HO-1 have been shown to have protective effects in cardiovascular diseases, including atherosclerosis, myocardial infarction, and heart failure. Nrf2 activation has been shown to reduce vascular inflammation and improve endothelial function, while HO-1 overexpression has been shown to reduce atherosclerosis and improve cardiac function.

Continuing research on the involvement of Nrf2 and HO-1 in different diseases has led to several promising discoveries and potential directions for future research. Some examples of ongoing research include investigating the mechanisms by which Nrf2 and HO-1 are involved in cancer, neurodegenerative diseases, and cardiovascular disease. Clinical trials are also evaluating the safety and effectiveness of Nrf2 activators and HO-1 inducers as therapeutic agents in these diseases. Additionally, research is exploring the roles of Nrf2 and HO-1 in other diseases, such as liver disease and pulmonary fibrosis, and developing novel activators and inducers to target these pathways for therapeutic purposes. As such, there is a growing interest in better understanding the functions of Nrf2 and HO-1 in disease and developing effective therapeutic strategies for managing them.

CONCLUSION

Oxidative stress occurs when an imbalance between reactive oxygen species and the body's defense system damages cells and their normal functions. Two important factors involved in managing this stress are Nrf2 and HO-1. Nrf2 is a type of protein that helps protect the body against oxidative stress by activating genes involved in antioxidant defense. HO-1 is an enzyme that helps to protect the body against oxidative stress through its antioxidant, anti-inflammatory,

and anti-cell death effects. When either Nrf2 or HO-1 are not working correctly, this can contribute to various diseases, including diabetes, cancer, and heart disease. Researchers are currently studying how to activate these factors and use them to treat disease alone or in combination with other therapies.

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