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Water Management – A Need of Hour

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Abstract:

Water is life for every living being on this earth. Water is called as 'life' in our culture. Without water life cannot survive on the earth. Every living being on the earth requires water in sufficient quantity. Whether it would be animals, birds, insects, algae, fungi etc. It's clear that everything that exists has a specific life span and everything that exists needs water.

Water is a nature's gift to living being. But it is observed thatpeople do not utilize water in an efficient way. As compare to foreign countries Indian people do not utilize water judiciously and the proportion of wastage is also high in India. So, it is need of hour to make region wise planning for water management and to improve awareness of water among people to take care the most useful nature's resource.

Introduction:

We cannot imagine Life on earth without water. Human being cannot survive without water for a single day. In our routine activities water is essential natural ingredient. Water is important raw material for living being. Water is a renewable resource of nature. From the existence of earth living being has able to survive on this planet due to water and still living being has been existed on earth.Water is available on earth in huge quantity and human being is large consumer of water on the earth. Water is available onearth in all forms i.e. liquid, gaseous, and solid. Demand for liquid form is more than gaseous or solid that is why water is called as 'liquid Gold.' Man can survive for 5 weeks without food but maximum 5 days without water. Man needs about 150 to 300 liters of water per day. Generally man requires water for his daily necessity i.e. drinking, cooking, washing utensils, bathing, flushing toilets, air cooling, gardening etc. municipal or civic purposes such as road washing, cleaning public lavatories, large markets and sewers and ornamental purposes of gardens, lawns, fountains, artificial waterfalls etc.; firefighting and industrial purposes such as power plants, refineries and steel, aluminum, glass, soap, fertilizer and paper manufacturing units.Animals or birds use water for drinking and bathing purposes. It means the requirement of water is unlimited and man is only large consumer of water.

India ranks second in world which receives maximum rainfall. Still there is scarcity of water in our country. The statement that 'water is available in much more quantity' is vague. What is required to do is efficient management of water is a need of hour. As compared to foreign countries Indian people do not judiciously make use of water. This happens because there is not much awareness in Indian people about the usefulness of water, just the mentality of Indian people is that water is available in our country in huge quantity.

Concept of Domestic Water Management:

Earth is the only planet of the solar system that is supporting life for ages just because of availability of water. Fresh water is a precious substance and availability of fresh water is rare thing on the planet though it is available in huge quantity on earth. But the reality is that only 3.5 per cent of the world's water is fresh i.e. in drinkable form and out of this 68% fresh water is trapped in ice and glaciers. Remaining 96.5 per cent water is salty and it cannot be drin. The population explosion witnessed in the latter half of the last century and the demand from various sectors of fresh water is increasing day by day. At one side the rising demand of fresh water and the explosion of population are putting pressure on available fresh water of the world. India has 17.7 per cent of the total population of the world.[5] But, the country has only 4 percent of the water resources present on the earth.

Day by day it is very hard to find fresh water due to pollution and increasing demand of water by various sectors i.e. industrial sector, agricultural sector, and domestic purpose. There are lot of physical and economic aspects of considering domestic water management aspect. In India out of more than 3000 towns, hardly 2000 towns have an organized water supply facility available at their town. Coverage of water supply in urban as well as rural sectors needs to be augmented. At present there is low daily per capita supply, inefficient distribution, high leakage and ill managed systems. In rural sector progress in water supply has been very slow. There are about six

lakh villages involved and which account for our 76 per cent population.

One in every seven persons on this planet lives in India. Today there is widespread realization that there can be no readymade solutions, that technology alone cannot solve problems, that we have to use all our ingenuity to find solutions which combine the best of the old practices with the benefits that modern science and technology can offer.

Objectives:

1) The objective of the study is to create awareness and importance of water among people
2) To develop the habit of reusing of waste water
3) To improve the ability of soil to hold water
4) To provide measures to re-fill the ground water level

Methodology:

The study is based on secondary source of data. The required data has been collected from various Muncipal Councils of Nanded District from their maintained books and records.

Measures to manage water in effective way: Following effective measures should be taken while using the precious substance of earth.

1. For kitchen particularly, careless wastage of water should be stopped and awareness should be created amongst the human about the value of water. So we should not use water more than what is actually required. Modern cooking systems like use of pressure cookers can save more than 25% of water.
2. In our routine kitchen activity water is mostly used for cleaning utensils, wiping floors, washing cloths, etc. So water should be judiciously used. Washing every second day in washing machine saves upto 130 liters of water (full load and half load takes the same quantity of water). By washing clothes in a wash tub instead of under a running tap saves around 200 liters of water.
3. Brushing teeth, washing hands, washing face can be done by taking water in a tumbler instead of running the tap for 5 to 10 minutes.
4. Instead of throwing the stored water (as people have tendency to store fresh water daily) can be used for washing, gardening, cleaning vehicles, cleaning floors and walls or can be used for toilets.
5. Washing vehicle can be done by taking two buckets of water instead of by using a running tap/pipe. Similarly, sprinkling water in the ground with mug instead of pipe will also save water.
6. The water remains after washing and rinsing of clothes and cleaning of utensils. These water should be stored and maybe used for flushing purposes.
7. Indian statistics show that 46.18% of agricultural laborers are constituted by women work force. Even in cultivators, females representation is almost equal or slightly less than males in many states, water being one of the major inputs utilized for crop production, judicious handling of water can definitely pave a tremendous breakthrough in optimum utilization of water.

Awareness programs sought for water protection and conservation:

The environmental scenario of India is very wide. Ours is a country highly diverse climatically, geologically, geographically, socially and economically. Therefore, awareness programs should be location specific. First we should concentrate on school going children and household women. Because children's are the future of country and they should know the importance of water. So, these can be possible by educating women of rural and urban areas. Women are the first source who can imbibe the importance of water on children's mind. Children's are to be made aware of health, diseases from water, conservation of water, protection of water resources, water and food contamination, refilling of wells and lakes. Non-government organizations have to play a significant role. In the directory of the Department of Environment, there are more than 200 non-Governmental organizations of which nearly 150 work in the area of environmental education and awareness. Moreover, children are to be told the real meaning of environment and the other associated factors which are really very close to water or which directly a causes of water pollution.

I) **Formal Environmental education:**Chief goals of environmental education should be:

- To improve the quality of environment
- To create an awareness among the people on environmental problems and water conservation
- To create an atmosphere so that people participate in decision making and develop the capabilities to evaluate the developmental programmes
- Design a syllabi for school going children from I[st] standard so that they can understand the importance of water from early childhood

II) Non-formal environmental education:
It is designed for any age group, working in social, economic, and cultural development of the community; they form groups of clubs and arrange exhibitions, public lectures, meetings, road showsand environmental campaigns at rural and urban regions.

Conclusions and recommendations:

Water is renewable resource it can be recycled by natural process. One of the main method is that it can be renewed by rain. Expanding human population resulted into expanding needs of man. With scientific progress and technological development man started utilizing natural resources at a much larger scale. Continuous increase in population caused an increasing demand for natural resources. This created a situation when the non renewable resources may come to an end after some time. As a result we would be using all those resources which are in fact the property of future generation. It is a matter of much concern. There must be some sort of balance between the population growth and the utilization of natural resources.

1. **Recycling and reuse of Municipal and industrial waste water:**
'Recycling' means internal use of water by the original user prior to discharge. While 'Reuse' refers to wastewater that is discharged from municipalities (75%), industries and irrigation are withdrawn by users other than dischargers. After treatment, reclaimed waters are diverted for irrigation. It is clearly evident in big cities like Delhi where the water scarcity is acute; the municipal sewage water is utilized for irrigating vegetable crops.
2. **Improving water use efficiency (UWE) through better technology:**
Agriculture sector consumes more than 85% of total water in the country. If we are able to save 7% of it, we will able to meet domestic and industrial demand. Hence it is imperative to adapt less water consuming or water saving methods of irrigations with an aim of producing more crops per drop. Such methods include micro irrigation (Drip, sprinkler, bubbler, spray and indigenous drip irrigation) methods. Farming In Israel was not an easy, but their farmers have developed various techniques by which the production of crops has increased drastically and now the country is exporting the farm products worldwide. Actually Israel is a desert land but the efficient and sustainable techniques innovated by their scientist and awareness regarding the techniques created amongst the farmers. Finally farmers adopted it in their farming activities.
3. **Rainwater harvesting:**
Rainwater harvesting is again the need of hour. It is a technique of collecting and storing of rain water. Rainwater is collected from the roof, or flat surface area and redirected to a tank, cistern, deep pit such as well, or borehole, aquifer, or a reservoir. So it can seeps down and restores the ground water. This will help to increase the ground water level, which came down drastically in last few decades.
4. **Tree Plantation:**
The habitant of villages, towns and cities should plant more and more trees in their nearby areas. There is a direct relation between tree plantation and water. The tree roots help in compacting the soil. The soil can store more significant quantities of water in it, which will increase the volume of groundwater level in their region. If soil erosion in any region is stopped, the water will automatically stop flowing to river.

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ग्रंथकार प्राध्यापकांच्या लेखनकार्यात महाविद्यालयीन ग्रंथालयाची भूमिका

संशोधक विद्यार्थी
प्रा. सदाशिव बाळासाहेब वरवटे
स्वामी रामानंद तीर्थ मराठवाडा विद्यापीठ,नांदेड

संशोधक मार्गदर्शक
डॉ. शिवाजी नारायणराव सोनटक्के
उपप्राचार्य, ग्रंथपाल कै. रसिका महाविद्यालय, देवणी
ता. देवणी जि.लातूर

सार :

प्रस्तुत शोध निबंधात ग्रंथकार प्राध्यापकांच्या लेखन कार्यातील महाविद्यालयीनग्रंथालयाची आवश्यकता व भूमिका काय असते. ग्रंथालय व माहिती सेवा केंद्र देत असलेल्या सेवा यावरच ग्रंथकाराचे किंवा उपभोक्त्यांचे समाधान अवलंबून असते. उपभोक्त्यांच्या माहिती विषयक गरजांचा शोध घेतल्याशिवाय त्यांच्या गरजांचे काटेकोरपण विल्षेशन केल्याशिवाय माहिती सेवांचे योग्य प्रकारे नियोजन केले जाते. कोणतेही लेखकार्य पूर्णतः नविन नसते त्याला आधार घ्यावा लागतो या आधाराचा शोध घेवून ग्रंथकार आपले लेखकार्य करीत असतो. हे कार्य गुणवत्ता पूर्ण होण्यासाठी त्यांना अद्यावत मुळस्त्रोतांचा वापर करणे गरजेचे आहे. यासाठी ग्रंथकारांना ग्रंथालयाकडून निशुल्क किंवा शुल्कासह विविध सेवा उपलब्ध झाल्यास त्यांचे लेखनकार्य पूर्ण करता येते. त्यासाठी त्यांना ग्रंथालयाची भूमिका महत्वाची ठरते.

शोधसंज्ञा : ग्रंथकार, प्राध्यापक, लेखनकार्य, ग्रंथालय, ग्रंथालयाची भूमिका.

आज माहिती तंत्र ज्ञानामध्ये प्रचंड प्रगती झाली आहे. या प्रगतीमध्ये ग्रंथालयाचाही समावेश आहे. समाजातील माहिती व तंत्रज्ञानाच्या गरजा वाढू लागल्या या गरजा भागवण्यासाठी ग्रंथालय आपल्यामध्ये बदल घडवून आणत आहेत. यामध्ये ग्रंथालय संगणकीकरण,Digital Library,Virtual Library असा बदल ग्रंथालयाने स्विकारला आहे. ग्रंथालयाचा विकास हा प्रामुख्याने ग्रंथालयाचे महत्व, योगदान यावर अवलंबून असतो. त्यामध्ये ग्रंथालय २१ व्या शतकामध्ये वाचकांच्या गरजा सक्षमपणे पूर्ण करण्याचा प्रयत्न करत आहेत. उपभोक्त्यांना आवश्यकते नुसार अद्यावत माहिती पुरवावयाचे काम ग्रंथालय करत आहेत. अशी अद्यावत व उपयुक्त माहिती ग्रंथालय ग्रंथपाल प्राध्यापकांच्या लेखनकार्यात आवश्यक असणारी ही माहिती देण्याचा प्रयत्न करते. अशी माहिती ग्रंथकार प्राध्यापकांना कशा पध्दतीने उपयुक्त ठरते किंवा त्या माहितीची लेखनकार्यात काय भूमिका आहे हे या शोध प्रबंधामध्ये स्पष्ट केले आहे.

शोधसंज्ञा व्याख्या :

ग्रंथकार:

"अशी व्यक्ती कीजी ग्रंथातील बौद्धिक मत प्रदर्शनास किंवा कलात्मक निर्मीतीस प्रामुखाने जबाबदार आहे" उदा. ग्रंथाचा लेखक हा त्या ग्रंथाचा ग्रंथकार आसतो.

प्राध्यापक

प्राध्यापक म्हणजे विद्यापीठाच्या कोणत्याही संचलित सलग्न किंवा स्वायत्व महाविद्यालयातील, स्वायत्त परिसंस्थेतील किंवा विभागातील मान्यताप्राप्त प्राध्यापक, सहयोगी प्राध्यापक सहायक प्राध्यापक, प्रपाठक, ग्रंथपाल, संचालक शारिरिक शिक्षक होय.

लेखनकार्य :

एखाद्या समस्ये संबंधी किंव एखाद्या परिस्थिती संबंधीत वस्तुनिष्ट लेखन केले जाते, तसेच एखादा विशिष्ट हेतू डोळयासमोर ठेवून माहितीचे संकलन केले जाते त्यास लेखनकार्य असे म्हणतात.

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ज्या ठिकाणी ग्रंथाचा संग्रह करून त्याची सुसंगत पध्दतीने मांडणी केली जाते यासर्व संग्रहाची व्यवस्था व संघटन केले जाते व या संग्रहाचा जास्तीत जास्त उपयोग करावा म्हणून प्रयत्न केला जातो अशा ठिकाणास ग्रंथालय असे म्हणतात.

ग्रंथालयाची भूमिका :

सर्वसाधारणपणे ग्रंथालय ही सामाजिक सर्जनशिलतेमध्ये महत्वाची भूमिका पार पाडतात आणि यामूळे ग्रंथालय ही व्यक्तिगत तसेच सामाजिक प्रगतिसाठी मदत करतात. या सर्वामुळे ग्रंथालयांना सामाजिक संस्था असे संबोधले जाते. ग्रंथालयाची भूमिका वाचकांना उपयुक्त सेवा प्रदान करून ज्ञान विकास करण्यास मदत करण्याची आहे. तसेच वैयक्तिक आणि सामाजिक प्रश्न सोडवण्यासाठी ग्रंथालयीन वाचन साहित्याचा उपयोग केला जातो.

ग्रंथकार प्राध्यापकांचे लेखनकार्य :

अ. ग्रंथलेखनकार्य

- पाठ्पुस्तक
- संदर्भग्रंथ
- संपादित ग्रंथ
- इतरग्रंथ

ब. संशोधन विषयक लेखनकार्य :

- संशोधन प्रकल्प
- शोधनिबंध
- शोधप्रबंध
- पी.एचडी
- एम.फिल
- मेजर रिसर्च प्रोजेक्ट
- मायनर रिसर्च प्रोजेक्ट

क. वृत्तपत्र व नियतकालिकेतील लेखकार्य

ड. सोशल मिडियातील लेखकार्य

- फेसबुक
- ब्लॉग
- व्हॉट्सअप
- ट्विटर

ग्रंथकारांच्या लेखनकार्यात ग्रंथालयाची भूमिका :

स्वातंत्र्यापूर्वी कालखंडात पाहिले जाते की, समाजप्रबोधनाचे काम हे प्रामुख्याने लेखक किंवा ग्रंथकारांनी केलेले दिसून येते पण त्यांच्या लेखकार्यास धार देण्याचे काम हे नेहमी ग्रंथालयाने केल्याचे आपणास दिसते ग्रंथालयाच्या उगमापासून ते आजपर्यंतचा इतिहास पाहिला तर आपणास असे पाहण्यात येते की, लेखन वाचकांचे मनोरंजन त्यांच्या व्यक्तिमत्व विकास आणि नवनविन शोध लावले जातात. ग्रंथकाराच्या लेखनाद्वारे घेतलेल्या माहितीच्या आधारे त्या समस्या जाणून घेवून त्यावर उपायोजना करण्याचे कार्य हे लेखनामुळे शक्य आहे असे लेखनकार्य वाढवण्यासाठी ग्रंथालयाची भूमिका अनन्य

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साधारण आहे. आजच्या माहिती तंत्रज्ञानाच्या युगामध्ये, लेखनकार्यात ग्रंथालय किती सक्षमपणे सेवा सुविधा देत आहेत व त्या सुविधा बाबतच्या समस्या जाणून घेणे हे या शोध निबंधाचे महत्व आहे.

लेखनकार्य व ग्रंथालय :

ग्रंथकारास त्याचे लेखनकार्य करत असताना वेगवेगळया परिस्थितीत ग्रंथालयाची आवश्यकता भासत असते अनेक प्रकारच्या संदर्भाची आवश्यकता, ती गरज ही केवळ ग्रंथालयच पूर्ण करू शकते. त्याचबरोबर ग्रंथकाराच्या मनात अनेक प्रश्न व विचार निर्माण होतात. त्या प्रश्नाची व विचारांची पूर्तता किंवा उत्तरे त्यांना केवळ ग्रंथालयातच प्राप्त होवू शकतात. ग्रंथकारास आवश्यक संदर्भग्रंथ किंवा संदर्भ ग्रंथाची पूर्तता ग्रंथालय करते त्यामुळे ग्रंथालयाची वेगळी भूमिका लेखनकार्यात दिसून येते.

ग्रंथपाल एक माहिती अधिकारी :

ग्रंथपालनाच्या व्यवसायात कार्यरत असताना अनेक ग्रंथकार, संशोधक, विद्यार्थी या वेगवेगळया वाचकांच्या संपर्कात आल्यामूळे त्यांच्याशी होणाऱ्या चर्चा या अनुशंगाने त्यांच्या विषयाशी होणारा परिचय, विविध विषयांशी नवनविन ज्ञान इत्यादी गोष्टीचा नित्यनियमाने येणारा संबंध यामुळे ग्रंथपालास संशोधनाची दृष्टी प्राप्त होते. त्यामुळे ग्रंथपालास माहिती अधिकाराचा दर्जा प्राप्त होवून त्याच्या ज्ञानाचा फायदा ग्रंथकारांना घेता येईल.

लेखनकार्यास पूरक वाचन साहित्याचा शोध :

सध्या माहिती तंत्रज्ञानाच्या युगात माहितीच्या विस्फोटामुळे योग्य व उपयुक्त, परिपूर्ण माहिती प्राप्त करणे ग्रंथकारास कष्टप्रद वाटते. जुने ग्रंथ, नियतकालिके, संदर्भग्रंथ अशा विविध प्रकारचे वाचनसाहित्य ग्रंथालयात उपलब्ध असते. अशावेळी नेमकी आणि महत्वाची माहिती ग्रंथकारास हवी असते. तसेच ग्रंथकारास लेखनकार्यास पुरक असणारी व ग्रंथलयात उपलब्ध नसलेले वाचन साहित्य उपलब्ध करावयाचे असेल अशा अनेक प्रकारच्या वाचन साहित्याचा शोध घेवून ते उपलब्ध करून देण्याचे क्षमता ग्रंथपालाच्या अंगी असल्याने ग्रंथकारास वाचन साहित्याचा शोध घेण्यास प्रत्यक्ष किंवा अप्रत्यक्षपणे ग्रंथालय भूमिका बजावतात

लेखनकार्यात सहकार्य :

ग्रंथकार ज्यावेळी प्रत्यक्ष लेखनकार्यास सुरूवात करतो त्यावेस ग्रंथलेखनपर, संशोधन स्वरूपाचे असते. अशावेळी त्यांच्या त्या स्वरूपावरून त्यांना ग्रंथालय सहकार्य करते. ग्रंथ, संशोधन प्रकल्प, प्रबंध अहवाल यांचा एक ठराविक आराखडा असतो. त्या चौकटीत राहूनच लेखनकार्य करावे लागते. संदर्भ देण्याच्या पध्दती, तळटीप देण्याच्या पध्दती, सूची सादर करण्याच्या प्रमाणक पध्दती याबाबत ग्रंथकारास फारसे माहित नसते. फोटो, मुळप्रतीचा दाखला, आलेख, नकाशे, चित्र–रेखाटणे इत्यादीचा वापर करावा लागतो या सर्वांचा नेमके कुठे समावेश करायचा याबाबतही ग्रंथकारास ग्रंथालयाची मदत होते.

पेटन्टस्, कॉपीराईट्स, ट्रेडमार्क इत्यादी संबंधी मार्गदर्शक :

लेखक लेखनकार्याच्या स्वामित्व हक्कासंबंधीचे कायदे याबाबत बऱ्यापैकी अनभिज्ञ असतात. आपल्या लेखनकार्याविषयी कोणती कायदेशिर काळजी घ्यावयाची असते पेटन्टस्, कॉपीराईट्स, ट्रेडमार्क यासारख्या कायद्याविषयी ग्रंथकारास ग्रंथालयातून मार्गदर्शन होते.

समारोप :

प्रस्तुत शोध निबंधात ग्रंथकार प्राध्यापकांच्या लेखन कार्यातील महाविद्यालयीनग्रंथालयाची आवश्यकता व भूमिका काय असते. ग्रंथकाराचे लेखनकार्य यशस्वी होण्यासाठी ग्रंथालयाचे किती व कसे महत्व आहे याविषयी चर्चा करण्यात आलेली आहे. ग्रंथकाराला ग्रंथालय व ग्रंथपाल यांच्याकडून त्यांच्या लेखनकार्यासाठी कसे मार्गदर्शन ठरू शकते या बाबतही विवेचन करण्यात आले आहे.

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Physico-Chemical Study Of Harsool Dam, Aurangabad, (M.S.) India.

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Abstract:

Water is one of nature's most amazing compounds, made up of two common elements: hydrogen and oxygen. Water plays a vital role in environmental ecosystems. It acts as a universal solvent for many more compounds than any other liquid and provides ionic balance and nutrients that sustain life. The assessment of water quality generally includes the analysis of physicochemical and biological parameters and reflects the abiotic and biotic state of the ecosystem. Freshwater quality is usually necessary to stabilize baseline conditions, establish quality standards, and monitor the aquatic environment. Changes in the aquatic environment due to anthropogenic contamination are increasing concern and require monitoring of surface waters and the organisms that live there. The present study deals with assessing the water quality, seasonal variations, and Correlation between parameters of Harsool Dam at Aurangabad [M.S.] India. The Physico-chemical characteristics were studied and analyzed from July 2008 - June 2009. The results revealed that the condition of these dam in various seasons concerning the parameters.

Keywords: water quality, seasonal variations, and Harsool Dam

INTRODUCTION

In many countries, water scarcity is becoming a growing obstacle for household supplies and economic activity in general. Water drawn from upstream water makes downstream water so scarce that some industries are forced to limit their activities seasonally. With the expansion of trade, irrigation, and people, the economic and ecological costs for investments in additional water supply also increase. Access to clean water remains an urgent human need in many countries. Part of the problem is pollution. Diseases that are overcome mainly by installing adequate water and sanitation systems cause enormous human suffering. The problem is exacerbated in some places by increasing water scarcity, making it difficult to meet growing demand. Dams are an inseparable part of our society and are built for various reasons, such as irrigation, energy production, industrial supplies, and clean water at increasing cost (Collier et al., 1998).

A reservoir, also called an artificial lake, is an artificial body of water created by the dam of a river. Several studies have carried out the changes in the biotic and abiotic factors of the river after the dam's construction. However, the reactions of waterways and river ecosystems to dams are complex and varied because they depend on supply. In local sediments, geomorphic restrictions, climate, dam. Structure, function, and critical attributes of Biota. Therefore, universal regulations cannot replace local knowledge by developing rules for the construction and operation of dams to protect local biodiversity (Power et al., 1996).

Point contamination is easy to identify and correct. Environmentally friendly sources of pollution, such as agricultural runoff and mine drainage, are more challenging to identify and control than those of municipalities or industries. Thermal infection occurs when the industry returns heated water to its source. Changes in water temperature can change the type and number of plants and animals in the area. Methods for controlling thermal contamination include cooling ponds, cooling towers, and dry cooling towers. The problem with water is often pollution. Pollution is caused by old lead pipes and solders that have been used in sanitary systems for years. Some bottled water contains many of the same contaminants found in tap water doses (Enger and Smith, 1995). In many cases, the cheapest and most effective way to reduce pollution is to avoid production and release it into the environment.

Climatic conditions are different in India, from February to May, monsoon from June to September, and winter from October to January. In tropical countries, there may be a direct relationship between the duration of the sun and the temperature. The present study was conducted to assess the water quality of the Harsool Dam at Aurangabad [M.S.] in India, which is essential for human use in this environment. Residents use the water for drinking, domestic, agricultural, and recreational purposes.

MATERIAL AND METHODS

Water samples were taken for physicochemical analysis at the Harsool Dam in Aurangabad [M.S.], India, early in the morning between 8:00 and 11:00 AM in the first week of each month from July 2008 - June 2009. Samples were collected in an acid-washed five-liter plastic container at a depth of 5 to 10 cm below the water's surface. Separate samples were collected to dissolve the oxygen in 250 ml bottles, and the dissolved oxygen was fixed in the field by adding an alkaline iodide-azide solution immediately after collection. The samples were analyzed directly and returned to the laboratory.

The status of the Dam water quality has been determined seasonally, that is, summer, monsoon, and winter. Physicochemical properties such as Total Dissolved Solids, Magnesium, Chlorides, Sulphates, Phosphate, Total Hardness, and Total Alkalinity have been seasonally determined in monthly variation in Site A. and B. using standard methods (APHA, 2005; Trivedi and Goel, 1987).

RESULT AND DISCUSSION

The water parameters were examined and recorded in three seasons: Summer, Monsoon, and Winter. The table shows seasonal data on the physicochemical parameters of the Harsool Dam in Aurangabad [M.S.] India. The present study deals with the physicochemical properties of the Harsool Dam at Aurangabad [M.S.] in India.

Total Dissolved Solids

TDS denotes mainly the various kinds of minerals present in the water. However, if some organic substances are also present more often in polluted waters, they may also contribute to the dissolved solids. Dissolved solids do not contain any gas and colloidal, etc. (Trivedy and Goel, 1984).

The Total Dissolved Solids values reached from 43 to 79 mg/l. The average Total Dissolved Solids values were maximum in winter 67.37±5.04 mg/l and minimum during summer 51.62±8.34 mg/l as recorded (Table No.1). In the Harsool dam, the Total Dissolved Solids were no positively and negatively correlated (Table 2). Sunkad and Patil, (2002) also made similar observations.

Magnesium

Magnesium is required universally by chlorophyll plants as the Mg - Porphyry component of the chlorophyll molecule and as a cofactor for various intracellular enzymatic transformations especially, in the algal, fungal and bacterial cells (Wetzel, 1975). Magnesium, calcium, and bicarbonate cause alkalinity, and carbonate, Sulphate, and chloride cause hardness in water (Jain and Jain, 1988).

The Magnesium values reached from 1.10 to 3.12 mg/l. The average Magnesium values were maximum in winter 2.60±0.33mg/l and minimum during monsoon 1.47±0.30 mg/l as recorded (Table No.1). In the Harsool dam, the magnesium positively correlated to Sulphates, and while it negatively correlated to Total Hardness (Table 2). Beriberi *et al.*, (1999) reported that magnesium showed a significant positive correlation with pH, electric conductivity, calcium, TA, and sulphates. Rao *et al.*, (1999) also noticed a similar observation.

Chlorides

A quality parameter of significance is the chloride concentration. Chloride concentration with natural waters results from the leaching of chloride-containing rocks and soils with which water comes in contact. Agricultural, industrial and domestic wastewaters discharged into surface water are also sources of chloride in the aquatic system. Chlorine in Free State, which is used as a disinfectant, will be converted into chlorides or combines with organic matter to form toxic compounds (Adoni, 1985).

The Chlorides values reached from 35.4 to 48.9 mg/l. The average Chlorides values were maximum in summer 45.75±0.97 mg/l and minimum during monsoon 40.28±3.2 mg/l as recorded (Table No.1). In the Harsool dam, the Chlorides positively correlated to magnesium, and while it is

negatively correlated to Total Hardness (Table 2). But high chloride concentration indicates the presence of a sufficient amount of disabled organic matter of animal origin, which on oxidation increases the nitrate content. Chloride relation with any other factor was not convincingly significant (Shinde *et al.*, 2010).

Sulphates

It is a naturally occurring anion in all kinds of natural waters. In arid and semiarid regions, it was found in notably higher concentrations due to soluble salts in soils and shallow aquifers. Biological oxidation of reduced sulphur species to Sulphate also increases its density. Rainwater has relatively high concentrations of Sulphate, particularly in the areas with high atmospheric pollution discharge of industrial waste, and domestic sewage in waters tends to increase its level. Most of the salts of Sulphate are soluble in water, and as such, it is not precipitated. However, it may transform sulphur and hydrogen sulphide depending upon the redox potential of the water (Trivedy and Goel, 1984).

The Sulphate values reached from 0.8 to 5.8 mg/l. The average Sulphate values were maximum in winter 4.27±1.41 mg/l and minimum during monsoon 1.45±0.41 mg/l as recorded (Table No.1). In the Harsool dam, the Sulphates positively correlated to magnesium, and while it no negatively correlated (Table 2). Rao *et al.*, (1999) reported the existence of positive co-relation with calcium, magnesium. Nandoni *et al.*, (2001), observed a negative co-relation of Sulphate with BOD. The high value of Sulphate during monsoon might be due to surface runoff, which brings more suspended solids along with organic and soluble salts. Monsoon months showed the maximum values indicating that this nutrient brought in from the allochthonous source; the low cost may attribute to its utilisation by the macrophysics (Singh, 2000).

Phosphate

Phosphorus in a water body may be of autochthonous origin by decomposing materials and from the sediments. It may be origin through the influents of the water body. In recent years the amount of influent phosphorus to the water body in increasing due to its varied uses. It may be through modern agricultural and domestic wastes. On the contrary, waters running through the sedimentary rock deposits and the lakes rich in organic matter contain higher phosphorus content (Wetzel 1975).

The Phosphate values reached from 0.1 to 0.4 mg/l. The average Phosphate values were maximum in monsoon 0.22±0.04 mg/l and minimum during summer

0.22±0.11 mg/l as recorded (Table No.1). In the Harsool dam, the Phosphate positively correlated to Total Hardness, while it was not negatively correlated (Table 2). Murugavel and Pandian (2000) also reported a positive correlation of phosphorus with water transparency, pH, free carbon dioxide, DO, and TA. this supports our findings.

Total Hardness

The hardness of water is of two types namely temporary hardness and permanent hardness. The temporary hardness, which is due to dissolved bicarbonates of calcium, magnesium, and another ion. Temporary hardness can be removed by boiling. The permanent hardness, which is due to the presence of chlorides, sulphates, calcium, magnesium, iron, and other heavy metals. Hard water used for washing purposes does not lather freely with soap and is used if drinking purposes cause undesirable effects on the digestive system (Jain and Jain, 1988).

The Total Hardness values reached from 43 to 72 mg/l. The average Total Hardness values were maximum in winter 66.12±5.38 mg/l and minimum during summer 49.87±3.09 mg/l as recorded (Table No.1). In the Harsool dam, Total Hardness positively correlated to Phosphate, and while it negatively correlated to Chlorides, Magnesium (Table 2). Rao *et al.*, (1999) also reported the positive co-relation of TH with calcium, TDS, magnesium, TA, chlorides, and phosphates and DO. These studies support our findings.

Total Alkalinity

In unpolluted freshwater, alkalinity remains constant apart from changes due to evaporation and precipitation. Because photosynthesis and respiration involve free carbon dioxide, and addition or removal of carbon dioxide does not alter alkalinity.

The Total Alkalinity values reached from 53 to 80 mg/l. The average Total Alkalinity values were maximum in monsoon 68.75±9.48 mg/l and minimum during winter 56.25±4.23 mg/l as

recorded (Table No.1). In the Harsool dam, the Total Alkalinity was no positively and negatively correlated (Table 2). A similar observation was also made by Shinde, *et al.*, (2011).

CONCLUSIONS

The present study shows detailed research regarding the quality of water in Harsool Dam at Aurangabad [M.S] India. The summer, monsoon, and winter seasons show different seasonal fluctuations of the other physical-chemical parameters. During the present investigation, the observed interval is lower than the permitted limit values specified by the ISI, which indicates that the dam's water is suitable for consumption. This study examines the physicochemical and biological factors to assess water quality, and it is clear that all parameters are also important. Physicochemical analysis, we found that the dam water sample is ecologically and ecologically balanced. To model water quality, a large number of parameters must examine more closely. These parameters were selected for their simple, fast, and continuous measurement in water quality monitoring stations. It can conclude that Total Dissolved Solids, Magnesium, Chlorides, Sulphates, Phosphate, Total Hardness, and Total Alkalinity represent the full range of quality parameters of drinking water, irrigation, aquatic life for surface water and aquaculture. In the present study, the positive and negative Correlation of the physicochemical parameters between them appears. Improve water quality; the level of contamination monitored continuously to maintain favorable conditions for the survival and reproduction of fish in the Harsool Dam in Aurangabad [M.S.], India

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Effect Of Pesticides On Human Health And Environment

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ABSTRACT:

Pesticides are the toxic chemical that are released to environment to kill, prevent, control, repel or mitigate the population of harmful pest of agricultural, domestic and industrial setting. The commonly used groups of pesticides are insecticides, fungicides, fumigants and rodenticides. Pesticides serve as a modifier that works as destroying pest. The main purposed of this paper is to critically look out major impact of pesticides towards the health and environment. The different literature of relevant topics are collected and reviewed on their adverse effect to environment and health. Those effects are very harmful to health as well as for the environment therefore control of their used in a proper way is necessary. By properly trained the farmers and other people regarding their effect and process of screening may lessen these pesticide problem.

KEYWORDS: pesticides, mitigate, environmental impact, harmful pest, fumigant, rodenticides.

INTRODUCTION:

Pesticides are toxic chemical substance or mixture of substance or biological agent that are deliberately released into the environment in order to kill, prevent, deters, control, destroy, repel or mitigate population of insect, weeds, rodents, fungi, or other harmful pest in agricultural, domestic and industrial setting. Pesticide serves as regulator or modifiers that work by destroying the pest. In Pesticides are toxic chemical substance or mixture of substance or biological agent that are deliberately released into the environment in order to kill, prevent, deters, control, destroy, repel or mitigate population of insect, weeds, rodents, fungi, or other harmful pest in agricultural, domestic and industrial setting. Pesticide serves as regulator or modifiers that work by destroying the pest. In agricultural field the insecticide are used to increase the production of quality through controlling pest and pest related disease. The main groups of commonly used pesticides are insecticide, fungicides, fumigants, and rodenticides.

Insect are the major fountain of crop vandalism. The use of pesticide has become a common practice and it increased many fold over the past few decade. It estimated that about 5.2 billion pound of pesticide are used worldwide annually [1]. Majority of pesticide are not particularly targeting the pest. Even they backwash non-target entity which invoke major problem to the society. It has been assess that only about 0.1% pesticide stretch out the target entity and remaining are taint with the surrounding environment [2]. Majority of framer unaware about pesticide type, level of poisoning, safety precaution and hazards on health and environment [3].

The over and misuse of pesticide has precedence to immense health problem, economic loss and various environmental problem. The resultant health problem of pesticide includes cancer, birth defect, reproductive problem, liver, kidney, and neural problem etc. In many developing countries majority of pesticide are associated with adverse effect on human health and environment due to the in judicial use of pesticide. On the other hand the overused of pesticide also precedence to the environmental pollution such as water, soil pollution, etc. and cause imbalance of ecosystem.

MATERIAL AND METHOD:

Though there was no specific method for reviewing articles. So, different literature of relevant topics were collected and studied thoroughly. Books and journals were collected and studied the article and papers about pesticides and toxicology. Besides library work different websites on internet was searched for necessary data. A notebook, pen pencil, and a pen drive/ hard disk are used as a tool for the present study.

RESULTS:

Misuse of pesticide induced tremendous effect on health and environment. The various effects of pesticides on health and environment are as follows -

Effect of pesticide on health:

Human beings are highly vulnerable to deleterious effect of pesticide due to nonspecific nature, haphazard application or misuse of pesticide. The pesticide enters human body through

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BIBLIOGRAPHIC ANALYSIS OF DOCTORAL DISSERTATIONS SUBMITTED TO SWAMI RAMANAND TEERTH MARATHWADA UNIVERSITY NANDED DURING THE PERIOD 1994-2021

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Abstract:

This Paper deals with origin of the research problem, interdisciplinary relevance, review of research and development in the subject, International/National status, significance of the study, statement of the problem, operational definitions, objectives of the study, hypothesis of the study scope and limitations, methodology, data collection, sources of data collection, data analysis, year wise distribution of Ph.D. theses, language wise distribution, guide wise distribution, quantum of doctoral dissertation by decade, distribution of research guides contributing Ph.D. work, outcome of the study, conspectus, acknowledgment etc.

Keywords:

Research, Study, Doctoral, Theses, Doctoral Dissertation and University etc.

Introduction:

a) **Origin of the research problem:**

Universities, temples and monasteries had large collections for the benefit of their students, devotees and visitors. Accounts of the world famous Taxashila and Nalanda Universities and the rich collections in their Libraries can be found in historical records. In medieval India, Libraries were not given much attention and the result was their delay. When British rule came to India in the eighteenth century, there were only a few libraries in the country and even during the British time, Library development was very slow.

b) **Interdisciplinary relevance:**

Libraries were largely neglected until the beginning of the twentieth century. In 1917, Education Commission under the Chairmanship of Sir Michael Sader, then Vice Chancellor of the University of Leeds, mentioned unsatisfactory conditions and poor facilities in Indian Libraries in its report. Libraries in general at this time were quite inadequate for all types of researchers and readers. The Commission recommended that Libraries be strengthened and that conditions and facilities be improved. Despite these recommendations, very little progress was made up to 1947. It was only after independence that proper attention was given to the libraries and much needed changes and improvements were made.

c) **Review of Research and development in the subject:**

The Indian contribution to world librarianship has been great. Indian even produced a genius in Dr. S. R. Rangnathan. Despites these accomplishments, little is known about Indian Libraries in the western world. The problems inherent in the creation of Library systems in developing countries are by their very nature overlooked by western scholars.

d) **International/National Status:**

Universities are always engaged in research especially applied research. India has invested cores of rupees in research. Swami Ramanand Teerth Marathwada University, Nanded is one of the most popular Universities in Maharashtra in general and Marathwada in particular. The researcher has Chosen the topic for present study is Doctoral Dissertations in Swami Ramanand Teeth Marathwada University, Nanded: Bibliographic Analysis.

It is a unique work which contains the contributions of Swami Ramanand Teerth Marathwada University over the last twenty six years in research leading to doctoral Degree. The work has analyzed Bibliometrically. It will be compilation of information about intellectual assets spread across near about doctoral dissertations. Hence the research work will serve as an accurate base not only for the Teachers, Librarians but also for the research scholars on International/National level.

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e) Significance of the study:

Man is an intelligent animal. Due to his greater curiosity, he always tries to discover new things, or to search the answers to unsolved problems. Man Concentrates on a concept and with the help of experiments and analysis come to a conclusion for prediction and ultimate control of events. Today, research has become an unending activity. Research consists of learning more and more about less and less until the researcher knows everything about nothing. The researchers are actively engaged in discovering the cause- effect relationship to develop generalization, principles or theories. Researchers are the specialists engaged in analyzing limited aspects of broad problems, through careful observations and the application of rigorous logic. Research is essentially an intellectual and creative which continuously broaden the frontiers of knowledge. The result of every research should be communicated freely and expeditiously to everyone. In this regards, Doctoral Dissertations in Swami Ramanand Teerth Marathwada University, Nanded: Bibliographic Analysis will be systematic analysis of doctoral dissertations awarded by University during the last twenty six years. The researcher has scientifically analyzed the theses by year, faculty, subject, guide and language wise etc. The researcher also provided the lists of recognized research centers and recognized research guides of the university with addresses. The researcher has prepared Rank -1 list of research guides in concern subjects. The Present study will be helpful to the researchers, teachers, librarians as well as policy makers as a research inventory tool.

Statement of Problem:

The statement of the problem of the present study is Doctoral Dissertations in Swami Ramanand Teerth Marathwada University, Nanded: Bibliographic Analysis.

Operational Definitions:

(a) Research:

Research is a systematic activity to reveal the truth. All around us, we notice that human advancement, inventions and discoveries are feasible because the researchers take pain to be curious and inquisitive. Kerlinger says, research is a Systematic, controlled, empirical and critical investigation of hypothetical propositions about the presumed relations among natural phenomenon. However, the Encyclopedia of Social Sciences defines research as the manipulation of generalizing, extending, correcting or verifying knowledge. That means research is a fact-finding process through the application of scientific methods.

(b) Study:

According to Illustrated Oxford Dictionary of English Language, (2007, p. 826) Study means the devotion of time and attention to acquiring information or knowledge, especially from books, the pursuit of academic Knowledge (continued their studies abroad). A thing that is or deserves to be investigate or examine (a subject) (Bibliometric Study). According to concise Oxford English Dictionary, (2007b, p.1432) Study means, A detailed investigation and analysis of a subject or situation, a thing that is or deserves to be investigated, done with deliberate and carefully effort.

(c) Doctoral:

According to Illustrated Oxford Dictionary of English Language, (2007 b, p. 237) of or for a degree of doctor. Also noun of this is Doctorate: The highest University Degree in any faculty, sometimes, honorary. According to Concise English Dictionary (2007c, p.421), Doctoral means: Relating to a doctorate and doctorate is the highest degree awarded by university faculty or other approved educational organization.

(d) Theses:

Theses is a long piece of writing based on your own ideas and research that you do as part of a University degree especially a higher degree such as Ph.D. (Source: http:// www.collinsdictionary.com).

(e) Doctoral Dissertation:

The Doctoral Dissertations which are products of research activity form an important source of information because apart from giving the experimental evidences, it also records a thorough review of works that have already been done in a particular field to show that the proposed work is not done elsewhere.

(f)University:

According to Illustrated Oxford Dictionary of English Language (2007g, p. 910) University means, An educational institution of Advanced learning and research conferring degrees. According to Concise Oxford English Dictionary, (2007h, p. 1519) University means, a high – level educational institution in which students' study for degrees and academic research is done. (SRTMU: Swami Ramanand Teerth Marathwada University: A name of university).

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numbers of doctoral dissertations, i.e. 325 (8.22%) were accepted by the university in the year 2013, while lowest number i.e. 05 (0.13%) doctoral dissertation was accepted in the year 1996.

Total number of 3954 doctoral dissertations has been produced during the last twenty six years period. It was also observed that on an average 152.07 i.e. 152 doctoral dissertations per year were accepted by the University.

Year wise Analysis also highlights that there is fluctuation in quantum of doctoral dissertations. Maximum doctoral dissertations are accepted by the University from 2002 to onwards because of the University Grant Commission released a circular of exemption in the NET/SET Examination for Ph.D. holders.

Table No. 01

Year wise Distribution of Ph.D. Theses

Sr. No.	Year	No. of Theses	Percentage	Sr. No.	Year	No. of Theses	Percentage
1	1996	5	0.13	14	2009	168	4.25
2	1997	11	0.28	15	2010	164	4.15
3	1998	13	0.33	16	2011	245	6.20
4	1999	21	0.53	17	2012	299	7.56
5	2000	41	1.04	18	2013	325	8.22
6	2001	36	0.91	19	2014	152	3.84
7	2002	166	4.20	20	2015	178	4.50
8	2003	86	2.18	21	2016	239	6.04
9	2004	84	2.12	22	2017	218	5.51
10	2005	143	3.62	23	2018	170	4.30
11	2006	116	2.93	24	2019	238	6.02
12	2007	174	4.40	25	2020	243	6.15
13	2008	138	3.49	26	2021	281	7.11

Language Wise Distribution:

Theses were submitted by the researchers in the various languages i.e. English, Hindi, Marathi and Urdu. The data regarding Language wise distribution of doctoral dissertations is presented in the Table No. 02.

Table No. 02

Language wise Distribution of Ph.D. Theses

Sr. No.	Language	No. of Theses	Percentage
1	English	2385	60.32
2	Hindi	243	6.15
3	Marathi	1278	32.32
4	Urdu	48	1.21

Table No. 02 indicates that of the 3954 doctoral dissertations, 2385 (60.32%) were in English, 1278 (32.32%) were in Marathi, 243 (6.15%) in Hindi, 48 (1.21%) were in Urdu respectively. It also presented with the help of bar chart.

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(iii) Objectives:

1. To know the availability status of Doctoral dissertations in the Swami Ramanand Teerth Marathwada University Library.
2. To trace the contribution of research in Swami Ramanand Teerth Marathwada University.
3. To Identify the subject wise analysis of research
4. To classify the doctoral dissertations by year, guide and Discipline.
5. To prepare rank list of top twenty Research guides in the University.
6. To know and identify the reasons behind the non-availability of doctoral dissertations in the University Library.
7. To prepare bibliography of doctoral dissertations accepted by SRTMUN.
8. To suggest ways and means to improve the availability status of doctoral dissertations in the University Library.

Hypothesis of the study:

1. Some Doctoral Dissertations are yet not available in the University Library which was accepted by the University.
2. Maximum theses are produced by the University in the discipline of Science.
3. The majority of the research guides guided to below ten researchers.
4. The maximum doctoral dissertations are accepted during the year 2000 onwards.

Scope and Limitations:

The University has established in 1994 and the study is for the period 1994 to 2021 (i.e. 26 years). The SRTM University has compiled doctoral dissertations for the period 1994 to 2015 in a book form. The researcher has collected the data 2015 to 2021 and analyzes the whole doctoral dissertations i.e. from 1994 to 2021 as per the objectives of the present study. The researcher has taken the serious efforts about bibliographical information regarding the availability and non – availability status of doctoral dissertations in the University Library. The present study is limited to doctoral dissertations accepted by Swami Ramanand Teerth Marathwada University, Nanded only. The researcher has covered the contribution in the minor and major research projects sanctioned by UGC during the period Jan. 2016 to Dec. 2021. The researcher has also covered the contribution in the patents of teachers of Swami Ramanand Teerth Marathwada University Nanded.

(iv) Methodology:

Researcher has applied Bibliometric Research method for the present study.

Data Collection:

In any research work data collection is vital part of the research. For the present study the bibliographical descriptions of doctoral dissertations available in the disciplines of sciences, Social Sciences and languages in the Swami Ramanand Teerth Marathwada University, Nanded is used for a data collection.

Sources of Data Collection:

1. https://shodhganga.inflibnet.ac.in:8443/jspui/handle/10603/5404
2. Ph. D. Section's Record of the University.
3. University website (i.e. www.srtmun.ac.in)
4. Compiled doctoral dissertations in book form 1994 to 2015 by the SRTM University.

Data Analysis:

The analysis of data has been presented in a systematic way with the help of graphs, charts, tables and other diagrams etc.

Year wise Distribution of Ph.D. Theses:

Table 01 represents the year wise distribution of doctoral dissertations which shows that the highest

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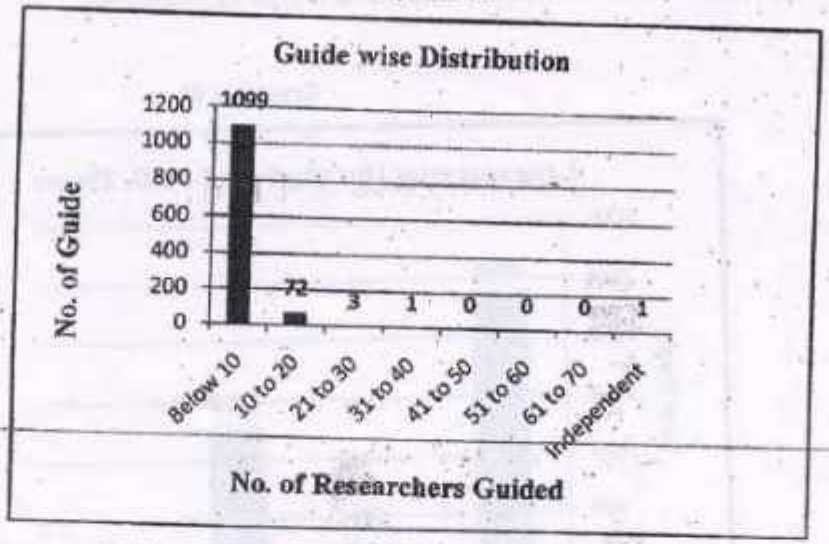
Graph No. 02



Quantum of Doctoral Dissertations by Decade:

Table No. 04

Quantum of Theses by Decade

Sr. No.	Year	No. of Theses	Percentage
1	1994-2000	91	2.30
2	2001-2010	1275	32.25
3	2011-2020	2307	58.35
4	2021	281	7.11

The Swami Ramanand Teerth Marathwada University, Nanded Established in 1994. After two years of gap. i.e. in 1996, the first doctoral dissertation was accepted. The data regarding quantum of doctoral dissertation by decade are presented in the table No. 04. Indicates that in the first six years that is during 1996-2000, there was only 91 (2.30%) doctoral degrees awarded. In the next ten years that is during 2001–2010, the university accepted 1275 (32.25%) degrees. It is also observed from the Table No. 04 that on an average 152.07 doctoral dissertations were accepted during last twenty six years Table No. 04. That the maximum doctoral dissertations i.e. 2307 (58.35%) were accepted during the year 2011-2020.

Distribution of Research Guides Contributing Ph.D. Work:

The Library is a storehouse of knowledge. Knowledge is Power. It is necessary to discover, invent, organize, preserve and disseminate Knowledge among the members of the society; Universities are always engaged in research especially applied research. India has invested cores of rupees in research. Swami Ramanand Teerth Marathwada University, Nanded is one of the most popular Universities in Maharashtra in General and Marathwada in particular. Bibliometric Analysis is a unique document which contains the contributions of Swami Ramanand Teerth Marathwada University, Nanded over the last twenty six years in research leading to doctoral degree. The work is analyzed Bibliomatrically. It is a compilation of information about Intellectual assets spread across 3954 doctoral dissertations. The researcher wants to know distribution of research Guides contributing Ph.D. work. The same data is presented in the table 05.

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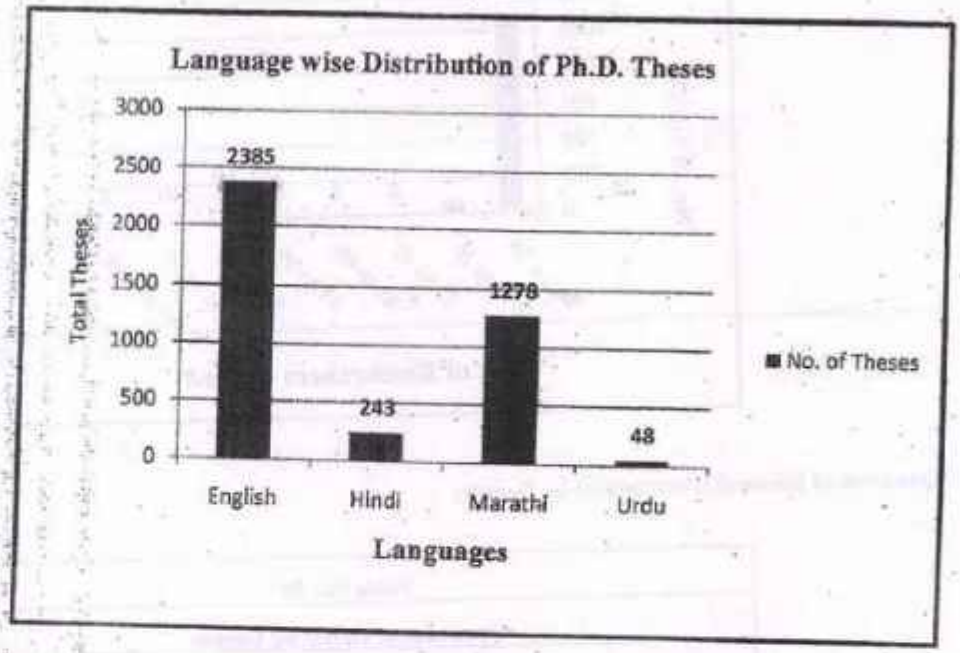
As per Table No.02 it was also observed that the Maximum doctoral dissertations 2385 (60.32%) were in English and minimum doctoral dissertations 48 (1.21%) were in Urdu.

Graph No. 01



Guide Wise Distribution:

However the same data was analyzed by a number researchers guided by the range is presented in the Table No. 03 represents the guide wise distribution of doctoral dissertations which shows that the Maximum i.e. 1099 (93.45%) guides guided below ten researchers. while 72 (6.12%) guides guided the researchers in the range of 10-20. 03 (0.26%) guides guided researches in the range of 21-30, However 01 (0.09%) guides guided the researchers in the range of 31-40. While 0 (0.00%) guides guided researchers in the range of 41-50, 0 (0.00%) guides guided researchers in the range of 51-60 and 61-70.

Table No. 03

Guide wise Distribution

Sr. No.	No. of Researchers Guided	No. of Guides	Percentage
1	Below 10	1099	93.45
2	10 to 20	72	6.12
3	21 to 30	3	0.26
4	31 to 40	1	0.09
5	41 to 50	0	0.00
6	51 to 60	0	0.00
7	61 to 70	0	0.00
8	Independent	1	0.09
[illegible]	[illegible]	[illegible]	[illegible]

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Conclusion:

Bibliometric research has developed a body of theoretical knowledge and group of techniques and applications based on the distribution of bibliographic data elements. The wider application of Bibliometric techniques is leading to the development of new and more precise techniques for grater economical and efficient management of the material and the Bibliometric studies are carried out on well established subject area.

The culmination of one's research contribution to the academic world as a doctoral researcher is accomplished via the dissertation. As a result, dissertations were analyzed because they serve as the best representation of the research interests of doctoral researchers at Swami Ramanand Teerth Marathwada University, Nanded.

Acknowledgement:

The above Minor Research Project entitled "Doctoral Dissertations in Swami Ramanand Teerth Marathwada University Nanded: Bibliographic Analysis" is Sanctioned by Swami Ramanand Teerth Marathwada University Nanded under the Scheme of Support for Minor Research Project.

I offer my Sincere thanks to Vice – Chancellor Hon Dr. Udhav Bhosle Saheb, Pro. Vice – Chancellor Hon. Dr. Jogendrasingh Bisen Saheb, Hon Dr. Mane, The Director, Innovation, Incubation and Linkages, The Dy. Registrar/Assistant Registrar Hon Dr. Sarita Yennawar, Academic Planning and Development Section and the Minor Research Project Sanctioning authority of Swami Ramanand Teerth Marathwada University, Nanded for Sanctioning and giving the opportunity to work on this Minor Research Project.

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Table No. 05

Distribution of Research Guides Contributing Ph.D. Work.

Sr. No.	No of Guides	No. of Research works	Sr. No.	No of Guides	No. of Research works
1	468	1	13	5	13
2	207	2	14	7	14
3	134	3	15	8	15
4	80	4	16	2	16
5	74	5	17	2	17
6	52	6	18	2	18
7	31	7	19	1	19
8	37	8	20	2	20
9	17	9	21	1	21
10	24	10	22	1	23
11	10	11	23	1	25
12	9	12	24	1	31

(v) Year-wise Plan of work and targets to be achieved:

Phase	Work	Duration
Phase I	Review of related literature	03 months
Phase II	Collection of Data	06 months
Phase III	Analysis & Interpretation	09 months
Phase IV	Project Compilation	06 months
Total Project duration		24 months

Outcome:

1. Bibliographical Details of Doctoral Dissertations accepted by SRTMUN.
2. Bibliographical Details of Doctoral Dissertations accepted by SRTMUN but not yet available in the SRTMUN Library.
3. Year wise Distribution of Doctoral Dissertations from 1994 to 2021.
4. Subject wise Productivity of Doctoral Dissertations.
5. Language wise Distribution of Doctoral Distributions.
6. Quantum of Doctoral Dissertation by Discipline.
7. Guide wise Distribution of Doctoral Dissertations.
8. Quantum of Doctoral Dissertations by Decade.
9. Distribution of Research Guides Contributing Ph.D. work.
10. Rank List of Guides.
11. Subject wise Rank – 1 Guides in SRTMUN.
12. Subject wise distribution of Non-Available Doctoral Dissertations.
13. Contribution of teachers of SRTMUN in Major and Minor Research Projects in Science during the year 2019-20.
14. Contribution of teachers of SRTMUN in Major and Minor Research Projects in Social Science, Humanities and Languages during the year 2019-20.

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Guest Editor

Dr. M.N.Kolpuke

Dr.D.S.Choudhari

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Internationalization of higher education: Prospects and challenges

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Indian higher education system is world's third largest in terms of students next to china and United States. After post 90s period liberalization, privatization and globalization has great impact on Indian higher education particularly the professional and technical education in LPG supported several government policies like private university bill, foreign education provider bill and also by allowing free entry of local private IT providers and related areas night and De wit quoted in OECD, 1999 "globalization is the flow of technology, economy knowledge people values, ideas..... across borders globalization affects is country in deferent way due to the nation individual's history, culture and priorities" Internationalization of higher education is one of the ways a country response to the impact of globalization yet, at the same time respects the individuality of the nation so internationalization and globalization are seen as different but dynamically linked concepts internationalization of higher education is the process of integration an international dimension into the teaching, research and services functions of the institution.

In the process of internationalization of higher education Indian higher education also has to build robust education system to attract foreign students we have witnessed that worlds first university was established in Takshashila in 700 BCE and in the 7th Century CE. The University of Nalanda has students and Scholars from china, Indonesia, Korea, Japan, Persia, Turkey, and from other parts of the world. Now a day's Indian students are adopting foreign education only approximately 45000 international students pursuing Indian higher education. India is on the 26th ranked country among the top destinations for international student's mobility. In comparison to hour students studying in foreign university, International students are less taking admission in Indian universities so there is a need to give quality education to prepare students to think globally and make global citizens, confident and capable of working in different countries over the world. Foreign students attract only to the reputed institutions so that we have create internationally reputed institutions to attract foreign student. This process of new education policy has given suggestion to promote internationalization of higher education. Here will discus suggestion of new education policies.

The first suggestion is given in NEP to internationalization of higher education to give internationally relevant education. Indian higher education should take liberty to create national and international curriculum to equip students with knowledge skills and competences to become global citizens. It is also suggested that NHEQE and similar qualification frame works in professional education must be aligned to receive internationally recognized qualifications. To attain this we require investment in quality academic infrastructure. Another suggestion by NEP is to create courses on Indian languages, arts, culture, history and traditions. Seeking to become attractive universities for foreign students we will receive funds to develop and offer spicily design courses. Other areas of strength in India such as STEM subjects, computer science, gaming and related topics are also attractive to foreign students; efforts must be tie these courses up with internship and industry attachment to make them more attractive.

NEP has suggested to collaborate with foreign university this collaboration will be facilitated for twinning programs. The enrolled students can complete their half coursein foreign university collaborated with us. With the help of MOU between two mutual universities these facilities can be run. It also suggest facilitating entry of international students and researches. The RSA will complete required formalities and will make all information available on a study in India portal, Set up by MHRD. NEP is also given suggestion to students exchange will be supported to have global experience. Also facility to stay and integration of foreign students with local communities. Faculty members of Indian institution will be encouraged to foreign universities vice versa. This comes under exchange programs assigned universities, short term assignments, jobs and short term programs in India and abroad. There should be research collaborations and offshore campuses it. MOOCs and open distance learning. Inviting foreign universities in India, Outreach and branding, and inter- university center for international education.

There are some challenges in making internationalization of higher education that are

1. Teaching quality: the first challenge that higher education in India is of quality teaching. Indian teachers are highly educated but not having training skills. So in the process of internationalization of higher education Indian teaching quality should be enhanced. Faculty shortages and the inability of state educational systems to attract retain well qualified teachers have been posing challenges to quality education for many years.

2. Cross cultural issues: In the Process of internationalization of higher education there is an issue of cross culture. Many students from different countries will study together and has different cultural background. Multicultural students have not easy to adjust one another.

3. Corruption in education: corruption in Indian education system has been threatened the quality education. Education has become one of the major contributors to black money people are looking to earn not to serve. In internationalization process esteemed university hire educational fees as per their needs.

4. Economic Challenges: Most of the Indian students belongs to middle class family they are not able to pay their education expenses near about seventy five percent of the total students community today have been facing the financial problems. To get international education one has to pay large amount which is a day dream for economically backward students

5. Privatization: in the process of making international of higher education the private institution will allow only those who are capable of paying them so the needy will left behind in privatization institutions become supreme to take decisions. The autonomy will create difference in learner.

6. Quota System : This is very controversial. This system eroding the quality education. Talent and identity is more important than your identity. This quota system is still a challenge

7. No skill based learning: Higher education system has no proper scheme of skill base education graduates need to acquire new skills especially vocational skills that can give them job.

In order to sustain the higher education there is need to increase of the number of institutes and also the quality of higher education to reach and achieve further requirement. Internationalization of higher education is the need of an hour to make our education global one.

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Single Stock Derivatives in India An overview

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Introduction :

In Indian financial system there are two types of market i.e. money market and capital market money market is market which consist of banks, financial institutions and sawkars, where as capital market consists of various financial instruments such as equity, derevatives, future and options. Here we are going to discuss one of the instrument of capital market that is options.

An option is a contract that allows the holder the right to buy or sell an underlying asset or financial instrument at a specified strike price on or before specified date, depending on the form of the option. The term option introduced to hedge the long market position for short time. It mean that if a buyer at a particular asset or product is willing to stay at a particular position but market is going negative then only option is used to hedge that position. Now a day's traders uses options as a primary investment to gain from market. There are some types of options on the basis of underlying assets.

1. Equity option
2. Bond option
3. Future option
4. Index option
5. Commodity option
6. Currency option
7. Swap option

Options are most often regarded as insurance against the price movements in the underlying stock or an index. It is a right to exercise the holders desire to buy (CALL) or sell (PUT). These options are priced based on the Holy Grail kind of formula called 'Black Scholer' model. The logic behind the gormulae is based on current underlying asset price, intrinsic value, time for expiry, volatility, interest rates and dividend, if any paid. As the expiry date nears, the option premium also tends to go down. However such fall happens only at the lag end of the option period. In normal periods, one can watch an interesting fact about the option premium price. It tends to move along with the value of the underlying asset. But the sprade between the value of underlying assets and the option pemium is wide enough to make huge profit. Investors can benefit from this sprade on the derivatives of the underlying. In this paper we are going to discuss various strategies that can be used to gain this spread.

Research Methodology :-

The research is of discreptive type to nature generally researcher used secondary sources of data collection such as Books, Magzines, New papers, website and research materials.

Objetive of Study :-

i. To introduce option concept of derivative market.
ii. To study indian derivative market as in single stock.

Limitation of Study :-

The researcher studied only historical background or derivative market in brief. He also discussed first stock list which are listed on NSE for single option trading.

Single Stock future concept :-

Stock futures are standardised agreements for future purchase and sale of individual stocks at agreed prices. Generally an individual share buy in cash or delivery be setteled as T + 2 days. In cash purchase of share having some limitations such as settelment or purchased share will credited on after T + 2 days after pruchase hence, it cannot be sold on the same day or before credited stock to the buyers D-Mat account. That time for the purpose of hedging or for speculation single stock future is used in a lesser amount of capital i.e. on primum, price.

In India single stock futures were permitted on NSE for trading on November [illegible] time total 31 stocks are introduced for single stock future trading these are as below :-

Name of the company
cement Co.Ltd.
Ltd.
petroleum corporation
Equipment Ltd.
's Lab.
Ind. Ltd.
Ambuja Cement Ltd.
Liever
Petrolcum Ltd.
Ltd.
Ltd
Ltd
Tech. Ltd.
Ltd.
& Toubro Ltd,
Mahindra & Mahindra Ltd
Mahangar Telephone Nigam Ltd.
Ranbaxy Labs Ltd.
Reliance Petroleum Ltd.
Reliance Industries Ltd.
Satyam computers
Sterlite Optical Techonology
TELCO Ltd.
Tata power Ltd.
Tata Iron & Steel Ltd.
Tata Tea Ltd.
State Bank of India
Videsh Sanchar Nigam Ltd.

Source : w.w.w.Nse.co.in

Introdction of single stock future is replacing badla trading into single stock future trading. According to R.H. Patil (2006) in relation with the introduction of SSFs, "Despite the obvious riskes that individual stock futures pose to the safety and intergrity of the capital market of the country, they have been introduced in a hurry in our country. In my opinion it was not wise for us to have introduced stock futures. All those who had mourned the death of badla are very happy that a similar product is now available for them to play their games."

Conclusion :-

In India, the success of single stock futures is unique. That concept of future to indian investor is familiar with the concept of Badla trading. The functions and features of Badla trading & future trading are same that's why traders were well familiar with that change.

The single stock futures were launched with lot many apprehensious in the Indian market, they are found to the safest between of all the derivative instruments, launched at that time. The problem raised against the instrument can hence be regarded as baseless, in the wake of experience till now. That individual sotck future is best concept of using as risk management tool.

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Research Article.....

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Respiratory Metabolism affected by mercuric chloride and aluminum sulfate in freshwater Catfish, *Clarias batrachus*

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ABSTRACT

Industries are the major sources of heavy metal pollution and it is released into water and soil. Heavy metals cause several ill effects to aquatic living organisms and environment (Muneeshkumar *et al.*, 2015). In recent work we present the knowledge and adverse effects of man-made activities such as industrial development throughout the world. Industrial waste contains amount of hazardous metals mix-up with the nearby water bodies and damage to the tissue of fishes and finally causing death. Respiration is one of the most vital physiological parameters on which many of the vital functions like growth as well as reproduction of fishes depends. Respiration is an important physiological body activity for each and every animal. Similar weighted catfishes *Clarias batrachus* were chosen for the study of respiration. They were found in the muddy fields of water which have barbles. The selected fishes were experimented with lethal concentration of both the compounds in the laboratory for two days. Winkler's method was used to measure the respiratory mechanism (Welsh and Smith, 1959). In this investigation it was found that the gradual descending trend of oxygen consumption when exposed to mercuric chloride and aluminum sulfate for 96 hrs. Alterations in oxygen consumption may be due to respiratory distress as a consequence of impairment in oxidative metabolism.

KEYWORDS

Mercuric Chloride, Aluminum Sulfate, *Clarias Batrachus*, Oxygen Consumption

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The problem of pollution of the water where the wastes are usually discharged has increased to a great extent in recent years. Aquatic life is strongly influenced by physical properties of a water body. It is known that heavy metals as well as agro-pollutants are potentially harmful to the aquatic lives. All pesticides applied for the pest control eventually pollute the water resources either in their original chemical form or in some degraded variety. On the other hand, all industries discharge their effluents indiscriminately in the adjoining water areas and frequently cause serious hazards to aquatic life.

Among the aqua fauna, fishes are affected to a significant extent (Muneeshkumar *et al.*, 2015). The consumption of aquatic oxygen in fishes is one of the most important tests to observe the entry of toxicant into the body of fishes. Use of recently developed chemicals and industrial wastes are well known for the adverse effects on the aquatic organisms. The toxicity of metal generally affects the central nervous system and extending towards the stress on physiological status of the fish. This physiological stress and status can be determined by the estimation of biochemical effects.

This change in physiological form causes the increase in the consumption of the oxygen for more work by the body of fish finally which leads to imbalance in the natural status of fish. In aquatic animals particularly in fishes, gills are the main respiratory organ. Water bore toxic contaminants damages initially to gills of fishes. Saroja (1959) literature review found that in aquatic ecosystem when contaminated by toxic pollutants it relates with the concentration of pollutants to which that much attention has not given. In the present study focus was given on respiratory study through oxygen consumption of *Clarias batrachus* when exposed to mercuric chloride and aluminum sulfate with different time period of 24 hrs, 48 hrs, 72 hrs, and 96 hrs.

Materials and Methods

All same sized (180-200 gm) weight of healthy freshwater *Clarias batrachus* test fishes were collected from the fisher man, Nanded. In order to their good settlement they were brought to the laboratory, cleaned by using 0.1% KMno4 to avoid dermal infection. The fishes then were made to settle for or aaclimatized15 days and later they were used for experimental work. The fishes were offered the small pieces of earthworm, rice or wheat flour balls. The fishes were exposed to mercuric chloride and aluminum sulfate concentrations. The respiratory metabolic function was measured by "Winkler's Method" (Welsh and Smith, 1959). For analysis of oxygen content from the sample, dark bottles having inlet and outlet for control separate bottles were used.

The selected animals were kept in a chamber and sample was collected for the estimation of oxygen. Sufficient time was given to the animal for both control and experimental. Then the samples were collected and analyzed for the oxygen uptake the difference between initial and final oxygen content was determined. The freshwater experimented catfish *Clarias batrachus* showed fluctuation in oxygen consumption uptake and oxygen after treating with mercuric chloride and aluminum sulfate up to 96 hours. The present observation show that due to the effect of mercuric chloride on oxygen consumption of catfish , it was recorded as 2.82, 2.19, 1.71 and 1.05 ml (C.C.) of O_2/ catfish/ hr. at the time of 24, 48, 72 and 96 hrs respectively in experimented group. In control group oxygen consumption was 3.17 ml (C.C.) of O_2/ catfish/ hr. which indicate that the descending order when compare with the normal group. The freshwater fish *Clarias batrachus* showed variations in total oxygen consumption of mercuric chloride and aluminum sulphte up to 96 hours. In present investigation total oxygen consumption of fish to the effect of aluminum sulfate was 2.51, 2.11, 1.71 and 0.98 ml (C.C.) of O_2/ animal/ hr. during 24, 48, 72 and 96 hours respectively in treated group. In control group total oxygen consumption was 2.98 ml (C.C.) of O_2/ animal/ hr. which indicate decreasing trend to compare with normal.

Results and Discussion

The recent observation made here, the effect of mercuric chloride and aluminum sulfate is showed clearly. As a result oxygen consumption was declined due to the more toxic effects of mercuric chloride as compare to aluminum sulfate on physiology of catfish *Clarias batrachus* (Landis *et al.*, 2002). The oxygen consumption was determined by the respiratory study. As per result it was found that the mercuric chloride was more toxic. They have capacity to change the respiratory function of the body of catfish. It changes the normal physiological working in respiration and oxygen consumption rate was reduced. Any change in oxygen consumption of catfish is for the reason that there was change in the aquatic environmental condition. It is often used to determinate metabolic fluctuation. Water contains mercuric chloride showed declined effect in oxygen consumption and rate of oxygen consumption (Agarwal *et al.*, 2000). Oxygen consumption was found to be decreased in all the experimented groups.

The oxygen consumption decreased when time exposure period increased by 24 hours to 96 hours. The mercuric chloride after entering in the respiration system of catfish it became complicated. It varies from metal to metal and also from species to species (Maula Reddy, 1988). It observed that there was oxidative respiratory dysfunction (Delgado *et al.*, 2006). Water pollutions are artificial process responsible for the threat of discharges from various sources (Vatakuru, 2005). The damage of organ depends upon the toxicants and the species of fish.

Table 1. Effect of mercuric chloride and aluminum sulfate on total oxygen consumption of catfish (*Clarias batrachus*)

S. N.	Name of the Compound	Consumption of Oxygen	Normal	Experimental			
				24 hrs	48 hrs	72 hrs	96 hrs
1	Mercuric Chloride	Total O_2Uptake in CC of O_2/Animal/ hr.	3.17+0.34	2.82+2.37	2.19+0.25	1.71+ 0.19	1.05+0.15
2	Aluminum Sulfate	Total O_2Uptake in CC of O_2/Animal/ hr.	2.98+0.34	2.51+0.18	2.11+0.10	1.71+10	0.98+0.16

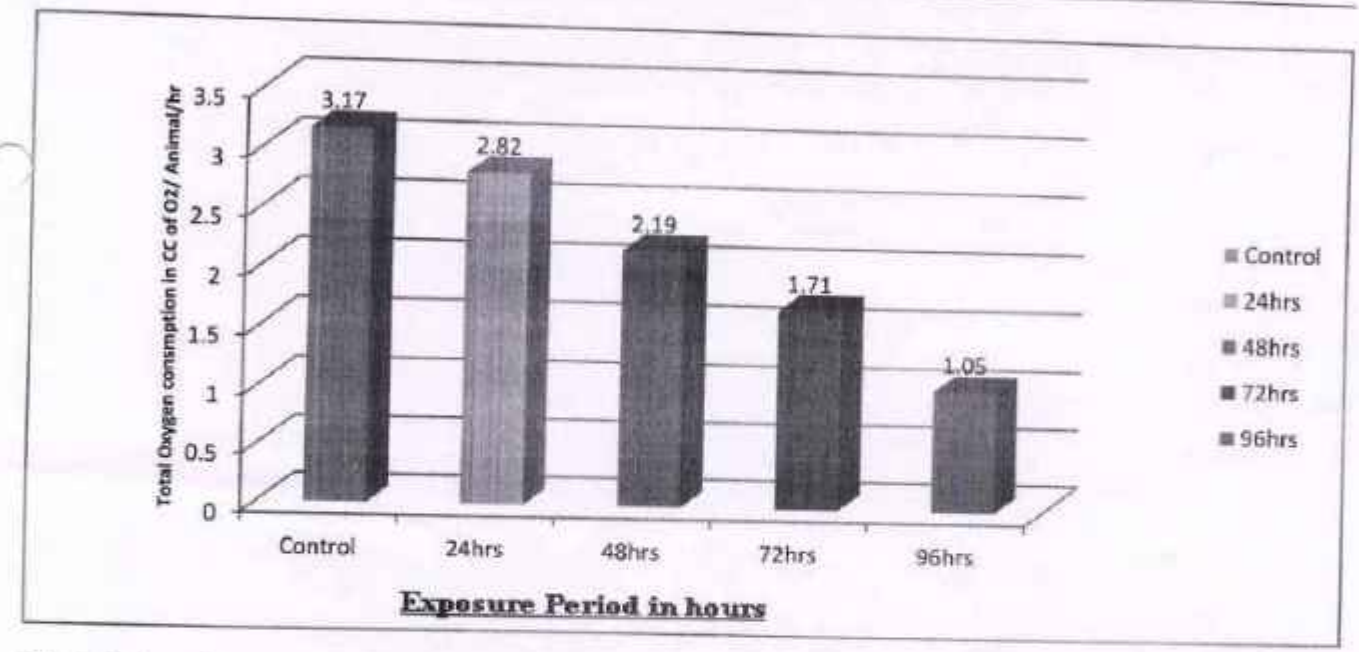

Fig 1. Effect of mercuric chloride on oxygen consumption of catfish (*Clarias batrachus*)

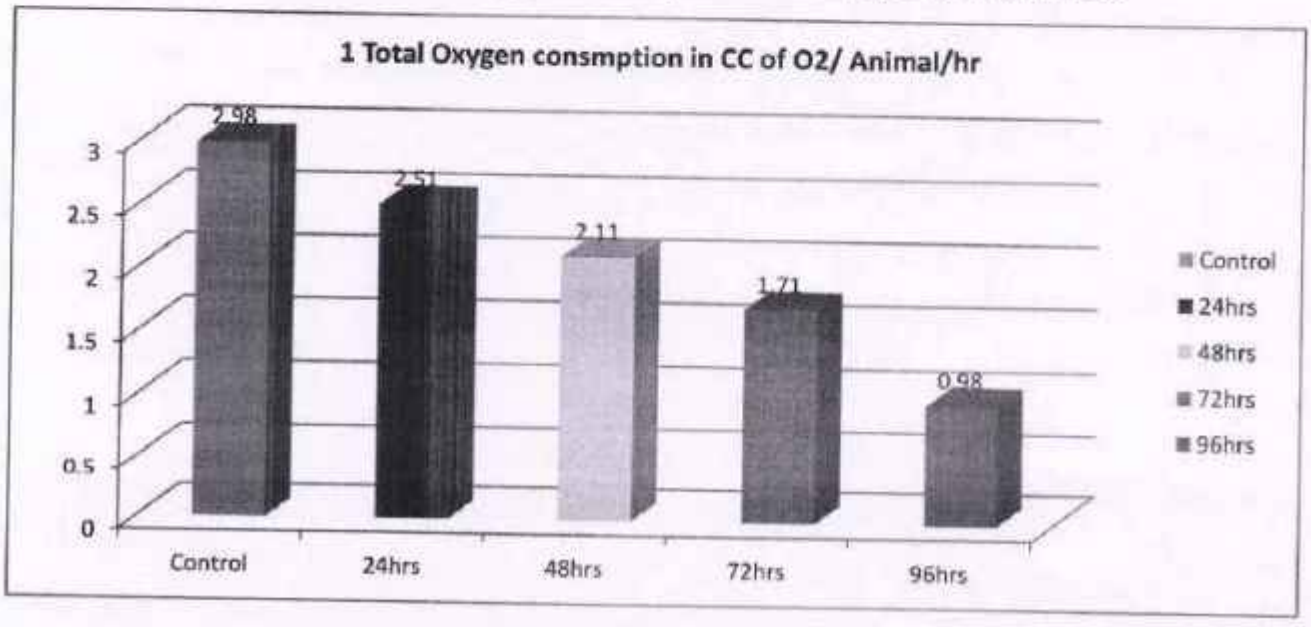

Fig 2. Effect of aluminum sulfate on oxygen consumption of catfish (*Clarias batrachus*)

Results and Discussion

Various toxicants dissolved in water and affect the fresh water aquatic life as well as marine water life (Balaji M., 1991). When freshwater catfishes are exposed to pollutants in water, the oxygen consumption of fishes was found to be decreasing, as a result of depletion of dissolved oxygen content in water. This increase in BOD level, reduction oxygen consumption in *Channa punctatus* when exposed to metasystox (Natarajan, 1981). Another effect of pesticide was noticed that on fresh water fish *Channa punctatus* and reported that rate of respiration declined in the fresh water fish (Ali, 1982).

Verma and Dale (1975) observed that oxygen consumption reduced due to the existence of suspended solid materials in the fresh water which would cause injury to aquatic animal and disturb normal life of fish. Magare and Patil (2000) reported a decrease in the rate of O_2 consumption in *Puntus ticto* exposed to endosulfan. The unusual behaviour of the fish, *Clarias batrachus* in stress condition may be due to obstructed functions of neurotransmitters. The gill opercular movements increased initially to support enhanced physiological activities in stressful habitat and later decreased may be due to mucus accumulation of gill. The toxic stress of pesticides has direct bearing on tissue chemical compounds (Tilak and Yacobu, 2002). This was also reported by (Chaudhary *et al.*, 2001).

The observed decrease in oxygen consumption by the whole animal may be due to the respiratory distress as a consequence of the impairment of oxidative metabolism. Several authors reported similar decline in whole animal oxygen consumption in different species of fishes exposed to toxicants (Ahmed *et al.*, 1981, Rangaswamy, 1984, Mushigeri *et al.*, 2002). Gills are the major respiratory organs and all metabolic pathways depend upon the efficiency of the gill for their energy supply and damage to these vital organs causes a chain of destructive events, which ultimately lead to respiratory distress (Joice, 2001). In consonance with this, he also reported that the depletion in O_2 consumption was due to the disorganization of the respiratory function caused by rupture in the respiratory epithelium of the gill.

It is also due to the disturbance in mitochondrial integrity and decreased activities of some mitochondrial enzymes (Ravinder, 1988). It is observed that the total oxygen uptake was reduced when exposed to concentration of 1.2 ppm of mercuric chloride. The physiological disturbance of metabolic respiratory activity may be an sign of stress caused due to the pollutants (Newell, 1973). The different workers reported that there was adverse effect of heavy metals on respiratory metabolism of aquatic animals. The Similar changes were also observed by (Chinnayya, 1971, Nagabhushanam, 1972 and Nagbhushanam *et al.*, 1981) there is significant drop in rate of oxygen consumption in fresh water fishes.

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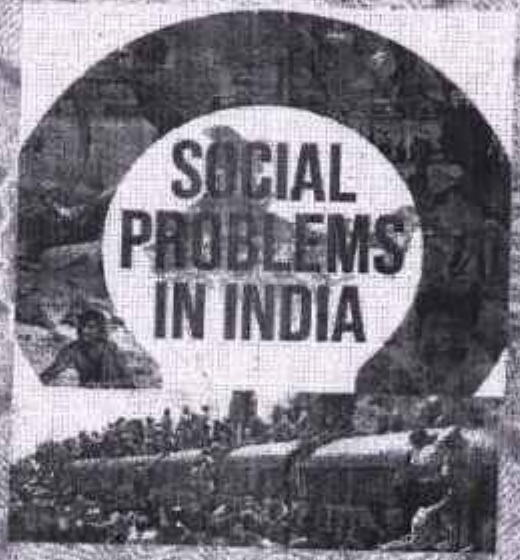

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ता. देवणी जि.लातूर

सार :–

सदर लेखात लेखकाने मराठवाडयातील लेखकांच्या लेखन कार्याचा अभ्यास केला आहे. लेखकांचे लेखनकार्याचा अभ्यास करताना त्यांची लेखनकला, लेखकांची साहित्य निर्मिती व लेखन साहित्य यांचा अभ्यास केला आहे. सदर लेखात मराठवाडयातील लेखकांच्या लेखनाचे उद्देश काय आहेत याचा विचार मांडला आहे. व मराठवाडयातील लेखकांचे लेखनकार्य विषयनिहाय असतात. त्या विषयांचा विचार याचा अनुभव अभ्यासकाने या संशोधन लेखनात मांडला आहे.

शोधसंज्ञा :– मराठवाडा, लेखक, लेखन, लेखनकार्य

प्रस्तावना :–

मराठवाडा ही संतांची, महंतांची समाजसुधारकाची त्याचबरोबर महानसाहित्यकांची कर्मभूमी आहे. मराठवाडा या कर्मभूमीमध्ये अनेक लेखकांनी/साहित्यकांनी आपल्या लेखनाच्या माध्यमातून मराठवाडयाच्या मातीचा, येथील संस्कृतीचा सुगंध जागतीक पातळीवर पोहचवून स्वातंत्र्य व स्वंयपूर्ण मराठवाडयाची अस्मिता, आण,बाण,शान मराठवाडयाच्या मातीचे पवित्र नात्याने व येथील संस्कृतीचे दर्शन अनेक लेखकांनी आपल्या कलाकृतीमधून मुखवत केले आहे. लेखन हा खऱ्या अर्थाने समाजाचा आरसा आहे. समाजातील वास्तव्य साहित्यातून लेखक मांडत असतो. लेखक हा समाजाचा घटक असल्यामुळे समाजामध्ये ज्या विविध घटना, घडामोडी, लेखकाला आलेल्या विविध अनुभवाची मांडणी साहित्यामधून प्रतिबिंबित करत असतो. अशा लेखकांच्या लेखनकार्याचा विचार आपणास या ठिकाणी करता येतो.

शोधसंज्ञा व्याख्या :–

मराठवाडा : महाराष्ट्र राज्यात सहा विभाग आहेत त्यापैकी मराठवाडा हा एक विभाग आहे. मराठवाडयात एकूण आठ जिल्हयांचा समावेश असून त्यामध्ये लातूर, नांदेड,परभणी, हिंगोली, औरंगाबाद, जालना , बीड व उस्मानाबाद या जिल्हयांचा समावेश होतो.

लेखक : ग्रंथातील विचारास,मत प्रतिपादनास जी व्यक्ती जबाबदार असतील त्या व्यक्तीस लेखक किंवा ग्रंथकार असे म्हणतात. लेखक हा निर्मितीक्षम कलावंत असतो. तरी तो नेहमीच एक विशिष्ट समाजाचा घटक असतो. त्याच्या कृतीउक्तीला नेहमीच एक सामाजीक परिमाण असते. लेखक ज्याचा एक घटक असतो त्या समाजाची जिवनपध्दतीच त्याच्या अनुभवाचे संदर्भक्षेत्र असते. आणि कलात्मक कुतुहलाचेही त्याच्या समाज जिवनातील विषयप्रश्न समस्या, श्रेय, नितीमुल्य, प्रेयकल्पना इ.विशेष म्हणजेच त्याचे समाजवास्तव्य त्याच्या लेखनाचे विषय ठरत असतात.

लेखनकार्य :– एखद्या समस्ये संबंधी किंवा एखाद्या परिस्थिती संबंधीत वस्तुनिष्ठ लेखन केले जाते. तसेच एखादा विशिष्ट हेतू डोळयासमोर ठेवून माहितीचे संकलन केले जाते त्यास लेखनकार्य म्हणतात.

मराठवाडयातील लेखकांच्या लेखनाचे उद्देश :–

मराठवाडयातील लेखक खुप मोठया प्रमाणात लेखकार्य करतात. हे लेखनकार्य करत असताना त्यांच्यापुढे लेखनाची काही उद्देश असतात. ते खालील प्रमाणे.

- लेखकाने केलेले चिंतन, मानवी जीवन, मानवी मन,सभोवतालचे निसर्ग, वाचनात आलेले साहित्य, प्रवासातील व फिरण्यातील अनुभव हे सांगावयाचे वाटते म्हणून लेखक लेखनकार्य करतात.
- लेखकांचा आत्मविष्कार, बालपणीचे व मोठयापणीचे अनुभव व्यक्तीच्या जीवनाचा केलेला उत्कृष्ट भावनाविष्कार, इतिहास व ऐतिहासिक, धार्मिक स्थळे यातून सांगणे हा उद्देश असतो.

➢ पौरानिक ऐतिहासिक काळातील व्यक्तींच्या व्यक्तचिंतनाच्या अंगाने घेतलेला शोध किंवा नव्याने केलेली व्यक्तिचित्रणात्मक, भावनाचित्रणात्मक मांडणी होय.

➢ संस्कृतील परंपरेची धोरवी, कौतुक किंवा टिका करण्याच्या हेतूने लेखन करणे वृत्तपत्रासाठी लेखनाची मागणी विषयानुसार संपादकांनी पत्र पाठवून मागितलेले लेख लिहण्याच्या उद्देशाने केलेले लेखन.

➢ सामान्य विषयातून असामान्यत्व स्पष्ट करणे

➢ ग्रामीण व शहरी जिवनाचे बदलते व्यक्तीजीवनातील परिणाम सांगण्यासाठी लेखन

➢ लेखकांना भेटलेली व भावलेली माणसे त्यांची व्यक्तिचित्रण लिहीण्यासाठी लेखन.

लेखनकला :

लिपीचा शोध लागण्यापूर्वी प्रथम मौखिक परंपरेतून ज्ञानाचे आदान–प्रदान होत असे. वेदकालात अशा पध्दतीने ज्ञानाचे आदान–प्रदान झाल्याचे दिसून येते. लिपीचा शोध जरी लागलेा नसला तरी चित्राद्वारे, सांकेतांच्याद्वारे, चिन्हांद्वारे संवाद साधला जात असे. पुढे जेव्हा लिपीचा शोध लागला त्या वेळेला वेगवेगळया प्रकारचे लेखन साहित्य वापरले गेले. भुर्जपत्र, कमलपत्र, चामडे, शीलालेख, ताम्रपट इत्यादी साधनांचा वापर केला जात असे. यामध्ये झाडाच्या साली, मातीच्या वीटा यांचाही वापर लेखन करण्यासाठी केला गेला. सुरूवातीच्या काळामध्ये चित्रयुक्त लिखाण होते. नंतर प्रत्यक्ष वस्तुच्या सहायाने चित्राच्या सहायाने विचारले स्पष्टीकरण होउ लागले. लेखन हे दृष्य संप्रेषणाचे चिन्ह मानले जाते. चित्रयुक्त लिखाणामुळे या चित्राच्या सहायाने विचाराचे स्पष्टीकरण होउ लागले. त्यामुळे अर्थ समजण्यास सुलभता आली.

लेखन साहित्य :–

मानवी जीवन व्यवहाराविषयक चित्रण, विवरण, अर्थनिर्णयन, भाष्य,अशा स्वरूपाच्या भाषिक अभिव्यक्तीस स्थुलमानाने साहित्य असे संबांधले जाते. जीवन व्यवहाराचे भावनिक, अध्यात्मिक, बौध्दीक अशा विविध अंगाने घडविलेले सर्जनशील, वैचारिक कल्पनात्मक वास्तव्य अशा भिन्नभिन्न स्तरावरचे सर्वांगीण सम्यक दर्शन साहित्याचे दर्शन वाचनास प्रतित होते. लिटरेचर या इंग्रजी शब्दाच्या मराठीमध्ये साहित्य किंवा वाङःमय हे पर्याय सामान्यतः समानार्थी म्हणून वापरले जातात. लिटरेचर या संज्ञेला काळाच्या ओघात अनेक लेखक वाङःमयेतिहासकार साहित्याच्या सर्वसमावेशक अर्थ विचारात घेवून नानाविध अर्थ व अर्थछटा यांची परिमाने बहाल केली यातून या संज्ञेचा अर्थ विस्तार होवून ती बहुआयामी व व्यापक विस्तृत बनली.

साहित्याचे वर्गीकरण लघुकथा, कादंबरी, कविता, महाकाव्य, खंडकाव्य, नाटक, शोकात्मिका, सुखात्मिका, प्रहसण अशा अनेक प्रकारामध्ये साहित्याचे वर्गीकरण केले जाते. परंतू वाङःमयाचे वर्गीकरण स्थुलमानाने ललितसाहित्य व ललित्तेतर साहित्य अशा प्रकारात केले जाते.

अ. ललितसाहित्य :–

ललित साहित्य हे लेखकाच्या कल्पनाशक्तीतून निर्माण होते. त्याला वास्तवातील घटना, व्यक्ति, प्रसंग तपशील हयांचा पायाभुत आधार असला तरी त्यातून सकारणारे अनुभव विश्व ही लेखकाची कल्पक निर्मिती असते. ललित साहित्याचे लेखन ही मूलतः व्यक्तिनिष्ठ, भावप्रेरित, कल्पनानिर्मित म्हणजेच प्रतिभानिर्मिती असते. सौदर्यसिध्दीच्या तत्वानुसार ते अवतरलेले असते. तदंतर्गत सुसंघटना ही प्रत्येक लिलित साहित्यकृतीपरत्वे एक वेगळी वैशिष्टयपूर्ण सुसंगता असते. काव्य, कथा, कादंबरी, नाटक हे लिलत साहित्य प्रकाराचे प्रमुख प्रकार होत. ललित वा लघुनिबंध, नाटयछटा आदि प्रकारांचा उल्लेख करता येईल.

१⅛ **काव्य** :– काव्य या प्रकाराची भावनेवर भिस्त आहे. काव्य हे एक भाषिक संघटना माननारे काव्याच्या रूपाचे व भाषेचे महत्व मानतात. काव्याचा एकच अर्थ निश्चित करणे कठीण आहे. पण काव्यात मात्र वाच्यार्थपिक्षा सुचितार्थाचे महत्व जास्त आहे. काव्यातून सर्वसाधारणपणे व्यक्त होतो. तो काव्यानुभव या रचनेला कथात्मकतेची जोड मिळाली ते कथाकाव्य होते. अगदी जुन्या काळी मुद्रणकला नव्हती त्याकाळी ग्रंथलेखन व ग्रंथपठण यासाठी पद्यलेखन सोयीचे होते. स्मरणसुलभता आणि श्रवणसुलभता या कारणासाठी पद्याचा स्विकार भारतात सारास झालेला आहे. पूर्णपणे गद्य प्रकृतीचा रामदासांचा दासबोध सुध्दा पद्यातच आहे.

२½ नाटक :— नाटक हा खुप जुन्या काळापासून बहुचर्चित साहित्यप्रकार आहे. नाटकाला भरतमुनींनी 'दृष्यकाव्य' म्हटले आहे. ते अर्थपूर्ण आहे. नाटकातून व्यक्त होतो तो नाटयानुभव नाटकात रचनात्मक सौंदर्याला (Structural Beauty) ला महत्व असते आणि त्यामुळे ते एका बाजूला साहित्याशी संबंध ठेवीत दुसऱ्या बाजुला वास्तुकलेशीही संबंध राखते.

3½ dlncjh \& "आधुनिक वाङ्:मयात सर्वात विस्तृत आणि अनेक उपप्रकार सामावणारा प्रकार म्हणजे कादंबरी'' किंवा कादंबरी हा कलाप्रकार सर्वसंग्राहक आहे. त्यात काव्यमय गद्येही चालते नाटयात्मक संघर्शही (षोकान्त किंवा विनोदी) चालतो तात्वीक गुंज्नगुजन चालते कादंबरीचा संबंध सर्वच ज्ञानशाखांशी प्रत्यक्षाप्रत्यक्ष येवू शकतो. कारण कादंबरीला एक ठरावीक रूप, आकृतीबंध नाही तिचा विस्तार केवळ लेखकाच्या मर्जीवर आहे. वाचकांची काळजी वाहणारा कादंबरी सारखा दुसरा प्रकार नाही. म्हणून त्याची नेहमी निवेदनात्मक शैलीदार भिस्त असते.

ब.ललितेतर साहित्य :—

ललितेत्तर साहित्याचे मुख्य उद्दिष्ट वाचकाला माहिती व ज्ञान देणे अशा स्वरूपाचे असते. त्यात प्रत्यक्ष वास्तावाला त्यातील तथ्यातालाच केवळ प्राध्यान्य असते. लेखकाच्या कल्पनाविलासाला त्यात अजिबात वाव नसतो.

शब्द हेच माध्यम स्वीकारून विविध ज्ञानशाखांमधील ललितेतर वाङ्:मय निर्माण होत असते. वैचारिक, शास्त्रीय, संशोधनपर, चर्चाचिकित्सात्मक, तत्वमीमांसक अशा विविध प्रकारच्या वाङ्:मयाचा समावेश त्यात होतो. अर्थशास्त्र, मानवशास्त्र, समाजशास्त्र, मानसशास्त्र अशा विविध सामाजिक शास्त्रांवरील तसेच मानव्यविधा विषयक ग्रंथ, भौतिकी, रसायनशास्त्र, प्राणीविज्ञान, वनस्पतीविज्ञान इत्यादी शास्त्रीय माहिती देणारे वातत्संबंधी चर्चा करणारे ग्रंथ संशोधनपर, वैचारिक लिखान आदींचा अंतर्भाव ललितेतर वाङ्:मयामध्ये केला जातो.

लेखकांचे लेखनकार्य विषयनिहाय

प्रत्येक लेखक आपले लेखनकार्य विषयानुसार करीत असतात. त्यामुळे उदगीर शहरातील लेखकांचे लेखन कार्य विषय निहाय आहे का हे जाणून घेण्यासाठी संशोधकाने प्रश्न विचारला असता लेखकांनी त्यांचे लेखन कार्य विविध विषयामधील केलेले पहावयास मिळते. लेखक त्यांचे लेखन कार्य नेहमी विषयनिहाय करतात. त्या विषयामध्ये खालील विषयांचा समावेश केलेला पहावयास मिळतो.

- ऐतिहासिक घटना
- आरोग्य विषयक
- ग्रामीण जीवन
- सामाजिक आशय
- स्त्री जाणीवा
- राजकीय घडामोडी
- चरित्रविषयक
- शिक्षण
- कौटुंबीक आशय
- जातीविषय
- धार्मिक आशय
- चरित्रात्मक
- शेतीविषय

या विविध विषयावर लेखकांनी आपले लेखनकार्य केले आहे. सामाजिक विषयावर सर्वात जास्त लेखन झालेले पहावयास मिळते. त्याच बरोबर स्त्री जाणीवा या विषयावर सुध्दा मोठया प्रमाणात लेखन झालेले पहावयास मिळते.

निष्कर्ष

आज मराठवाडयातील लेखकांच्या लेखन कार्याचा अभ्यास केलास लेखकांचे लेखनकार्याचा अभ्यास करताना त्यांची लेखनकला,त्याचे लेखनकार्याचा उद्देश वेगवेगळे आसतात. लेखन कार्य करत आसताना कोणतेही लेखन पुर्णत: नवीन नसते त्याला कशाचा तरी अधार आसतो या अधारातील सुसंगतीचा अधारे लेखकांच्या लेखन पुर्ण करतात.

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Original Article

In Silico Molecular Docking Againstc-KIT Tyrosine Kinase and ADME Studies of 4-Thiazolidinone Derivatives

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ABSTRACT

Nowadays, the molecular docking approach is used to model the interaction between a small molecule and a protein at the atomic level, which allow us to characterize the behaviour of small molecules in the binding site of target proteins and to elucidate fundamental biochemical processes, C-KIT, a receptor tyrosine kinase, is involved in intracellular signalling, and the mutated form of C-KIT plays a crucial role in the occurrence of some cancers. In this research, we designed novel thiazolidine-4-one derivatives of 3-ethyl-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one with various benzilidine groups attached to the five-membered imino-thiazolidinone ring and studied molecular docking against C-KIT Tyrosine kinase target protein (1T46). The docking studies of these compounds showed the good interaction of the synthesized molecules with the 1T46 target protein. The ADME studies of these molecules have also been studied to identify which of the synthesized molecules have the potential to cross the Human Intestinal lining (HIA) and the BBB barrier. Out of the 18 molecules studied, 12 derivatives exhibited the good potential to be absorbed by the intestine out of which only one molecule was able to indicate the potential to cross the BBB barrier. There were 5 molecules that could not cross both barriers. These studies could reveal which functionalities present attached to the thiazolidine-4-one could assist in human intestinal absorption and the crossing of the BBB barrier.

Introduction

Computational docking methods are used to screen various possible compounds, searching for new compounds with specific binding properties, or testing a range of modifications of an existing compound. Due to the rapid rise in the amount of molecular biological data available, the computer-aided analysis of molecular interactions becomes more realistic in addition to which as of now the computer prediction of the interaction

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between proteins and small molecules has advanced to the point that it allows accurate prediction of bound conformations and affinity.

Likewise, the binding of small molecule majorly organic compounds which are ligands to large protein targets is significant to both understanding biological processes and designing drugs [1]. As many proteins regulate biological functions by interacting with small molecules, these receptor proteins are often the prime targets for therapeutic agents. Therefore, a detailed understanding of interactions between small molecules and proteins may form the basis for a rational drug-design strategy which is attractive in drug development concept due to two reasons: it may facilitate the development of more selective therapeutic agents with fewer undesirable side effects and will offer some hopes for reduction of the enormous costs and time required in traditional random screening protocols for drug discovery. Hence, by assuming the receptor structure is available in the PDB database, a major challenge in lead discovery and optimization is to predict both ligand orientation as well as binding affinity which could often be referred to as "molecular docking" [2,3].

Molecular docking has become an increasingly important tool for drug discovery and is the most widely employed technique whose goal is to predict the position and orientation of a ligand (a small molecule) when it is bound to a protein receptor or enzyme. The completion of the human genome project has resulted in broadening the scope of new therapeutic targets in drug design and discovery. Accordingly, the advancement in strategies such as excessive high-throughput protein purification, crystallography, and nuclear magnetic resonance (NMR) spectroscopy has been providing structural information of protein–ligand and protein complexes. This leads to the advancement which resulted in the development of computer-aided drug design, also known as molecular docking [4-5]. Molecular docking is a key tool in structural molecular biology and computer-assisted drug design which tries to predict the structure of the intermolecular complex formed between two or more constituent molecules, further trying to predict the position and orientation of a ligand when it is bound to a protein to know the predominant binding modes of a ligand with a protein of known three-dimensional structure. Simply this can be mentioned that docking is a method that predicts the preferred orientation of one molecule to a second when bound to each other to form a stable complex. Usually, these binding partners are biological macromolecules (e.g., protein, DNA/RNA, and peptide) or small molecules (e.g., endogenous ligands and drugs) and their preparations for the docking is just as important as the docking itself [6,7]. The computational approaches are currently being used for screening large databases of compounds to identify potential lead drug molecules. Hence, it can be mentioned that its main application lies in structure-based virtual screening for the identification of new active compounds towards a particular target protein [8]. It can also be stated that for a selected set of structures of a protein and a ligand, the ultimate goal of all docking methods is to predict the structure of the resulting complex and the biological activity of a given ligand.

In this study, molecular docking is performed between receptor i.e. protein molecule and ligand i.e. the novel thiazolidin-4-one derivatives which were already synthesized by the authors. They are the novel thiazolidine-4-one derivatives of 3-ethyl-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-onewhich belong to an important group of heterocyclic compounds containing sulphur, nitrogen, and carbonyl group in the 4th position in a five-member ring [9,10]. They are an important class of bioactive molecules with diverse biological activities, so it is often called "wonder nucleus". Furthermore, thiazolidinone gives out various derivatives which attracted great attention due to the diversity of their biological effects [11] such as antidiarrheal [12], antimicrobial [13], antidiabetic [14,15], antiarrhythmic activity[16], anticancer [17-26], anti-HIV [27], Ca^{2+} channel blocker [28], cardioprotective

[29], anti-ischemic [30], cyclooxygenasesinhibitory [31], and anti-platelet activating factor [32].

C-KIT, a receptor tyrosine kinase, is intricate in intracellular signalling, and the mutated form of C-KIT has important role in existence of some cancers. The role of C-KIT has directed to the thought that inhibiting c-Kit kinase activity can be a goal for cancer therapy [33]. The encouraging results of inhibition of c-Kit for treatment of cancers have been detected in some cancers like gastrointestinal stromal tumour, acute myeloid leukemia, melanoma, and other tumours, and these results have stimulated attempts toward improvement of using c-Kit as a capable target for cancer therapy [34]. The main procedure of handling the cancers is chemotherapy, in which anti-tumour compounds are administered to patients. This treatment is thought to be effective, particularly in the early stages of the disease, but it does not permanently cure the patient or totally extinguish cancer. Many factors are associated to the treatment catastrophe, among which we can remark the stage of the disease, the battle of tumour cells to the drugs, and the side effects of the action as the drugs used kill both the cancer cells and the normal cells, often becoming resistant to treatment [35]. It is therefore important to develop effective anti-cancer therapeutic agents with well-defined pharmacokinetic properties.

Therefore, concerning the potentiality of thiazolidinone compounds and CKIT as potential target for cancer theory, we decided to conduct molecular docking against C-KIT Tyrosine kinase target protein (1T46) of the novel thiazolidine-4-one derivatives of 3-ethyl-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-onewithvarious benzilidine groups attached to the five-membered imino-thiazolidinone ring.

Experimental

Docking studies

In this study, the affinity and binding modes of the examined molecules against the target protein were determined. First, the water molecules were removed from the crystal structures of target proteins, retaining only main-chain amino acids which are essential for binding. The co-crystallized ligands were used as the reference ligands to predict the binding pockets (Figure 1) and later ligand was removed. Then, the polar hydrogen atoms were added to protein structures to protonate them. The structures of the examined compounds were drawn by using ChemDraw Ultra 7.0 and BIOVIA Discovery Studio Visualizer 2021 which were later saved by using PDB formats. Next, the saved files were opened by using MGL AutoDock Tools software where the protein preparation was done and selected as macromolecule then saved in PDBQT format. The configuration file was created which contained receptor name, ligand name, output file name, X, Y, and Z coordinates of the grid box, and also the size X, Y, and Z of the grid box. Then, the ligand was prepared and any rotatable bonds if available were added. Thereafter, the Command Prompt was opened and AutoDock Vina software was used for running the docking process for each target receptor by ligand by entering necessary codes or commands. In each case, 9 docked structural poses, affinity, and RMSD data were generated by using the algorithm. The output from the Vina split software was further analysed and visualized by using BIOVIA Discovery Studio Visualizer 2021.

Figure 1 depicts the structure of the protein **1T46** on which molecular docking of all 18 earlier synthesized compounds have been performed.

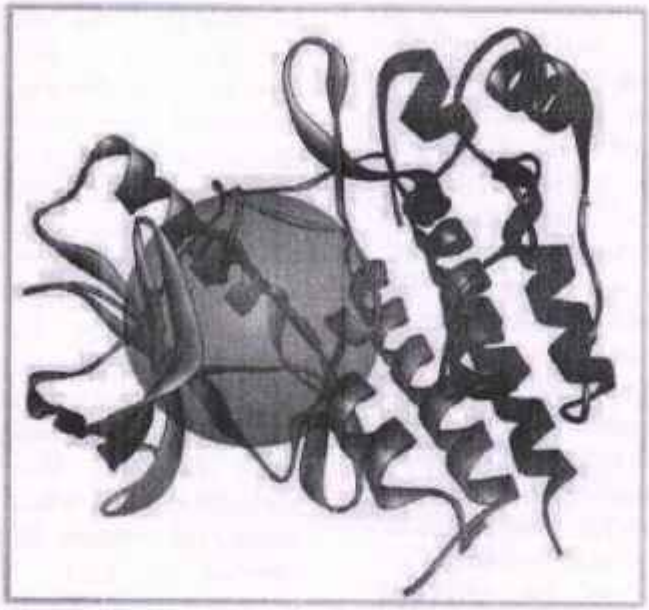


Figure 1. Proteins used for molecular docking - 1T46, C-KIT Tyrosine Kinase target protein

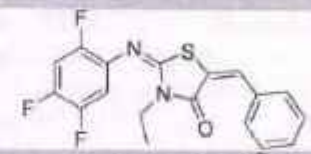
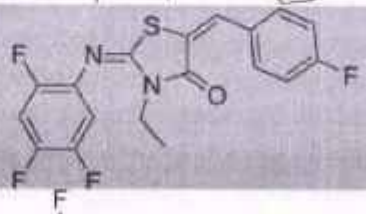
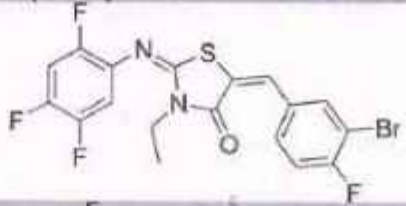
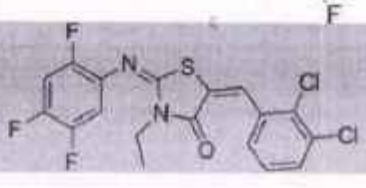
ADME study

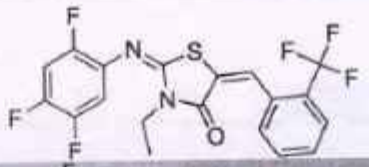
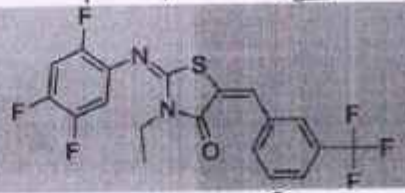
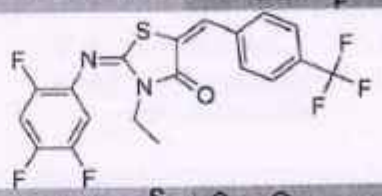
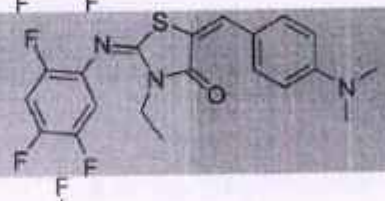
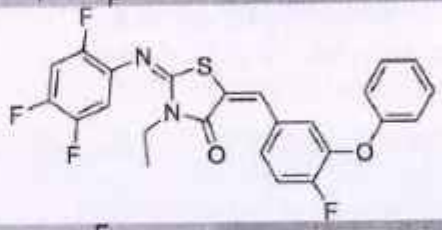
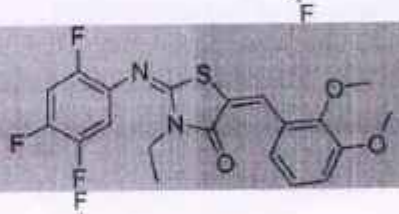
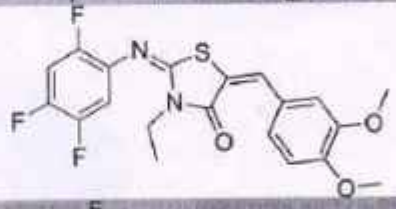
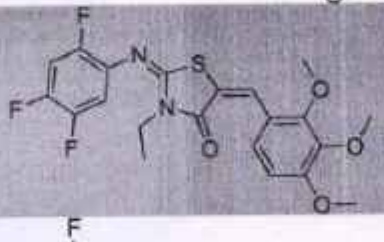
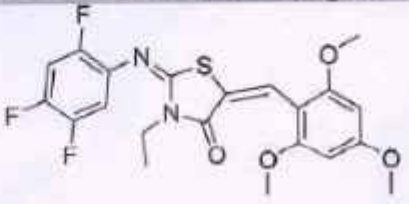
ADME study had been performed by using the Swiss ADME site (SwissADME). Primarily the structures were created with the help of ChemDraw Ultra 7.0 software and later uploaded on the Swiss ADME website to generate Smiles. These Smiles were used to generate ADME analysis data.

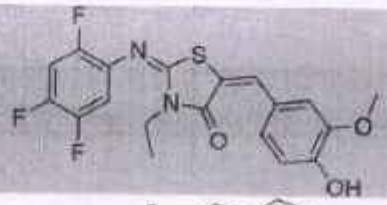
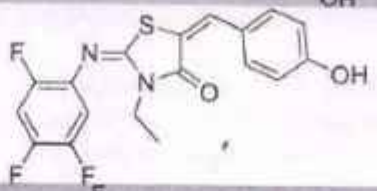
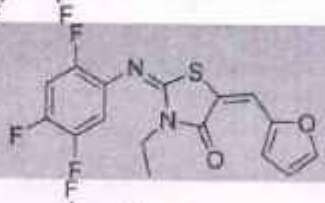
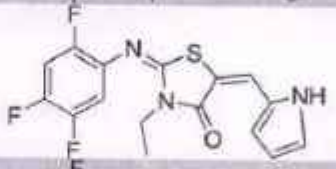
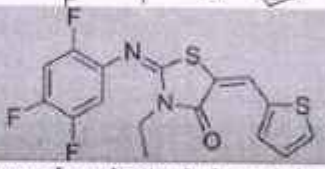
Results and Discussion

Molecular docking

Table 1. Molecules and their characteristics

Molecule No.	Name	Structure	Affinity (kcal/mol)
1	5-Benzylidene-3-ethyl-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-10.0
2	3-Ethyl-5-(4-fluoro-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-9.7
3	5-(3-Bromo-4-fluoro-benzylidene)-3-ethyl-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-7.2
4	5-(2,3-Dichloro-benzylidene)-3-ethyl-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-10.2

5	3-Ethyl-5-(2-trifluoromethyl-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-9.4
6	3-Ethyl-5-(3-trifluoromethyl-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-9.0
7	3-Ethyl-5-(4-trifluoromethyl-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-11.1
8	5-(4-Dimethylamino-benzylidene)-3-ethyl-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-7.6
9	3-Ethyl-5-(4-fluoro-3-phenoxy-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-7.8
10	**5-(2,3-**Dimethoxy-benzylidene)-**3-**ethyl-**2-(2,4,5-**trifluoro-phenylimino)-thiazolidin-**4-**one		-9.5
11	**5-(3,4-**Dimethoxy-benzylidene)-**3-**ethyl-**2-(2,4,5-**trifluoro-phenylimino)-thiazolidin-**4-**one		-9.4
12	3-Ethyl-2-(2,4,5-trifluoro-phenylimino)-5-(2,3,4-trimethoxy-benzylidene)-thiazolidin-4-one		-7.1
13	3-Ethyl-2-(2,4,5-trifluoro-phenylimino)-5-(2,4,6-trimethoxy-benzylidene)-thiazolidin-4-one		-6.6

14	3-Ethyl-5-(4-hydroxy-3-methoxy-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-9.5
15	3-Ethyl-5-(4-hydroxy-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-9.5
16	3-Ethyl-5-furan-2-ylmethylene-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-9.5
17	3-Ethyl-5-(1H-pyrrol-2-ylmethylene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-9.1
18	3-Ethyl-5-thiophen-2-ylmethylene-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one		-9.2

➢ 3-Ethyl-5-(4-trifluoromethyl-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one docking results against **1T46**

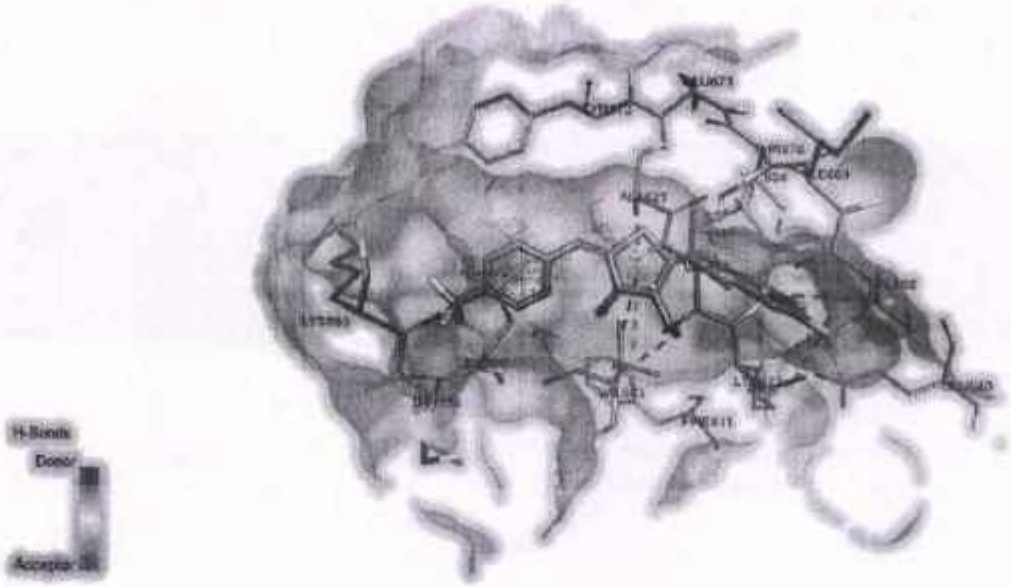


Figure 2. Molecular docking 3D interaction output of 3-Ethyl-5-(4-trifluoromethyl-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one, **7** against 1T46

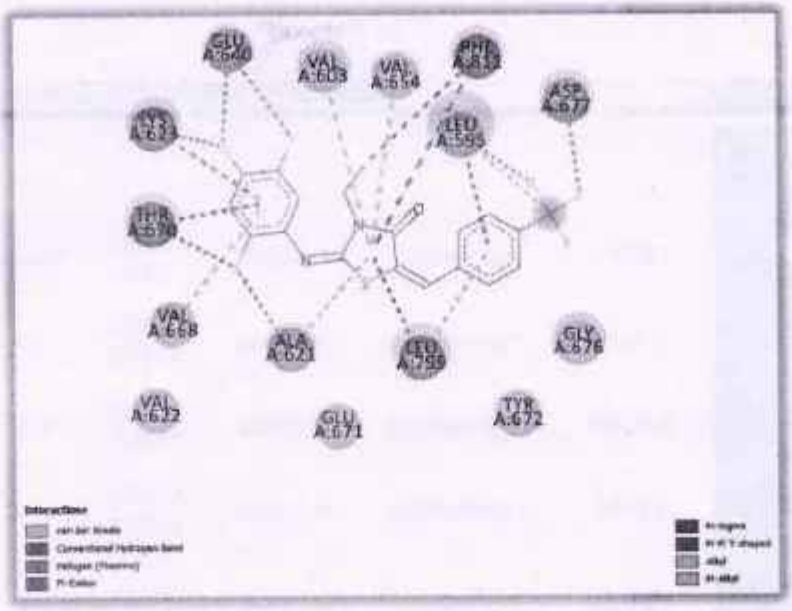


Figure 3. Molecular docking 2D interaction output of 3-Ethyl-5-(4-trifluoromethyl-benzylidene)-2-(2,4,5-trifluoro-phenylimino)-thiazolidin-4-one, 7 against 1T46

To visualize the interactions their 2D diagram and 3D interactions (color of bond interaction is justified in the table) of H-bonds, i.e. donor and acceptor are shown.

Table 2. Total Number of Favourable Interactions: 20

Sr. No.	NAME	COLOUR	DISTANCE	CATEGORY	TYPES OF BONDS	FROM	BONDS	TO	BONDS
1	A:LYS623:HZ3 - :UNK0:F24		2.81639	Hydrogen Bond;Halogen	Conventional Hydrogen Bond;Halogen (Fluorine)	A:LYS623:HZ3	H-Donor;Halogen Acceptor	:UNK0:F24	H-Acceptor;Halogen
2	A:THR670:HG1 - :UNK0:F23		2.56331	Hydrogen Bond;Halogen	Conventional Hydrogen Bond;Halogen (Fluorine)	A:THR670:HG1	H-Donor;Halogen Acceptor	:UNK0:F23	H-Acceptor;Halogen
3	A:LEU595:O - :UNK0:F27		3.2834	Halogen	Halogen (Fluorine)	A:LEU595:O	Halogen Acceptor	:UNK0:F27	Halogen
4	A:ALA621:O - :UNK0:F23		3.61139	Halogen	Halogen (Fluorine)	A:ALA621:O	Halogen Acceptor	:UNK0:F23	Halogen
5	A:GLU640:CD - :UNK0:F24		3.06836	Halogen	Halogen (Fluorine)	A:GLU640:CD	Halogen Acceptor	:UNK0:F24	Halogen
6	A:GLU640:OE1 - :UNK0:F25		2.9049	Halogen	Halogen (Fluorine)	A:GLU640:OE1	Halogen Acceptor	:UNK0:F25	Halogen
7	A:ASP677:OD2:		3.11815	Halogen	Halogen (Fluorine)	A:ASP677:OD2:	Halogen Acceptor	:UNK0:F	Halogen

	B - :UNK0:F 28					B	r	28	
8	A:LYS6 23:NZ - :UNK0	4.24359	Electrostatic	Pi-Cation	A:LYS62 3:NZ	Positive	:UN K0	Pi-Orbitals	
9	A:LEU5 95:CD2 - :UNK0	3.7209	Hydrophobic	Pi-Sigma	A:LEU5 95:CD2	C-H	:UN K0	Pi-Orbitals	
10	A:THR6 70:CG2 - :UNK0	3.43386	Hydrophobic	Pi-Sigma	A:THR6 70:CG2	C-H	:UN K0	Pi-Orbitals	
11	A:LEU7 99:CD1 - :UNK0	3.4092	Hydrophobic	Pi-Sigma	A:LEU7 99:CD1	C-H	:UN K0	Pi-Orbitals	
12	:UNK0: C14 - A:PHE8 11	3.74416	Hydrophobic	Pi-Sigma	:UNK0:C 14	C-H	A:P HE8 11	Pi-Orbitals	
13	:UNK0 - A:PHE8 11	5.76464	Hydrophobic	Pi-Pi T-shaped	:UNK0	Pi-Orbitals	A:P HE8 11	Pi-Orbitals	
14	:UNK0: C26 - A:LEU5 95	4.64106	Hydrophobic	Alkyl	:UNK0:C 26	Alkyl	A:LE U59 5	Alkyl	
15	:UNK0 - A:LYS6 23	4.58266	Hydrophobic	Pi-Alkyl	:UNK0	Pi-Orbitals	A:LY S62 3	Alkyl	
16	:UNK0 - A:VAL6 68	5.40553	Hydrophobic	Pi-Alkyl	:UNK0	Pi-Orbitals	A:V AL6 68	Alkyl	
17	:UNK0 - A:VAL6 03	4.69753	Hydrophobic	Pi-Alkyl	:UNK0	Pi-Orbitals	A:V AL6 03	Alkyl	
18	:UNK0 - A:ALA6 21	3.90841	Hydrophobic	Pi-Alkyl	:UNK0	Pi-Orbitals	A:AL A62 1	Alkyl	
19	:UNK0 - A:VAL6 54	5.47997	Hydrophobic	Pi-Alkyl	:UNK0	Pi-Orbitals	A:V AL6 54	Alkyl	
20	:UNK0 - A:LEU7 99	5.48695	Hydrophobic	Pi-Alkyl	:UNK0	Pi-Orbitals	A:LE U79 9	Alkyl	

The structure of 3-Ethyl-5-(4-trifluoromethyl-benzylidene)-2-(2, 4, 5-trifluoro-phenylimino)-thiazolidin-4-one as a ligand has been subjected to molecular docking with a protein molecule that would act as a receptor. Docking results observed 9 poses out of which pose having the lowest affinity (kcal/mol) was selected as the best docking pose and was considered for the ligand interaction. Here, 20 favorable interactions were observed where the ligand has bonded at the chosen pocket site in the selected pose. The given table demonstrates the information about the bonds between the ligand and amino acids which contains bond distance, types of bonds, from where the bond is forming and their types. The ligand formed two hydrogen bonds [conventional hydrogen bond with fluorine], five halogen bonds [with fluorine], one electrostaticbond [pi-cation] and twelve hydrophobic interactions [pi-sigma,pi-pi T-shaped, alkyl and pi-alkyl].

ADME study

The results of ADME studies of the 18 compounds have been depicted (Figure 4). Molecules with the absorption potential through the intestine appear in the white portion, while the absorbed molecules with

the potential to cross the BBB barrier appear in the yellow portion. The study shows that molecules **1, 2, 8, 10, 11, 12, 13, 14, 15, 16, 17,** and **18** are capable of being absorbed through the human intestine (HIA). Out of these 12 molecules only molecule **1** is observed to be capable of crossing the BBB barrier. This molecule demonstrates the good permeability potential across the BBB and has no substituents on the phenyl ring attached to the thiazolidin-4-one ring. Likewise, this molecule is demonstrated to follow all five rules of Lipinski's Rule, with no violations of any rule.

Molecule **8** indicates the good potential to be able to cross the BBB barrier, due to the presence of two methyl groups attached to the amine's nitrogen. The presence of heterocycles furan and pyrrole (as in molecules **16** and **17**) are close to the potential molecules that could cross the BBB barrier, while the thiophene presence (as in molecule **18**) decreases its potential to do so, probably due to larger size of sulphur, as compared with oxygen and nitrogen. The molecules **10, 11, 12, 13, 14,** and **15** having methoxy and hydroxyl groups are the good candidates that could be absorbed by the intestine.

Molecules **5, 6,** and **7** possessing $-CF_3$ functionalities, and molecule **9** possessing phenoxy group and fluoro groupson the phenyl ring attached to the thiazolidin-4-one ring, show no potential for absorption through the intestinal lining. The presence of halogen atoms –Br and –Cl is indicated to hamper its potential for intestinal absorption, as observed in molecules **3** and **4**. However, if only the –F group is present on the ring, the intestinal absorption improves and demonstrates more potential to cross the BBB barrier, as observed in the case of molecule **2**.

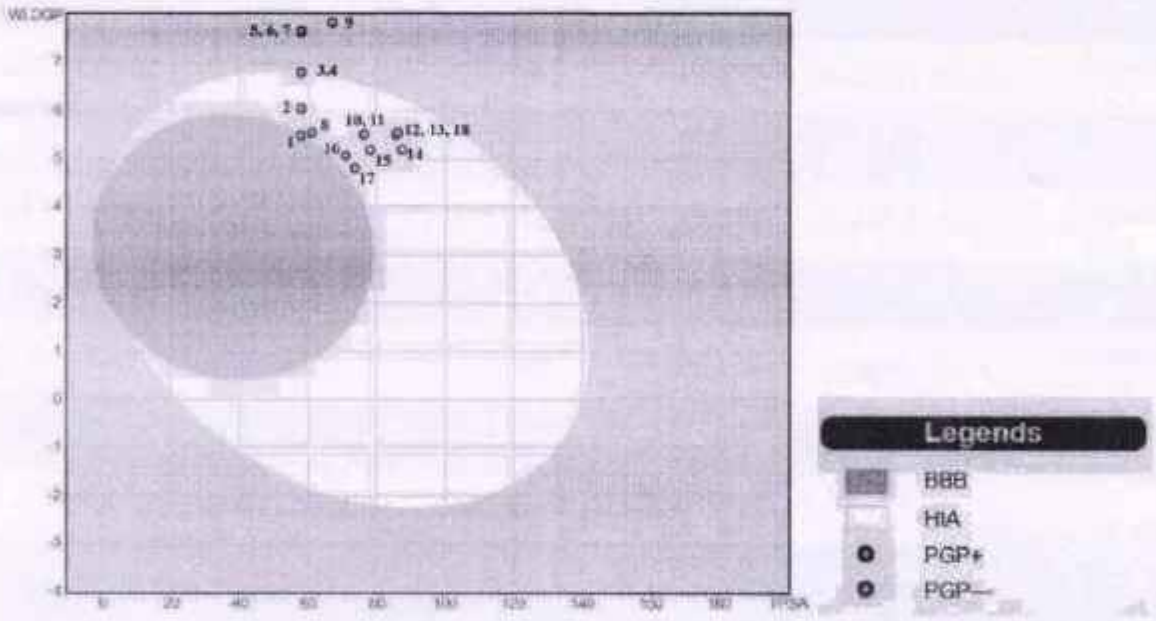


Figure 4. ADME Boiled egg Diagram

Table 3. Physicochemical Properties

Molecule No.	Formula	Physicochemical Properties				
		MW	Number of H-bond acceptors	Number of H-bond donors	MR	TPSA
Molecule 1	$C_{18}H_{13}F_3N_2OS$	362.37	5	0	96.85	57.97
Molecule 2	$C_{18}H_{12}F_4N_2OS$	380.36	6	0	96.81	57.97
Molecule 3	$C_{18}H_{11}BrF_4N_2OS$	459.26	6	0	104.51	57.97
Molecule 4	$C_{18}H_{11}Cl_2F_3N_2OS$	431.26	5	0	106.87	57.97
Molecule 5	$C_{19}H_{12}F_6N_2OS$	430.37	8	0	101.86	57.97
Molecule 6	$C_{19}H_{12}F_6N_2OS$	430.37	8	0	101.86	57.97
Molecule 7	$C_{19}H_{12}F_6N_2OS$	430.37	8	0	101.86	57.97
Molecule 8	$C_{20}H_{16}F_3N_3OS$	405.44	5	0	111.06	61.21
Molecule 9	$C_{24}H_{16}F_4N_2O_2S$	472.45	7	0	123.33	67.2
Molecule 10	$C_{20}H_{17}F_3N_2O_3S$	422.42	7	0	109.84	76.43
Molecule 11	$C_{20}H_{17}F_3N_2O_3S$	422.42	7	0	109.84	76.43
Molecule 12	$C_{21}H_{19}F_3N_2O_4S$	452.45	8	0	116.33	85.66
Molecule 13	$C_{21}H_{19}F_3N_2O_4S$	452.45	8	0	116.33	85.66
Molecule 14	$C_{19}H_{15}F_3N_2O_3S$	408.39	7	1	105.37	87.43
Molecule 15	$C_{18}H_{13}F_3N_2O_2S$	378.37	6	1	98.88	78.2
Molecule 16	$C_{16}H_{11}F_3N_2O_2S$	352.33	6	0	89.12	71.11
Molecule 17	$C_{16}H_{12}F_3N_2OS$	351.35	5	1	91.2	73.76
Molecule 18	$C_{16}H_{11}F_3N_2OS_2$	368.4	5	0	94.73	86.21

Table 4. Lipophilicity

Molecule No.	Lipophilicity					
	iLOGP	XLOGP3	WLOGP	MLOGP	Silicos-IT Log P	Consensus Log P
Molecule 1	3.45	4.88	5.5	4.12	5.5	4.69
Molecule 2	3.67	4.98	6.06	4.51	5.92	5.03
Molecule 3	3.84	5.68	6.82	5.11	6.6	5.61
Molecule 4	3.87	6.14	6.81	5.11	6.79	5.74
Molecule 5	3.72	5.77	7.67	4.95	6.58	5.74
Molecule 6	3.7	5.77	7.67	4.95	6.58	5.73
Molecule 7	3.73	5.77	7.67	4.95	6.58	5.74
Molecule 8	3.73	5.01	5.56	4.39	5.18	4.78
Molecule 9	4.41	6.51	7.85	5.25	7.04	6.21
Molecule 10	3.97	4.83	5.52	3.83	5.63	4.76
Molecule 11	3.76	4.83	5.52	3.83	5.63	4.71

Molecule 12	4.08	4.8	5.52	3.5	5.71	4.72
Molecule 13	4.39	4.8	5.52	3.5	5.71	4.79
Molecule 14	3.62	4.5	5.21	3.61	5.09	4.41
Molecule 15	3.07	4.53	5.2	3.54	5.02	4.27
Molecule 16	3.31	3.98	5.09	2.85	4.89	4.02
Molecule 17	3.09	3.71	4.83	2.85	5.02	3.9
Molecule 18	3.43	4.6	5.56	3.7	6.13	4.69

Table 5. Water Solubility

	Water Solubility											
Molecule No.	ESOL LogS	ESOL Solubility (mg/ml)	ESOL Solubility (mol/l)	ESOL Class	Ali LogS	Solubility (mg/ml)	Solubility (mol/l)	Class	Silicos-IT LogSw	Silicos-IT Solubility (mg/ml)	Silicos-IT Solubility (mol/l)	Silicos-IT class
Molecule 1	-5.32	1.74E-03	4.81E-06	Moderately soluble	-5.83	5.33E-04	1.47E-06	Moderately soluble	-6.72	6.83E-05	1.88E-07	Poorly soluble
Molecule 2	-5.48	1.26E-03	3.32E-06	Moderately soluble	-5.94	4.40E-04	1.16E-06	Moderately soluble	-6.99	3.88E-05	1.02E-07	Poorly soluble
Molecule 3	-6.4	1.84E-04	4.01E-07	Poorly soluble	-6.66	9.99E-05	2.17E-07	Poorly soluble	-7.77	7.78E-06	1.69E-08	Poorly soluble
Molecule 4	-6.51	1.32E-04	3.07E-07	Poorly soluble	-7.14	3.12E-05	7.24E-08	Poorly soluble	-7.9	5.44E-06	1.26E-08	Poorly soluble
Molecule 5	-6.19	2.81E-04	6.52E-07	Poorly soluble	-6.76	7.55E-05	1.75E-07	Poorly soluble	-7.55	1.20E-05	2.79E-08	Poorly soluble
Molecule 6	-6.19	2.81E-04	6.52E-07	Poorly soluble	-6.76	7.55E-05	1.75E-07	Poorly soluble	-7.55	1.20E-05	2.79E-08	Poorly soluble
Molecule 7	-6.19	2.81E-04	6.52E-07	Poorly soluble	-6.76	7.55E-05	1.75E-07	Poorly soluble	-7.55	1.20E-05	2.79E-08	Poorly soluble
Molecule 8	-5.56	1.11E-03	2.73E-06	Moderately soluble	-6.04	3.74E-04	9.22E-07	Poorly soluble	-6.8	6.40E-05	1.58E-07	Poorly soluble
Molecule 9	-6.94	5.37E-05	1.14E-07	Poorly soluble	-7.72	9.05E-06	1.92E-08	Poorly soluble	-9.16	3.25E-07	6.89E-10	Poorly soluble
Molecule 10	-5.48	1.40E-03	3.33E-06	Moderately soluble	-6.17	2.87E-04	6.79E-07	Poorly soluble	-6.93	4.95E-05	1.17E-07	Poorly soluble
Molecule 11	-5.48	1.40E-03	3.33E-06	Moderately soluble	-6.17	2.87E-04	6.79E-07	Poorly soluble	-6.93	4.95E-05	1.17E-07	Poorly soluble
Molecule 12	-5.56	1.25E-03	2.76E-06	Moderately soluble	-6.33	2.11E-04	4.67E-07	Poorly soluble	-7.03	4.22E-05	9.33E-08	Poorly soluble
Molecule 13	-5.56	1.25E-03	2.76E-06	Moderately soluble	-6.33	2.11E-04	4.67E-07	Poorly soluble	-7.03	4.22E-05	9.33E-08	Poorly soluble
Molecule 14	-5.2	2.24E-03	5.49E-06	Moderately	-6.0	3.58E-04	8.77E-07	Poorly soluble	-6.24	2.34E-04	5.74E-07	Poorly soluble

	6			soluble	6							
Molecule 15	-5.18	2.48E-03	6.56E-06	Moderately soluble	-5.89	4.83E-04	1.28E-06	Moderately soluble	-6.14	2.75E-04	7.28E-07	Poorly soluble
Molecule 16	-4.67	7.48E-03	2.12E-05	Moderately soluble	-5.17	2.36E-03	6.69E-06	Moderately soluble	-5.95	3.99E-04	1.13E-06	Moderately soluble
Molecule 17	-4.5	1.12E-02	3.19E-05	Moderately soluble	-4.95	3.94E-03	1.12E-05	Moderately soluble	-5.94	4.00E-04	1.14E-06	Moderately soluble
Molecule 18	-5.16	2.53E-03	6.87E-06	Moderately soluble	-6.14	2.70E-04	7.33E-07	Poorly soluble	-5.99	3.77E-04	1.02E-06	Moderately soluble

Table 6. Pharmacokinetics

Molecule No.	Pharmacokinetics								
	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s)
Molecule 1	High	Yes	No	Yes	Yes	Yes	No	No	-5.05
Molecule 2	High	No	No	No	Yes	Yes	No	No	-5.08
Molecule 3	High	No	No	No	Yes	Yes	No	No	-5.07
Molecule 4	High	No	No	No	Yes	Yes	No	No	-4.57
Molecule 5	Low	No	No	No	Yes	Yes	No	No	-4.83
Molecule 6	Low	No	No	No	Yes	Yes	No	No	-4.83
Molecule 7	Low	No	No	No	Yes	Yes	No	No	-4.83
Molecule 8	High	No	No	No	Yes	Yes	No	No	-5.22
Molecule 9	Low	No	No	No	Yes	Yes	No	No	-4.56
Molecule 10	High	No	No	No	Yes	Yes	No	No	-5.45
Molecule 11	High	No	No	No	Yes	Yes	No	No	-5.45
Molecule 12	High	No	No	No	Yes	Yes	No	No	-5.65
Molecule 13	High	No	No	No	Yes	Yes	No	No	-5.65
Molecule 14	High	No	No	No	Yes	Yes	No	No	-5.6
Molecule 15	High	No	No	No	Yes	Yes	No	Yes	-5.39
Molecule 16	High	No	No	Yes	Yes	Yes	No	Yes	-5.62
Molecule 17	High	No	No	Yes	Yes	Yes	No	Yes	-5.81
Molecule 18	High	No	No	Yes	Yes	Yes	No	No	-5.28

Table 7. Druglikeness

Molecule No.	Druglikeness					
	Lipinski Violations	Ghose Violations	Veber Violations	Egan Violations	Muegge Violations	Bioavailability Score
Molecule 1	0	0	0	0	0	0.55
Molecule 2	1	1	0	1	0	0.55
Molecule 3	1	1	0	1	1	0.55
Molecule 4	1	1	0	1	1	0.55
Molecule 5	1	1	0	1	1	0.55
Molecule 6	1	1	0	1	1	0.55
Molecule 7	1	1	0	1	1	0.55
Molecule 8	1	0	0	0	1	0.55
Molecule 9	1	1	0	1	1	0.55
Molecule 10	0	0	0	0	0	0.55
Molecule 11	0	0	0	0	0	0.55
Molecule 12	0	0	0	0	0	0.55
Molecule 13	0	0	0	0	0	0.55
Molecule 14	0	0	0	0	0	0.55
Molecule 15	0	0	0	0	0	0.55
Molecule 16	0	0	0	0	0	0.55
Molecule 17	0	0	0	0	0	0.55
Molecule 18	0	0	0	0	0	0.55

Table 8. Medicinal Chemistry

Molecule No.	Medicinal Chemistry			
	PAINS Alerts	Brenk Alerts	Leadlikeness Violations	Synthetic Accessibility
Molecule 1	0	3	2	3.7
Molecule 2	0	3	2	3.7
Molecule 3	0	3	2	3.72
Molecule 4	0	3	2	3.73
Molecule 5	0	3	2	3.83
Molecule 6	0	3	2	3.8
Molecule 7	0	3	2	3.8
Molecule 8	1	3	2	3.93
Molecule 9	0	3	2	4.03
Molecule 10	0	3	2	3.93
Molecule 11	0	3	2	3.87
Molecule 12	0	3	2	4.08
Molecule 13	0	3	2	4.07
Molecule 14	0	3	2	3.77
Molecule 15	0	3	2	3.67
Molecule 16	0	3	2	3.68
Molecule 17	0	3	2	3.71
Molecule 18	0	3	2	3.67

Conclusion

The synthesized thiazolidin-4-one derivatives have revealed the good interactions with the C-KIT Tyrosine Kinase (1T46) target protein, which indicates the good anti-viral potential of the molecules. The ADME studies show that groups like fluoro, hydroxyl, methyl, and methoxy demonstrate the good human intestinal absorption, which is not the case if chloro, bromo, and trifluoromethyl groups are attached to the heterocyclic ring. The *in-silico* methods can illustrate which functional groups in the molecules could aid in absorption in the body. This could give a proper direction to the synthetic organic chemist for synthesizing bio-active derivatives of thiazolidin-4-one.

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Efficient Organocatalytic Chiral Synthesis of (*R*)-Pipecolic Acid

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Abstract

Aldehyde obtained from unsymmetrical cleavage of cyclohexene by ozonolysis is subjected to L-proline catalyzed asymmetric α-amination reaction to obtain chiral amino alcohol with >99% ee which is subsequently converted into (*R*)-6-(hydroxymethyl)piperidin-2-one and (*R*)-pipecolic acid. Overall, a short and efficient asymmetric synthesis of (*R*)-pipecolic acid is described employing organocatalytic asymmetric α-amination of aldehyde as key step.

Keywords: organocatalysis; α-amination of aldehyde, pipecolic acid; unsymmetrical ozonolysis

1. Introduction

Functionalized piperidine derivatives are versatile building blocks for synthesis of various natural and unnatural bioactive molecules (Figure 1) [1,2]. (*R*)-Pipecolic acid (**1**) is one of the simplest members of substituted piperidine family. As it provides foundation for extension [3-9] to more complex and functionalized biologically active derivatives, it attracted synthetic chemists around the globe. This resulted in number of asymmetric synthesis [10-36] of (*R*)- and/or (*S*)-pipecolic acids based on enzymatic transformations, asymmetric hydrogenation, auxiliary directed alkylation, ring closing metathesis, and from chiral building blocks. Recently Greck et al. [26] synthesized (*R*)-pipecolic acid (**1**) using L-proline catalyzed α-amination of aldehyde derived from cyclohexene via ozonolysis. (*R*)-6-(Hydroxymethyl) piperidin-2-one (**2**), another member of piperidine family, is part of an important class of antitumor agents and is useful for the synthesis of pipecolic acid derivatives [37-41]. Recently Kumar et al. reported synthesis of **3** starting from L-aspartic acid [41]. In general, design and synthesis of conformationally constrained α-amino acids has attracted considerable attention from the synthetic and medicinal chemistry communities.

In the recent years, the area of asymmetric organocatalysis has provided several new transformations for obtaining chiral building blocks [42-47]. In this context, proline, a naturally occurring α-amino acid with secondary amine functionality, cheap and available in both enantiomeric forms and because of utility in different reactions, has emerged as the most practical and versatile organocatalyst [48]. Proline has also been found to be an excellent asymmetric catalyst for α-amination [49-53] of aldehydes and ketones.

As a part of our research program aimed at achieving asymmetric synthesis of biologically active molecules using organocatalysis [54-57], we wish to report organocatalytic asymmetric synthesis of (*R*)-pipecolic acid via (*R*)-6-(hydroxymethyl)piperidin-2-one using L-proline catalyzed α-amination of aldehyde as the key step.

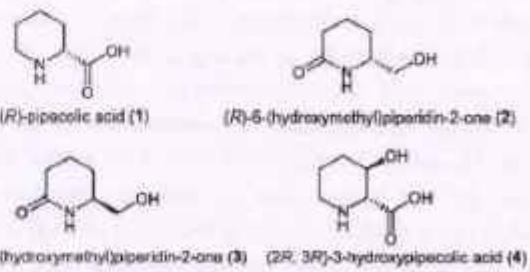

Figure 1 Structure of various piperidine derivatives

2. Results and discussion

From retrosynthetic analysis (Scheme 1), it was envisaged that (*R*)-pipecolic acid (**1**) and (*R*)-6-

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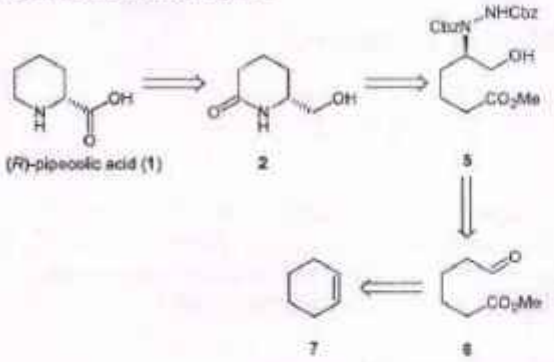
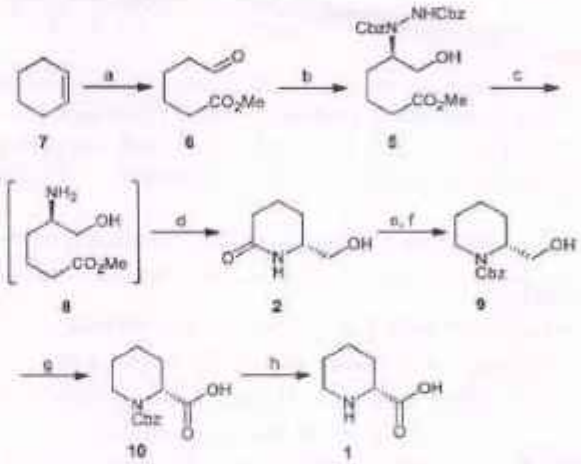
(hydroxymethyl)piperidin-2-one (**2**) could be synthesized from the aldehyde **6** using L-proline catalyzed α-amination to install required chirality. The aldehyde **6** could be derived from cyclohexene **7** using unsymmetrical ozonolysis.



Scheme 1 Retrosynthetic analysis of (*R*)-pipecolic acid

The synthetic approach began with commercially available cyclohexene **7** as outlined in Scheme 2. Ozonolysis [58-59] of cyclohexene **7** in CH_2Cl_2/MeOH in the presence of sodium bicarbonate at -78 °C followed by treatment with acetic anhydride and triethylamine afforded unsymmetrically cleaved functionalized aldehyde **6** in 82% yield [57]. Aldehyde **6** was subjected to α-amination with dibenzyl azodicarboxylate and L-proline (10 mol %) at 0 °C in CH_3CN followed by reduction with sodium borohydride in methanol at 0 °C (List protocol [49]) to furnish chiral amino alcohol **5** in 79% yield. The chiral purity of amino alcohol **5**, as determined by chiral HPLC analysis [60] was found to be >99%. The compound **5** was then subjected to W2 Raney Nickel-catalyzed hydrogenation in methanol with catalytic glacial acetic acid for benzylcarbamate deprotection and *N*-*N* bond cleavage affording crude aminoalcohol ester **8**. The crude aminoalcohol ester **8** on reflux in ethanol for 5h in presence of catalytic pyridine afforded (*R*)-6-(hydroxymethyl)piperidin-2-one (**2**) in 81% yield over two steps. The spectroscopic data of compound **2** was in accordance with data reported in the literature [40].

The hydroxylactam **2** on reduction with $BH_3.Me_2S$ in presence of $BF_3.Et_2O$ in THF under reflux condition for 24h afforded aminoalcohol which was immediately protected as benzyl carbamate using benzyl chloroformate and $NaHCO_3$ in dioxane: H_2O (1:1) at 0 °C affording compound **9** in 86% yield. Alcohol **9** on treatment with pyridinium dichromate in DMF at room temperature for 5h afforded acid **10** in 71% yield. Palladium-on-carbon catalyzed hydrogenation of benzyl carbamate **10** afforded (*R*)-pipecolic acid (**1**) in 93% yield. The physical and spectroscopic data of pipecolic acid **1** were in full agreement with the literature data [16]. Although Greek's approach [26] for (*R*)-pipecolic acid (**1**) also involves ozonolysis and L-proline catalyzed amination of aldehyde, but our approach is different one.



Scheme 2 *Reagents and conditions*: (a) O_3, $NaHCO_3$, CH_2Cl_2, MeOH, -78 °C then Ac_2O, Et_3N, 0 °C, 82%; (b) dibenzyl azodicarboxylate, L-proline, CH_3CN, 0 °C, 2h and rt, 1h then $NaBH_4$, MeOH, 0 °C, 5 min, 79%; (c) Raney Ni, H_2 (60 psi), cat. AcOH, MeOH, rt, 24h; (d) EtOH, reflux, 5h, 81% over two steps; (e) $BH_3.Me_2S$, $BF_3.Et_2O$, THF, reflux, 24h; (f) CbzCl, $NaHCO_3$, dioxane:H_2O (1:1), 0 °C, 86% over two steps; (g) pyridinium dichromate, DMF, rt, 5h, 71%; (h) Pd/C, MeOH, H_2 (20 psi), 4h, 93%.

3. Conclusion

In conclusion, proline-catalyzed α-amination approach has been successfully applied to the synthesis of (*R*)-6-(hydroxymethyl)piperidin-2-one and (*R*)-pipecolic acid. The present method is easily amenable for the synthesis of a variety of piperidine alkaloids. Currently, studies in this direction are in progress.

4. Experimental

4.1. General information

All reagents and solvents were of analytical grade or were purified by standard procedures prior to use. IR spectra were recorded on a Perkin-Elmer 68B infrared spectrophotometer. The ^1H (200 MHz/ 400 MHz) and ^{13}C (50 MHz/ 100 MHz) NMR spectra were recorded on a Bruker AC-200/ AC-400 spectrometers using TMS as internal standard. In ^{13}C NMR spectra, the carbon resonances were assigned by use of DEPT

experiments. Mass spectra were recorded at an ionization energy 70 eV on API Q STARPULSAR spectrometer using electrospray ionization. Elemental analysis data were obtained on a Carlo-Erba CHNS-O EA 1108 elemental analyzer. Optical rotations were measured on Jasco P-1020 polarimeter. Progress of the reactions was monitored by TLC on Merck silica gel 60 F254 precoated plates, and compounds were visualized by fluorescence quenching, by use of I_2, or by charring after treatment with a *p*-anisaldehyde–AcOH–H_2SO_4 mixture in EtOH. Column chromatography was performed on flash silica gel (230–400 mesh size).

4.2. Methyl 6-oxohexanoate 6

Yield: 8.871 g (82%); colourless liquid; IR ($CHCl_3$) ν_{max} 2987, 2952, 1735, 1714, 1252, 678 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ= 1.60-1.67 (m, 4H), 2.28-2.35 (m, 2H), 2.41-2.47 (m, 2H), 3.64 (s, 3H), 9.74 (t, 1H); ^{13}C NMR (50 MHz, $CDCl_3$): δ= 21.2, 24.0, 33.4, 43.1, 51.3, 173.5, 202.0 ppm.

4.3. (5*R*)-Methyl-5-(N,N'-(dibenzyloxycarbonyl) hydrazinyl)-6-hydroxyhexanoate 5

To a cooled solution of dibenzyl azodicarboxylate (90%, 8.25 g, 25 mmol, 1 equiv) and L-proline (287 mg, 2.49 mmol, 10 mol %) in CH_3CN (200 mL) at 0 °C, aldehyde **6** (3.600 g, 25 mmol) was added and the reaction mixture was allowed to stir at the same temperature for 2 h and then warmed to 20 °C within 1 h. After the reaction mixture became colourless, it was cooled to 0 °C, treated with EtOH (20 mL) and $NaBH_4$ (1.2 g), and was stirred for 5 min at 0 °C. The reaction mixture was worked up by adding aqueous ammonium chloride solution and extracting with ethyl acetate (3 x 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (pet. ether–ethyl acetate = 85:15).

Yield: 8.769 g (79%); viscous liquid; $[\alpha]_D^{25}$ = +27.6 (*c* 1.16, $CHCl_3$); ee >99% [50]; IR ($CHCl_3$) ν_{max} 3453, 2997, 1733 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ ppm 1.52-1.72 (m, 4H), 2.31 (t, *J* = 8 Hz, 2H), 3.50 (s, 3H), 4.13-4.24 (m, 2H), 4.67-4.83 (m, 1H), 5.15 (s, 4H), 7.33 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.3, 28.0, 34.5, 51.5, 58.6, 60.5, 67.8, 68.2, 127.7, 127.9, 128.1, 128.4, 135.5, 155.4, 156.6, 166.1 ppm; Elemental Anal. Calcd for $C_{23}H_{28}N_2O_7$: C, 62.15; H, 6.35; N, 6.30. Found: C, 62.18; H, 6.29; N, 6.27.

4.4. (*R*)-6-(Hydroxymethyl)piperidin-2-one 2

The solution of **5** (6.0 g, 13.51 mmol) in MeOH (100 mL) and acetic acid (10 drops) was treated with Raney nickel (6 g, excess) under H_2 (80 psi) atmosphere for 24 h. The reaction mixture was filtered over celite and concentrated to give crude γ-amino ester **8** which on stirring in EtOH (20 mL) in presence of catalytic pyridine at 50 °C for 5h to furnish crude cyclized product. Purification by silica gel column chromatography afforded lactam **2**.

Yield: 1.289 g (74%); white solid; mp 73 °C (Lit. 74 °C [40]); $[\alpha]_D^{25}$ = -22.5 (*c* 1.05, $CHCl_3$) {Lit. for *S*-isomer $[\alpha]_D^{25}$ = +22.2 (*c* 1.0, $CHCl_3$) [40]}; IR ($CHCl_3$) ν_{max} 3351, 2954, 1668, 1461, 1377, 1112, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ ppm 1.33-1.52 (m, 1H), 1.64-1.76 (m, 1H), 1.81-1.97 (m, 2H), 2.28-2.46 (m, 2H), 3.21 (broad s, 1H), 3.41-3.52 (m, 1H), 3.55-3.71 (m, 2H), 6.40 (broad s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 24.9, 31.3, 54.7, 65.7, 171.1 ppm; ESI-MS: *m/z* = 152.21 $[M + Na]^+$.

4.5. (*R*)-1-(Benzyloxycarbonyl)-2-(hydroxymethyl) piperidine 9

To the solution of lactam 2 (0.516 g, 4 mmol) in THF (20 mL) under argon atmosphere was added $BF_3.Et_2O$ (0.564 g, 4 mmol, 1 equiv) and boron-dimethyl sulfide (0.304 g, 4 mmol, 1 equiv) drop wise. Once H_2 evolution ceased, the solution was refluxed for 24h. The reaction mixture, washed with water, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the residue as crude amino alcohol which was used in the next reaction without further purification.

To cooled solution of amino alcohol and $NaHCO_3$ (0.403 g, 4.8 mmol, 1.2 equiv) in 1,4-dioxane: water (1:1, 20 mL) was added benzyl chloroformate (0.818 g, 4.8 mmol) at 0 °C and stirred at that temperature for 2h. The pH of reaction mixture was adjusted to 2 with dilute HCl and extracted with diethyl ether (2 x 50 mL), washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain crude product. Purification by column chromatography afforded carbamate **9**.

Yield: 0.856 g (86%); mp 53 °C (Lit. 49-52 °C [16]); $[\alpha]_D^{25}$ = -30.4 (*c* 1.15, $CHCl_3$). {Lit. $[\alpha]_D^{25}$ = +30.3 (*c* 1.15, $CHCl_3$) for *S*-isomer [16]}; ^1H NMR (200 MHz, $CDCl_3$): δ ppm 1.39-1.68 (m, 6H), 1.82 (broad s, 1H), 2.85-3.06 (m, 1H), 3.59-3.68 (m, 1H), 3.80-3.85 (m, 1H), 4.07 (d, *J* = 12.6 Hz, 1H), 4.32-4.46 (m, 1H), 5.14 (s, 2H), 7.25-7.36 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$): δ = 19.3, 24.8, 25.0, 40.0, 52.8, 60.5, 66.7, 127.5, 127.7, 128.4, 136.6, 156.3 ppm; ESI-MS: *m/z* = 272.34 $[M + Na]^+$.

4.6. (*R*)-N-(benzyloxycarbonyl)-pipecolic acid 10

To a solution of alcohol **9** (0.400 g, 1.60 mmol) in DMF (10 mL) was added pyridinium dichromate

(2.416 g, 6.4 mmol, 4 equiv) at room temperature and stirred at that temperature for 5h. After completion of reaction, as seen by TLC analysis, reaction mixture was diluted with water (100 mL) and extracted with EtOAc (2 x 30 mL), washed with water, brine, dried over anhydrous Na_2SO_4, concentrated under reduced pressure to obtain crude product. The crude product was purified by flash column chromatography to obtain pure acid **10**.

Yield: 0.299 g (71%); mp 83 °C (Lit. 84 °C [13]) $[\alpha]_D^{25}$ = +76.8 (*c* 0.2, CH_2Cl_2) {Lit. $[\alpha]_D$ = +77.6 (*c* 0.2, CH_2Cl_2) [13]}; ^{1}H NMR (400 MHz, $CDCl_3$): δ ppm 1.33-1.47 (m, 2H), 1.65-1.72 (m, 3H), 2.24-2.33 (m, 1H), 2.98-3.13 (m, 1H), 4.08 (dd, *J*= 8 Hz, 11 Hz, 1H), 4.89-5.02 (m, 1H), 5.16 (s, 2H), 7.32 (m, 5H), 10.63 (broad s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6, 24.5, 26.5, 41.7, 54.3, 67.5, 127.7, 127.9, 128.6, 136.4, 156.6, 177.3 ppm.

4.7. (*R*)-Pipecolic acid 1

A solution of acid **10** (0.200 g, 0.76 mmol) in ethyl acetate (20 mL) was stirred under H_2 (20 psi) in presence of catalytic 10% Pd/C (50 mg) for 4h. The catalyst was filtered through a bed of celite. The celite bed was again washed with water. The combined filtrate was concentrated under vacuum to obtain (*R*)-pipecolic acid **1**.

Yield: 0.091 g (93%); mp 271 °C (Lit. 271-274 °C [22]); $[\alpha]_D^{25}$ = +26.9 (*c* 1.15, water) {Lit. $[\alpha]_D^{25}$ = +26.3 (*c* 1, water) [22]}; ^{1}H NMR (400 MHz, D_2O): δ ppm 1.61-1.73 (m, 3H), 1.85-1.92 (m, 2H), 2.26-2.30 (m, 1H), 2.99-3.06 (m, 1H), 3.43-3.46 (m, 1H), 3.89 (dd, *J* = 8 Hz, 10 Hz, 1H); ^{13}C NMR (100 MHz, D_2O): δ = 21.30, 21.32, 25.7, 43.7, 57.0, 172.0 ppm; Elemental Anal. Calcd for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 55.81; H, 8.55; N, 10.81.

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6. Conflicts of interest

There are no conflicts to declare.

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ARTICLE

Organocatalytic Chiral Synthesis of Centrally Acting Muscle Relaxant (*S*)-Mephenesin

Sharad P. Panchgalle[1,✉], Vijaykumar S. More[2], Abhay S. Bondge[3] and Kalimoddin I. Momin[4]

ABSTRACT

Chiral synthesis of centrally acting muscle relaxant (*S*)-mephenesin was achieved using L-proline catalyzed α-aminoxylation of 3-(2-methylphenxoy)propanal as chirality induction step. The chiral synthesis started with commercially available 2-cresol and was accomplished in four steps with overall yield 56%. The enantiomeric excess of final product (*S*)-mephenesin is >98%. The chiral purity was determined by chiral-HPLC using Chiralcel-OD column. The synthesis involves oxidation of primary alcohol to aldehyde with iodoxybenzoic acid (IBX) as one of the steps.

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KEYWORDS

Mephenesin, Organocatalysis, L-Proline, α-Aminoxylation, Aldehyde, Iodoxybenzoic acid.

INTRODUCTION

Among the common proteogenic α-amino acids, only glycine is achiral and others are chiral molecules. Proteins made up of these amino acids are chiral in nature. Proteins are important biomolecules found in cells of living organisms. Enantiomers show different reactions with other chiral molecules. This indicates that the living organism have different interaction with the enantiomers. In some cases, one enantiomer gives desired effect on living organism and other enantiomer gives severe side effects. Due to this scientific community turned towards chiral drug molecules instead of racemic drug molecules. The quest of chiral drug molecules can be fulfilled by resolution of racemic mixture [1-4] and asymmetric synthesis [5-8]. The resolution of racemic mixture is not the perfect solution for getting chiral molecules because half material will be waste in this method. To overcome drawbacks of resolution of racemic mixture, chemists designed asymmetric synthesis by using chiral catalysts. In last century, metal-ligand catalyst ruled over the scientific community [9-12]. Use of organometallic compounds as catalyst have limitations such as high toxicity of metal, disposal of metal catalyst after use, *etc*. In last few decades, use of chiral organic molecules as catalyst has emerged as front runner and the world came across the term "organocatalysis" [13-18]. Organocatalysis gained the recognition in the form of 2021 Nobel Prize in Chemistry to Prof. Benjamin List and Prof. David W.C. McMillan. In recent years, many organocatalytic reactions are reported for getting variety of chiral molecules and chiral building blocks [19-23].

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In year 2003, Hayashi *et al.* [24], MacMillan *et al.* [25] and Zhong [26] independently reported the organocatalytic α-aminoxylation reaction of aldehyde for synthesis of chiral 1,2-diols. This method of preparation of chiral 1,2-diol has several favourable things such as cheap antipodes of proline, low catalyst loading (10-20 mol%), high enantioselectivity and high yield of 1,2-diols.

3-Aryloxypropane-1,2-diols (Fig. 1) are chiral building blocks for bioactive compounds. Some important 3-aryloxy-proane-1,2-diols are listed in Fig. 2. Literature survey revealed that there are many routes for chiral 3-aryloxypropane-1,2-diols involving use of metal catalyst such as osmium tetroxide (OsO_4) for dihydroxylation [27], Jacobson catalyst for hydrolytic kinetic resolution [28,29] and enzymatic resolution [30,31].

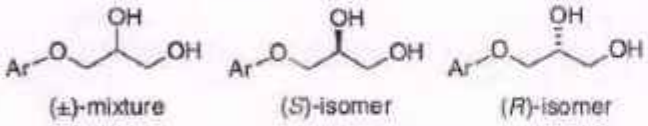


Fig. 1. 3-Aryloxy-1,2-propanediols

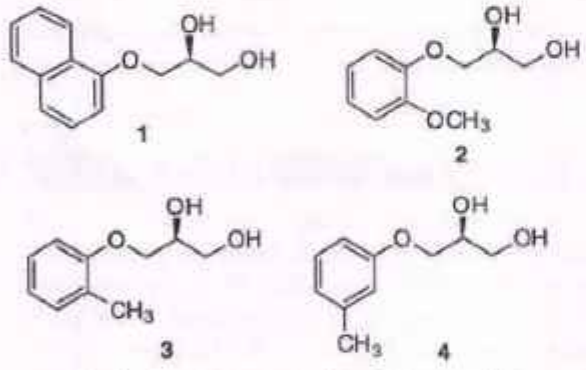


Fig. 2. Some important 3-aryloxy-1,2-propanediols

Our group was first to apply L-proline catalyzed asymmetric α-aminoxylation reaction for synthesis of chiral 3-aryloxypropane-1,2-diols. In 2009, the synthesis of (*S*)-3-(1′-naphthoxy)propane-1,2-diol (**1**) in > 98% ee and subsequently compound **1** converted into β-blockers *viz.* (*S*)-propranolol and (*S*)-naftopidil [32]. Using the same methodology, the organocatalytic asymmetric synthesis of (*S*)-guifenesin (**2**) and subsequently conversion of compound **2** into antihypertensive drug (*S*)-moprolol and skeletal muscle relaxant (*R*)-methocarbamol [33] is also reported.

(*S*)-Mephenesin (**3**) is a well-known centrally acting muscle relaxant. Literature has some reports for synthesis of compound **3**. Earlier reports involve dihydroxylation [27] of alkene with OsO_4, enzymatic resolution of racemic diol [30] and chiral pool approach [34]. Till date, nobody synthesized (*S*)-mephenesin (**3**) using organocatalysis. With our organocatalytic expertise towards the synthesis of chiral 3-aryloxypropane1,2-diol, we planned asymmetric synthesis of (*S*)-mephenesin (**3**) using L-proline catalyzed α-aminoxylation reaction of aldehyde.

EXPERIMENTAL

Reagents and solvents were of analytical grade or were purified by standard procedures prior to use. IR spectra were recorded on a Perkin-Elmer 1615 FT infrared spectrophotometer. ^{1}H (200 MHz) and ^{13}C (50 MHz) NMR spectra were recorded on a Bruker AC-200 spectrometer. The carbon resonances were assigned by use of DEPT experiments. Mass spectra were recorded at an ionization energy 70 eV on API Q STARPULSAR spectrometer using electrospray ionization. Microanalytical data were obtained on a Carlo-Erba CHNS–O EA 1108 elemental analyzer. Optical rotation was measured on Jasco P-1020 polarimeter. Progress of the reactions was monitored by TLC on Merck Silica Gel 60 F_{254} precoated plates and compounds were visualized by fluorescence quenching, by use of I_2 or by charring after treatment with a *p*-anisaldehyde–AcOH–H_2SO_4 mixture in ethanol. Column chromatography was performed on flash silica gel (230-400 mesh size).

3-(2-Methylphenoxy)propanol (7): To a 100 mL two-necked round bottom flask equipped with reflux condenser and rubber septum was charged 2-cresol (**6**) (2.160 g, 20 mmol) and 10% aqueous NaOH solution (20 mL) and stirred. After formation of homogeneous solution, 3-bromopropanol (3.056 g, 22 mmol) was added and refluxed for 6 h. The progress of reaction was checked by TLC analysis. After completion of reaction, the reaction mixture extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layer was washed with water (1 × 50 mL), brine, dried over anhydrous Na_2SO_4, filtered and concentrated on rotary evaporator under reduced pressure. Residue was purified by flash column chromatography (silica gel) using EtOAc-petroleum ether (15:85) as an eluent, affording the alcohol **7**. Yield: 2.357 g (71%); yellow oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 2.01-2.13 (m, 2H), 2.22 (s, 3H), 3.88 (t, J = 6 Hz, 2H), 4.12 (t, J = 6 Hz, 2H), 6.82-6.91 (m, 2H), 7.12-7.20 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 15.85, 31.81, 59.29, 64.59, 110.52, 120.02, 126.11, 126.48, 130.25, 156.58.

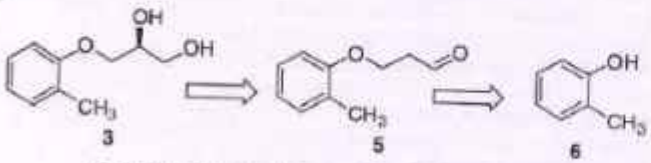
3-(2-Methylphenoxy)propanal (5): To a 50 mL two neck round bottom flask equipped rubber septum and two-way stop cork with argon balloon was added alcohol **7** (2.098 g, 12.63 mmol) and anhydrous DMSO (15 mL) and stirred. To this stirring solution was added iodoxybenzoic acid (IBX, 5.304 g, 18.94 mmol, 1.5 equiv.) and content of flask was stirred at room temperature for 2 h. The reaction mixture was diluted with water (10 mL) and then with diethyl ether (100 mL). The two layers were separated and diethyl ether layer was filtered through a bed of celite. The filtrate was washed with water (2 × 50 mL), brine, dried over anhydrous Na_2SO_4, filtered and concentrated on rotary evaporator under reduced pressure to afford aldehyde **5**. Yield: 1.866 g (90%); yellow oil; IR ($CHCl_3$, cm^{-1}): 3064, 3004, 2958, 2837, 2358, 2046, 1725, 1593, 1504, 1253, 744; ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 2.17 (s, 3H), 2.87-2.94 (m, 2H), 4.32 (t, J = 6 Hz, 2H), 6.82-6.91 (m, 2H), 7.11-7.20 (m, 2H), 9.88 (t, J = 1.77 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 15.85, 43.00, 61.44, 110.76, 110.95, 120.59, 126.59, 130.50, 156.30, 200.36 ppm.

(*S*)-3-(2-Methylphenoxy)propane-1,2-diol or (*S*)-mephenesin (3): To a 100 mL two-necked round bottom flask equipped rubber septum and two-way stop corked with argon balloon was added aldehyde **5** (0.901 g, 5.494 mmol) and nitrosobenzene (0.587 g, 5.494 mmol) and acetonitrile (50 mL) and stirred at -20 °C. To this stirring solution was added L-proline (0.126 g, 1.095 mmol, 20 mol %). The reaction

mixture was stirred at -20 °C for 24 h. To this cooled reaction mixture, methanol (25 mL) and $NaBH_4$ (0.313 g, 8.236 mmol) was added and reaction mixture was stirred for 10 min at -20 °C. Phosphate buffer was added to reaction mixture for quenching of reaction. The reaction mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated on a rotary evaporator under reduced pressure to afford crude aminoxy alcohol. The crude aminoxy alcohol was used as it was for next step. To a single necked round bottom flask containing crude aminoxy alcohol was added methanol (30 mL) and then added 10% Pd/C (70 mg) carefully. The reaction mixture was then stirred under a hydrogen atmosphere (1 atm. of H_2) for 6 h. The reaction was monitored by TLC analysis. After completion of the reaction, the reaction mixture was filtered through a celite pad and then concentrated to near dryness. Purification by flash column chromatography (silica gel) using EtOAc-petroleum ether (40:60) as an eluent afforded (*S*)-mephenesin **3**. Yield: 0.880 g (88%); white crystals; m.p.: 90-91 °C [Lit. [34] m.p.: 90-91 °C]; $[\alpha]_D^{25}$ = -19.16 (*c* 0.910, hexane:2-propanol 4:1) [Lit. [30] $[\alpha]_D^{25}$ = -19.16 (*c* 0.910, hexane:2-propanol 4:1)] ee >98% [Chiral HPLC analysis: Chiralcel OD (250 × 4.6 mm) column; eluent: 2-propanol: petroleum ether 7.5:92.5; flow rate: 1 mL/min, detector: 220 nm t_R = 15.85 min, t_S = 15.18 min]; IR ($CHCl_3$, cm^{-1}): 3448, 3064, 3004, 2881, 2580, 1652, 1647, 1593, 742 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ ppm: 1.63 (brs, 2H), 2.22 (s, 3H), 3.73-3.91 (m, 2H), 3.93-4.20 (m, 3H), 6.80-6.92 (m, 2H), 7.12-7.19 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 16.17, 63.79, 68.97, 70.54, 111.06, 120.93, 126.58, 126.87, 130.74, 156.37 ppm; LC-MS: *m/z* = 205.16 (M⁺ + Na); Anal. calcd. (found) % for $C_{10}H_{14}O_3$: C, 65.92 (65.87); H, 7.74 (7.76).

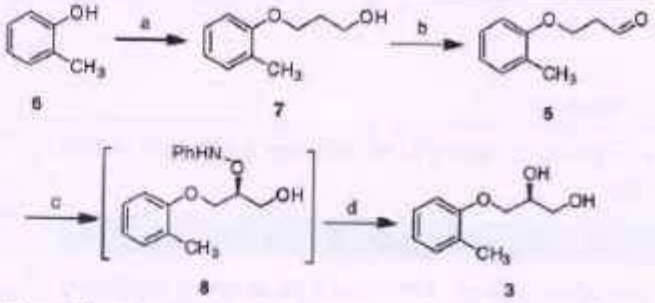
RESULTS AND DISCUSSION

The retrosynthetic analysis of (*S*)-mephenesin (**3**) shows that compound **3** can be easily obtained from aldehyde **5** through L-proline catalyzed α-aminoxylation reaction and aldehyde **5** can be easily obtained from 2-cresol (**6**) (**Scheme-I**).



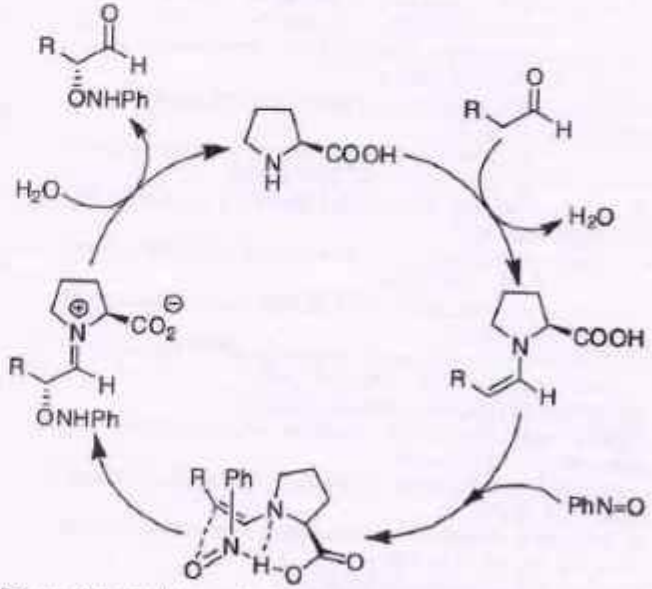
Scheme-I: Retrosynthetic analysis of (*S*)-mephenesin

As per retrosynthetic analysis, we started the synthesis of (*S*)-mephenesin (**3**) with commercially available 2-cresol **6** (**Scheme-II**). 2-Cresol (**6**) on refluxing with 3-bromopropanol in presence of aqueous NaOH solution undergoes Williamson reaction and afforded alcohol **7** in 71% yield. The oxidation of primary alcohol **7**, carried out by treating it with 2-iodoxybenzoic acid (IBX) in anhydrous DMSO at room temperature, gave aldehyde **5** in 90% yield. The triplet at 9.88 δ ppm in ^1H NMR spectra and peak at 200. 36 δ ppm in ^{13}C NMR spectra confirmed the presence of aldehyde group in compound **5**. For α-aminoxylation reaction, a solution of aldehyde **5** in acetonitrile treated with nitrosobenzene in presence of L-proline



Scheme-II: Reagents and conditions: (a) 3-bromopropanol, 10% aq NaOH, reflux, 6 h, 71%; (b) 2-iodoxybenzoic acid, $(CH_3)_2SO$, rt, 2 h, 90%; (c) Nitrosobenzene, L-proline, CH_3CN, -20 °C, 24 h then $NaBH_4$, MeOH, -20 °C, 0.5 h; (d) 10% Pd/C, MeOH, H_2, rt, 6 h, for two steps 88%

(20 mol%) at -20 °C for 24 h and resultant solution then treated with $NaBH_4$ in methanol in same pot to afford crude aminoxy compound **8**. The crude aminoxy compound **8** without purification treated with H_2 gas (1 atm) in presence of 10% Pd/C in methanol resulted in breaking of O-N bond and afforded (*S*)-mephenesin (**3**). The ^1H NMR spectra of (*S*)-mephenesin (**3**) shows the methine proton at C-2 overlapped with two methylene protons of C-1 at 3.93-4.20 δ ppm. The ^1H NMR spectra and ^{13}C NMR spectra of (*S*)-mephenesin (**3**) were in good agreement with the structure. The optical purity of (*S*)-mephenesin (**3**) was determined by chiral HPLC using Chiralcel OD (250 × 4.6 mm) column and was found to be >98%. The catalytic cycle for α-aminoxylation reaction of aldehyde is shown in **Scheme-III**.



Scheme-III: Catalytic cycle of L-proline catalyzed α-aminoxylation of aldehyde

Conclusion

An efficient and enantioselective synthesis of centrally acting muscle relaxant (*S*)-mephenesin was achieved in 56% overall yield starting with commercially available 2-cresol. The L-proline catalyzed α-aminoxylation reaction of aldehyde was the chirality induction step and afforded >98% optical purity. High yields, high ee, availability of starting material and organo-

catalytic green asymmetric reaction are highlights of this approach.

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Demonetisation: A Boon Or Bane

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Abstract

Demonetisation was effectively planned by the think-tank but suddenly declared in an unplanned way to curb black money in Indian economy. The cash ban caused considerable damage to the wheels of the economy in the form of forced unemployment. The Indian informal sector, which provides 80 percent of total employment was much affected. The reverse migration of work force necessitated them to adopt to a meal per day. Nearly, 2.5 lakh workers in leather industry, 20,000 workers in diamond industry 15% to 20% of daily wagers in Jewel sector have become jobless. The Gross Domestic Product (GDP) estimate was reduced to 7.1% from 7.6% for the year 2016-17 by the Government itself. The International Monetary Fund (IMF) has also lowered the GDP forecast to 6.6% for 2016-17. New Investments fell by 50% in post cash ban. Rupee value also declined by 1.69% on 15.12.16. The surgical strike on black money has derailed the investors' confidence in the stock market in the beginning. The cost of Demonetisation is estimated at Rs. 4.3 trillion including the GDP losses. The Government felt the impact is transient, but the economists viewed it as firing cannonballs to kill mosquitoes. To conclude, Demonetisation is a long pending measure to curb black money. In addition, the govern- ment has to employ in time all other pertinent measures in an exigent mode to make the cash ban a grand success.

Keywords

Demonetisation, Brexit 2016, fake indian currency notes network, private final consumption expenditayre, cash centric, AMRUT, RERA, Benami Transaction Act, CBDT, industrial lobby, cyber security, USSR, CIS, corporate governance reforms.

Introduction

The Indian Govt. gave an unexpected shock to its citizens on 8th Nov, 2016 by nullifying high value currency. The three big surprises of 2016 viz., Brexit 2016, Donald Trump Win and the India's Demonetization created an uncertainty in the Indian economy[1]. The Annual Report of Reserve Bank of India (RBI) 2015- 16 revealed that total bank notes circulated in India were valued at Rs. 16.42 trillion of which nearly 86% were of Rs. 500 and Rs. 1000 denomination.

The Demonetisation of such high value notes grinded the Indian economy to a virtual halt.

Cash Is King

The informal sector which provides nearly 80% of total Indian employment is cash centric. The sector consists of 21000 unorganized markets, 38.3 million small and medium size enterprises. About 92% of the trade in Fast Moving Consumer Goods (FMCG) is taking place across petty shops (Kiranas) in India[3]. As the note ban move was sudden and unplanned, it caused considerable inconvenience to the daily wagers and working class. The earlier attempts to demonetize the notes in 1946 and 1978 did not affect the working class since less than 5% of population had access to those high value notes[4]. The recent step to cash ban is a bold step and daring to implement because outcome is uncertain.

Statement of the Problem

Since independence, corruption, black economy and sponsored terrorist act were a major hurdle for India's economic growth. For instance, India stood 76th rank out of 168 nations in International Corruption Index 2015. Moreover, the Income Tax raid held between April 2014 and Nov 2016 unearthed nearly Rs. 31,277 crore black money and Rs. 2164 crore worth of undisclosed assets[5]. The RBI had detected nearly 6.5 lakh fake notes of higher value in circulation as per its Annual Report 2016[6]. From 2013, 205 out of 608[7] districts in India were badly affected by terrorism and such incidents are more frequent at present. This provoked the Indian Army to conduct surgical attacks on enemies. Fake Indian Currency Notes (FICN) Network is funding the terror networks in India. Because of this India lost nearly 707 lives and more than 3200 were injured so far. The recent bout of

Demonetisation was a long pending affair as Rome was not built in a day. Finally the govt. announced the cash ban on Nov 8, 2016 anticipating the short term pain for long term gain to the society.

Transient Impact of Demonetization

Demonetisation has caused a sudden breakdown in Indian commercial eco system. Cash centric sectors were virtually shutdown. The rural population became job loss. Poor and working people have been dislocated and their livelihoods were irreparably damaged. Farmers could not buy inputs, private hospitals refused to treat patients who had only old notes. Some of the working class found difficulty in buying food and forced to adopt a meal per day. Wedding and other social events were disrupted because the working class did not have access to structural set up to adopt to this shock doctrine economics.

Demonetisation And Employment

The job creation is always a challenge to the Govt. even before demonetization. The cash ban resulted in more job losses in various sectors of the economy. Nearly 2.5 lakh workers in leather industry and 15% to 20% of daily wagers in jewel sector became jobless[8]. Majority of ceramic tiles units were closed in Gujarat. In Surat, more than 20,000 workers in diamond sector lost their job. The Demonetisation results in reverse migration of work force thereby crores of people lost their earnings[9]. According to Sitaram Yecherury, CPI, since 8th No 2016, four lakh jobs were vanished and more than 31.9 million textile workers have not been getting wages. All India Manufacturers Association (AIMA) projected a drop in employment of 60% and loss in revenue of 55% to its member units during post demoneti- zation. Indian infrastructure sector saw a cut of 35% in its employment mainly due to cash crunch[10].

The Budget 2017-18 created a positive impact on Indian job market. According to Rituparna Chakraborty, Teamlease, budget directly suggests employment for youth in tourism, footwear, leather, textile and manufacturing industries. Relaxation of tax on corporate from 30% to 25% will increase the employment by 5 to 10%. As investment focus on infrastructure, it also going to boost employment in the sector. The digital payments also encourage job creation in cyber security and allied sector.

Demonetization and Investments

As per the World Bank Report, Capital formation in India has downward trend since 2011. In addition, Demonetisation has created an uncertainty in the flow of investments. New investments fell by 50% in post demonetization. The investment proposals which were 227 prior to cash ban declined to 177 till 31st December 2016. The value of investment proposals were dropped from Rs. 81.8 thousand crore to Rs. 43.7 thousand crore during the period. The Private Final Consumption Expenditure (PFCE) reduced from 7.5% in 2015-16 to 5.5% in 2016-17[11].

But the Govt.'s commitment to macroeconomic stability like lowering inflation, reduced bank rate and bank deposit rate, the sharp reduction in current account deficit became strong fundamentals for India to attract more investments. The Govt. of West Bengal received investment proposals worth Rs. 2.35 lakh crore on January 2017[12]. The union budget 2017-18 also paved way for a healthy investment atmosphere in Indian economy.

Demonetisation and Gdp

The contraction in cash supply slowdown the GDP. The Govt. Of India also lowered its GDP estimate from 7.6% to 7.1% for 2016-17[13]. In addition, the International Monetary Fund (IMF) has also lowered its forecast for Indian GDP from 7.5% to 6.6% for the year 2016-17[14]. Dr. Montek Singh Ahluwalia, former Deputy Chairman, Planning Commission also projected India's GDP between 5% to 5.5% for the year 2016-17 mainly due to demonetization. But Amercain Rating Agency 'Fitch' projected India's GDP at 6.9% from earlier 7.4% for the fiscal year 2017[15]. The Indian rating agencies ICRA and CARE also down grade the GDP to 6.8% in FY 17. According to Mahesh Vyas, CMIE, India's GDP growth will shift down to 6% per annum for next five years from 2017-18 because of demonetization[16]. But budget 2017-18 stated that Demonetisation will bring clear and bigger GDP because effect of cash ban is not expected to spill over to 2017-18. The GDP growth is projected between 6.75% to 7.5% for 2017-18. The capital expenditure is increased by almost 25% in budget. The fiscal deficit is 3.2% in 2017-18 and 3% in 2018-19. The Revenue deficit

for 2017-18 is at 1.9%. The FOREX reserve is at $361 billion in January 2017 which is enough to cover the next 12 months imports bill[17].

Demonetisation and Rupee

The demand and supply of currency will determine its value. Since demonetization, Rupee has depreciated by 1.69% from Rs. 66.63 to 67.75 on 15.12.16. Such declining trend will continue till currency circulation is fully restored. The currency circulation which was 11.8% on November 4, 2016 reduced to 6.5% on 20.01.2017. The US Fed Interest hike from 0.5% to 0.75% resulted in fund outflow i.e., nearly $1.4 billion Foreign Investors Fund was pulled out of Indian Stock Market from November 7, 2016 to December 12, 2016. In addition, FOREX reserve also dropped from $367.04 billion to $359.67 billion during the corresponding period[18]. The cash withdrawal limit was lifted for current accounts from February 1, 2017 onwards. The savings bank account holder's cash withdrawal limit likely to do away by February 2017 end. The end of such transitional pain will augment the money circulation in near future which has positive impact on Rupee. The Protectionism policy of Donald Trump, the US Fed Interest policy change finally resulted in strengthening the value of USD. The RBI fixed the reference rate of Rs. at 68.2043 against USD on 27.01.2017[19].

Demonetisation And Real Estate

Indian real estate is cash intensive. In addition, the sector had been witnessing a slowdown for the past three years. Since demonetization, nearly 37% declined in property registration in Mumbai. The rate of home sales had fallen by 50% and price by 20%. Union budget 2017-18 has focused a good deal in real estate which is beneficial to home buyers, developers and investors. The proposed infrastructure status to affordable housing, including a pledge to build one crore rural homes in next two years become a boost to Indian reality. According to Sunil Rohokale, ASK Group, the infrastructure status to reality opens up a lot of avenues to raise capital domestically from Insurance companies and pension funds. The policies like Smart Cities, Housing for All by 2022, AMRUT, Real Estate (Regulatory and Development) Act, Benami Transaction Act including GST Act will bring more transparency in the sector. But pricing is a major problem to all stakeholders in the Industry.

Digitalization and Demonetisation

In India, the average no of card transaction per inhabitant is mere 6.7 compared to UK (201.7). India is emerging as digital India. Now it is at the cusp of a massive digital revolution. The Govt. had assumed that a significant portion of illegal assets is stored in the form of high value currency. Till 30.12.2016, around Rs. 14.97 trillion banned notes were deposited into banks which equals to 96.5% of total banned notes. It means that only Rs. 54,000 crore notes failed to make it back. The 96.5% deposits include Rs. 80,000 crore of repayment of loans, Rs. 25000 crore deposited in dormant accounts, Rs. 16,000 crore deposited in co-operatives and Rs. 13,000 crore deposited in Regional Rural Banks. Besides, more than Rs. 2 lakh deposited in each account over 60 lakh bank accounts during the period[20]. As identifying black money in the mess takes time, the goal post of cash ban was shifted towards digital economy. Generally, the cash drive economy ultimately resulted in mounting of black money. The digitalization makes services faster, formal and accountable. The mobile wallet transaction per day rose 12 times in post demonitistion. As average value of transactions had fallen from Rs. 750 to Rs. 500, people started to use digital way even for petty expenses. "PayTM" showed three fold rise and "Oxygen" by 160% rise during the post shock therapy. The rural masses have started embracing digital payments through mobile wallets. Specific tax incentives and prizes offered for digital mode of payments to motivate people to follow digital way.

Indian Stock Market - Post Demonetisation

Actually the surgical strike on black money shook the investors' confidence. The BSE SENSEX experienced a bit lower of 6% on the very next day of cash ban. As Warren Buffet rightly said, 'be fearful when others are greedy', the volatility in the stock markets caused uncertainty in nothing but buying opportunities. BSE SENSEX climbed the best weekly gain in 8 months of 0.63% on 27.01.2017. The Nifty also gained 0.45% during that weekend[21]. According to Porinju veliyath, Equity Intelligence India, Demonetisation drive brought a long term positive impact on Indian formal

sector. To compete with informal sector, the formal sector has to mobilize huge investments from th stock market.

The Union Budget 2017-18 is continued with tax exemption for long term capital gain from shares which raised BSE SENSEX by 485.68 points and Nifty by 155.1 points on the day of budget itself[22].

TABLE 1.1: SIMPLE MOVING AVERAGE PRICE OF BSE SENSEX BEFORE AND AFTER DEMONETISATION

Name of the Company	10-06-2016 to 26-01-2017 average 100%	29-07-2016 to 26-01-2017 average	%	09-12-2016 to 26-01-2017 average	%	Market price on 27-01-2017 average	%
Adani Ports	248	262	112.10	278	122.58	304	105.6
Asian Paints	1015	1041	90.64	920	95.57	970	102.5
Axis Bank	512	519	89.84	460	92.38	473	101.3
Bajaj Auto Ltd	2702	2761	98.78	2669	105.63	2854	102.1
Bharti Airtel Ltd	335	329	93.73	314	96.72	324	98.21
Cipla Ltd	545	558	104.59	570	106.42	580	102.3
Coal India Ltd	311	317	97.43	303	102.25	318	101.9
Dr.Reddy's Laboratories Ltd	3133	3159	98.63	3090	95.60	2995	100.8
GAIL (India)	399	408	108.77	434	120.80	482	102.2
HDFC Bank	1208	1232	99.50	1202	106.95	1292	101.9
Hero Motocorp	3188	3253	96.96	3091	100.88	3216	102.0
Hindustan Unilever Limited	869	870	95.40	829	98.50	856	100.1
HDFC	1284	1319	96.96	1245	107.01	1374	102.7
ICICI Bank	254	260	102.36	260	107.09	272	102.3
Infosys	1076	1031	90.43	973	87.55	942	95.8
ITC	240	245	98.75	237	107.08	257	102.0
L & T	1424	1452	96.63	1376	101.12	1440	101.9
Lupin Ltd.	1530	1530	96.93	1483	97.52	1492	100.0
M&M	1334	1336	896.85	11964	93.85	1252	100.1
Maruti Suzuki	4842	5148	109.60	5307	122.18	5916	106.3
NTPC Ltd	154	158	106.49	164	115.58	178	102.6
ONGC	166	175	118.07	196	123.49	205	105.4
PowerGrid Corporation of India	171	179	109.94	188	119.88	205	104.6
Reliance Industries Ltd	1021	1033	101.67	1038	100.39	1025	101.1
State Bank of India	234	248	108.97	255	113.68	266	105.9
Sun Pharmaceutical Industries Ltd	745	730	88.46	659	86.04	641	97.9
Tata Consultancy Services Ltd	2433	2399	93.22	2268	96.92	2358	98.6
Tata Motors Ltd	483	505	99.59	481	112.22	542	104.5
Tata Steel Ltd	376	390	110.90	417	124.73	469	103.7
Wipro	508	494	91.73	466	91.73	466	97.2

Source: WWW.BSE30 Sensex.com

Table 1.1 exhibits the simple moving average prices of BSE SENSEX before and po Demonetisation drive. The BSE SENSEX 30 shares' average prices of 50 days, 150 days and 20

days from the market price on 27.01.2017 taken for the study. It shows that the prices of Asian paints, Axis bank, Bharti Airtel, Dr. Reddy lab, Hindustan Unilever, Infosys, Lupin Ltd., M&M, Sun Pharma, TCS, Wipro declined marginally during the study period.

Challenges Unleashed By Demonetization

According to CMIE, the total transaction cost of Demonetisation including the GDP losses around Rs. 4.3 trillion[23]. But eradication of corruption, black money and terrorism is far most important. In 2012, the Central Board of Direct Taxes (CBDT) opined that Demonetisation may not be a solution to solve black economy. It is so because the black assets are largely held in the form of benami properties, bullion in and out of India.

During the cash ban, the tax authorities have conducted 556 surveys, 253 searches and 289 seizures. They seized Rs. 112.29 crore new high denomination curren- cies and Rs. 18 lakh fake new currencies. Over 75% funds officially recorded as received by Indian political parties between 2004 and 2014 were from unknown sources. Such donations lead to formations of Industrial lobby in our parliament. The unexpected large scale land purchase outside future smart cities in advance of November 8, 2016 may be attributed to the role of industrial lobby[24]. It is learnt that 58% of GDP is under the control of 1% population which is against the philosophy of prevention of concentration of economic power in few hands. It is aptly mentioned that nearly 4 tons of gold were purchased by the economic offenders in 48 hrs after the announcement of note ban of Nov 8, 2016. The Govt. has to act in time to implement Benami Transaction Act, Real Estate (Regulation and Development) Act, Bank Reforms, Restructuring Informal Sector and speed of ongoing digital payments besides ensure cyber security.

The Govt. has to ensure both formal and informal sector should co-exist in country like India where inequality remains high. The 29 state owned banks wrote off Rs. 1.14 lakh crores of bad debts between 2013 and 2015 in which farmers were expected to get the benefits[25]. Recently the number of farmers' suicide shows an increasing trend. So transparency and accountability must be strongly imposed in all sectors of the economy. The RBI's Corporate Governance Reforms 2015 in Indian public sector banks has to be implemented properly on a continuous basis with needed changes.

Conclusion

The success of Demonetisation depends on the way in which it is being executed. In 1991, Union of Soviet Socialist Republic (USSR) introduced Demonetisation which led to creation of Commonwealth of Independent States (CIS). Such move in North Korea made people homeless while cash ban in Nigeria in 1984 resulted in complete collapse of their economy. It is known that the Govt. machinery was unprepared to meet the challenges of cash crunch when it is implemented. There were nearly 62 amendments and notification during the first 3 weeks of its announcement. Consumer's confidence was fully shaken psychologically which require a comprehensive strategy to boost domestic consumption by improving purchasing power of working class. India is rich but Indians are poor. So a steady but low rate of inflation is always vital to protect the poor Indians who are daily wagers.

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SIMPLE AND EFFICIENT SYNTHESIS OF BIS-(4-HYDROXYCOUMARIN-3-YL)METHANE DERIVATIVES USING L-GLUTAMIC ACID AS CATALYST

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ABSTRACT

In the present study, we reports synthesis of bis-(4-hydroxycoumarin-3-yl)methaneby the one-pot-multicomponent reaction of different substituted aromatic aldehyde/heterocyclic aldehydes and 4-hydroxycoumarine in the presence of L-Glutamic acid (5mol %) as a catalyst in water : ethanol (1:1). The reaction mixture was stirred at reflux temperature for specified period of time. We found that this is a facile and efficient method for the synthesis of bis-(4-hydroxycoumarin-3-yl)methane. The prominent features of this method are the inexpensive reagents, simple and safe experimental procedure, easy and clean workup, short reaction times (05-40 min), excellent yield (52-99 %), no toxic waste and environmentally benign method.

KEYWORDS: 4-Hydroxycoumarine, bis(4-hydroxy coumarin-3-yl)methane, L-Glutamic acid.

INTRODUCTION

Coumarins constitute an intrinsic class of naturally occurring compounds in the area of natural products and synthetic organic chemistry. Bis-(4-hydroxycoumarin-3-yl) methane derivatives are of much interest because their wide range of biological activities which play very significant role as drug in the medicinal and pharmaceutical chemistry. Bis-4-hydroxycoumarine derivatives shows significant biological/pharmaceutical activity such as anticoagulant,[1] anti-microbial,[2] pesticides,[3] anticancer,[4] anti-inflammatory[5] activities.

These biological activities of coumarins raised our interest in synthesizing some new coumarins derivatives.

L-L-Glutamic acid is an amino acid which is acts as an efficient catalyst in the organic chemistry to synthesize various biologically important compounds such as, dihydropyrimidinones,[6] 1,2,4,5-tetrasubstituted imidazoles under thermal, solvent-free conditions,[7] polyfunctionalized dihydro-2-oxypyrroles[8] and 2,4,5-Triaryl-*1H*-imidazoles.[9]

The study of literature it reveals that, bis-(4-hydroxycoumarin-3-yl)methane derivatives are synthesized using catalysts and ionic liquids such as $RuCl_3{\cdot}nH_2O$,[10] sulfated titania(TiO_2/SO_4),[11] SiO_2-OSO_3H NPs,[12] Nano silica chloride (nano SiO_2Cl),[13]n-Dodecylbenzene Sulfonic Acid (DBSA),[14]tungstate sulfuric acid (TSA),[15] choline chloride–oxalic acid,[16] Cobalt(II) chloride hexahydrate ($CoCl_2.6H_2O$),[17]succinimide-N-sulfonic acid,[18] $NaHSO_4/SiO_2$/Indion 190 resin,[19] Fe_3O_4 nanoparticles,[20] Nano TiO_2@KSF,[21]Phosphotungstic acid,[22] $[MIM(CH_2)_4SO_3H][HSO_4]$[23] andPOImD.[24]

However, most of these reported methods include disadvantages such as low yield, costly reagents or catalysts, drastic reaction conditions, environmental pollution, long reaction time, complicated operations. So to overcome these disadvantages we have developed a new simple, green and efficient method to synthesis of bis-(4-hydroxycoumarin-3-yl) methane by the one-pot reaction of 4- hydroxycoumarine and various substituted benzaldehyde on reflux in ethanol: water (1:1) as solvent.

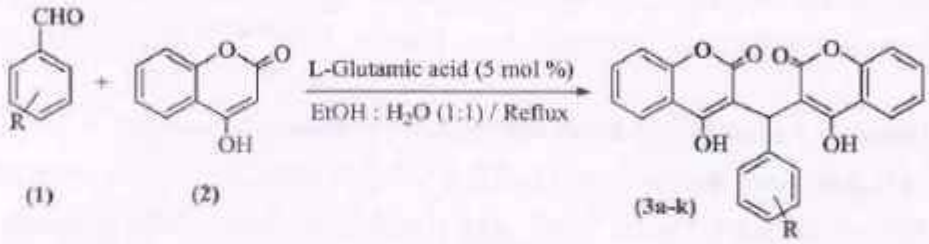
Experimental

a) Material and Methods

Chemicals were purchased from Merck, Fluka and Aldrich chemical companies. All yields refer to isolated products unless otherwise stated. Melting points were determined in an open capillary. NMR spectrum recorded at 500 MHz with tetramethylsilane as internal standard and dimethylsulfoxide DMSO-d_6 as solvent on Bruker Avance Neo 500 MHz NMR spectrometer; Fourier transform infrared (IR) spectra were obtained as KBr discs on a Perkin Elmer spectrum 400 FT-IR/FT-FIR spectrometer and mass spectra on LCMS Water's Synapt-XS Maldi TOF HDMS spectrometer.

b) General Procedure for the Synthesis of Bis-(4-hydroxycoumarin-3-yl) methane derivatives

In a 50 ml round bottom flask, a mixture of substituted aromatic aldehydes (1mmol), and 4-hydroxycoumarine (2 mmol) in the presence of catalytic amount of L-Glutamic acid (5 mol %) was stirred at reflux temperature in ethanol: water (1:1) (10 ml) for 5-40 minutes. The progress of the reaction was monitored by thin layer chromatography by using TLC plates at 70 % polarity (ethyl acetate: n-hexane) and TLC was observed under UV-lamp. After the appropriate time, the mixture was cooled then poured on ice cold water, the solidified product and filtered out 3(a-k). The crude solid material was purified by recrystallization from ethanol. Then the melting point of the product was determined by open capillary method and was uncorrected. Some principal products were characterized by FT-IT, FT-NMR, and LC–MS spectroscopic analysis from commercial agencies.



Spectroscopic analysis of compounds

3-((4-chlorophenyl)(4-hydroxy-2-oxo-2H-chromen-3-yl)methyl)-4-hydroxy-2H-chromen-2-one (3c)

M.F.: $C_{25}H_{15}O_6Cl$; Mol. Weight: 446.12, M.P. 257 °C; IR (KBr, cm^{-1}): 3415 (-OH), 3074, 2950, 2936 (Ar-H), 1668 (>C=O), 1565, 1490, 1404 (Ar-C=C), 1093(C-O), 816,782, 765 (C-Cl); ^{1}H-NMR (500 MHz, DMSO-d_6, δ ppm): 10.12 (s, 2H, -OH), 7.96-7.89 (m, 3H, Ar-H), 7.61-7.56 (m, 3H, Ar-H), 7.36-7.17 (m, 6H, Ar-H), 6.32 (s, 1H, CH); ^{13}C-NMR (500 MHz, DMSO-d_6, δ ppm): 166.35, 165.80, 164.52, 152.21, 139.65, 137.69, 131.65, 131.04, 129.85, 129.54, 128.63, 128.58, 127.76, 123.87, 123.46, 118.24, 115.77, 103.64, 35.61. (39.50 for DMSO solvent); LC-MS (m/z): 447 (M+1).

3, 3'-(3-Nitrophenyl)methylene)bis(2-hydroxy-4H-chromen-4-one) (3d)

M.F.: $C_{25}H_{15}NO_8$; Mol. Weight: 457.12, M.P. 237 °C; IR (KBr, cm^{-1}): 3414 (-OH), 3071, 2928, 2861 (Ar-H), 1641, 1617 (C=O), 1528, 1449 (Aromatic C=C), 1564, 1347 (NO_2), 1100 (C-O); ^{1}H-NMR (500 MHz, DMSO-d_6, δ ppm): 10.12 (s, 2H, OH), 8.22 -7.87 (m, 4H, Ar-H),

7.63 -7.51 (m, 4H, Ar-H), 7.34 -7.26 (m, 4H, Ar-H), 6.39 (s, 1H, CH); ^{13}C-NMR (500 MHz, DMSO-d_6, δ ppm): 173.14, 170.63, 166.69, 164.26, 152.37, 147.72, 144.33, 133.62, 131.46, 129.35, 124, 123.26, 121.07, 120.45, 118.87, 115.68, 102.90, 51.23, (39.58-39.25 for DMSO solvent), 36.20; LC-MS (m/z): 458 (M+1).

3, 3'-(4-Nitrophenyl)methylene)bis(2-hydroxy-4H-chromen-4-one) (3e)

M.Fo.: $C_{25}H_{15}NO_8$; Mol. Weight: 457.12, M.P. 230 °C; IR (KBr, cm^{-1}): 3414(OH), 2934, 2855,(Ar-H), 1618 (C=O), 1564, 1348, (NO_2), 1113 (C-O); ^{1}H-NMR (500 MHz, DMSO-d_6, δ ppm): 11.02 (s, 2H, OH), 7.95-7.93 (d, 2H, Ar-H), 7.62-7.60 (d, 2H, Ar-H), 7.37-7.25 (m, 5H, Ar-H), 6.88-6.73 (m, 3H, Ar-H), 6.53 (s, 1H, CH);^{13}C-NMR (500 MHz, DMSO-d_6, δ ppm): 166.01, 164.24, 152.18, 145.60, 131.77, 126.31, 124, 123.69, 123.52, 123.34, 118.27, 115.79, 104.13, (39.58, 39.42, 39.25 for solvent DMSO), 32.66.; LC-MS (m/z): 458 (M+1).

3, 3'-(Thiophen-2-ylmethylene)-bis-(4-hydroxy-2H-chromene-2-one) (3j)

M.F.: $C_{23}H_{14}SO_6$; Mol. Weight: 418.112, M.P. 214 °C; IR (KBr, cm^{-1}): 3474, 3414, (Ar-OH), 3114, 2928, 2726, 2600, (Ar-H), 1639, 1616 (C=O), 1565, 1495, 1449, (Aromatic C=C), 1097, 1050(C-O).; ^{1}H-NMR (500 MHz, DMSO-d_6, δ ppm): 11.53 (s, 2H, OH), 8.11-8.12 (d, 1H, Ar-H), 7.90-7.92 (d, 1H, Ar-H), 7.58-7.61 (m, 4H, Ar-H), 7.45-7.46 (d, 1H, Ar-H), 7.30-7.38 (m, 4H, Ar-H), 6.43 (s, 1H, CH); ^{13}C-NMR (500 MHz, DMSO-d_6, δ ppm): 166.30, 164.35, 152.34, 150.01, 145.47, 131.69, 127.99, 123.97, 123.44, 123.12, 118.44, 115.80, 103.23, (39.58, 39.42, 39.25 for DMSO solvent) 36.64; LC-MS (m/z): 419.06 (M+1).

RESULT AND DISCUSSION

In continuation of our previous studies on catalyzed organic reactions, we found that the condensation reaction of aromatic aldehyde (1) and 4-hydroxycoumarine (2) in the presence of catalytic amounts of L-Glutamic acid leads to formation of bis-(4-hydroxycoumarin-3-yl) methane derivatives (3) (Scheme-VIII).

Initially, we used 4-chlorobenzaldehyde (1c) and 4-hydroxycoumarine as the model reaction system to investigate the reaction at 0, 2.5, 5, 7.5 and 10 mol % of L-Glutamic acid in ethanol: water (1:1, v: v) at reflux temperature. The product (**3b**) was obtained in 0, 52, 99, 99 and 99 % yield, respectively. This indicates that the use of 5 mol % of L-Glutamic acid is sufficient to promote the reaction (Table-4.4).

Table 1: Optimization of amount of catalyst L-Glutamic acid for synthesis of compound (3c).

Entry	Amount of catalyst (mol %)	Time (min)	Yield (%)
1	0	30	0
2	2.5	30	52
3	5	30	99
4	7.5	30	99
5	10	30	99

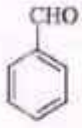
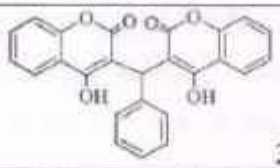
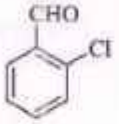
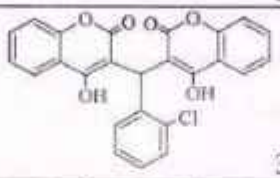
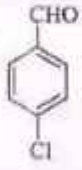
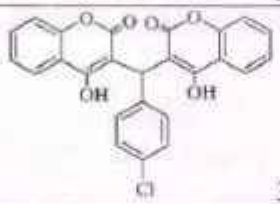
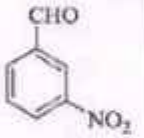
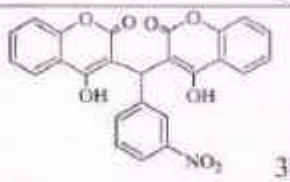
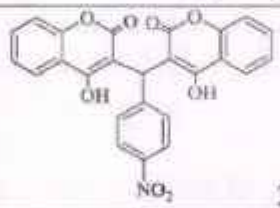
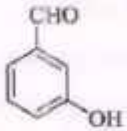
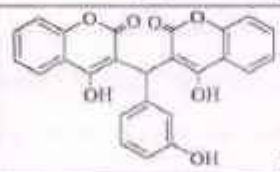
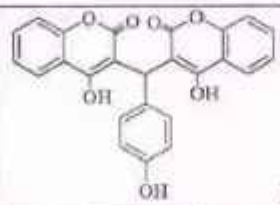
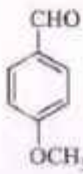
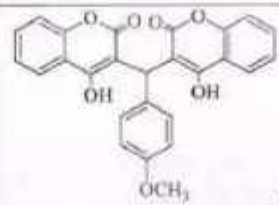
To determine the effect of solvent such as water, ethanol and mixture of water and ethanol at room temperature as well as reflux temperature to obtain varies yield. Ethanol: water (1:1) stand out as the best solvent system of choice among the solvents tested because of the rapid conversion and excellent yield (99 %) of desired product, where's the product formed in yields (52~99 %) by using other solvents (Table-2, Entry 1~10).

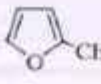
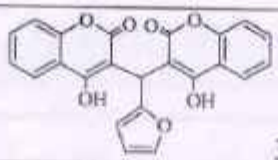
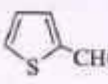
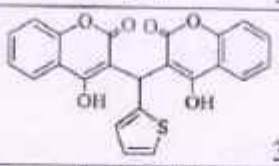
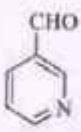
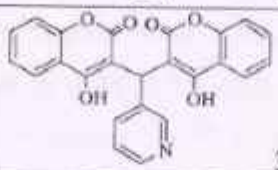
Table-2: Screening of solvents for the synthesis of bis-(4- hydroxycoumarin-3-yl)methane (3c).

Entry	Solvents	Temp	Amount of catalyst(mol %)	Time	Yield (%)
1	Ethanol	R.T.	5 mol%	22 Hrs	75
2	Water: Ethanol (1:1)	R.T.	5 mol%	6:30 Hrs	69
3	Water	R.T.	5 mol%	3 Hrs	79
4	Ethanol	Reflux	5 mol%	35 min	77
5	Water	Reflux	5 mol%	25 min	82
6	Water: Ethanol (1:1)	Reflux	5 mol%	5 min	99
7	Water: Ethanol (1:2)	Reflux	5 mol%	5 min	77
8	Water: Ethanol (1:3)	Reflux	5 mol%	5 min	70
9	Water: Ethanol (1:4)	Reflux	5 mol%	5 min	67
10	Water: Ethanol (1:5)	Reflux	5 mol%	5 min	62

To study the generality of this process, variety of examples were illustrated for the synthesis of bis-(4- hydroxycoumarin-3-yl) methane derivatives (3a-k) and the results are summarized in Entry-1-11, Table-3. The reaction is compatible for various substituents such as $-NO_2$, -OH, $-OCH_3$, -Cl and hetero cyclic aldehyde. The formation of desired product has been confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectroscopic analysis techniques and compared with the corresponding literature data.

Table 3: L-Glutamic acid catalysed synthesis of bis-(4-hydroxycoumarin-3-yl)methane (3a-k).

Entry	Aldehyde	Product	Time (min)	Yield (%)	MP (°C) Found	MP (°C) Reported
1		 3a	05	76	226	228-230[22]
2		 3b	05	78	225	224-226[19]
3		 3c	05	99	256	258-259[23]
4		 3d	20	91	236	234-236[13]
5		 3e	23	88	228-230	232-234[13]
6		 3f	30	81	262	256-258[24]
7		 3g	34	72	219	222-224[13]
8		 3h	40	73	248	247-249[13]

9		 3i	40	52	210	199-201[22]
10		 3j	25	85	212-214	212[22]
11		 3k	08	90	>300	-

[a]*Reaction conditions:* 1 (2 mmol), 2 (1 mmol), L-Glutamic acid (5%) ethanol at reflux temperature;

[b] Isolated yields

CONCLUSION

L--Glutamic acid is an easily available, inexpensive and efficient catalyst for the synthesis of Bis-(4-hydroxycoumarin-3-yl) methane derivatives from various substituted benzaldehyde (1 mmol) and 4-hydroxycoumarine (2 mmol) in the presence of L-Glutamic acid (5 mol %) as a catalyst was refluxed with magnetic stirring in ethanol: water (1:1) (10 ml) solvent for 05-40 minutes. The remarkable advantages of this method are the, short reaction times, easy work up, catalyst is simple and safe to handle and high yields. We believe that this method is a useful addition to the present methodology for the synthesis of Bis-(4- hydroxycoumarin-3-yl) methane derivatives.

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Synthesis of 1, 8-dioxo-octahydroxanthenes derivatives using Rochelle salt catalyst under microwave irradiations

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Abstract: Herein, we reports synthesis of 1, 8-dioxo-octahydroxanthenes derivatives by the one-pot-multicomponent reaction of different substituted aromatic aldehyde/heterocyclic aldehydes and dimedone in the presence of Rochelle salt (10 mol %) as a catalyst in water under microwave irradiations at 450 Watt for specified period of time. We found that this is a green, facile and efficient method for the synthesis of 1, 8-dioxo-octahydroxanthenes derivatives. The prominent features of this method are the inexpensive reagents, simple and safe experimental procedure, easy and clean workup, short reaction times (2-5 min), excellent yield (80-96 %), no toxic waste and environmentally benign method.

Keywords: Dimedone, 1, 8-dioxo-octahydroxanthenes, Rochelle salt.

I. INTRODUCTION

Rochelle salt is potassium sodium tartrate tetrahydrate (a double salt of tartaric acid) having molecular formula $KNaC_4H_4O_6 \cdot 4H_2O$. Study of literature indicates that it is efficient catalyst used for the synthesis of used for the synthesis of substituted chromenes and benzochromenes,[1] 2, 4, 5-trisubstitutedimidazoles.[2]

Xanthenes derivatives are essential heterocyclic because of their agricultural bactericide and pharmacological activities.[3] 1,8-Dioxo-octahydroxanthenes are derivatives of xanthenes, in which substituted 4-aryl pyran ring is present in the middle and two fused cyclohexen-2-one rings (dimedone) on the left and right sides. These xanthenediones received attention due to their different biological activities, like antimicrobial,[4-5] antioxidant,[6-9] leishmanicidal,[10] anti-tubercular,[11] agents and photosensitizer in photodynamic therapy.[12]

In literature several strategies have been reported for the synthesis of 1, 8-dioxo-octahydroxanthene derivatives such as $Cu(NO_3)_2{\cdot}3H_2O$ in acetonitrile/reflux,[13] $InCl_3$ and $(HPO_3)_n$,[14] W-doped ZnO nanocomposite,[15] Silicotungstic acid ($H_4SiW_{12}O_{40}$)/reflux,[16] $Fe_3O_4@SiO_2$-$SnCl_4$ /in ethanol under ultrasonic irradiation,[17] Ionic liquid [cmmim][BF_4] under microwave irradiation,[18] Cu(II)-Fur-APTES/GO,[19] FeNP@SBA-15,[20] Succinic acid,[21] Choline chloride-oxalic acid,[22] and Sulfacetamide.[23] However, most of the methods possesses some disadvantages like tedious work up, drastic reaction conditions, toxic solvents, sluggish and poor yields of the products, and so forth, which demands for further development of a novel catalyst for synthesis of xanthenes with an easy, cost-effective, simple, efficient, and greener method.

Herein, we have carried out the synthesis of 1, 8-dioxo-octahydroxanthene derivatives from dimedone and different substituted benzaldehydes and hetroaldehyde using Rochelle salt catalyst in water solvent under microwave irradiation.

II. EXPERIMENTAL

a) Material and Methods

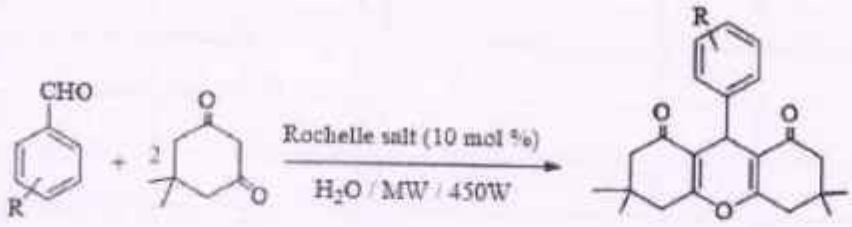
The chemicals were obtained from Fisher Scientific, Loba Chemie Pvt. Ltd., Sigma-Aldrich and used without further purification. All yields refer to isolated products unless otherwise stated. Melting points were determined by an open capillary using heavy paraffin oil in Thieles tube and are uncorrected. Pre-coated silica gel TLC (thin-layer chromatography) plates were used for investigation of rates of reactions under UV lamp. NMR spectrum recorded at 500 MHz with tetramethylsilane as internal standard and $CDCl_3$ as solvent on Bruker Avance Neo 500 MHz NMR spectrometer; Fourier transform infrared (IR) spectra were obtained as KBr discs on a Perkin Elmer spectrum 400 FT-IR/FT-FIR spectrometer and mass spectra on LCMS Water's Synapt-XS Maldi TOF HDMS spectrometer.

b) General procedure for the synthesis of 1, 8-dioxo-octahydroxanthene derivatives:

A mixture of aromatic aldehyde (1 mmol), dimedone (2 mmol), and Rochelle salt (10 mol %) as catalyst were taken in a 50 mL round bottom flask containing 5 mL water. The contents of the beaker were irradiated under microwave at 450 W for appropriate time as shown in Table 1. The progress of the reaction was monitored by thin layer chromatography. After completion of the reaction, the reaction mixture was cooled to room temperature, cold water was added and solid product obtained. It was filtered off and was purified by recrystallization from ethanol. Melting points were determined by open capillary tube using heavy paraffin oil in Thiele tube. Melting points are uncorrected and are compared with the reported literature values.

III. RESULTS AND DISCUSSION

In the this section, we have carried out the Rochelle salt (10 mol %) catalysed synthesis of 1, 8-dioxo-octahydroxanthene derivatives from substituted aromatic aldehydes, dimedone (active methylene compound) in water under microwave irradiated at power 450 Watt.



1(a-k) 2 3(a-k)

Scheme: 1: Synthesis of 1, 8-dioxo-octahydroxanthene derivatives using Rochelle salt catalyst under microwave irradiation

To investigate the influence of microwave irradiation on rate of reaction and yield of the product, we carried out a series of experiments at different power levels of the microwave. The obtained results at different power levels are summarized in Table-1. The observed results, indicates that the titled compounds (3a–k) can be synthesized with high purity and yield at power level 450 Watt (Entry 4, Table 1).

Table 1: Optimization of reaction condition for the synthesis of 1, 8-dioxo-octahydroxanthene (3a) under microwave set up

Entry	Power (Watt)	Time (min)	Yield (%)
1	200	25	40
2	350	10	60
3	400	6	85
4	450	2	96
5	600	2	96
6	700	2	96

To determine the adequate amount of catalyst for the faster conversion of reactants into product with better yield, we have carried out the model reaction (4-nitrobenzaldehyde and dimedone) with different concentration of catalyst Rochelle salt at 2.5, 5, 7.5, 10 and 12.5 mol % gives the yield of desired product 45, 60, 86, 96 and 96 % respectively (Entry 1-5, in Table-2). The result obtained proved that 10 mol % amount of Rochelle salt catalyst is sufficient to accelerate the reaction.

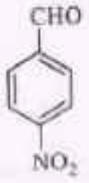
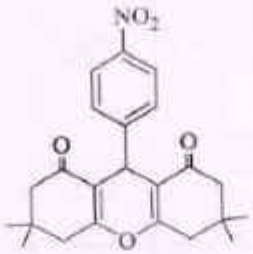
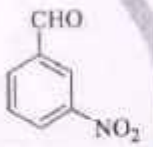
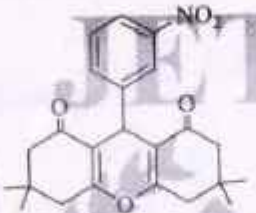
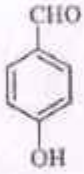
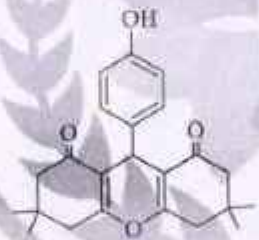
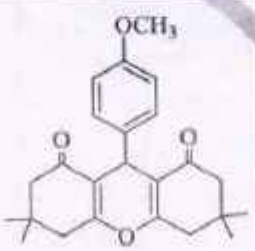
Table 2: Optimization of amount of catalyst Rochelle salt for the synthesis of 1, 8-dioxo-octahydroxanthene (3a) under microwave irradiation conditions (450 Watt)

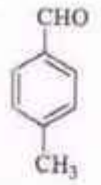
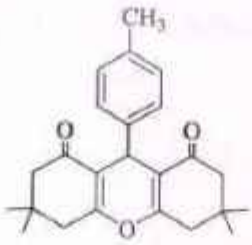
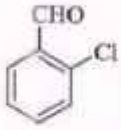
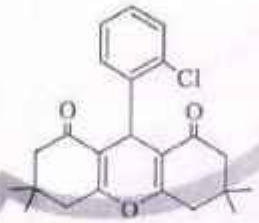
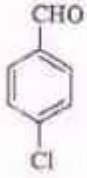
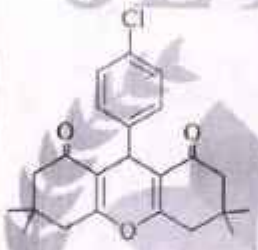
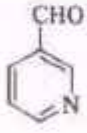
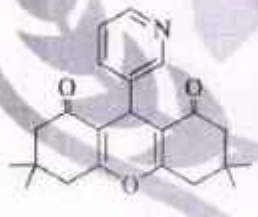
Entry	Concentration (mol %)	Yield (%)
1	2.5	45
2	5	60
3	7.5	86
4	10	96
5	12.5	96

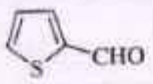
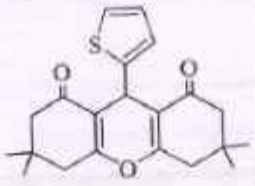
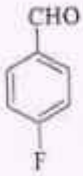
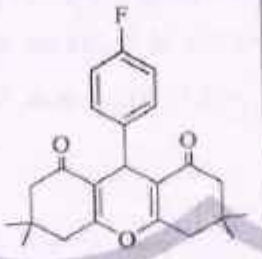
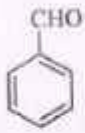
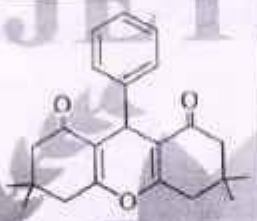
Scope and general applicability of the this methodology were studied by subjecting a broad range of structurally diverse aromatic aldehydes, having electron withdrawing (nitro) and electron donating groups (methyl, methoxy, hydroxy, chloro) as well as hetero aromatic aldehydes (pyridine-3-carbaldehyde, thiophene-2-carbaldehyde and furan-2-carbaldehyde), with dimedone under the found optimized conditions power level at 450W in the presence of 10 mol% Rochelle salt catalyst (Entry1-11, Table-3).

It is observed that all the reactions are taking place within shorter reaction time from 2 to 5 minutes with good to excellent (80-96 %) yield of the product. The obtained results indicate that the aldehydes having electron donating groups were reacts slowly as compared to aldehydes having electron withdrawing groups.

Table 3: Rochelle salt catalyzed synthesis of 1, 8-dioxo-octahydroxanthene (3a-k) derivatives under the optimized reaction conditions

Entry	Aldehydes	Product	Time (min)	Yield (%)	MP (°C) Found	MP (°C) Reported
1		 3a	2	96	222-224	223-225[17]
2		 3b	2	95	166-168	169-172[20]
3		 3c	4	80	246-248	244-247[20]
4		 3d	5	90	240-242	241-243[17]

5		 3e	5	81	216-218	216-218[20]
6		 3f	3	93	224-226	227-230[20]
7		 3g	3	94	226-228	230-232[23]
8		 3h	3	83	206-208	204-206[18]

9		 3i	2	85	166-168	162-164[23]
10		 3j	2	92	226-228	230-231[20]
11		 3k	2	90	202-204	201-203[17]

Spectroscopic analysis data of the principal compounds:

3,3,6,6-tetramethyl-9-(4-nitrophenyl)-3,4,5,6,7,9- hexahydro-1H-xanthene-1,8(2H)-dione (3a):

IR (KBr, cm^{-1}): 2961, 2870, 2589, 1636, 1620, 1512, 1464, 1411, 1380, 1117-1016; ^{1}H-NMR (500 MHz, $CDCl_3$, δ ppm): 8.13-8.11(d, 2H, Ar-H), 7.25-7.23 (d, 2H, Ar-H), 5.53 (s, 1H, CH), 2.50-2.23 (m, 8H, $4CH_2$), 1.23 (s, 6H, $2CH_3$), 1.11 (s, 6H, $2CH_3$); ^{13}C-NMR (500 MHz, $CDCl_3$, δ ppm): 197.61, 190.95, 189, 160.55, 146.58, 146.11, 127.66, 123.50, 119.65, 114.69, 52.88, 46.98, 46.39, 41.37, 33.25, 31.47, 29.49, 28.03, 27.46, 25.92; LC-MS (m/z): 396.224 (M+1); (M. F. & M. Wt. $C_{23}H_{25}NO_5$ and 395.2).

3,3,6,6-tetramethyl-9-(pyridine)-3,4,5,6,7,9- hexahydro-1H-xanthene-1,8(2H)-dione (3h):
IR (KBr, cm^{-1}): 3095, 3046, 2932, 2821, 1637, 1623, 1500, 1468, 1411, 1146; ^{1}H-NMR (500 MHz, $CDCl_3$, δ ppm): 8.40-8.36 (m, 2H, Ar-H), 7.39-7.19 (m, 2H, Ar-H), 5.54 (s, 1H, CH), 2.39-2.22 (s, 8H, $4CH_2$), 1.16 (s, 6H, $2CH_3$), 1.06 (s, 6H, $2CH_3$); ^{13}C-NMR (500 MHz, $CDCl_3$, δ ppm): 197.53, 190.28, 160.48, 140.53, 146.88, 134.59, 133.96, 123.01, 119.64, 114.61, 52.87, 46.71, 41.36, 31.47, 31.39, 31.01, 29.52, 28.02, 27.48, 25.91; LC-MS (m/z): 352.18 (M+1); (M.F. & M. Wt. $C_{22}H_{25}NO_3$ & 351.2).

IV. CONCLUSION

We have developed a new green, simple and efficient methodology for the synthesis of 1, 8-dioxo-octahydroxanthene derivatives from substituted aromatic aldehydes, dimedone (active methylene compound) in the presence of Rochelle salt (10 mol %) catalyst in water medium under microwave irradiated at power 450 Watt.

V. ACKNOWLEDGEMENTS

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CATALYST FREE MULTI-COMPONENT SYNTHESIS OF 5-AMINO-1,3-DIARYL-*1H*-PYRAZOLE-4-CARBONITRILES IN ENVIRONMENT FRIENDLY MEDIUM AND THEIR BIOLOGICAL EVALUATION

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Abstract: The sequential Knoevengel-cyclo condensation reaction involving aromatic aldehydes, malononitrile, and phenyl hydrazine in water and ethanol at room temperature is described as an efficient, one-pot, three-component synthesis of an extensive variety of heterocyclic compounds that are extremely relevant to the scientific community.

Keywords: Three-component synthesis, Catalyst free, 5-Amino pyrazole, Green chemistry.

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Introduction

The field of science has lately taken an interest in the possible applications of heterocyclic compounds linked by nitrogen. To create these heterocyclic compounds, the cyclization reaction of suitable linear compounds is a common and well-known method [1-3]. Pyrazoles containing heterocyclic compounds were the go-to for the pharmaceutical and agricultural sectors for a long time. These compounds have been found to have a variety of useful properties, including anti-tumor, anti-bacterial, anti-microbial, anti-fungal, anti-inflammatory, analgesic, anti-depressant, anti-convulsant, and antipyretic effects. fights against parasites, malaria, cancer, and viruses [4-10]. Research on pyrazole derivatives is highly valued in the pesticide chemical community because of these molecules' herbicidal and insecticidal effects [11-19]. Coordination chemistry has made extensive use of pyrazole-containing molecules as ligands [20]. Prior research [21, 22] indicated that 5-amino-4-cyanopyrazole derivatives had antibacterial action.

Other routes can be taken to synthesize pyrazole derivatives [23-25]. The two most prevalent ways to create 1,3,4,5-tetrasubstituted pyrazoles are 1,3-dipolar cycloadditions of diazo compounds onto triple bonds [27], and oxidative N-N bond creation of enamines and nitriles [28]. Two other approaches to functionalized prefabricated trisubstituted pyrazoles include nucleophilic substitution and transition metal-catalyzed C-N bond creation. Many heterocyclic compounds can be synthesized using nitriles as an intermediate [30-32]. We have successfully produced novel pyrazole compounds by employing aromatic aldehydes, malononitrile, and phenyl hydrazine derivatives in a tandem Knoevengel cyclo-condensation reaction in water and ethanol at room temperature.

Experimental:

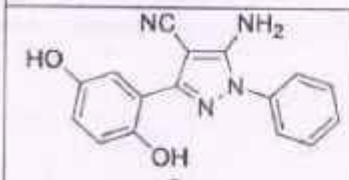
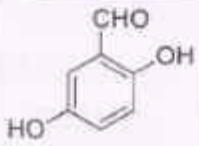
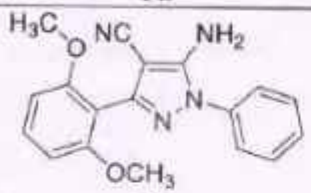
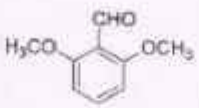
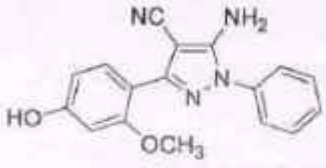
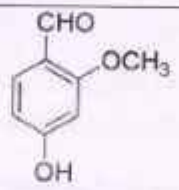
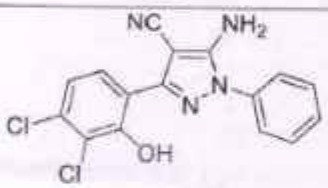
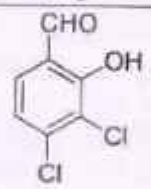
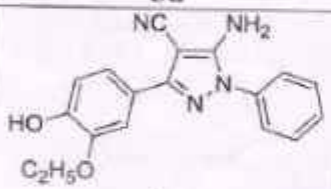
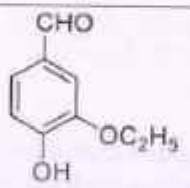
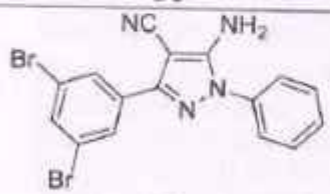
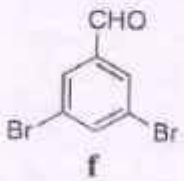
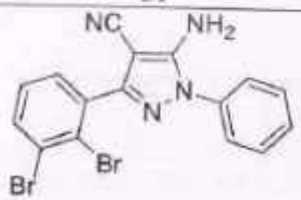
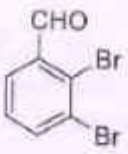
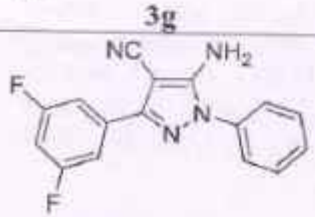
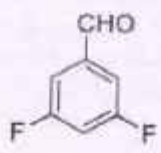
Chemicals and apparatus:

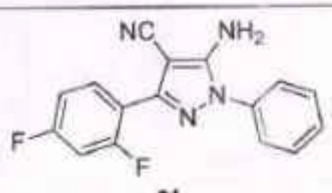
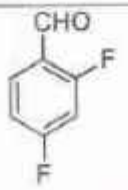
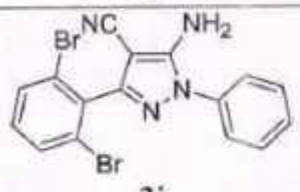
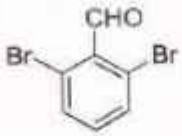
All chemicals were used directly after purchase from Merck or B. L. D. Pharma Companies. Using a **BRUKER AVANCE III HD NMR 500 MHz** spectrometer (in ppm) for ^{1}H NMR. The internal standard was tetramethyl silane (TMS). Singlet (*s*), doublet (*d*), triplet (*t*), quadruplet (*q*), and multiplet (*m*) are the abbreviations for nuclear magnetic resonance (NMR) signals. Uncorrected melting points were measured using an open capillary tube. FT(IR) spectra were recorded on Brucker FT-IR instrument on KBr pellets. Mass spectra of the prepared derivatives were recorded on Bruker IMPACT HD instrument.

General procedure for the preparation of 5-amino-1,3-diphenyl-1*H*-pyrazole-4-carbonitrile derivatives: An aromatic aldehyde (1 mol), malononitrile (1 mol), and phenyl hydrazine (1 mol) were added to a 50 mL mixture of water and ethanol (1:1) in a 250 mL round-bottomed flask while the ingredients were at room temperature. Once the reaction was complete (as monitored by TLC), crystals of the product were formed. These crystals were recovered via filtration and subsequently recrystallized from ethanol to achieve pure products.

Scheme: Greener Synthesis of 5-amino-3-aryl-1-phenyl-1*H*-pyrazole-4-carbonitrile from phenyl hydrazine, malononitrile, and substituted benzaldehydes

Table 1: Yield, colour, reaction time, and physical constants of the products (**3a-j**)

Products	Aldehyde	Colour	Yield (%)	Reaction time (min.)	m.p. (°C)
 **3a**	 **a**	Yellow powder	76.37	25	207-210
 **3b**	 **b**	Orange powder	73.97	20	194-196
 **3c**	 **c**	Yellow powder	69.78	30	176-178
 **3d**	 **d**	White powder	80.47	45	172-174
 **3e**	 **e**	Red-brown powder	70.36	120	171-173
 **3f**	 **f**	Brown powder	79.19	35	197-199
 **3g**	 **g**	Brown powder	78.74	40	195-197
 **3h**	 **h**	Yellow powder	81.66	20	167-169

 **3i**	 i	Yellow powder	79.40	50	170-172
 **3j**	 j	Brown powder	73.78	45	197-199

5-Amino-3-(2,4-dihydroxyphenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3a):
Yellow powder (71.57 %), M.P. = 211°C, FT(IR) spectrum (KBr) 3322, 2953, 2952, 2202, 1684, 1595, 1441, 1250, 737, 683 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 10.19 (s, 1H), 7.84 (s, 1H), 7.34 (d, 2H), 6.73-7.33 (m, 8H). UV spectrum (λ_{nm}) 324, 282. MS (m/z): 290.13 $(M)^+$. (Anal. Calcd for $C_{16}H_{12}N_4O_2$: C, 65.75; H, 4.14; N, 19.17; O, 10.95 %. Found: C, 65.48; H, 4.06; N, 18.72, O, 10.92 %.

5-Amino-3-(2,3-dimethoxyphenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3b):
White powder (68.99 %), M.P. = 125 °C, FT(IR) spectrum (KBr) 3292, 2237, 1684, 1248, 736, 684 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 7.62 (*d*, 2H), 7.62 (*d*, 2H), 6.88-7.60 (*m*, 8H), 3.95-4.01 (*s*, 6H). UV spectrum (λ_{nm}) 355, 270. MS (m/z): 323.10 $(M)^+$. (Anal. Calcd for $C_{18}H_{16}N_4O_2$: C, 67.49; H, 5.03; N, 19.49; O, 9.99 %. Found: C, 66.39; H, 4.99; N, 19.42, O, 9.90 %.

5-Amino-3-(2-hydroxy-4-methoxyphenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3c):
White powder (73.53 %), M.P. = 157 °C, FT(IR) spectrum (KBr) 3408, 3290, 2210, 1599, 1250, 735, 685 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 5.84 (*s*, 1H), 4.26-4.27 (*d*, 2H), 6.88-7.65 (*m*, 8H), 1.51-1.55 (*s*, 3H). UV spectrum (λ_{nm}) 363, 277. MS (m/z): 301.08 $(M)^+$. (Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.66; H, 4.61; N, 18.29; O, 10.45 %. Found: C, 66.61; H, 4.59; N, 18.21, O, 10.38 %.

5-Amino-3-(3,4-dichloro-2-hydroxyphenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3d):
White powder (76.11 %), M.P. = 163 °C, FT(IR) spectrum (KBr) 3444, 3339/3295, 2193, 1645, 1251, 732, 690 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 11.56 (*s*, 1H), 7.66-7.69 (*d*, 2H), 6.94-7.32(*m*, 7H). UV spectrum (λ_{nm}) 383, 318. MS (m/z): 338.34 $(M)^+$. (Anal. Calcd for $C_{16}H_{10}N_4OCl_2$: C, 55.67; H, 2.92; N, 16.23; O, 4.64; Cl, 29.34 %. Found: C, 55.60; H, 2.89; N, 16.16, O, 4.22; Cl, 29.29 %.

5-Amino-3-(3-ethoxy-4-methoxyphenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3e):
Red-brown powder (70.36 %), M.P. = 172 °C, FT(IR) spectrum (KBr) 3326, 2192, 1599, 1250, 744, 685 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 11.78 (*s*, 1H), 8.173 (*d*, 2H), 7.31-7.93 (*m*, 7H), 7.02-7.11 (*s*, 5H), 3.55 (*s*, 3H). UV spectrum (λ_{nm}) 334, 273. MS (m/z): 332.33 $(M)^+$. (Anal. Calcd for $C_{19}H_{18}N_4O_2$: C, 68.25; H, 5.43; N, 16.76; O, 9.57%. Found: C, 68.00; H, 5.34; N, 16.11, O, 9.49%.

5-Amino-3-(3,4-dibromophenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3f):
Yellow powder (79.19 %), M.P. = 178 °C, FT(IR) spectrum (KBr) 3306, 1924, 1589, 1252, 749, 653, 633 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 7.48-7.92 (*d*, 2H), 6.94-7.75 (*m*, 8H). UV spectrum (λ_{nm}) 330, 274. MS (m/z): 418.00 $(M)^+$. (Anal. Calcd for $C_{16}H_{10}N_4Br_2$: C, 45.96; H, 2.41; N, 13.40; Br, 38.22 %. Found: C, 45.69; H, 2.33; N, 13.22; Br, 38.17 %.

5-Amino-3-(2, 5-dibromophenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3g):
Yellow powder (74.40 %), M.P. = 176 °C, FT(IR) spectrum (KBr) 3302, 2216, 1563, 1252, 752, 693, 635 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 8.20 (*d*, 2H), 6.95-7.96 (*m*, 8H). UV spectrum (λ_{nm}) 337, 309. MS (m/z): 420.95 $(M)^+$. (Anal. Calcd for $C_{16}H_{10}N_4Br_2$: C, 45.96; H, 2.41; N, 13.40; Br, 38.22 %. Found: C, 45.91; H, 2.37; N, 13.27; Br, 38.19 %.

5-Amino-3-(3,4-difluorophenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3h):
Yellow powder (77.51 %), M.P. = 148 °C, FT(IR) spectrum (KBr) 3304, 2233, 1596, 1249, 1250, 753, 693 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm)

7.55-7.63 (*d*, 2H), 6.87-7.54 (*m*, 8H). UV spectrum (λ_{nm}) 336. MS (m/z): 297.09 $(M)^+$. (Anal. Calcd for $C_{16}H_{10}N_4Cl_2$: C, 64.86; H, 3.40; N, 12.62; F, 18.91 %. Found: C, 64.80; H, 3.33; N, 12.55; F, 18.85 %.

5-Amino-3-(2,5-difluorophenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3i):
Yellow powder (79.40 %), M.P. = 151 °C, FT(IR) spectrum (KBr) 3250, 2213, 1594, 1250, 1238, 747, 688 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 7.68 (*d*, 2H), 6.95-7.75 (*m*, 8H). UV spectrum (λ_{nm}) 333, 287. MS (m/z): 297.08 $(M)^+$. (Anal. Calcd for $C_{16}H_{10}N_4Cl_2$: C, 64.86; H, 3.40; N, 12.62; F, 18.91 %. Found: C, 64.83; H, 3.36; N, 12.57; F, 18.88 %.

5-Amino-3-(2,4-dibromophenyl)-1-phenyl-1*H*-pyrazole-4-carbonitrile (3j):
Yellow powder (77.51 %), M.P. = 168 °C, FT(IR) spectrum (KBr) 3396, 2208, 1599, 1247, 750, 693, 639 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ (ppm) 7.96 (*d*, 2H), 6.95-7.89 (*m*, 8H). UV spectrum (λ_{nm}) 317. MS (m/z): 428.96 $(M)^+$. (Anal. Calcd for $C_{16}H_{10}N_4Br_2$: C, 45.96; H, 2.41; N, 13.40; Br, 38.22 %. Found: C, 45.93; H, 2.37; N, 13.39; Br, 38.19 %.

Antimicrobial Activity:
We used synthetic substances for a variety of fungal and bacterial samples (clinical isolates), and all of the samples were purchased as dry powder for this experiment. Candida albicans MCC1439 and Saccharomyces cerevisiae MCC1033 were among the fungus strains examined. Before being sub-cultured on antimicrobial agent-free potato dextrose agar, the mold isolates were preserved in sterile water to guarantee their vitality and purity. Both Escherichia coli MCC 2412 and Pseudomonas aeruginosa MCC 2080 were Gram-negative bacteria, but Bacillus subtilis MCC 2010 and Staphylococcus aureus MCC 2010 were Gram-positive bacteria. In Pune, India, at the National Centre for Molecular Research, we bought these living organisms. There was no antibacterial action at the concentrations tested when using dimethyl formamide (DMF) to dissolve the compounds and preserve the solution at 4 °C. In contrast to fungi, which can be cultured in potato dextrose agar and Sabaouraud liquid media, bacteria can be grown in nutritional broth (NB; Difco) and nutrient agar (NA).

Antibacterial screening:
To evaluate the antimicrobial efficacy of the produced chemicals, we utilized a panel of four bacteria: two gram-positive (S. aureus MCC 2010 and B. subtilis MCC 2010) and two gram-negative (E. coli MCC2412 and P. aeruginosa MCC2080). Autoclaving the Muller Hilton agar medium at 15 lbs/in2 for 15 minutes was done for the purpose of antibacterial testing. To determine whether newly manufactured antibiotics were effective against bacteria, the disc diffusion method was employed. Floating the culture in sterile distilled water allowed the inoculum to be diluted to a concentration of approximately 108 cfu/mL to test for antibacterial activity. The desired microbial strains were introduced to 20 mL of Muller Hilton agar medium by swabbing it onto petri dishes. Before adding 100 µL of a 4.0 mg/mL solution of each chemical reconstituted in DMSO, 6 mm diameter wells were bored into the pre-inoculated plates using a clean borer. Every plate was incubated for 24 hours at 37 °C. Every plate was incubated for 24 hours at 37 °C. The zone of inhibition surrounding the wells was used to evaluate the antibacterial activity of all produced drugs. The two solvents utilized as controls were streptomycin and dimethyl sulfoxide (DMSO).

Antifungal Activity:
Two different types of fungi were tested using the cup-and-plate technique to see how well the compounds performed. Candida albicans MCC1439 and Saccharomyces cerevisiae MCC1033 were the strains used. The discs were 6 mm in diameter and 1 mm thick. We injected the test fluid into them using a micropipette. After that, the dishes were maintained at 37 °C for an additional 72 hours. The effect of the experimental solution on the implanted fungus's development became obvious during this time. The inhibition ring's size was measured after 36 hours of storage at 37 °C. There have been investigations into the minimum inhibitory doses of chemicals that are believed to possess antifungal properties. After overnight incubation, the minimum inhibitory concentration (MIC) of a fungal medication is defined as the concentration at which noticeable microbial development was inhibited. Clinical laboratories used the minimum inhibitory concentration (MIC) to confirm microbial resistance to existing antimicrobials and to find out how effective new antimicrobials were.

Results and Discussion:
Researchers performed a catalytic screening at room temperature using several catalysts and 1 mmol of aromatic benzaldehyde, phenyl hydrazine, and malononitrile, respectively. There was shown to be no significant effect of catalyst type on pyrazole yield by reaction condition screening. A base catalyst was not necessary to obtain the

desired 5-amino-4-cyanopyrazole derivatives after a remarkable yield was achieved after 2 hours of reaction at room temperature in a solvent mixture of water and ethanol (1:1 v/v).

Consequently, phenyl hydrazine acts as both a nucleophile and a catalyst for the Bronsted base reaction. So, the bases didn't affect the reaction's yield per se. Based on this, we monitored the reaction yield about the phenyl hydrazine concentration. Adding more phenyl hydrazine does not increase the production of 5-amino-1,3-diphenyl-1*H*-pyrazole-4-carbonitrile. Reducing the amount of phenyl hydrazine did not, however, result in total conversion.

In these ideal circumstances, this three-component process can be extended to include a broad range of aromatic aldehydes, malononitrile, and phenyl hydrazine derivatives. There were high product yields when malononitrile was used. Interestingly, high product yields were achieved with even low nucleophilic malononitrile. Also, dialdehydes were employed to successfully produce bis poly-substituted pyrazoles in large quantities. To further explore the reaction's bounds, aldehydes containing electron-drawing substituents on the aromatic ring were also utilized. The bulky aldehydes that were sterically present were converted into the necessary products with relative ease. To increase the reaction's applicability, researchers looked into using heteroaryl aldehydes.

Findings from experiments evaluating the three-component coupling capability of several aliphatic aldehydes. Aliphatic aldehydes were not effective in this one-pot, catalyst-free reaction, though. Because aromatic aldehydes are more reactive towards nucleophilic addition, this tendency was primarily caused by the fact that aliphatic aldehydes are less reactive. Schematic 1 shows the steps used to synthesize 5-amino-1,3-diphenyl-1H-pyrazole-4-carbonitrile in a very selective manner. In situ preparation of 5-amino-1,3-diphenyl-1H-pyrazole-4-carbonitrile derivatives is possible, as suggested by this method, by condensation of aromatic aldehyde, phenyl hydrazine, and a very reactive malononitrile.

Since nitrile may be easily transformed into other functional groups, the recently found method offers strong empirical proof of this assertion. Remarkably, a catalyst-free reaction was carried out with remarkable selectivity and minimal atom waste. To our knowledge, no single vessel has ever been used to carry out a Knoevenagel reaction, Michael-type reaction, ring closure, and subsequent aromatization without the need for a catalyst.

The structures of 5-amino-1,3-diphenyl-1H-pyrazole-4-carbonitrile derivatives were inferred by spectroscopic examinations. Compounds **3a**, **3c**, and **3d** exhibited a wide band in the 3444-3322 cm^{-1} area due to the υ(O-H) stretching of the aromatic hydroxyl groups. The (O-H) group for compound 4a was determined to be represented by bands at 2952 and 1441 cm^{-1}. Bands in the 3350-2953 cm^{-1} area of the infrared spectra of compounds **3a-3j** were interpreted as the (N-H) stretching of the grafted amine groups. The FT-IR spectra of all the compounds that were synthesized show the presence of the C=N stretching vibration band between 1684 and 1545 cm^{-1}.

In the ^1H NMR spectra of compounds **3a**, **3c**, **3d**, and **3e** ($CDCl_3$, 500 MHz), the presence of an aromatic ring -OH is indicated by the singlet at δ5.84-11.78. The phenyl ring showed a doublet in the range of 6.73 to 7.96. Between 7.34 and 8.20, the NH_2 group added to a 2H singlet. 3H was also given another singlet in the area δ1.54-4.01 because of the methoxy group connected to the aromatic ring.

Antimicrobial evaluation:

The new compounds were evaluated for their antibacterial and antifungal activity against various bacterial and fungal strains in vitro using the broth microdilution method. These strains included Gram-positive and Gram-negative bacteria such as *Staphylococcus aureus* (MCC 2010), *Bacillus subtilis* (MCC 2010), *Escherichia coli* (MCC 2412), and *Pseudomonas aeruginosa* (MCC 2080). All bacterial isolates were cultured in nutritional broth for 24 h at 37 °C. Fungal spore suspensions were collected using tween 80 from 7-day-old cultures of fungi cultured on sabouraud dextrose agar at 25 °C for 24 h. The final bacterial and fungal inoculum ODs were 0.2–0.3 and 0.5, respectively. Preparing the stock solutions with DMSO does not affect the measured concentrations. Bacteria and fungi doubled at a concentration of 1000 µg/mL. Powdered medications like fluconazole and streptomycin were commonly used to treat fungal and bacterial infections. After being incubated at 37 °C for 24 h and at 25 °C for 48 hours, antibacterial and antifungal activities were assessed, respectively.

The study's standard treatment was streptomycin, a broad-spectrum antibiotic having a minimum inhibitory concentration (MIC) of 10 mg/mL against the bacterial species. Suppression zones ranged from 12-16 mm for *E. coli* (MCC 2412), 10-12 mm for *B. subtilis* (MCC 2010), 12-15 mm for *P. aeruginosa* (MCC 2080), and 9-13 mm for *S.* [illegible] (MCC 2010). Compared to other bacterial

species, *S. aureus* was more susceptible to **3a**. It was also discovered that **3e** (19mm) was more effective than the gold standard drug. The effectiveness of the reference medication was found to be lower than **3d** against *P. aeruginosa*. It was shown that **3j** was the most potent chemical against *E. coli*.It was shown that the median inhibition zones for *C. albicans* (MCC1439) and *S. cerevisiae* (MCC1033) were 8-17 mm and 10-17 mm, respectively, when treated with the standard drug *fluconazole* (MIC = 50 µg/ml). The medication is more effective than the gold standard against both *C. albicans* (MCC1439) and *Saccharomyces cerevisiae* (MCC1033), with a minimum inhibitory concentration (MIC) of 54 µg/mL.

Table 2: Antibacterial activities of the product (3a-j)

Compound	*S. aureus*	*B. subtilis*	*E. coli*	*P. aeruginosa*
3a	12	10	15	12
3b	10	12	12	15
3c	9	11	13	13
3d	13	10	14	14
3e	11	12	16	15
3f	12	11	12	12
3g	11	10	15	14
3h	12	12	13	12
3i	13	10	16	15
3j	12	11	15	11
Std	12	11	12	12

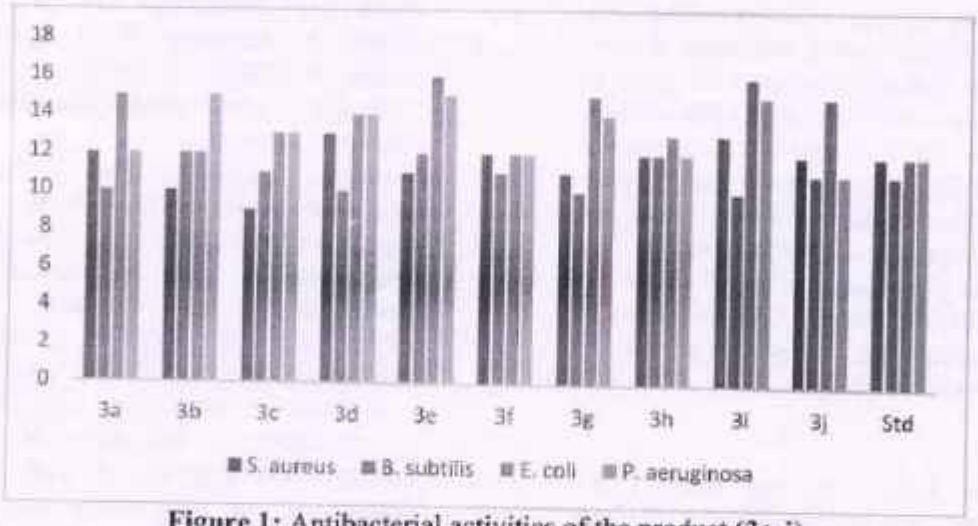


Figure 1: Antibacterial activities of the product (3a-j)

Table 3: Antifungal activities of the product (**3a-j**)

Compound	*Candida albicans*	*Saccharomyces cerevisiae*
3a	16	11
3b	10	15
3c	13	16
3d	14	13
3e	8	15
3f	10	12
3g	9	13
3h	8	16
3i	17	17
3j	16	16
Fluconazole	15	11

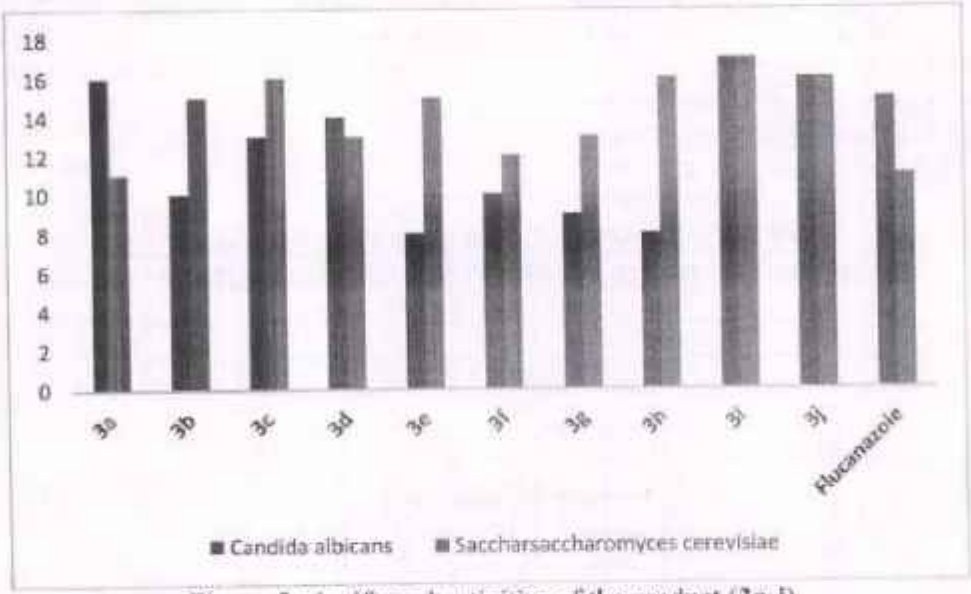


Figure 2: Antifungal activities of the product (**3a-j**)

Conclusions:

Applying a multicomponent reaction method, we have demonstrated the one-step synthesis of poly-substituted amino pyrazole analogs. Fast, good to excellent yields were attained without the need for a catalyst in this reaction, which had additional advantages including easy experimental workup and no hazardous by-products. The use of catalysts, toxic organic solvents, or dehydration is not necessary for the procedure we detail above for dealing with pyrazole systems. An eco-friendly strategy for synthesizing these compounds is presented by this methodology.

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DESIGN, SYNTHESIS, IN *VITRO* ANTIMICROBIAL, AND CYTOTOXIC STUDIES OF A NEW SERIES OF PYRROLO[2,3-*d*] PYRIMIDINEHYDRAZIDEHYDRAZIDE DERIVATIVES

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Abstract:
This study examines the design and synthesis of a newly manufactured pyrrolo[2,3-*d*]pyrimidinehydrazide (PPH) derivative. The PPH derivatives are designed to contain bromine atoms in positions 2, 3, 4, 5, and 6. The microwave technique is used as a novel and reliable method for the preparation of this type of PPH derivative. Spectral and elemental studies were used to provide a comprehensive description of the chemical structure of the PPH derivatives **2–7** that were constructed. By using the disc diffusion method, each drug was put through an in vitro antimicrobial test against six different microorganisms. In comparison to streptomycin, which had a concentration of 25.0 µg/ml, it was discovered that compounds 2, 4, and 5 exhibited the highest levels of activity against *E. coli* (11.5, 15.5, and 23.4 µg/ml, respectively). Furthermore, compound **7** demonstrated potential cytotoxic effects against *artemia salina*, with an IC_{50} value of 18.5 µg/ml.

Keywords: Pyrrolo[2,3-*d*]pyrimidinehydrazide, Elemental studies, Cytotoxic studies

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INTRODUCTION

As a result of the capability of nitrogen-containing heterocycles to generate hydrogen bonding, van der Waals forces, hydrophobic effects, π-stacking interactions, and dipole–dipole interactions with biological targets, the Food and Drug Administration (FDA) has approved more than eighty percent of the drugs that are currently on the market [1-5]. It is usual for pyrrolopyrimidine derivatives to exhibit a wide range of biological and pharmacological features, and these derivatives can be found in a variety of small molecule drug discovery programs [6]. These derivatives are nitrogen-fused heterocycles.

The pyrrolo[2,3-*d*]pyrimidinehydrazide derivatives hold a significant position among the pyrrolopyrimidine compounds. These compounds possess a wide range of biological properties, including anti-bacterial [7], anti-diabetic agents [8, 9], antiviral [10, 11], anti-inflammatory [12, 13], anti-hypertensive activity [14], anti-protozoal activity [15], and they have demonstrated potent anticancer activity, which makes them an effective tool for DNA interaction [16-18].

This work is a continuation of our research efforts that have been centered on the synthesis of novel nitrogen-containing heterocycles that possess anti-microbial activity [19–22]. In recent times, we have been paying close attention to the process of preparing new pyrrolo[2,3-*d*]pyrimidinehydrazide derivatives. These derivatives are predicted to exhibit biological activity, and they are prepared under conditions that are both environmentally friendly and time-saving via microwave assistance.

A new series of pyrrolo[2,3-*d*]pyrimidine hydrazide derivatives with the bromine atom on carbon 2, 3, 4, 5, and 6were prepared by us using our reliable method under microwave-assisted conditions. The purpose of this study was to evaluate the anti-microbial activity of these compounds as a first study for this particular type of pyrrolo[2,3-*d*]pyrimidinehydrazide as an anti-microbial agent. Additionally, the molecular docking study was displayed and discussed during the presentation.

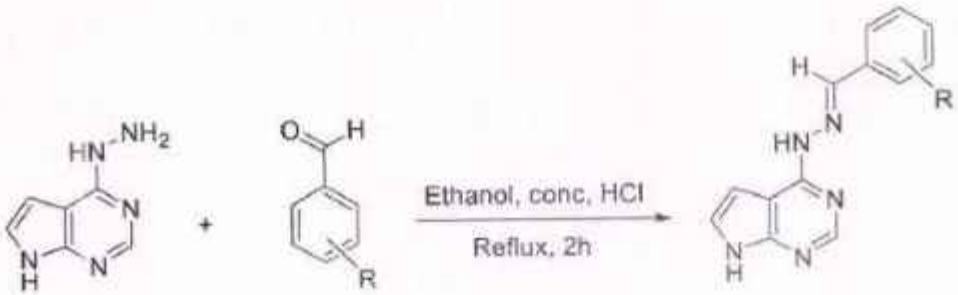
EXPERIMENTAL

Materials and methods

The melting points of all the compounds were recorded using a digital Gallen Kamp MFB-595 equipment, which may have been inaccurately calibrated. The following chemicals were utilized without additional purification: pyrrolo[2,3-*d*]pyrimidine, 2,3,4-tribromobenzaldehyde, hydrazine hydrate, 2,3-dibromobenzaldehyde, 2,4-dibromobenzaldehyde, 2,5-dibromobenzaldehyde, 2,6-dibromobenzaldehyde, 3,4-dibromobenzalde hyde, and 3,5-dibromobenzaldehyde. A Brucker spectrophotometer was used to record infrared spectra (cm^{-1}) with a KBr pellet. Bruker spectrometers operating in deuterated dimethyl sulfoxide (DMSO-d_6) were used to record the ^{1}H-NMR and ^{13}C-NMR spectra, at 400 MHz and 100 MHz, respectively. Chemical shift (δ ppm), multiplicity (*s*=singlet, *d*=doublet, *t*=triplet, *m*=multiplet), and coupling constant (*J* in Hz) were the following reported in ^{1}H-NMR spectra, which were allocated relative to deuterated solvent signals. At CIF Pune University's micro-analysis center, we documented elemental analyses. The recently produced chemicals were tested for purity using the TLC method [10].

Formulation of PPH compounds (1-7):

To prepare the compounds (**1-7**), one mmol of pyrrolo[2,3-*d*]pyrimidine-hydrazide and one mmol of substituted dibromobenzaldehydes were refluxed in 20 ml of ethanol for 2 hours. The cooled liquid was then dumped onto a bed of ice water. To get affords **1–7**, the precipitate was filtered off and recrystallized from ethanol.



Scheme 1: Preparation of compounds **1-7**

2.2.1. 4-{(2E)-2-[(2,3-dibromophenyl) methylide ne]hydrazinyl}-7H-pyrrolo[2,3-*d*]pyrimidine(1).

Yield % 75.66, m.p. 189-190°C, IR:υ_{max}/cm^{-1} 3110 (-NH- aromatic), 3178 (-NH- aliphatic), 2815 (-CH=), 1582/1479 (>C=C<), 1655 (>C=NN-), 1233 (C-F), 1070 (-N-N-), 741 (benzene ring), 688 (C-Br).^{1}H-NMR (DMSO-d$_6$) δ: 14.25 (s, 1H, -NH- aliphatic), 12.97 (s, 1H, NH, aromatic), 8.73 (s, 1H, -CH=), 8.46 (s, 1H, pyrimidine-H), 7.09-8.01 (m, 6H, aromatic-H)). Anal. Calcd. for $C_{13}H_9Br_2N_5$(395.05): C, 39.52; H, 2.30; Br, 40.45; N, 17.73. Found: C, 39.48; H, 2.17; Br, 40.09; N, 17.67.

2.2.2. 4-{(2E)-2-[(2,4-dibromophenyl)met hylidene]hydrazinyl}-7H-pyrrolo[2,3-*d*]pyrimi dine (2).

Yield % 73.79, m.p. 195-196°C, IR:υ_{max}/cm^{-1} 3139 (-NH- aromatic), 3292 (-NH- aliphatic), 2884 (-CH=), 1590/1478 (>C=C<), 1661 (>C=NN-), 1291 (C-F), 1029 (-N-N-), 687 (benzene ring).^{1}H-NMR (DMSO-d$_6$) δ: 14.41 (s, 1H, -NH- aliphatic), 12.94 (s, 1H, NH, aromatic), 8.49 (s, 1H, -CH=), 7.20-7.56 (m, 6H, aromatic-H (7.20 (1H, *d*, (*J* = 3.88Hz), 7.34 (1H, *dd*, (*J* = 7.62, 1.62Hz), 7.45 (1H, *dd*, (*J* = 8.00, 1.75Hz), 7.48 (1H, *dd*, (*J* = 8.03, 1.62Hz), 7.56 (2H, *d*, (*J* = 3.88Hz)). Anal. Calcd. for $C_{13}H_9Br_2N_5$(395.05): C, 39.52; H, 2.30; Br, 40.45; N, 17.73. Found: C, 39.39; H, 2.26; Br, 40.11; N, 17.68.

2.2.3. 4-{(2E)-2-[(2,5-dibromophenyl) methylidene]hydrazinyl}-7H-pyrrolo[2,3-*d*]pyrimidine (3).

Yield % 74.89, m.p. 189-192°C, IR:υ_{max}/cm^{-1} 3096 (-NH- aromatic), 3195 (-NH- aliphatic), 2982 (-CH=), 1587/1477 (>C=C<), 1624 (>C=NN-), 1224 (C-F), 1001 (-N-N-), 731 (benzene ring).^{1}H-NMR (DMSO-d$_6$) δ: 11.82 (s, 1H, -NH- aliphatic), 11.69 (s, 1H, NH, aromatic), 7.51 (s, 1H, -CH=), 7.05-8.28 (m, 6H, aromatic-H (7.05 (1H, *d*, (*J* = 3.86Hz), 7.27 (2H, *dd*, (*J* = 8.40, 1.08Hz), 8.28 (2H, *s*), 7.48 (1H, *dd*, (*J* = 8.03, 1.62Hz), 7.56 (2H, *d*, (*J* = 3.88Hz)). Anal. Calcd. for Anal. Calcd. for $C_{13}H_9Br_2N_5$(395.05): C, 39.52; H, 2.30; Br, 40.45; N, 17.73. Found: C, 39.50; H, 2.27; Br, 40.33; N, 17.53.

2.2.4. 4-{(2E)-2-[(2, 6-dibromophenyl) methylidene]hydrazinyl}-7H-pyrrolo[2,3-*d*]pyrimidine (4).

Yield % 80.97, m.p. 196-198°C, IR:υ_{max}/cm^{-1} 3127 (-NH- aromatic), 3289 (-NH- aliphatic), 2948 (-CH=), 1581/1475 (>C=C<), 1662 (>C=NN-), 1224 (C-F), 1023 (-N-N-), 687 (benzene ring).^{1}H-NMR (DMSO-d$_6$) δ: 14.42 (s, 1H, -NH- aliphatic), 12.94 (s, 1H, NH, aromatic), 8.66 (s, 1H, pyrimidine H), 8.11 (s, 1H, -CH=), 6.81-7.52 (m, 6H, aromatic-H (7.52 (1H, *d*, (*J* = 3.89Hz), 7.04 (1H, *dd*, (*J* = 1.64, 1.43Hz), 6.87 (2H, *dd*, (*J* = 1.68, 1.53Hz), 6.81 (1H, *d*, (*J* = 3.89Hz)). Anal. Calcd. for $C_{13}H_9Br_2N_5$(395.05): C, 39.52; H, 2.30; Br, 40.45; N, 17.73. Found: C, 39.40; H, 2.21; Br, 40.19; N, 17.70.

2.2.5. 4-{(2E)-2-[(3,4-dibromophenyl) methylidene]hydrazinyl}-7H-pyrrolo[2,3-*d*]pyrimidine (5).

Yield % 73.33, m.p. 187-188°C, IR:υ_{max}/cm^{-1} 3046 (-NH- aromatic), 3290 (-NH- aliphatic), 2684 (-CH=), 1585/1476 (>C=C<), 1660 (>C=NN-), 1223 (C-F), 1023 (-N-N-), 682 (benzene ring).^{1}H-NMR (DMSO-d$_6$) δ: 14.52 (s, 1H, -NH- aliphatic), 12.48 (s, 1H, NH, aromatic), 8.66 (s, 1H, pyrimidine H), 8.09 (s, 1H, -CH=), 6.81-7.53 (m, 5H, aromatic-H (6.81 (1H, *d*, (*J* = 3.90Hz), 6.89 (1H, *d*, (*J* = 1.68Hz), 7.14 (1H, *d*, (*J* = 1.68Hz), 7.53 (1H, *d*, (*J* = 3.90Hz). Anal. Calcd. for $C_{13}H_9Br_2N_5$(395.05): C, 39.52; H, 2.30; Br, 40.45; N, 17.73. Found: C, 38.95; H, 2.26; Br, 40.22; N, 17.69.

2.2.6. 4-{(2E)-2-[(3, 5-dibromophenyl) methylidene]hydrazinyl}-7H-pyrrolo[2,3-*d*]pyrimidine (6).

Yield % 77.76, m.p. 183°C, IR:υ_{max}/cm^{-1} 3109 (-NH- aromatic), 3194 (-NH- aliphatic), 2985 (-CH=), 1575/1506 (>C=C<), 1629 (>C=NN-), 1206 (C-F), 1046 (-N-N-), 695 (benzene ring).^{1}H-NMR (DMSO-d$_6$) δ: 11.87 (s, 1H, -NH- aliphatic), 11.74 (s, 1H, NH, aromatic), 8.28 (s, 2H, Ar H), 7.56 (s, 1H, -CH=), 6.93-7.70 (m, 3H, aromatic-H (6.93 (1H, *d*, (*J* = 3.86Hz), 7.34 (1H, *d*, (*J* = 0.54Hz). Anal. Calcd. for $C_{13}H_9Br_2N_5$(395.05): C, 39.52; H, 2.30; Br, 40.45; N, 17.73. Found: C, 38.99; H, 2.29; Br, 40.41; N, 17.72.

2.2.7. 4-{(2E)-2-[(2,3,4-tribromophenyl) methylidene]hydrazinyl}-7H-pyrrolo[2,3-*d*]pyrimidine (7).

Yield % 79.04, m.p. 186°C, IR:υ_{max}/cm^{-1}3021 (-NH- aromatic), 3118 (-NH- aliphatic), 2973 (-CH=), 1582/1480 (>C=C<), 1648 (>C=NN-), 1251 (C-F), 1026 (-N-N-), 731 (benzene ring).^{1}H-NMR (DMSO-d$_6$) δ: 11.93 (s, 1H, -NH- aliphatic), 11.66 (s, 1H, NH, aromatic), 8.66 (s, 1H, pyrimidine H), 8.12 (s, 1H, -CH=), 6.81-7.53 (m, 4H, aromatic-H (6.81 (1H, *d*, (*J* = 3.89Hz), 7.12 (2H, *d*, (*J* = 1.95Hz), 7.53 (1H, *d*, (*J* = 3.89Hz). Anal. Calcd. for $C_{13}H_8Br_3N_5$(473.95): C, 32.94; H,

1.70; Br, 50.58; N, 14.78. Found: C, 32.91; H, 1.69; Br, 50.55; N, 14.75.

Antimicrobial activity:

The study used gram-positive Staphylococcus aureus MCC 2010 and gram-negative Bacillus subtilis MCC 2010 microorganisms to test the antibacterial effectiveness of the chemicals that were produced. Bacillus subtilis (MCC 2010), Escherichia coli (MCC 2412), Staphylococcus aureus (MCC 2408), and Pseudomonas aeruginosa (MCC 2080) were the bacterial strains utilized in this investigation. To mimic the conditions usually used in an antibacterial test, the Muller Hilton agar medium was autoclaved at a pressure of 15 lbs/in2 for 15 minutes. To test whether the newly produced chemicals were effective against bacteria, the researchers used the disc diffusion method [19-22]. A decrease in the organism count to around L108 colony-forming units per milliliter (cfu/mL) was achieved by modifying the inoculum and suspending the culture in sterile distilled water to evaluate the antibiotic effect. Bacterial strains were cultured by swabbing 20 mL of Muller Hilton agar medium from Petri plates. The Petri dishes were then incubated for 15 minutes to allow the cultures to be absorbed. A 6-millimeter-diameter well was bored using a sterile borer. Afterward, 100 µ of a DMSO-reconstituted solution containing 4.0 mg/mL of each chemical was added to the polluted plates. An entire 24-hour period was spent incubating each plate at a temperature of 37 °C. An entire 24-hour period was spent incubating each plate at a temperature of 37 °C. To measure the antibacterial activity of each drug, the area of inhibition surrounding the test wells was measured. Dimethyl sulfoxide (DMSO) was used as the negative control, and streptomycin was used as the positive control [23-25].

Antifungal Activity:

Cup and plate experiments incorporating the compounds were conducted with two separate fungus species [25, 26]. The Candida albicans (MCC1439) and Saccharomyces cerevisiae (MCC1033) strains are the ones being studied. The discs, which were 1 mm thick and 5 mm in diameter, were filled with the test solution using a micropipette. The plates were then kept in an incubator set at 37 °C for a whole week. During this time, the test solution diffused throughout the body, preventing the injected fungus from growing. After incubating at 37°C for 36 hours, the inhibitory zone's diameter was measured. The inquiry included testing chemicals with substances that were thought to have antifungal characteristics using minimum inhibitory concentration (MIC) studies. After a total of 24 hours of incubation, the concentration of an antifungal drug at which all measurable microbial growth is successfully suppressed is called the minimum inhibitory concentration (MIC). The minimum inhibitory concentration (MIC) approach is used in diagnostic laboratories to validate microbial resistance to antimicrobial drugs and to evaluate the efficacy of newly developed antimicrobial agents.

***In vitro* cytotoxicity:**

A bioassay using brine shrimp was used to evaluate the cytotoxicity of the chemicals that were produced [27]. The shrimp eggs were placed in a specific area of the aquarium. The opposite half was filled with a fake seawater solution consisting of 38 g of NaCl and 1000 ml of water from the faucet. The entire process of hatching and developing into nauplii takes two days for shrimp. To perform a bioassay, the newly developed crustaceans were removed. Mixed with various strengths of dry components- 2.5, 5.5, 7.5, 10, and 12.5 mg/mL sample vials were filled. By dissolving the complexes in DMSO, their cytotoxicity was evaluated. Using a Pasteur pipette, ten live shrimp were added to each test tube. A control group was included to guarantee that the test technique and results obtained from the drug's cytotoxic activity were valid. After a day, the tubes were examined under a microscope to record any findings and count the number of nauplii that survived. Five separate replicates, each with three runs, made up the experiment. Many statistical tests, including LC50, LC90, chi-square, and 95% CI, were performed on the collected data. The numerical values were adjusted using Abbott's technique, as described in reference [28], whenever deaths occurred within the control group.

% deaths = [(test-control)/control] x 100.

RESULTS AND DISCUSSION

There are two methods for producing pyrrolo[2,3-*d*]pyrimidine (PP) hydrazones. The Schiff bases were produced when PPH was afforded a reasonable yield (80%) by refluxing PP over ethanol for around 12 hours. The Schiff bases of PPH were synthesized with an outstanding yield of 85% using the microwave technique (MW) in a reaction condition with ethanol for 2 hours at 60 °C. This process yielded compounds **1–7**. These findings demonstrated that the Schiff bases' reaction times were shortened by microwave

irradiation. In addition, compared to refluxing conditions, heating with a microwave is more efficient for creating pure chemicals in good to outstanding yields.

FT(IR) spectra:

To determine the degree of bonding between the molecule and the methoxy group of the benzaldehyde, the free PPH was compared to the FT(IR) spectra of the compounds that were formed. Using a limited spectrum of bands, the impact of PPH vibration on substituted bromobenzaldehydes was examined. No stretching vibrations have been detected in any of the produced compounds containing aldehyde (CHO) or amino (NH_2) groups, indicating that they are all fully developed. By contrast, the azomethine (HC=NN-) group generated a strong new band at 1573-1662 cm^{-1} [29]. The presence of an aromatic (NH) bandwidth in the 3054 - 3110 cm^{-1} region has led some to speculate that the prepared compounds must exist [30, 31]. All of the compounds have been classified based on the analysis of the aldehydic (-CH=) bands at 2815-2882 cm^{-1}. Two strong lines at 1493–1590 and 1441–1483 cm^{-1} are seen in the infrared spectra of**1–7** compounds; these lines are associated with the aromatic ring's >C=C group. The strongest bands are at 1318–1330, 728–738, and 654-687 cm^{-1}. Compounds **1-7** display FT(IR) spectra that are compatible with aromatic (C-N), di/ trisubstituted benzene ring, and monosubstituted benzene ring structures. The **1-7** molecule's aromatic C-Br group was identified by a band at 687-691 cm^{-1} in the FT(IR) spectra.

^{1}H NMR spectra:

All of the developed compounds' wide singlet signals in the ^{1}H NMR spectra, which range from 11.82 to 14.41 ppm, are due to the aromatic -NH- group in the pyrrolyl ring. All of the compounds that are made have an aldehydic -CH= group assigned to them in the 7.48-8.49 ppm range, and the aliphatic -NH- singlet peak is visible in the 11.69-12.94 ppm range. Since there is no broad singlet signal at 9.84 ppm (2H) corresponding to the -NH_2 of PPH, the 1H NMR spectra of all the produced derivatives show that the amino group was successfully substituted by the Schiff base [32]. A singlet for the pyrimidine proton between 6.98 and 8.28 ppm is visible in the ^{1}H-NMR spectra of compounds **1-7**. When looking at ^{1}H NMR spectra from different publications, you may find that they have the same bands [33].

Antibacterial activity:

According to **Table 1**, all of the microorganisms that were tested were susceptible to the chemicals that were researched. The minimum inhibitory concentrations (MICs) for these compounds ranged from 0.5 to 64 µg/mL. The reference drug was *ciprofloxacin*, which is a broad-spectrum antibiotic that had a MIC of 10 µg/mL against the bacterial species. For Staphylococcus aureus, the inhibition zones ranged from 10 to 18 mm (MCC 2010), while for Pseudomonas aeruginosa, they ranged from 8 to 29 mm (MCC 2080).

Table 1: Antibacterial studies of **1-7**compounds

Compound	Antibacterial Activity (zone of inhibition)			
	S. aureus	***B. subtilis***	***E. coli***	***P. aeruginosa***
1	15	15	19	15
2	17	18	23	16
3	16	0	24	19
4	13	0	23	16
5	12	17	15	25
6	13	12	16	29
7	10	11	10	10
Ciprofloxacin	10	10	12	11

The most effective bacteria against S. aureus, when considering all bacteria collectively, are the **1**, **2**, and **7** strains. Compounds **1-6** showed superior efficacy compared to the industry benchmark ciprofloxacin. The compound **7** exhibited reduced antibacterial efficacy against P. aeruginosa. The results demonstrated that **6** surpassed the suggested method of delivery. The against E. coli. Refer to sections **1**, **2**, and **4** for information on B. subtilis. The antibacterial activity is most likely caused by the more effortless penetration of the cell walls of lipophilic microorganisms. The molecule's capacity to traverse the lipid cell membrane of gram-negative bacteria is mainly attributed to the lipophilic alkyl chain. The results indicate that there is a negative

and the antibacterial activity. This can happen when the size of the carbon chain is too large to traverse the bacterial cell membrane [34].

Antifungal activity:

In response to the reference drug fluconazole (MIC 50 µg/ml), the inhibition zones of Candida albicans (MCC1439) and Saccharomyces cerevisiae (MCC1033) were found to be 6-17 mm and 7-20 mm, separately. All of the substances tested showed substantially higher fungicidal activity than the reference medication, as proven by the data shown in **Table 2**. A minimum inhibitory concentration (MIC) of 54 µg/mL was found for all the substances that were tested against Candida albicans (MCC1439) and Saccharomyces cerevisiae (MCC1033).

Table 2: Antifungal studies of 1-7compounds

Compound	*Candida albicans*	*Saccharomyces cerevisiae*
1	12	14
2	14	11
3	0	16
4	6	20
5	0	16
6	13	11
7	17	9
Fluconazole	9	12

***In vitro cytotoxicity*:**

Table 3 displays the findings of the evaluation of the cytotoxicity of the substances on Artemia salina. According to literature, the half-life (LD_{50}) values vary between 3.99 and 9.67 x 10-4 µM/mL, which represents the concentration at which 50% of the organisms were impacted.

Table 3: Brine shrimp bioassay of **1-7**compounds

Compound	LD_{50} (M)
1	$>6.45 \times 10^{-4}$
2	$>4.22 \times 10^{-4}$
3	$>5.25 \times 10^{-4}$
4	$>4.49 \times 10^{-4}$
5	$>7.31 \times 10^{-4}$
6	$>4.66 \times 10^{-4}$
7	$>3.99 \times 10^{-4}$

CONCLUSION

Various substituted bromo benzaldehydes were used to prepare several new derivatives of PPH. The results acquired from several analytical techniques, such as FT-IR, UV-vis, NMR spectral studies, and electrochemical data, support the creation of the proposed compounds. The compounds that were produced underwent a battery of analytical tests, including ^{1}H NMR, UV-vis, elemental analysis (C, H, N), and FT-IR spectroscopy. After collecting the spectra, they were examined. Based on the results, modified bromo benzaldehydes and PPH should be mixed in a ratio of 1:1. The antibacterial activity of all the compounds that were produced was substantial. Every one of the synthetic chemicals has extremely high cytotoxicity levels when applied to vulnerable cell types.

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Analysis of Authorship Pattern of SAJLIS UGC- CARE Research Journal Published during 2015-2017

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ABSTRACT

The present study contains a Content analysis of UGC-CARE listed (SAJLIS) South African Journal of Libraries and Information Science . The study covers articles published between 2015 and 2017. The study includes yearwise subject-wise distribution of contributions in the field of library and information subject Authorship pattern, prolific contributors to the journal. In the field of LIS, it is observed that collaborative research is predominated, the degree of collaboration in SAJLIS is 0.9638 which clearly indicates its dominance upon individual contribution. Library professional are conducting more research work to develop the LIS professional. The scope of publication of research articles in the (SAJLIS) South African Journal of Libraries and Information Science. The research in library and information subject of is going internationally.

Keywords: Bibliometrics, Bibliography, Authorship pattern, Geographical distribution, Citation Analysis

Introduction-

The South African Journal of Libraries and Information Science, SAJLIS has since 2002 been published as the official research journal of the Library and Information Association of South Africa (LIASA). LIASA was established in 1997 supported by an overwhelming majority of members of the LIS associations that had accommodated the interests of the library and information services (LIS) the African Library Association of South Africa (ALASA), and the South African Institute for Librarianship and Information Science (SAILIS) voted to dissolve. Although the name has changed slightly at various stages in its existence, the volume numbering of the Journal has been continuous since the first issue of South African Libraries 1933 this was the quarterly journal of the South African Library Association. "Content analysis of the manifest and latent content of a body of communicated material (as a book journal or any information source) through a classification, tabulation, and evaluation of its key symbols and themes in order to ascertain its meaning and probable effect." Content analysis is essentially a systematic analysis of the occurrence of

words, phrases, concepts, and so on in books, films, and other kinds of materials. (ALA Glossary of Library and Information Science, 1983).

1. SCOPE AND LIMITATIONS OF THE STUDY

The present study has been undertaken in order to know the nature and contents of articles in the SAJLIS research. SAJLIS is an official publication SAJLIS. It publishes original research articles by renowned library professionals on all aspects of library and information science. The aim of the journal is to provide a forum for the librarian to publish their research findings and also to open new vistas for further research. It is one of the leading journals being published for from South Africa Country. The major limitations of the present study are - The study is limited to the articles of Vol. 81 to 83 to from years 2015to 2017.

2.SOURCES OF DATA

In order to analyze the SAJLIS, the primary sources used by the researcher are the issues of the journal volume 81 to 83 for the period years 2015-2017.Six issues of the journals are taken as the sources of data. All the issues are minutely scanned to collect the necessary data.

3. VARIABLES CONSIDERED FOR ANALYSIS

The following variables were considered for analysis to draw meaningful conclusion:

4.1 Total number of articles appeared during the period 2015-2017

4.2 Subject-wise breakup articles

4.3 Authorship pattern and collaborative authors

4.4 Number of pages per article

4.5 The prolific contribution to the journal

4. OBJECTIVES OF THE STUDY

1) Year-wise distribution of the contribution
2) Subject-wise distribution of contribution
3) Authorship pattern
4) Prolific contributors to the journal
5) Average length of the article per volume

5. METHODOLOGY:

Document analysis was the major techniques used by the investigators for the current study. A specially prepared data sheet was used for analyzing the 16 issues of the SAJLIS manually. Data items for source contributions included authors name, number of authors, and institutional contributions of the contribution, number of pages, and subject of articles. After collection of all these data, the analysis was done manually. The method used by the investigators for the analysis of data collected, was purely manual. To draw meaningful conclusions various techniques have to be

used for the analysis. They are documental analysis, calculation of percentages and averages, preparation of frequency tables, diagrammatical representation and statistical analysis.

6. DATA ANALYSIS & INTERPRETATION

6.1 Year wise Research articles published in SAJLIS

Table 1

Publication Year	Volume	Research Articles	Percentage of Publication
2015	81	16	43%
2016	82	12	32%
2017	83	14	35%
Total	**03**	**42**	**100%**

Analysed that a total of 14 articles were published in SAJLIS during the year between 2015 and 2017. Out of the 41contributions from the selected three years, 43% (16) research articles were published in Volume 81 during the year 2015, 32% (12) research articles were published in Volume 82 in 2016 and 35% (14) research articles were published in volume 83 during the year 2017. This analysis reveals that more research articles was published during the year 2015 when compared to the years 2012 and 2014

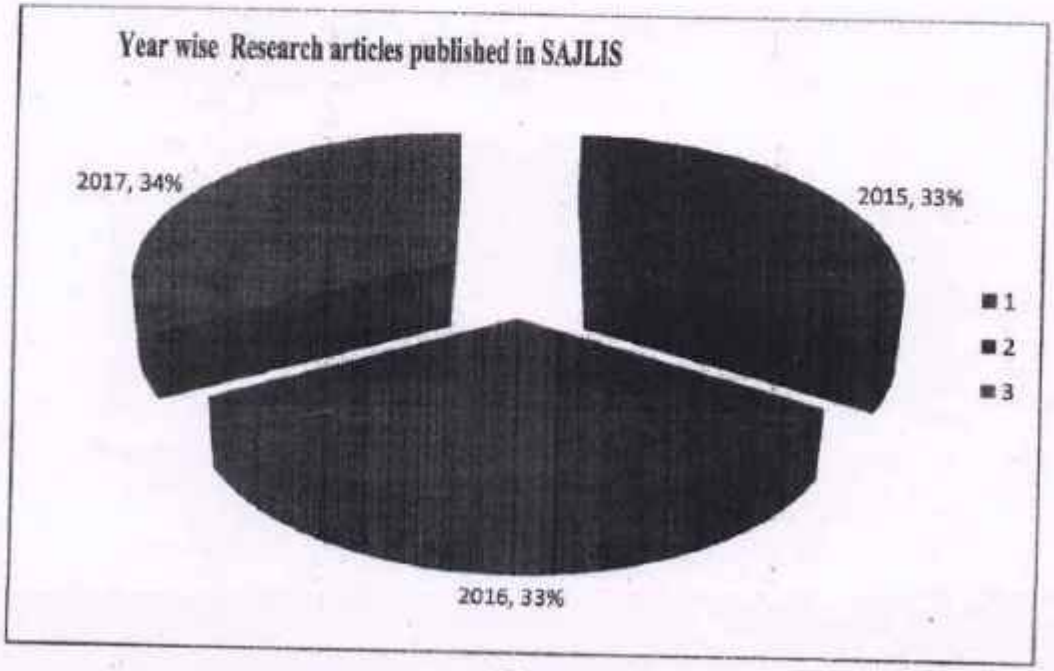

Figure 1

6.2 Subject wise distribution of articles.

Table 2

S.N.	Topic Title	No. of Articles	Percentage
1.	Open source	5	12%
2.	End user	3	8%
3.	Automation	7	16%
4.	Retrieval system	3	8%
5.	E-book	4	9%
6.	Collection management	3	8%
7.	University library	2	5%
8.	Digital repository	5	12%
9.	Digital information	6	14%
10.	Digital collections	4	9%
		42	100%

The table 2 analysed that majority of the articles contributed which appeared under the subject Automation 7(16%) followed by digital information (14%) open source and digital repository (12%) e-books and digital collection (9%) end user, retrieval system and collection management (8%) and 5% on university library). This study reveals that majority of the automation are conducting research and publishing their research findings in library automation and according to that automation was most important and current subject,

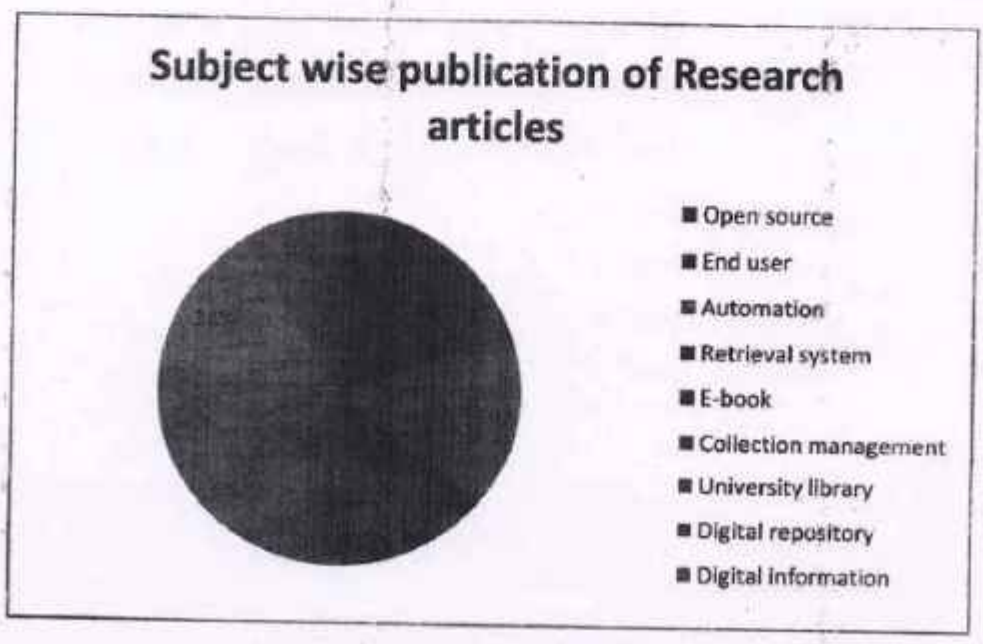

Figure 2

6.3 Yearwise Authorship pattern of the contribution.

Table 3

S.N.	No. of Authors	No. of Author Contributed Articles	Total Number of Author	Percentage
1	Signal Author	11	11	26%
2	Two Authors	23	46	55%
3	Three Authors	5	15	12%
4	More than Three Authors	3	12	7%
	Total	42	95	100%

The table no.3 Analysis of the 95 authors contributions (articles) reveals that there are 23 contributions (55%) by two authors, 11 contributions (26%) by solo author, 5 contributions
(12%) by Three authors contributions (7%) by more than three authors, This analysis reveals that more number of authors desires to write collaboratively and only less number of people likes to produce individual write up work by less than two authors.

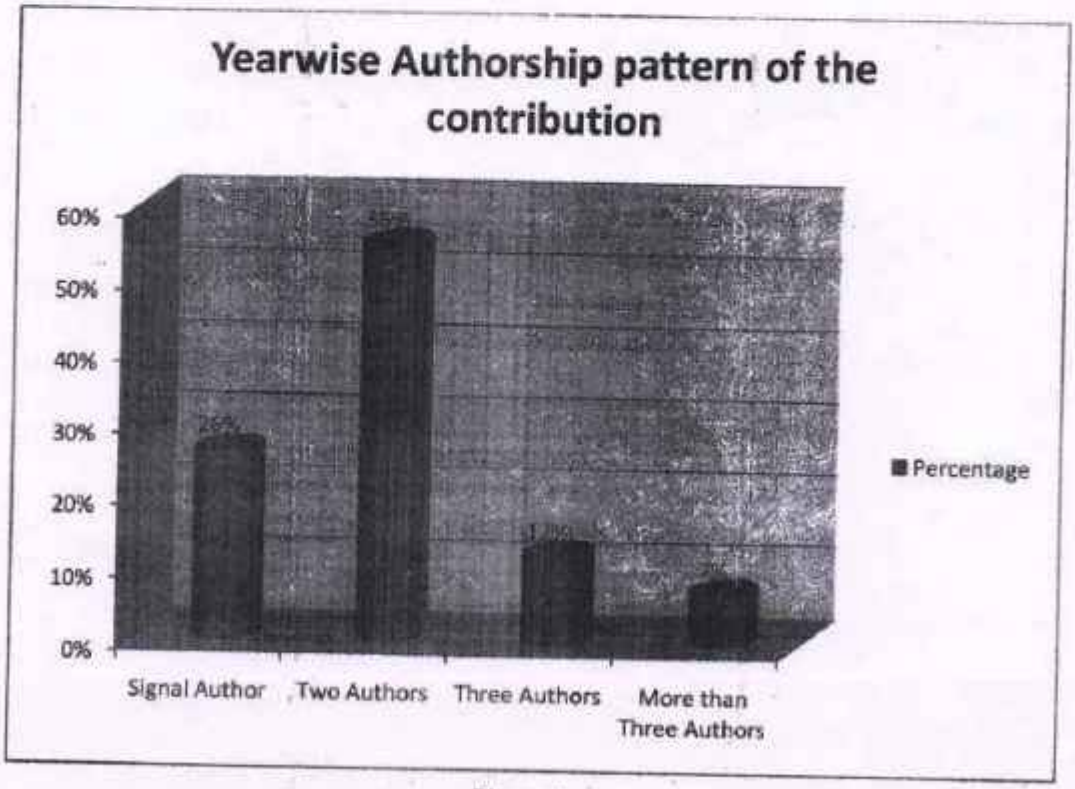

Figure 3

6.4Most Prolific Contributors Journal

Table 4

S.N.	Ranked Author	Articles Contributed 2015-2017	Level of Rank	Percentage
1	Omwoyo Bosire Onyancha	5	1	12%
2	Elisha Chiware	4	2	10%
3	Peter G.Underwood	3	3	6%
4	Irvine Kadzenga	2	4	5%
5	Single Article Published	26	5	67(2%)
		42		100%

Table -7, reveals that the list contains the names of 4 authors with more than two articles contributed during the period of 2015-2017. The contributions from all of them when taken solo contribution is 26 (2%) out of the total contributed articles (42) is found from solo author. Omwoyo Bosire Onyancha has obtained first rank(12%) contributed 5 articles have been published. Elisha Chiware is on rank fourth (10%) on third rank Peter G.Underwood 3(6%) and 2(5%) is second rank the author Irvine Kadzenga

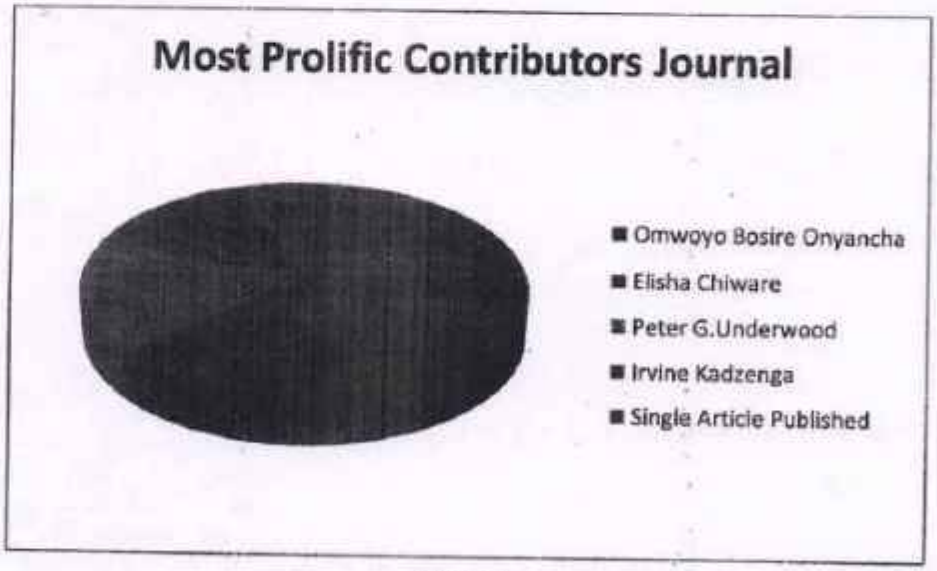

Figure 4

6.5Average page length of the article per volume

Table No.5

Page Length	No. of Articles	Percentage
Three Pages	3	7%
Four Pages	8	19%

Five Pages	11	27%
Six Pages	9	21%
Seven pages	6	14%
More Than Seven Pages	5	12%
Total	42	100%

Table 5, shows that the majority of the articles 11 (27%) have the length of five pages, 9 (19%) have length of six pages,8(19%) with length of with four pages, 6 (14%) articles with seven pages, 5 (12%) articles with more than seven three pages, 3 (7%) articles with three pages,

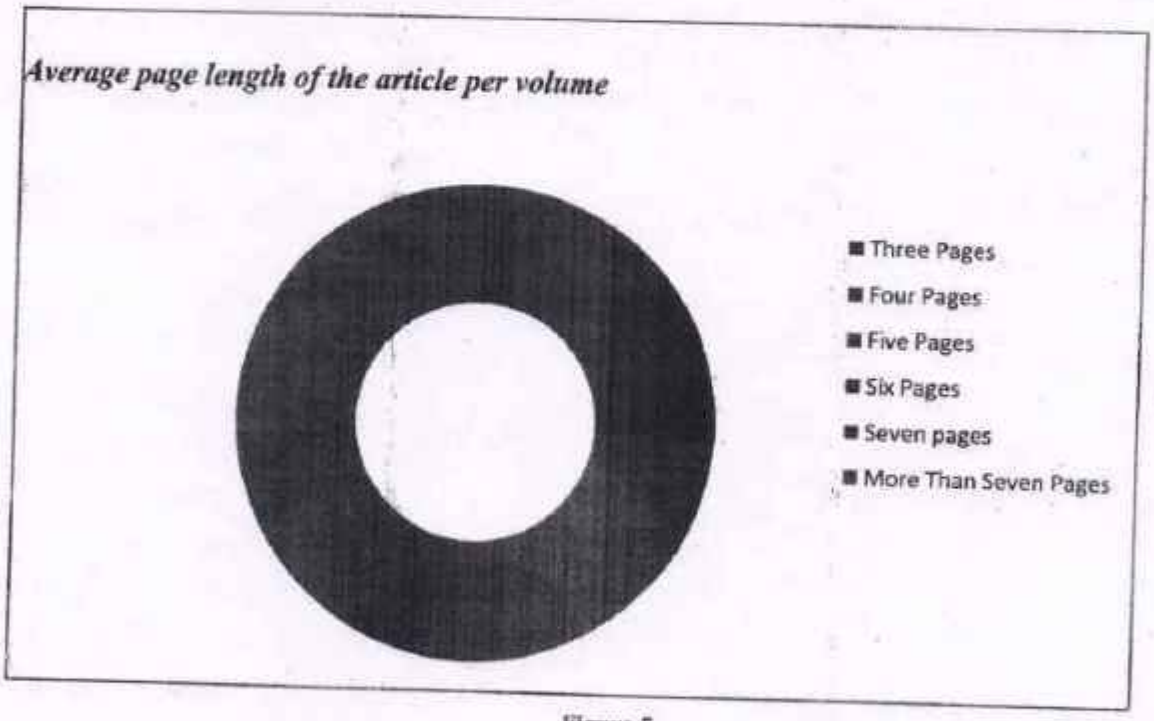

Figure 5

6.6.CITATION ANALYSIS

Year wise Distribution of Citations

The references provided by the authors at the end of their articles are the basis of citation analysis. Citation traces a connection between two documents. one which cites and the other which is cited. Citation analysis is one of the popular methods applied to derive
the following benefits

Year wise Distribution of Citations

Year	Vol No.	Issue	Citation	Percentage
2015	81	2	147	28%
2016	82	2	164	31%
2017	83	2	203	39%
Total	03	06	514	100%

Table No.6:

The above table shows that maximum number of citations 203 (39 %) produced in 2017 followed by 164 (31%) citations in 2016 and 147 (28%) citations in 2015.

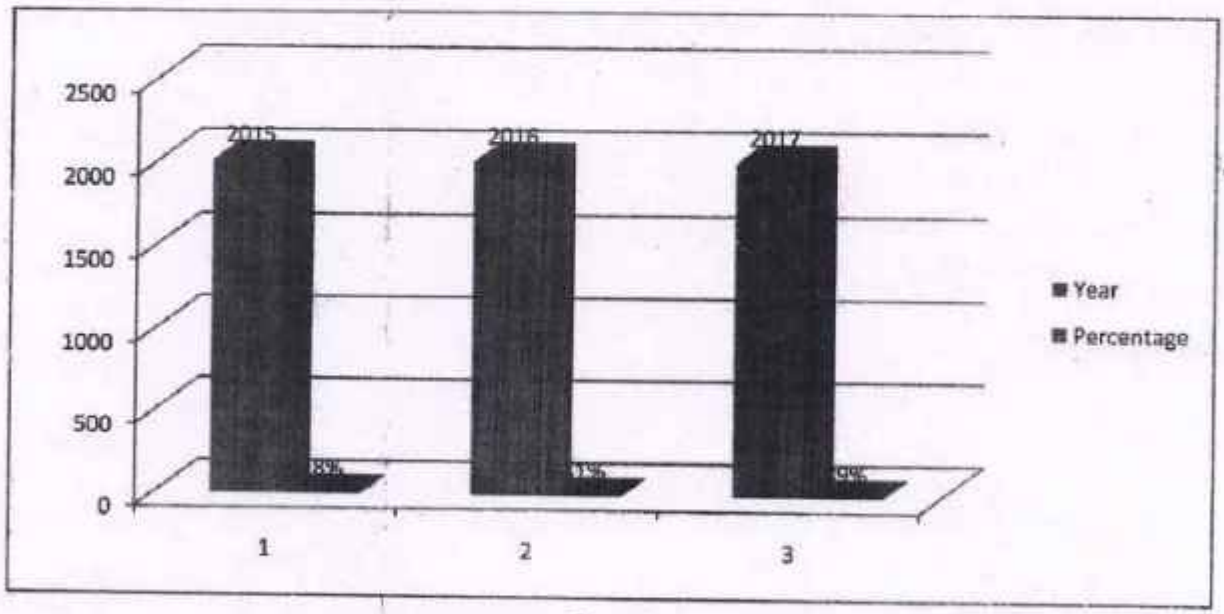

Figure6

7.Major Findings of the Study:

1. Majority of the research articles was published in 2017.
2. It is found that library professionals are conducting research and publishing their research in Automation ,digital information, open source, digital repository-books and digital collection.
3. Multiple authorship or collaborative research predominates in writing of articles.
4. Citation pattern has been followed very systemically in research articles.

8.CONCLUSION:

The content and bibliometric analysis of the UGC- CARE listed journal (SAJLIS) South African Journal of Libraries and Information Science in the 81 to 82 volumes of the research shows the various characteristics of the published

literature in library and information science.The publication trend totally depends on the productivity pattern of the authors. Now a days we can see the team research or collaborative research is visible in all the areas of knowledge, as in the LIS it is shown also.The present study also reveals that the trend collaborative research is increasing in the LIS. The study revealed that Maximum number subject trends is automation and digital information it is 16% and 14% .Study also concluded that the most prolific author is Onwoyo Bosire Onyancha which is on number one 1rank.Citationa ratio also been considered in this research i.e (514)39% citations are cited in the year 2017 while writing a research paper by researchers

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Contents

POLLUTION GENERATING SOURCES ITS EFFECT AND CONTROL

R. A. Kunale

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ABSTRACT

Environment is the natural world, for example the air, water and land in which plants, animal and people live. Contamination of this environment causes pollution of environment. Pollution is a term that covers all the ways pollutants get into the air, water, soil and cause damage to natural resources or all living beings. It can be produced from natural and artificial sources like volcanoes, forest fires, earthquakes, industrial wastes, pesticides, insecticides etc. Pollution can cause respiratory problems, heart diseases, lung cancer etc. It will also lead to water contamination and damage to natural resources is challenging to understand the effects of pollution. It can affect nature, human beings, and animals and play a vital role in adverse climate change. Depletion of natural resources and destroying habitats are significant effects of pollution. Pollution is global problem and it can harm humans by breathing in smoke or consuming contaminated food. Moreover, it can cause health problems such as asthma, cancer, and heart diseases. It also affects nature by destroying plants, animals, and natural habitats.

Keywords:*Pollution, environment, remedies, natural resources.*

Introduction

The activities of human created various environmental issues such as deforestation, global warming, and depletion of scarce natural resources.In the simple terms, pollution is defined as the contamination of the physical and biological constituents in the earth's atmosphere. It affects human life and the natural environment to a very great extent.Due to air pollution, diseases that can occur to human beings are asthma, various skin diseases, cancer, etc. Therefore, it is the essential need of the hour to take serious steps to reduce pollution to its core. In 1997, environmentalist Charles Moore discovered the world's largest collection of floating trash the Great Pacific Garbage Patch ("GPGP") while sailing from Hawaii to California. And in the last 20 years, it's only gotten worse a 2018 study has found that the vast dump of plastic waste swirling in the Pacific Ocean is now bigger than France, Germany, and Spain combined far larger than previously feared. From milk jugs and abandoned fishing gear to polymer molecules small enough to penetrate human skin and be unknowingly inhaled, plastic is now suspected of contributing to a host of ailments, including infertility, autism, thyroid dysfunction, and certain cancers.

Environmental issues continue to attract attention at all levels. It is time now urgent call to action, at a personal level, we can minimize environmental pollution by taking public transport or carpools to reduce vehicular smoke, avoiding firecrackers at festivals and celebrations can also cut down on air and noise pollution, not using fertilizers and pesticides which can cause both water and soil pollution, and switching over to organic farming. The government can also bring strict rules and regulations to lessenindustrial pollution.Pollution degrades our natural resources, from the water we drink to the air we breathe. The different types of pollution listed as follows:

1. **Air Pollution**: Air pollution is the contamination of air in the atmosphere when harmful or excessive quantities of substances such as smoke and harmful gases from industries, CFCs and oxides produced by automobiles, the burning of solid wastes, etc. are introduced into the environment.
2. **Water Pollution**: This refers to the contamination of natural resources of water, due to the addition of harmful chemical, biological or physical materials, which includes industrial wastes, oil spills, domestic and farm wastes, pesticides, as well as mining and agricultural wastes, to water resource which make it unusable.
3. **Soil Pollution**: Land/Soil Pollution occurs due to the degradation of the

earth's surface by different commercial, industrial, agricultural and domestic activities. Causes of soil pollution also include mining, deforestation, dumping of e-waste and other industrial wastes, usage of harmful chemicals such as insecticides, pesticides, etc.

4. **Noise Pollution:** Excess noise due to sounds created by machines, loudspeakers, microphones, loud music, noise from industries, construction and civil engineering works etc. lead to noise pollution.
5. **Less natural resources due to Land occupation**:As the world embraced urbanization, mother nature witnessed the greener lands getting transformed into modern cities and metropolises. What followed is a trail of natural disasters signaling that something is wrong with the planet earth. Consuming more natural resources disturbs the cycle of nature.
6. **Space debris**: Manmade satellites occupied the place in space.Space debris, or space junk, consists of discarded launch vehicles or parts of a spacecraft that float around in space hundreds of miles above the Earth, risking collision with a satellite or spacestation.While space debris is unlikely to affect space travel, it will lead to significant problems for spaceflight around Earth. The risk would be highest for objects orbiting at an altitude of around 1,000 kilometres (620 miles), which is used for communications and Earth observation.

1. Pollution control: Some simple remedies to reduce pollution are listed below

Say no to crackers

Air and Noise pollution caused by fire crackers can increase the impact of pre-existing problems and disorders of patient related to heart, respiratory and nervous system. Radioactive and poisonous elements are used to spread the color in the sky when cracker burst, which can increase the risk of cancer.

Use Public Transportation

Emissions from vehicles account for 40 per cent of the air pollution and using public transportation can help in reducing that. Here, we can reduce emissions by using public transport which can contribute in making the air cleaner.

Turn off the lights, fans and water taps when not in use

Turning off the lights when you leave your room can help save energy. It can also help reduce carbon emission and other harmful greenhouse gases. Hence, turning off your lights is a simple way to help protect the environment and save the planet.

Recycle, reduce and reuse

Learn how reducing, reusing, and recycling can help you, your community, and the environment by saving money, energy, and natural resources. Reducing, reusing and recycling waste helps save landfill space by keeping useful materials out. The amount of energy and natural resources needed to produce the raw materials are limited.

Segregate your waste

The simple ways to practice waste segregation are keep separate containers for dry and wet waste in the kitchen. Also keep two bags for dry waste collection- paper and plastic, for the rest of the household waste.Keep plastic from the kitchen clean and dry and drop into the dry waste bin. Send wet waste out of your home daily.

Say no to plastic

A single plastic bag takes up to 1000 years to decompose as it contains non-renewable petrochemicals. Hence plastic bags will stay for a more extended period and damage our mother nature. Plastic pollution is a problem that the whole world is facing together. We are finding microplastic pieces in our waterways, in the food we eat, and in the water we drink. Collectively, we need to take action and say no to plastic.Plastic waste does not degrade at a sustainable rate. The more we continue to make, the more waste continues to build up.

When plastic waste is not disposed of properly, it ends up in the environment, which is causing devastating impacts. Each single-use plastic item we use today adds to the mass problem of tomorrow and beyond. So say no to use plastic.

Plant more trees

The world's forests absorb a third of global emissions every year. Particles, odors and pollutant gases such as nitrogen oxides, ammonia and sulfur dioxide settle on the leaves of a tree. Trees absorb these toxic chemicals through their stomata, or 'pores', effectively filtering these chemicals from the air. Trees can improve air quality in direct and indirect ways. Indirectly, they can help by shading surfaces and reducing temperatures. If buildings are shaded by trees, it reduces the need for conventional air conditioning, and the emissions of greenhouse gases that come with it.

Use of fans instead of ACs

Researchers also conducted a cost-benefit analysis on the environmental impact and found the total benefit of using fans to reduce air conditioner use from a greenhouse emissions perspective.

Try to recycle industrial waste

Industrial waste should be treated and reused. Use the sustainable industrial development process.

To sum up, any type of pollution is harmful to the environment with serious consequences like global warming, uneven climatic changes, etc. Due to our greediness and illegal human activities, the innocent lives of animals are lost.

Conclusion

Environment pollution is the introduction of harmful materials into the environment that disturb the cycle of nature. These materials are called pollutants. They can be created by human activity like industrial activity, and natural like volcanic ash. Pollutants damage the quality of water, air and land. Air and water carry pollution into the ocean currents and migrating fish. It is among the many things that harm our planet once greener and healthier than it is now. It is a dangerous phenomenon that is contributing to an array of health issues among human and animal.

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A Review on New Education Policy 2020

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Abstract:

The New National Education policy was approved by the union cabinet on 29 july , 2020 to overhaul the country's education system . It will bring **transformation** reforms in the school and **higher education** system in the country.. The aim of new police is the universalize of education from pre–school to secondary level with 100% **Gross Enrollment Ratio** (GER) in school education by 2030.The NEP proposes some changes including opening up of Indian higher education to foreign **universities, introduction** of a four – year multidisciplinary undergraduate program with multiple exit options. **The NEP 2020** aims at making India a global Knowledge superpower .

Introduction:

Government of India started various schemes like Sarva Shiksha Abhiyan, Mid-Day Meal, Adult Education and Skill Development Scheme, National Means cum Merit Scholarship Scheme, National Program for Education of Girls at Elementary Education, Kasturba Gandhi BalikaVidyalaya, Scheme for Infrastructure Development in Minority Institutions, BetiBachao, BetiPadhao, etc. to educate the every citizens of India.Education is the most powerful weapon to change the world". This is said by Nelson Mandela who said this after observing the power of education. Education is the means that brings economic growth, social prosperity and political stability in the society. Education makes the people confident to put their views and showcase their immense potential. It is education that enabled citizens of a county to participate in the governance process and strengthen the democracy.

Importance of education has been appreciated and education has been promoted by the Governments of most of the countries in the world. Working in the field, most of the countries isproviding free education to all its citizen. In some of the countries free education is a constitutional right of every citizen and people of any age group, religion, caste, creed are entitled to receive free education. Education makes the life of people better by transforming the personality of the individual. It makes them feel confident and opens the way for success.

Well educated population is necessary for a country's growth. This can be done only when we understand the importance of education. By the education the population of a country will be equipped with the vibrant knowledge, progressive attitude and skills and this will be the boon for the country. The same can be achieved by spreading awareness about the importance of Education in the country basically in the rural areas. If the people are educated then they will become capable of earning a livelihood by themselves and so for the nation. They will become taxpayer and by this tax the county will prosper.

In 2020, came the New Education Policy (NEP) and launched on 29th July 2020. The idea was put forward by former **ISRO Chief K. Kasturirangan** who discussed the ongoing issue and transitions in the education system. He aimed to create an impact on everyone ranging from primary school to the workplace. It was approved by the union cabinet and has successfully made revolutionary reforms in the Indian education paradigm.

Major Highlights of NEP

1) On 29 July 2020, the new education policy came into existence.

2) The Union Cabinet of India approved the Education Policy.

3) The National Education Policy (NEP 2020) describes India's vision for a new education system.

4) This new policy is the replacement of the previous Education Policy of 1986.

5) By 2040, India's education system is expected to be transformed under this policy.

6) Under this policy, the state expenditure on education will be hiked from 3% to 6%.

7) It enforces the use of local language for instructing students up to class 5.

8) The new model 5+3+3+4 is introduced stating 3 years of preschool and 12 years of schooling.

9) Exams will be held only in classes 2, 5, and 8 instead of every academic year.

10) The main aim is to reduce classroom load from students and make them more interdisciplinary and multi-lingual.

This revised policy expands the age group for mandatory schooling from 6-14 years to 3-18 years. This new system will provide you with 12 years of schooling with three years of Aanganwadi/ pre-schooling.

· **Foundation Stage-** this stage begins from age 3 to 8 years in Anganwadi or pre-school education and class 1 & 2 system. This system possesses only multi-level play activity, interactive school activity, and basic learning of literature and numerals.

· **Preparatory Stage-** 3 years from age 8 to 11. This stage includes class 3- class 5. This system will consist of the basic learning of all subjects and their activities.

· **Middle Stage-** 3years from age 11 to 14. This stage includes class 6- class 8. This system consists of the practical learning of arts, social activities, humanities, science, and mathematics with corresponding internships to experience the working environment in the described fields.

· **Secondary Stage-** 4 years from age 14 to 18. This stage includes class 9- class 12. This system consists of multidisciplinary education, Critical analysis and thinking, students' choice of subjects, and expertise in it.

In school education, the policy focuses on overhauling the **curriculum on experiential** learning and critical thinking. The current 10 + 2 system in the school will be replaced by a new 5+3+3+4 curricular structure. The mid-day meal **programme** will be extended to pre- **school children**.

The Higher Education Commission of India (HECI) will now set up a regulatory body for the entire higher education. Norms, regulations, accreditation, and academic standards will be the same for both the private and public sectors. Thus, providing you with the opportunity to give one common entrance exam for higher education, multiple exit and entry wherein you can start and end your education allowing you to join back without losing your credits. The policy also proposes that all **universities and colleges** must aim to become multidisciplinary by 2040.

Conclusion:

A New Education Policy has been sanctioned by our government in July 2020 after 34 years, for bringing the changes in the National Education System. The New Education Policy has its objective of making the learning process more efficient by enhancing students thinking and creative ability. The New Education Policy includes several changes in the school level as well as higher education.This policy will boost employment in the country and will radically changeour education system.

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