A GREEN AND EFFICIENT ONE-POT SYNTHESIS OF POLYHYDROQUINOLINE DERIVATIVES CATALYZED BY AMMONIUM CHLORIDE UNDER AQUEOUS MEDIA

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ABSTRACT

An efficient and eco-friendly one-pot four component synthesis of polyhydroquinoline derivatives from dimedone, aromatic aldehydes, ethylacetoacetate and ammonium acetate in the presence of catalytic amount of ammonium chloride under aqueous media is reported.The present approach of this protocol offersuse of green solvent, short reaction time, high yields, operational simplicity and simple workup.

Keywords: *Polyhydroquinoline, one-pot synthesis, eco-friendly, aqueous media*

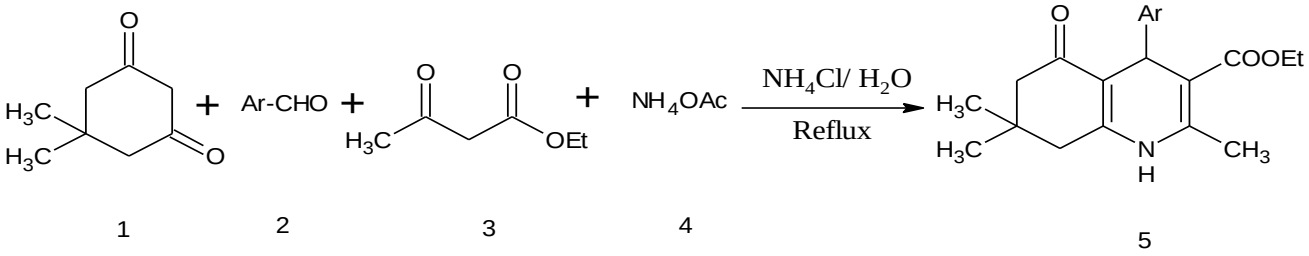
Introduction

Heterocyclic compounds particularly containing nitrogen have attracted considerable attention in modern synthetic chemistry as these compounds play a key role in the fields of natural products, medicinal chemistry and materials chemistry. Among the important heterocyclic compounds, Quinolines having 1,4-dihydropyridine nucleus has attracted the enormous attention of organic and pharmaceutical chemists because of their significant biological activity and pharmacological properties[1-2].1,4-Dihydropyridines possess a range of biological activities, some of the biological activities exhibited by them are anti-atherosclerotic, bronchodilator, vasdilator, hepatoprotective, anti-hypertensive, anti-diabetic, geroprotective and antitumor agents[3-6]. 1,4- DHPs exhibit variety of pharmacological and medicinal properties and have been found to be effective as calcium channel blockers [7] and thus used in the therapeutic treatment of cardiovascular diseases [8]such as hypertension, angina pectoris, supraventricular tachycardia [9]. Literature have disclosed that these compounds also exhibits certain medicinal applications such as chemo sensitizer in tumor therapy, memory enhancing power, platelet anti-aggregatory activity, neuroprotectant, anti-inflammatory activity, antithrombotic activity [10-12].

In recent years, from the environmental and economic view point it is advisable to develop environmentally benign processes and avoid the use of solvents which are hazardous, responsible for environmental pollution and suspected human carcinogens. The use of water as an eco-friendly and easily available solvent in chemical reaction is the new trend in organic synthesis and important area of research. The use of water as a solvent shows valuable gains as it is most abundant and non-toxic. Water is polar solventhence immiscible with majority of organic compounds, therefore the water soluble by-products stays and isolation of organic compound is easy. Multicomponent reaction (MCR) is one of the most powerful and efficient tools in organic synthesis for the fabrication of biologically important compounds in the perspective of green chemistry. Multicomponent reactions offer advantages of atom economy, high yields and one-pot operation and aregreatly influenced by selection of suitable solvent and efficient catalyst [13-15].

Commonly used method reported for the synthesispolyhydroquinoline derivatives involves the one-pot, four component reaction of dimedone, aromatic aldehydes, ethyl acetoacetate and ammonium acetate in the presence of a variety of catalyst. The synthesis of these heterocyclic molecules is therefore extensively studied in the presence of organic solvents and catalysts [16-21].Recently the synthesis of polyhydroquinoline derivatives have been carried out using microwaves [22], ionic liquids [16], TMSCl-NaI [23], metal triflates [24], molecular iodine [25], $SiO_2/NaHSO_4$[26], $SiO_2/HClO_4$[27], ceric ammonium nitrate [28], tetrabutylammonium hydrogen sulfate [29], fermenting baker's yeast [30], organocatalyst [31]. Many of these methods are unsatisfactory as they suffer from

disadvantages such a use of toxic organic solvents, longer reaction times, low yield, and tedious workup procedures.Therefore the development of a new green and convenient method using a readily available catalyst in aqueous media for the synthesis of 1,4-Dihydropyridines is highly desirable. Herein, we wish to report an efficient, green and ammonium chloride catalyzed synthesis of polyhydroquinoline derivatives via a one-pot four component condensation reaction between dimedone, aromatic aldehydes, ethyl acetoacetate and ammonium acetate in the presence of ammonium chloride in refluxing water (Scheme 1).



1 2 3 4 5

Scheme1. Synthesis of polyhydroquinoline derivatives catalyzed by NH_4Cl under aqueous media

Experimental
Materials and Methods

All the chemicals were purchased from LOBA Chemie and used as received without any further purification. All the reactions were monitored by thin-layer chromatography (TLC) using aluminum plates coated with silica gel using petroleum ether and ethyl acetate (60/40) as eluent and visualized with either UV light or an iodine chamber. Melting points were recorded by melting point apparatus. IR spectra were recorded onKBr disc on a Perkin-Elmer FTIR Spectrophotometer. The ^{1}H NMR spectrawere recorded in $CDCl_3$at room temperature on a VARIAN USA, Mercury plus 300 NMR Spectrometer using TMS as an internal standard.

Typical experimental procedure for the synthesis of polyhydroquinoline derivatives

In a typical experimental procedure a mixture of aromatic aldehyde (10 mmol), dimedone(10 mmol), ethyl acetoacetate (10 mmol), ammonium acetate (10 mmol) and ammonium chloride (20 mol %) in water was refluxed for the appropriate time as summarized in Table 1. After completion of the reaction as monitored by TLC, the reaction mixture was cooled and poured in ice cold water. The solid product obtained was filtered, washed with water and dried. Further purification was accomplished by recrystallization from ethanol to obtain pure polyhydroquinoline derivatives.

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(phenyl)-5-(*6H*)-oxoquinolin-3-carboxylate (5a)

M.P.: 200-202 ^{0}C. IR (KBr): 3290, 3076, 2969, 1698, 1608, 1060, 690 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ 0.96 (s, 3H), 1.05 (s, 3H), 1.21 (t, J=7.3Hz, 3H), 2.12-2.30 (m, 4H), 2.30 (s, 3H), 4.08 (q, J=7.1Hz, 2H), 5.09 (s, 1H), 6.62 (s, 1H), 7.06-7.212 (m, 1H), 7.20-7.24 (m, 2H), 7.28-7.33 (m, 2H).

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(4-chlorophenyl)-5-(*6H*)-oxoquinolin-3-carboxylate (5b)

M.P.: 247-248^{0}C. IR (KBr): 3274, 3190, 3076, 1706, 2961, 1603, 1492, 1214, 849 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ0.95 (s, 3H), 1.06 (s, 3H), 1.16 (t, J=7.1Hz, 3H), 2.11-2.33 (m, 4H), 2.35(s, 3H), 4.02 (q, J=7.1Hz, 2H), 5.02 (s, 1H), 6.48 (s, 1H), 7.12-7.20 (m, 2H), 7.25-7.28 (m, 2H).

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(4-methoxyphenyl)-5-(*6H*)-oxoquinolin-3-carboxylate (5c)

M.P.: 258-260^{0}C. IR (KBr): 3276, 3201, 3076, 2951, 1701, 1605, 1492, 1215, 847 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ0.92 (s, 3H), 1.02 (s, 3H), 1.22 (t, J=6.9Hz, 3H), 2.10-2.30 (m, 4H), 2.35 (s, 3H), 3.75 (s, .3H), 4.02 (q,

J=7.1Hz, 2H), 4.98 (s, 1H), 6.39 (s, 1H), 6.69 (d, J=8.5, 2H),7.20 (d J=8.5, 2H).

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(3-nitrophenyl)-5-(*6H*)-oxoquinolin-3-carboxylate (5d)

M.P.: 180-182 ^{0}C. IR (KBr): 3290, 2969, 1607, 1532, 1160, 752 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ0.91 (s, 3H), 1.04 (s, 3H), 1.22 (t, J=7.1Hz, 3H), 2.09-2.30 (m, 4H), 2.36 (s, 3H), 4.02 (q, J=7.1Hz, 2H), 4.90 (s, 1H), 6.32 (s, 1H), 6.72 (d, 1H), 7.22-7.15 (m, 2H),7.38(d, 1H).

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(4-hydroxyphenyl)-5-(*6H*)-oxoquinolin-3-carboxylate (5e)

M.P.: 226-228 ^{0}C. IR (KBr): 3365, 2968, 1710, 1640, 1590, 1480, 1385, 1220, 782 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ 0.93 (s, 3H), 1.04 (s, 3H), 1.26 (t, J=7.1Hz, 3H), 2.15-2.33 (m, 4H), 2.40 (s, 3H), 4.06 (q, J=7.1Hz, 2H), 4.95 (s, 1H), 5.36 (s, 1H), 6.45(s, 1H), 6.75-6.78 (m, 2H), 7.03-7.06 (m, 2H).

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(4-hydroxy-3-methoxyphenyl)-5-(*6H*)-oxoquinolin-3-carboxylate(5f)

M.P.: 214-216 ^{0}C. IR (KBr): 3392, 3291, 3098, 1690, 1612, 1020, 732 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ0.90 (s, 3H), 1.02 (s, 3H), 1.21 (t, J=7.1Hz, 3H), 2.11-2.30 (m, 4H), 2.35 (s,3H), 4.02 (q, J=7.1Hz, 2H), 4.92 (s, 1H), 5.36 (s, 1H), 6.45(s, 1H), 6.68-6.70 (d, 2H), 7.5 (m, 1H).

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(5-bromo-2-hydroxyphenyl)-5-(*6H*)-oxoquinolin-3-carboxylate (5g)

M.P.: 210-212 ^{0}C. IR (KBr): 3316, 3107, 2962, 1736, 1616, 1475, 1230, 777 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ 0.92 (s, 3H), 1.02 (s, 3H), 1.22 (t, J=7.1Hz, 3H), 2.13-2.32 (m, 4H), 2.42 (s, 3H), 4.05 (q, J=7.1Hz, 2H), 4.96 (s, 1H), 5.38 (s, 1H), 6.55(s, 1H), 7.7(m, 1H), 6.72 (m, 1H), 7.8 (d, 1H)

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(4-methylphenyl)-5-(*6H*)-oxoquinolin-3-carboxylate (5h)

M.P.: 264-266 ^{0}C. IR (KBr): 3280, 3099, 2962, 1698, 1610 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ0.91 (s, 3H), 1.06 (s, 3H), 1.21 (t, J=7.1Hz, 3H), 2.21-2.39 (m, 4H), 2.12 (s, 3H), 4.025(q, J=7.1Hz, 2H), 5.00 (s, 1H), 6.41 (s, 1H), 6.96 (d, 2H), 7.02 (d, 2H).

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(2,4-dimethoxyphenyl)-5-(*6H*)-oxoquinolin-3-carboxylate (5i)

M.P.: 198-200 ^{0}C. IR (KBr): 3280, 3200, 3098, 1698, 1610, 1020 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ0.92 (s, 3H), 1.05 (s, 3H), 1.21 (t, J=7.1Hz, 3H), 2.08-2.30 (m, 4H), 2.34 (s, 3H), 4.02 (q, J=7.1Hz, 2H), 3.72 (s, 3H), 3.65 (s, 3H), 4.98 (s, 1H), 6.40 (s, 1H), 6.69 (m, 1H), 6.01 (d, 1H), 7.02 (m, 1H).

Ethyl 1,4,7,8-tetrahydro-2,7,7-4-(2-thienyl)-5-(*6H*)-oxoquinolin-3-carboxylate (5j)

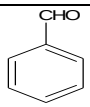
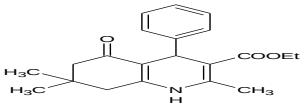
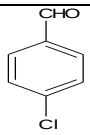
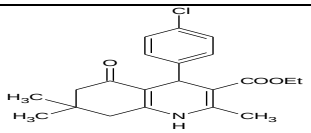
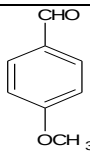
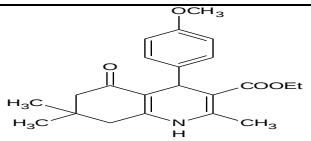
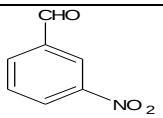
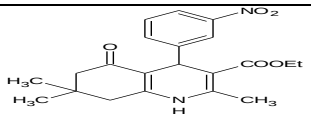
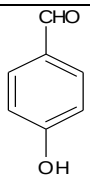
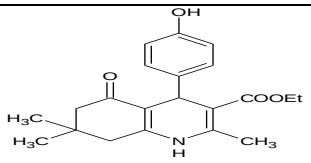
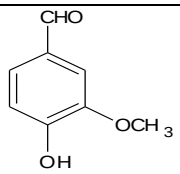
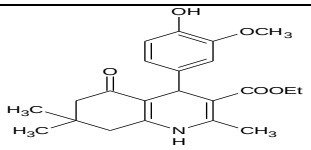
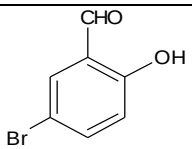
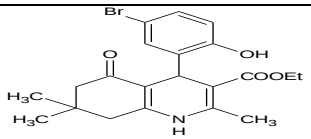
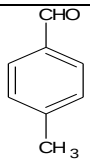
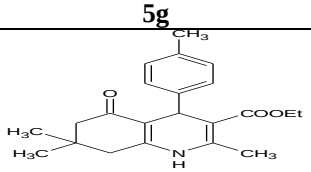
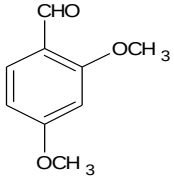
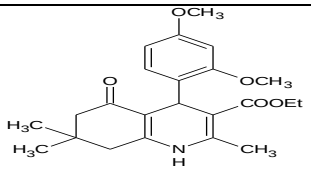
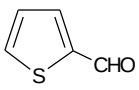
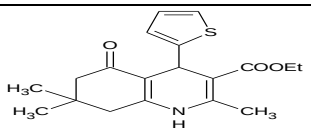
M.P.: 280-282 ^{0}C. IR (KBr): 3292, 3211, 3065, 1689, 1602, 1067, 685 cm^{-1}; ^{1}HNMR ($CDCl_3$, 300 MHz): δ 0.95 (s, 3H), 1.07 (s, 3H), 1.25 (t, J=7.1Hz, 3H), 2.10-2.30 (m, 4H), 2.36 (s,3H), 4.03 (q, J=7.1Hz, 2H), 4.95 (s, 1H), 6.439 (s, 1H), 7.12(m, 1H), 7.2 (m, 1H), 7.8 (m, 1H).

Results and Discussion

Synthesis of polyhydroquinoline derivatives **(5a-5j)** was studied via one-pot four component reaction of dimedone**1**, an aldehyde **2**, ethyl acetoacetate **3** and ammonium acetate **4** in presence ammonium chloride as a catalyst in water (Table 1).In order to investigate the optimal loading of ammonium chloride catalyst, a catalytic performance was surveyed on the model reaction. For optimization, we have synthesized polyhydroquinoline derivative (5a) fromdimedone (10 mmol), benzaldehyde (10 mmol), ethyl acetoacetate (10 mmol) and ammonium acetate (10 mmol) under reflux inwater with different amount of catalyst as a model reaction.To generalize the scope of present method, reaction was studied by using different aldehydes bearing electron withdrawing to electron donating groups under the optimized conditions. The reaction under the influence of ammonium chloride in aqueous media proceeds smoothly in all cases to yield corresponding products with very good to excellent yields with reduced reaction time. As a result of this improved protocol, it was confirmed that the reaction time is significantly reduced from hours to minutes. The reproducibility of the result and purity of the compound was checked by TLC. The easy

workup of reaction in which pouring the reaction mixture in ice water to get the solid product in good yield and sufficiently pure. The present method is found better to the available methods in regards with environmentally benign, inexpensive and commercially available catalyst and simplicity of workup.

Table 1. Synthesis of polyhydroquinoline derivatives with various aldehydes using NH_4Cl catalyst

Entry	Ar-CHO	Product[a]	Time (min)	Yield[b] (%)	M.P. (^{0}C)
1		 **5a**	35	95	200-202
2		 **5b**	65	87	247-248
3		 **5c**	40	92	258-260
4		 **5d**	90	86	180-182
5		 **5e**	100	86	226-228
6		 **5f**	20	88	214-216
7		 **5g**	50	84	210-212
8		 **5h**	80	95	264-266
9		 **5i**	130	90	198-200
10		 **5j**	110	92	280-282

[a] Products were characterized by IR and ^{1}H NMR spectroscopy
[b] Isolated yield

Conclusion

In conclusion, we have developed a simple, rapid, efficient and green method for the preparation of polyhydroquinoline derivatives using ammonium chloride catalyst under aqueous medium. The notable features of this one-pot protocol are the short reaction time, high yield, green solvent and operational simplicity. This method does not involve the use of organic solvents and thus is an environmentally benign, useful and attractive process.

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PHYSICOCHEMICAL AND PHYTOCHEMICAL ANALYSIS OF DIFFERENT EXTRACTS OF WITHANIA SOMNIFERA RHIZOME

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ABSTRACT

The present article associated with study of Physicochemical Phytochemical and analysis of Withania somnifera rhizome. Withania somnifera also known as ashwagandha is a source of naturally active compounds used by people worldwide for many ailments. Withania somnifera is a well known Indian medicinal plant widely used in the treatment of many clinical conditions in India. Root of Withania somnifera which has various therapeutic actions such as a sedative, diuretic, anti- inflammatory, and an anti-stress agent. The current investigation deals with extraction and detection or screening of active phytochemical compounds from different extracts of Withania somnifera root. Physicochemical screening of rhizome powder showed 5.5% total ash, 3.0 % water soluble ash, 16 % water soluble extractives, and P^H 5.3.Phytochemical screening of different extractions revealed the presence of phenols,flavonoids, tannins, saponins, alkaloids, steroids, terpenoids, glycosides.

Keywords: *Withania somnifera, therapeutic, Phytochemical Physicochemical*

Introduction

Plant have been playing important role in curing the diseases of human being since time immemorial. The medicinal value of plants is due to some chemically active substances that produce a definite physiological action on the human body. Some important bioactive constituents of plants are alkaloids, tannins and flavonoid and phenolic compounds [1]. These compounds are synthesized by primary or rather secondary metabolism of living organisms. Secondary metabolites are chemically and taxonomically extremely diverse compounds with obscure function. They are widely used in the human therapy, agriculture, scientific research, veterinary and many other areas [2].Plants are used medicinally in different countries and are the source of potential and powerful drugs [3].Plant synthesizes different types of chemical compounds, which can be differentiated on the basis of their chemical class, functional groups and bio synthetic origin into primary and secondary metabolites [4]

Withania somnifera is popularly known as Ashwagandha or Winter Cherry and Indian ginseng is considered one of the most important herbs in Ayurvedic indigenous medical systems for over 3000 years and is commonly used in Indian traditional health care systems[5].It is a perennial plant belonging to the order Solanaceae [6]. It is mostly cultivated in many regions of India like Madhya Pradesh, Punjab, Gujarat and Rajasthan.

Materials and Methods

Plant Material Collection: The Plant Withania somnifera were collected from forest area of Akola district as per the standard method [7]. The plant was identified and authenticated From Dr.A.V.oke, Department of Botany, Shri Shivaji College of Arts Commerce and Science, Akola. Fresh rhizomes were collected then bring to the laboratory and thoroughly washed with distilled water and shade dried at 28 ± 2 ºC. The dried roots were ground well into a fine powder in a mixer grinder. The powder was stored in a polythene bags at room temperatures.

Preparation of the extract

The powder plant material was subjected to hot continuous extraction in a soxhlet apparatus. The powder plant drug was successively extracted with methanol, Acetone, chloroform, Ethyl acetate and hot water. The liquid extracts were collected in tarred conical flask. The solvent was removed by distillation. These extracts were used to study to various qualitative chemical tests and determine the presence of different phytoconstituents.

Preliminary Phytochemical Screening Phytochemical screening of the Withania somnifera was done by the standard procedures prescribed by Kokate and Harborne [8, 9].

Preliminary Physicochemical screening such ash values, extractive values, moisture content etc. were determined as per procedure mentioned in accordance with WHO guideline 5, 6.

Result and Discussion

Phytochemical analysis was performed on the hot water, methanol acetone chloroform and ethyl acetate extract of Withania somnifera. Hot water extract was found to contain proteins, amino acids, alkaloids, phenolic compounds, glycoside, and carbohydrate. Methanolic extract contains carbohydrates, glycosides, alkaloids, flavonoids, saponins Acetone extract conain steroid carbohydrate, protein, glucoside. chloroform extract contain carbohydrate glucoside and ethyl acetate extract contain alkaloids, phenolic, compounds carbohydrate, protein. (Table1.) This work is beneficial for analyzing the quality and purity of the crude drug.

Phytochemical analysis of Withania somnifera root

Table no.1 Phytochemical analysis of Withaniasomnifera root

Sr.No.	Test	Hot water	Methanol	Acetone	Chloroform	Ethyl Acetate
I	**Alkaloids**					
	Mayer's Te	+	+	+	-	+
II	**Flavonoids**					
	Lead acetate test	-	+	-	-	+
III	**Phenolic compound andTannins**					
	FeCl3 test	+	+	-	+	+
IV	**Terpenoids**					
	Liebermann Burchards Test	-	-	-	-	-
V	**Steroids**					
	salkowski test	+	+	+	-	-
VI	**Carbohydrates**					
	Fehling's Test	+	+	+	+	+
VII	**Protein**					
	Millon's Test	+	+	+	-	+
VIII	**Saponins**					
	Foam Test	+	+	-	-	-
IX	**Glucosides**					
1	Keller-Killiantest	+	+	+	+	-
2	Legal's test	+	+	+	+	-

Where, += present and - = absent

Physicochemical Parameter

Table No.2 Physicochemical analysis of Withania somnifera root

Sr.No.	Physicochemical Parameter	Results
1.	**Ash Values**	
	Total Ash	**5.5 %**
	Water soluble ash	**3.0 %**
	Acid insoluble ash	**1.2 %**
2	**Extractive values**	
	Chloroform extractives	**0.28 %**
	Water soluble extractives	**16 %**
3	Moisture content	**5 %**
4	PH	**5.3**

Physicochemical evaluation of *Withania somnifera root* was shown that the result of physicochemical constant found within limit (table no.2).This indicates that quality and purity of raw material was good enough. Rhizome of plant was having 5.5% of total ash, 3.0% water soluble ash and acid soluble ash is about 1.2%.The water soluble extractive values was 16%.So the plant shows high water soluble ash and water soluble extractive values. The result of moisture content 5 % implies that extract is properly dried and stored. The PH value of crude drug was found to be near about 5.3 indicates acidic nature of rhizome. These data will be helpful for identifying and ascertaining the quality of the collected crude drug Table no.2

Conclusion

The phytochemical investigation revealed the presence of various phytochemical constituents such as alkaloids, flavonoids, amino acids, carbohydrate, proteins, saponin and tannins. Phytochemical constituents confirmed utilization of root for therapeutic medical treatment. The people of India are turning to usage of medicinal plants and phyto-chemicals in health care. Ayurveda, Unani, Siddha and other traditional systems of medicine are the ancient systems of medicine and utilize numerous numbers of medicinal plants. All studied standardization parameters like phytochemical screening provide the knowledge in the identification authentication of Withania somnifera.The physicochemical like PH, total ash, acid insoluble ash, water soluble extractive were observed.These values can be utilized to detect adulteration. All studied standardization of physicochemical parameters provide the knowledge in identification and authentication of Withania somnifera *root.*

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CANCER & ANTICANCER DRUGS: A REVIEW

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ABSTRACT

The development of chemotherapy using conventional anticancer drugs has been hindered due to some drawbacks associated with their poor water solubility and poor pharmacokinetics, resulting in severe adverse side effects and multidrug resistance in patients. Nano carriers were developed to palliate these problems by improving drug delivery, opening the age of nano medicine in oncology. However, despite attractive results being obtained in preclinical studies, many well-designed nano drugs fell short of expectations when tested in patients, evidencing the gap between nano particle design and their clinical translation. The aim of this review is to evaluate the extent of nano therapeutics used in oncology. The reasons that prevent nano drugs from expanding to clinic are discussed, and therefore the effort that has got to be taken to require full advantage of the good potential of nano medicine is highlighted

Introduction

Cancer may be a disease characterized by uncontrolled multiplication and spread of abnormal sorts of the body's own cells. The branch of drugs concerned with the study, diagnosis, treatment and prevention of cancer is Oncology. Cancer may affect people in the least ages, even fetuses, but the danger of most varieties increase with age.[1] All cancers begin in cells, the body's basic unit of life. The body is formed from many sorts of cells. These cells grow and divide in a controlled way to produce more cells as they are required to keep the body healthy. When cell get older or damaged, they die and are replaced with new cells. However, sometimes this orderly process goes wrong. The genetic material [DNA] of a cell can become damaged, producing mutations that affect normal cell growth and division. When this happens, cells don't die once they should and new cells form when the body doesn't need them. The extra cells may form a mass of tissue called a tumor. Targeted drug delivery is considered as a method in which drug-carrier complex, delivers drug to the pre-selected cell in a specific manner. The drug should reach the target cell[s] with the maximum concentration or with maximum effect. [2], [3]. Chemotherapy and radiation therapy are major clinical treatment used for the control of early stages of tumor but these methods has severe side effects. Nature has provides human a spread of useful sources mainly plants for discovery and development of medicine against dreadful diseases. Traditional herbs are an efficient system for the treatment of cancer. Drugs from medicinal plants are found to be comparatively less toxic and side effects [4]. This study is carried to perform brief description about cancer, medicinal plants and cancer drugs that have anticancer activity. Study reviewed of cancer, anticancer drugs and anticancer medicinal plants like Turmeric, Vinca, Wheat grass, Neem, Taxus and Aloe vera in treatment or/and chemoprevention of cancer.

Nanoparticles

Nanoparticles are solid colloidal particles ranging from 10 to 1000 nm in size, they consist of micromolecular materials in which the active ingredients [drug or biologically active material] is dissolved, entrapped, encapsulated, adsorbed, or attached[5]. Nanospheres have a monolithic-type structure [matrix] during which drugs are dispersed or adsorbed onto their surfaces or encapsulated within the particles. Nanocapsules are the vesicular system during which the drug is confined to a cavity consisting of an inner liquid core surrounded by a polymeric membrane. In this case the active substance is usually dissolved in the inner core, but may also be adsorbed to the capsule surface. [6,7]. Apart from this, nano particles have some following advantages: Provide a targeted delivery of the drug, Protect drug from degradation, Decrease of toxic side effects, Improve the bioavailability

of the drug, Cheaper and stable, Provide patient compliance[8, 9].

Nanotechnology

Nanotechnology is the preparation of Nanosized structures containing the API [10]. Nanotechnology is defined because the study and use of structures within the size range of 1 to 100 nm. The goal of nanotechnology is to diagnose as accurately and early as possible and to treat as effectively as possible with none adverse effects using controlled and targeted drug delivery approach [11].
Important Drug Delivery System developed using Nanotechnology principles are Nano particles, Solid Lipid Nano particles, Nano suspension, Nano emulsion, Nano crystals [12].

Types of Cancers

*Carcinomas
*Sarcoma
*Lymphomas
* Leukemias
*Adenomas

Factors Influencing Cancer

***Age:**
Cancer most commonly develops in older people; 78% of all cancer diagnoses are in people 55 years of
age or older. Anyone can develop cancer. However, the risk of being diagnosed with cancer increases significantly with age.

*Obesity and Physical activity

Obesity and lack of physical activity are associated with increased risk at various cancer sites, including breast and endometrial cancer. [14]

Tobacco and Smoking

The consumption of tobacco is the leading cause of cancers. The regular use of tobacco via smoking, chewing, snuffing, which is responsible for 65% to 85% cancer incidences in men and women, respectively. [15]

Alcohol consumption

Alcohol consumption also considered as one of the major cause of colorectal cancer as per a recent monograph of WHO. Annually, about 9.4% new colorectal cancer cases are attributed to the consumption of alcohol, globally [15].

Radiation

In the developed and developing countries, the radiations are also notorious carcinogens. About 10% cancer occurrence is due to radiation effect, both ionizing and non-ionizing. The major sources of radiations are radioactive compounds, ultraviolet [UV] and pulsed electromagnetic fields. [13]

Plant as a Source of Anti-cancer Compounds

Plant derived compounds, which are the important source of clinically useful anti-cancer drug, has shown to have probable for treatment or prevention of cancer in humans. In the treatment of cancer, plant features a long history; quite 3000 plant species are reported by Hartwell which are utilized in treatment of cancer. [17]
Plants also as plant derived compounds have played significant role within the development of variety of clinically used anti-cancer agents. Chemotherapy, being a serious treatment used for the control of advanced stages of malignancies and as a prophylactic against possible metastasis, exhibits severe toxicity on normal tissues. Plants are used for treating various diseases of citizenry and animals. They maintain the health and vitality of people and also cure diseases, including cancer without causing toxicity. More than 50% of all modern drugs in clinical use are of natural products, many of which have the ability to control cancer cells. [18].

Influence of Aging on Drug Pharmacokinetics

With increasing age, multiple physiological parameters alter, which can substantially influence the PK of anticancer drugs. In elderly patients, the PK profile can be influenced by changed distribution, metabolism and elimination parameters, while changes in absorption rarely led to clinically-relevant differences. Changes in gastric pH may have variable impacts on anticancer drug absorption, while absorption of sophistication II oral therapeutic drugs, including tyrosine kinase

inhibitors and endocrine agents, increases with increasing gastric pH. Another example includes capecitabine, with a higher absorption in elderly patients with a higher gastric pH, similar to increased absorption in the fed compared to the fasted state. These multifactorial and sophisticated changes make it difficult to predict internet effect of aging on the PK profile of a selected drug administered to elderly carcinoma patients. Besides these physiological changes, multiple other factors contribute to the complexity of anticancer drug treatment within the elderly patient. Firstly, elderly patients often have several comorbidities and receive comedication which will negatively affect anticancer treatment. For instance, patients with diabetes mellitus encountered more chemotherapy-related toxicities when receiving adjuvant chemotherapy for breast cancer compared to the non-diabetic control group. [19]

A higher fat proportion within the elderly patient may end in impaired anticancer drug disposition and increased toxicity from various chemotherapy regimens. Furthermore, comorbidities were determined to significantly influence mortality rates in elderly patients diagnosed with cancer. [20]

List of Anticancer Plant

Sr.no	Plant Name	Family	Chemical responsible for anticancer Activity
01	Turmaric	Zingiberacea	Curcumin
02	Vinca	Apocynacea	Vinblastine, vincristine, vinorelbine and vindesine
03	Wheat grass	Grasses	Chlorophyll, selenium and lactrile
04	Neem	Meliacacea	Flavonoids [rutin and Quercetin]
05	Taxus	Texaceae	Pactitaxel, taxol
06	Aleo vera	Xantharrhoeaceae	Aloeenodin, emodin

List of Some Anticancer Drugs

These are Docetaxel, Paclitaxel, Anthracyclines, Doxorubicin, Epirubicin, Alkylating Agents, Cyclophosphamide, Vinca-Alkaloids, Vinorelbine [Intravenous], Vinorelbine [Oral], Anti-Metabolites, Fluorouracil, Capecitabine.

Conclusion

Cancer after disorder is that the second leading explanation for death. Cancer is that the abnormal growth of cells in our bodies which will cause death. For treatment of cancer there are very synthetic compounds are present but they need many adverse effect as compared to medicinal plants that have anticancer activity. Medicinal plants that have anticancer activity has role in treatment also as chemo preventive purpose for cancer. Some medicinal plant like turmeric, vinca, taxus, neem, aloe vera, broccoli, etc that have chemical constituents as curcumin, vincristine, vinblastine, taxol and various anticancer classes of constituents like vitamins, flavonoids, phenolics compounds, anthraquinones, carotenoids, diterpenoids, coumarins, tannins, saponins and other miscellaneous compounds have their important role in treatment and in prevention of cancer.

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APPLICATION OF NEMEROW'S POLLUTION INDEX (NPI) FOR WATER QUALITY ASSESSMENT OF DHARMABAD TEHSIL DIST. NANDED

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ABSTRACT

The pollution index is a powerful tool for assessing water quality. To remit the problem of lacking good quality of water in some sites of Dharmabad Tehsil, it is the comprehensive pollution index, one of the earliest methods for water should be assessed objectively and reasonably. The water samples from various locations of Dharmabad Tehsil were collected in 2020. The NPI was calculated for the water samples. The samples were analysed for various physiochemical parameters viz. pH, Electrical Conductivity, Turbidity, Fe, TH, Mg, F, Ca, TDS, NO3, and SO4. The results were compared with standards (BIS: 10500:2012). It was revealed from the results that the improved Nemerow's index method can be more comprehensive and more objective to reflect the status of water. The present study shows that the NPI values of some sampling stations showed high NPI values and water samples to bring an acute awareness among the people about the quality of groundwater by taking specific locations for analysis.

Keyword: *Ground Water, Surface Water, Water Quality, Nemerow's Pollution Index, Physiochemical Parameters.*

1. Introduction

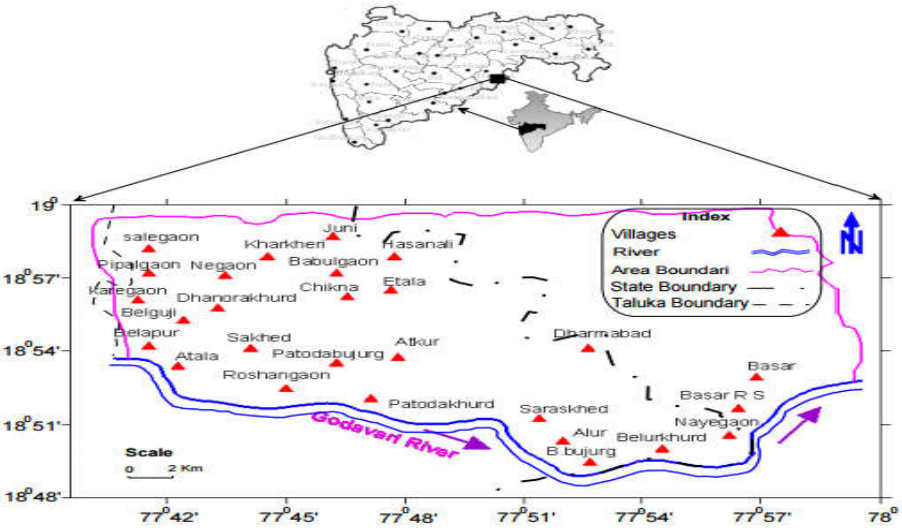
Water is formed by combination of two Hydrogen ions and one oxygen ion from atmosphere and it is mainly gathered and stored in seas, oceans and lakes. 97.41% water on the earth is concentrated in seas and oceans is saline and it cannot be used for consumption, as it is 0.99% of water is in the form of ice which is found near the poles. It is also not useful. 1.40% of rainwater percolates in the ground and becomes a ground water. and only 0.20% of water which is very less on the surface of the earth is available in the form of rivers, lakes, streams, and wetland is known as surface water(Gurjarand *et al.,* 2008). Water found in rivers, lakes, streams, and wetland is known as surface water. Water that percolates into the ground is called ground water, which contain about 0.31% of the total water on earth. (Ahluwalia)Groundwater is one of earth's most vital renewable and widely distributed resources as well as an important source of water supply throughout the world. The quality of water is a vital concern for mankind since it is directly linked with human welfare. In India, most of the population is dependent on groundwater as the only source of drinking water supply(Balakrishnan,2011).But the present scenario on ground water contamination worldwide is increasingly affected by pollution that comes from industrial and agricultural activities either due to unawareness, lack of vision, negligence, or high cost of waste discarding and treatment, which results in pollution. The great movement of urban poor and extension of cities and sudden development of industries and factories cuts of the bordering productive agriculture land, encroachment on water bodies, groundwater quality changes and wetland pollutions (Nazari *et al*. ,1993).

In view of the ground contamination, increasing population and industrial as well as urban expansion, the production of wastewater and its disposal on land and water bodies has grown rapidly. Hence, regular monitoring is required to develop a strategy to manage the environmental hazards due to wastewater pollution and to improve water quality of ground and surface water for aquatic ecosystem and disease-free human population, respectively.Usually, the quality of water is analysed by its physical, chemical, and biological parameters. If the study contains a large number of samples and each sample is analysed on the basis of the concentrations of many parameters; than the evaluation of water quality becomes very complicated task. To overcome this task Horton (1965) proposed the first Water quality Index Method WQI. A water quality index converts a large water quality data set into the form which is understandable and useable for the general people. It expresses the overall water quality of a certain location based on several water quality parameters with a single number. It is a

valuable mathematical instrument which transforms large water quality data into a single number and can represent the water quality level of the area with single word Water quality indices transform a large data set into a much condensed and informative form and help to extract the fundamental facts about the characteristics of the samples. There are two main methods to calculate water quality index i.e., Weighted Arithmetic Index and Nemerow's Pollution Index. In the present study Nemerow's Pollution Index have been adopted to assess the status of existing water quality and to identify the physiochemical parameters causing pollution respectively. Researcher collect the water samples from various locations of Dharmabad Tehsil in 2020, NPI was calculated for the water samples. The experimental analysis was done for various Physiochemical parameters such as pH, Electrical Conductivity, Turbidity, Fe, TH, Mg, F, Ca, TDS, NO3 and SO4.The results are compared with standards of BIS: 10500:2012. The results show that the improved Nemerov's index method can be more comprehensive and more objective to reflect the status of water, the present study attempts to show the NPI values of some sampling stations showed high NPI value and water samples from to bring an acute awareness among the people about the quality of ground water by taking specific locations for analysis.

2. Study Area

Dharmabad is situated 80 km towards south east of Nanded district located at 18.9° North Latitude and 77.85° East Longitude and at 359 meters (1177feet) altitude above the mean sea level. Groundwater is the major source of water, used for domestic purposes. Pioneer Distilleries Limited, a subsidiary of United Spirit Limited is engaged in manufacturing of Alcohol. The factory is situated at Dharmabad of Nanded district of Maharashtra.



Figer 1: Location Map of the Study Area

3. Methodology

Nemerow's Pollution Index (NPI)

Nemerow's Pollution Index (NPI) is a simplified pollution index introduced by Neme (Rathod et al., 2011) which is also known as Raw's pollution index (RPI). It is given as

NPI = *Ci* / Li

Were,Ci----- Observed value of i^{th} parameter,

Li-----Permissible limit of i^{th} parameter

4. Result and Discussion

Ground water is one of the earth's widely distributed, renewable and most important resources. It is

generally considered least polluted compared to other inland water resources, but studies indicate that

ground water is not suitable for drinking purpose without proper treatment (Sudhakar *et al*., 2014 b) The pH NPI values varies from 0.81 to 0.92 in all sampling stations the NPI is in permissible range The EC NPI value varies from 0.72 to 1.06 in all sampling stations very high NPI value in sample number S5. The Fe NPI value varies from 0.03 to 1 in all sampling stations very high NPI value in sample number S8. Total Hardness NPI Value range from 0.6 to 1. Mg NPI range from 0.8 to 1.7 in sampling stations S2, S5 had recorded very high NPI Value indicated that unsuitable for drinking purpose. The Fluoride concentration in all sampling stations range from 0.7 to 1.2 of NPI level. The S5 and S6 sampling station indicated that high fluoride levels of NPI, remaining all sampling stations were within the limited range Ca NPI levels from 0.4 to 1.7 While the Total dissolved Solids NPI range from 0.8 to 1and NO3 NPI range from 0.4 to 1.01.The results show that the method is correct and reasonable as per Cheng,*et al*., (2007).

Table 1: NPI Value of parameters-2020

Parameter		S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	BIS Limit
PH	Analysi s value	7.8	7.7	7.5	7.8	7.7	6.9	7.8	7.7	7.5	7.5	8.5
	NPI value	**0.92**	**0.91**	**0.9**	**0.92**	**0.91**	**0.81**	**0.92**	**0.91**	**0.88**	**0.9**	
E.C	Analysi s value	1208	1310	1308	1200	1485	1312	1120	1011	1003	1012	1400
	NPI value	**0.86**	**0.94**	**0.9**	**0.86**	**1.06**	**0.94**	**0.8**	**0.72**	**0.72**	**0.7**	
Fe	Analysi s value	0.1	0.2	0.1	0.2	0.01	0.1	0.2	0.3	0.1	0.1	0.3
	NPI value	0.33	0.67	0.3	0.67	0.03	0.33	0.67	1	0.33	0.3	
TH	Analysi s value	208	190	250	280	301	209	290	180	250	270	300
	NPI value	**0.69**	**0.63**	**0.8**	**0.93**	**1**	**0.7**	**0.97**	**0.6**	**0.83**	**0.9**	
Mg	Analysi s value	24	32	27	26	51	38	29	24	25	27	30
	NPI value	0.8	1.07	0.9	0.87	1.7	1.27	0.97	0.8	0.83	0.9	
F	Analysi s value	0.8	0.7	0.6	0.8	1.2	1	0.9	0.8	0.7	0.5	1
	NPI value	**0.8**	**0.7**	**0.6**	**0.8**	**1.2**	**1**	**0.9**	**0.8**	**0.7**	**0.5**	
Ca	Analysi s value	30	40	60	80	30	45	32	30	30	30	75
	NPI value	0.4	0.53	0.8	1.07	0.4	0.6	0.43	0.4	0.4	0.4	
TDS	Analysi s value	490	400	470	480	502	485	478	460	450	500	500
	NPI value	0.98	0.8	0.9	0.96	1	0.97	0.96	0.92	0.9	1	
No3	Analysi s value	22	23.1	38	39	45.3	41	39.1	38.2	37.5	36	45
	NPI value	0.49	0.51	0.8	0.87	1.01	0.91	0.87	0.85	0.83	0.8	

5. Conclusion

The Nemerow index method is used to evaluate groundwater quality. Based on the data of the Dharmabad Tehsil, due to the importance of water quality issuesNPI values of some sampling stations showed high NPI values, Hence, better management of water systems is required for the regional supply of water for irrigation, industrial and domestic uses, and water samples to bring an acute awareness among the people about the quality of groundwater by taking specific locations for analysis.

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BIOLOGICAL STUDY OF NEWLY SYNTHESIZED PYRIMIDINE DERIVATIVES

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ABSTRACT

A series of novel 4-(2-amino-6-(substituted phenyl)pyrimidine-4-yl)-2,6-dibromobenzene-1,3-diol, were synthesized from different substituted 2,3-dibromo-1-(3,5-dibromo-2,4-dihydroxyphenyl)-3-(substitutedphenyl)propane-1-one and guanidine hydrochloride were dissolved in ethanol. Double the quantity of sodium hydroxide was dissolved in minimum amount of water and added to reaction mixture. After 6Hrs. reflux, it was poured into 250 ml of water and recrystalized the structures of the compounds were elucidated by elemental and spectral (IR, ^{1}H NMR,) analysis. The synthesized compounds were checked for biological evaluation i.e. antimicrobial, antifungal study.

Keywords: *Chalcone, Pyrimidine, biological evaluation, antimicrobial, antifungal study.*

Introduction

The chemistry of heterocyclic compounds is as logical as that of aliphatic or aromatic compounds. Their study is of great interest both from the theoretical as well as practical importance. Various compounds such as alkaloids, essential amino acids, vitamins, haemoglobin, hormones, large number of synthetic drugs and dyes contain heterocyclic ring systems. There are large number of synthetic heterocyclic compounds, like pyrrole, pyrrolidine, furan, thiophene, piperidine, pyridine and thiazole having important application and many are important intermediates in synthesis. Fused pyrimidines continue to attract considerable attention because of their great practical usefulness, primarily due to very wide spectrum of biological activities. This is evident in particular from publications of regular reviews on the chemistry of systems where the pyrimidine ring is fused to various heterocycles such as purines, pteridines, quinazolines, pyridopyrimidines, triazolopyrimidines, pyrazolopyrimidines, pyrimidoazepines, furopyrimidines and pyralopyrimidines.

Materials& Methods

Step I - Synthesis of 1-(3,5-dibromo-2,4-dihydroxyphenyl)ethanone

In hot glacial acetic acid, fused zinc chloride was added and refluxed till solid was dissolved. Then powdered 2,4-dibromobenzene-1,3-diol was added and refluxed for eight hours. The reaction mixture was cooled and then poured in acidulated water. The solid obtained was filtered, washed with water and recrystallized from rectified spirit to obtain titled compound. Thus following compounds were synthesized.

Step II - Synthesis of (E)-1-(3,5-dibromo-2,4-dihydroxyphenyl)-3-(subsitutedphenyl)prop-2-en-1-one (3a-d)

In ethanol solvent, 2,4-dibromobenzene-1,3-diol and Substituted aromatic aldehyde were added. To this mixture, drop wise added 10 % of KOH solution with constant stirring. The reaction mixture was kept overnight. Then this mixture was poured over HCl and crushed ice. The product (E)-1-(3,5-dibromo-2,4-dihydroxyphenyl)-3-(subsitutedphenyl)prop-2-en-1-one (3a-d) was filtered and recrystalized from ethanol.

Step III – Synthesis of 2,3-dibromo-1-(3,5-dibromo-2,4- dihydroxyphenyl)-3-(substituted phenyl)propane-1-one (4a-d)

An equimolar quantity of (E)-1-(3,5-dibromo-2,4-dihydroxyphenyl)-3- (substituted phenyl)prop-2-en-1-one (3a-d) were dissolved in glacial acetic acid by warming. The solution was cooled at room temperature and treated with the solution of bromine in glacial acetic acid till the yellow color of bromine of persisted. The solution was allow to stand overnight, when crystal of 2,3-dibromo-1-(3,5-dibromo-2,4- dihydroxyphenyl)-3-(substituted phenyl)propane-1-one (4a-d) separated out.

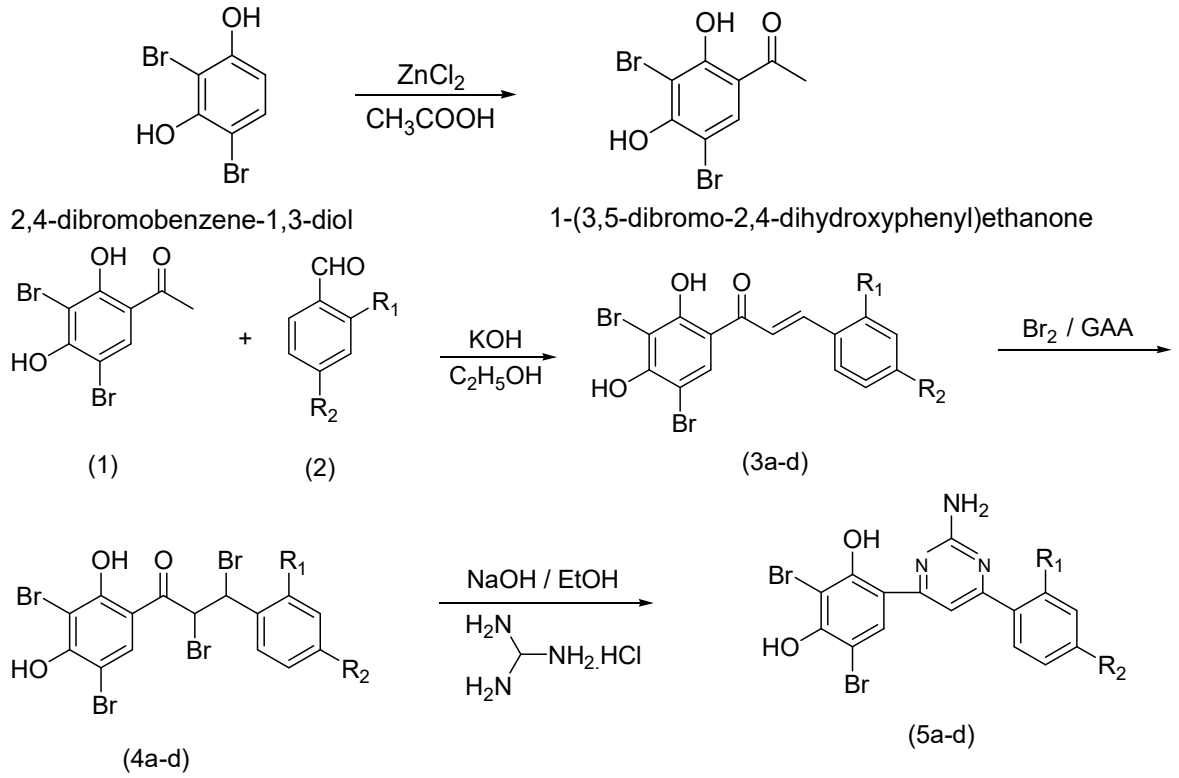
Step IV - Synthesis of Pyrimidine Derivatives (5a-d)

An equimolar quantity of 2,3-dibromo-1-(3,5-dibromo-2,4- dihydroxyphenyl)-3-(substituted phenyl)propane-1-one (4a-d) and guanidine

hydrochloride were dissolved in ehhanolic sodium hydroxide solution and stirred for about 5-6 hours. This was then poured into cold dilute hydrochloric acid with continuous stirring for an hour and kept in refrigerator overnight and participate obtained was filtered and dried. It was then recrystalized using petroleum ethanol.

Result & Discussion

Scheme



The structure of synthesized compound has been elucidated by IR and H^1 NMR analysis. IR spectra shows absorption band at expected values. H^1 NMR showed the proton of aromatic ring at excepted chemical shift and integral value. The probable mechanism has been suggested for the formation of Pyrimidine derivatives.

Table1: Physical property of compounds
Spectral Analysis (Compound No. 5d)

Comp ounds	R_1	R_2	Molecular Formula	MP◦C	%Yield	R.F. Value	% Nitrogen	
							Found	Calculated
5a	OMe	OMe	$C_{18}H_{15}O_4N_3Br_2$	170	42%	0.65	10.89	10.85
5b	NO_2	H	$C_{16}H_{10}O_4N_4Br_2$	187	36%	0.61	11.19	11.91
5c	OMe	H	$C_{17}H_{13}O_3N_3Br_2$	150	39%	0.68	10.32	11.40
5d	H	OMe	$C_{17}H_{13}O_3N_3Br_2$	151	52%	0.62	09.68	10.71

IR analysis (wave number in cm^{-1}) 3100-3000 (Ar-H stret.), 3200-3300(-OH stret), 3200-3250(-NH_2stret), 1675-1575(-NH stret), 1610-1620 (C=N stret), 1550-1475(N-O stret), 2815-2832(O-CH3 stret).

NMR analysis (δ ppm): 4.00 (-NH_2, 2H),5.35 (-OH,1H) ,6.8-8.0 (Ar-H , 7H), 3.73(-OCH3, 3H).

Biological evaluation

The antimicrobial and antifungal activity of all newly synthesized compounds was evaluated against gram-negative Escherichia coli, Pseudomonas aeruginosa, and gram-positive bacteria Staphylococcusaureus, Bacillus subtilis.The culture of each microbes species was incubated at 37 °c and the zone of inhibition on agar plates (diffusion method) was measured after 24 hrs. Most of these compounds were found active.

Antifungal Activity

Sr. No.	Compounds	Antifungal Activity	
		A. Niger	B. Albicans
1	5a	14	16
2	5b	16	19
3	5c	15	14
4	5d	16	12

Antioxidant Activity:

Total phenolic content

Total phenolic content was determined as described by Prior et al. [21]. Briefly, 500 µg of compound in 100 µL of methanol was mixed with 100 µL of 1 N Folin–Ciocalteu reagent. Following incubation for 5 min, 200 µL of 20% Na_2CO_3 was added. Absorbance at 730 nm was measured in plate reader after 10 min and the concentration of phenolic compounds was calculated using standard curve of gallic acid (500–5000 ng; R^2=0.967). The results were expressed as mg gallic acid equivalent (mg GAE) g^{-1} .

Pyrimidine derivatives

Sr.No	Sample	µgGAE/mg
1	4-(2-amino-6-(2,4-dimethoxyphenyl)pyrimidin-4-yl)-2,6-dibromobenzene-1,3-diol	20
2	4-(2-amino-6-(2-nitrophenyl)pyrimidin-4-yl)-2,6-dibromobenzene-1,3-diol	09
3	4-(2-amino-6-(4-methoxyphenyl)pyrimidin-4-yl)-2,6-dibromobenzene-1,3-diol	12
4	4-(2-amino-6-(2-methoxyphenyl)pyrimidin-4-yl)-2,6-dibromobenzene-1,3-diol	11

Compound Sr. no. 1 to 4 shows good antimicrobial and antifungal activity and antioxidant activity. On the basis of screening data it was observed that these heterocyclic compounds can be easily used against treatment of disease caused by test microbes.

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STUDIES OF SOME INNER TRANSITION METAL IONS COMPLEXES WITH HYDROXY SUBSTITUTED CHALCONE AT 0.1 M IONIC STRENGTH

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ABSTRACT

In this present investigation is attempt to make the explain Proton-ligand stability constants and metal-ligand stability constants of 1-(5-bromo-2-hydroxyphenyl)-3-(4-methoxyphenyl) prop-2- en-1- One (L_2) studied with inner transition metal ions like La(III), Pr(III) and Nd(III) were determine by pH-metric study at 0.1 M ionic strength. (30±1^{0}C) in 70% Dioxane- water mixture by Bjerrum method as adopted by Calvin Wilson. 1:1 and 1:2 complexes were formed in between 1-(5-bromo-2-hydroxyphenyl)-3-phenylprop-2-en-1-one (L_2) and La (III), Pr (III) and Nd(III). Valuesof Pk and log k were evaluated and compared from resultant data.

Keywords: *Substituted chalcone, Dioxane – water mixture, stability constant.*

1. Introduction

Stability constants forehead plays a critical role in the identification and increase in efficiancy of ligand design for selective complexation of metal ions in solution. Thus, it is important to assess the potential of metal-binding ligand organic in the complex formation process. During the complex formation in aqueous medium, two types of stabilities are considered, one is the thermodynamics stability, and the other is kinetic stability. This stability may be affected by various factors like nature of central metal ion and ligands, chelating effect, etc are useful for the determination of stability constants. Various modern techniques are used to determine the stability constant of simple as well as mixed ligand compound.

Bjerrum[1] and Calvin[2] were given the good contribution in the field of stability constants of organic ligands and their metal complexes. S.G. Sonkamble.[3] have done Lots of work on metal complexes with organic ligands in aqueous or mixed solvents (ethanol-water, methanol-water and dioxane-water) and various methods are also available in the literature for calculation of stability constants. The binary complex of 1-(2'-hydroxy Phenyl)-3-Phenyl Propane-1, 3-dione (β-diketone) Prepared from 2'-hydroxy acetophenone ware studied in presence of iron (III), Cadmium (II), Cobalt (II), Nickel (II), Zinc (II) cations in various aquo-organic media using pH metric measurements at 298K and 0.1M ionic strength.

M.W.Shaikh et al.[4] studied Proton-ligand stability constants and metal-ligand stability constants of 1-(5-bromo-2-hydroxyphenyl)-3-phenylprop-2-en-1-one studied with inner transition metal ions like La(III), Sm(III) and Nd(III) were determine by pH-metric study at 0.1 M ionic strength.

Noor Mohammad et al.[5] were investigated pH metric studies of Cu (II)ions with the pyrazole derived from 3(4-nitrophenyl)-4-benzoyl 5(2-hydroxy-4-bromo-phenyl) pyrazole and 3(4-chlorophenyl)-4- benzoyl 5(2-hydroxy-4-nitro-phenyl) pyrazole . R.B. Dhake[6] investigated the metal-ligand and proton–ligand stability constant of Ce(III) with Clobetasol propionate was determined at various ionic strength by pH metric titration .

R.P Giram et al.[7] have studied the stability constants and thermodynamic parameters of transition metal complexes of substituted aminothiazole Schiff bases. Thorat et al.[8] have been studied The complex formation between Pr(III) & Sm(III) metal ions and 3-(2-hydroxy-3-nitro-5-methylphenyl)-5-(3-nitrophenyl)isoxazoline , 3-(2-hydroxy-3-nitro-5-methylphenyl)-5-(4-chlorophenyl)isoxazoline, 3-(2-hydroxy-3-nitro- 5-methylphenyl)-5-(2-furyl)isoxazoline. Thakur et al.[9] studied the complex formation between Cu(II), Ni(II) & Co(II) metal ions with 1-(5-bromo-2-hydroxyphenyl)-3-phenylprop-2-en-1-one and 1-(5-bromo-2-hydroxyphenyl)-3-(4-methoxyphenyl)prop-2-en-1-one chalcones at 0.1M ionic strength (26±1^{0}C) in 70% Dioxane- water mixture by Bjerrum method as adopted by Calvin Wilson.

2. Experimental methodology

2.1 Material and Methods

All chemicals used are of AR grade. The ligand (L_2) was synthesized in the laboratory by reported protocol. The stock solution of the ligand was prepared by dissolving required amount of ligand in a70% (Dioxane + water) mixture.

2.2 General procedure

Types of Titrations
i) Free acid HNO_3 (0.01 M)
ii) Free acid HNO_3 (0.01 M) and ligand (20 x 10^{-4}M)
iii) Free acid HNO_3 (0.01 M) and ligand (20 x 10^{-4}) and metal ion (4 x 10^{-4}M) against standard 0.1N NaOH solution.The ionic strength of all the solutions was maintained constant 1M by adding appropriate amount of KNO_3 solution. All the titrations were carried out in 70% (Dioxane+water) mixture and the reading were recorded for each 0.1 ml addition. The graph of volume of alkali added (NaOH) against pH were plotted. The ligand involved in the present work may be considered as a monobasic acid having only one dissociable H+ ion from phenolic -OH group and it can therefore, be represented as HL. The dissociating equillibria can be shown as.

$HL \rightleftharpoons H^+ + L^-$

By the law of mass action, we have,

$K=[HL]/([H^+][L^-])$ (1)

Where, the quantities in bracket denote the activities of the Species at equilibrium.

3. Result and Discussion

3.1 Calculation of Proton-Ligand Stability Constant (n_A)

The plots between volume of NaOH and pH of the solution were used to determine the proton ligand stability constant (representing the replacement of H+ ions from functional group of ligand with respect to pH value). The horizontal difference (V_2-V_1) was measured accurately between the titration curves of free acid and acid + ligand. It was used to calculate the formation number n at various pH values and fixed ionic strength μ = 0.1 M using Irving and Rossotti's equation [1, 2].

$$\bar{n}_A = \gamma - \frac{(E_0+N)(V_2-V_1)}{(V_0+V_1)TL^0} \qquad \text{----------(2)}$$

Where, V^0 is the initial volume of the solution. E^0 and T_L^0 are initial concentrations of the mineral acid and ligand respectively. V_1 and V_2 are the volumes of alkali of normality N during the acid and ligand titration at given pH. γ is the replaceable proton from the ligand. The data of n_A obtained at various pH along with the horizontal difference for some representative systems are represented in Table 1. The metal ligand Ligand formation number (n) is estimated by Irving- Rossotti's equation.

$$\bar{n} = \frac{(E_0+N)(V_3-V_2)}{(V_0+V_2)Tm^0} \qquad \text{----------(3)}$$

Where, the notations have the same meaning as given in earlier equation. The horizontal difference (V_3-V_2) between the metal complex (A+M+L) and reagent (A+L) curve is used to evaluate the value of n using Irving Rossotti's equation.

Table 1 Proton ligand stability constant (pK)

Ligand	System	pK	
		Half integral method	Point wise method
L2	1-(5-bromo-2-hydroxyphenyl)-3-(4-methoxyphenyl) prop-2- en-1- One	8.5921	7.2422

Table 2: Metal-ligand stability constant (log K)

System	$LogK_1$	$LogK_2$	Δ LogK
La(III)+L_2	5.5723	2.4958	3.0765
Pr(III)+L_2	4.7653	2.6950	2.0703
Nd(III)+L_2	4.5755	2.6950	1.8805

Conclusion

From the titration curves, it is observed that the departure between acid + ligand (A+L) curve and acid + ligand + metal (A+L+M) curve for all systems started from pH 3.6 this indicated the commencement of complex formation. Also change in colour from yellow to orange in the pH range from 3.9 to 8.6 during titration showed the complex formation between metal and ligand.

The difference between $LogK_1$ and $LogK_2$ is less than 2.5, indicating the simultaneous formation of 1:1 and 1:2 complexes when the difference is more then 2.5, then in such a case a stepwise complex formation takes place. From the table 2, it is observed that the difference between log K_1 and log K_2 values are not sufficiently large that indicates the simultaneous formation of complex between metal ion and ligand. The values of log K_1 and log K_2 (table 2) for La (III)–L_2 is comparatively more than the Pr (III) +L_2 and Nd (III) +L_2 hence stepwise complex formation takes place. Pr (III)-L_2 Nd (III)–L_2 forms simultaneous formation of 1:1 and 1:2 complexes.

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BIODIVERSITY MAINTAINS THE ECOLOGICAL BALANCE NECESSARY FOR HUMAN SURVIVAL

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ABSTRACT

The Melghat Tiger Reserve is situated in the Satpura range of hills within the 'Central Highlands' province of the Deccan Biogeographic Zone of Peninsular India. MTR in the southern Satpuras is located in Dharni and Chikhalda Tahasils of Amravati District of Maharashtra (21^0 15' N to 21^0 45' N Latitude and 76^0 57' E to 77^0 30' E Longitude) about 50 km from Parathwada. The Tiger Reserve is bounded on three sides by the forests of the East, West and South Melghat Divisions and by the Tapti River to the North and Betual District of Madhya Pradesh in the north and northeast. The present research work was done due to its richness in species diversity, vegetation types, medicinally significant, and its topography, all have direct influenced on divergence of species.Even the vegetation cover was studied, plants counted, and species enlisted. Accurate data of tree size and number was prepared. In present study occurrence of tree vegetation, morphodiversity and Identification of species was done. It was observed that Biodiversity maintains the ecological balance necessary for human survival. So, there is a great need for the storage and managing of this data to be protected and secure.

Keywords: *Biodiversity,Vegetation, Ecology, Melghat*

Introduction

Central India represents the major forest cover of the country. Melghat Tiger Reserve is one of them, having tropical dry deciduous type of forests. The Melghat forest cover in this area is so large, complex and huge that it is very much difficult to understand it properly. The biodiversity is usually studied now by taxonomist who takes great pains in collecting, identifying, documenting and describing the elements of diversity. But the approach usually is very materialistic. The plant morphodiversity and its cultural associations were rarely studied, recorded or understood. Traditional knowledge and relationship with bioresources have been largely responsible for biodiversity in India. For better management of bioresources this needs appreciation and respect.

A species may be defined as a group of organisms which are able to interbreed freely under natural conditions to produce viable offsprings. Species diversity refers to variety of living species within a geographic area (Glowka, 1994). An area with a greater number of closely related species is not as diverse as the some area with the same number of species which are not closely related.Species are well known and are distinct units of diversity. Each species can be considered to have a particular "role" in ecosystem, so the addition or loss of single species may have consequences for the system as a whole. Conservation efforts often being with the recognition that a species is endangered some way; change in the number of species in an ecosystem is readily obtainable and easily understandable measure of how healthy the ecosystem is.Genetic diversity refers to the differences in genetic make-up between distinct species as well as the genetic variations within a single species. This is the least visible and, arguably, least studied level of biological diversity. More genetic diversity in a species or population means a greater ability for some of the individuals in it to adapt to change in the environment. Less diversity leads to uniformity, which is a problem in the long term, as it is unlikely that any individual in the population would be able to adapt to changing conditions.Since the genes are the fundamental unit of natural selection, and thus evolution, some scientists argue that the real unit of biodiversity is genetic diversity.

It encompasses the broad differences between ecosystem types, and the diversity of habitats and ecosystem processes within each ecosystem type.Ecosystem diversity deals with species distribution and community patterns, the role and function of key species, and combines species functions and interactions. The term "ecosystem" here represents all levels greater than species: associations, communities, ecosystems, and the like.

Review of Literature

Hedge et al., (1998) studied variation in bark thickness in a tropical forest community of Western Ghats in India. They examined the relation between bark thickness and girth in a large sample of trees from evergreen and semi-evergreen rain forest. There was a significant tendency for bark thickness to increase with tree girth. They concluded that bark thickness and occurrence of gums and resins were physiogenomic-structural attributes of value in characterizing tree communities created by different levels of disturbance.Seetharam et al., (2000) worked on structure, composition, regeneration, status and plant diversity of Bidar District of North-eastern Karnataka. On the basis of dominance of the series of plant communities occurring in the forest were a) Chloroxylon swietenia-Anogeissus latifolia-Acatia chundra. b) Albazia amara-Bauhinic racemosa-Lannea coromendelica, c) Dalbergia paniculata-Butea monosperma-Soymida febrifuca. Total of 243 species belonging to 197 genera and 54 families were recorded from 15 transects. The girth and height distribution of trees and shrubs of the different classes showed 'L' shaped curve.Hajra et al., (2002) studied population structure of corridor forest through density diameter relationship between Rajaji and Corbett National Park, Uttarnchal, India. The diameter distribution curves showed that in most of the cases there was an equal representation of individuals in the intermediate girth classes. In many cases the old trees with higher girth at breast height (gbh) values were seen to be exceptionally less thus leading to the preponderance of intermediate aged stands. Therefore the results obtained indicated that all communities show a more or less equal distribution of individuals in the intermediate gbh classes.

Pant (2003) worked on the structure, composition, regeneration status and plant and animal diversity of the North and South Betul forest divisions in Madhya Pradesh. Diversity of plant species tended to decrease in old growth stands, steep slopes, very disturbed area i. e. areas around villages or recently felled coups, very dry areas, areas that had experienced fires in the recent past etc. Areas in valley flats, riparian areas, remote and less disturbed areas etc. showed a high diversity.Udayan et al., (2003) surveyed medicinal plants conservation areas located in Karnataka for the study of plant diversity. Intensive field work undertaken during all seasons resulted in authentic collection of 933 medicinal plant species represented by 147 Families, including 556 genera. Of the 933 medicinal plants, 912 were native Angiosperms, 20 Pteridophytes and 1 Gymnosperm. Among the 147 Families, the families Rubiaceae, Euphorbiaceae, Asteraceae, Laminaceae, Fabaceae, Acanthaceae, and Apocynaceae shared a large proportion of medicinal plant species. Their study revealed that a high percentage of medicinal plants were recorded from dry deciduous scrub forest. Kumar et al., (2003) surveyed medicinal plant species of Indian Thar with respect to total number of species occurring in forest areas. The first 10 families having larger than expected number of the medicinal species included, in decreasing order, Fabaceae, Solanaceae, Lamiaceae, Euphorbiaceae, Tiliaceae, Malvaceae, Mimosaceae, Menispermaceae, Acanthaceae and Capparaceae. The high used families have 57 species out of a total of 65 (87.7%) as household remedies, 28 species out of a total of 34 species as traditional remedies and all the 17 as commercialized remedies. Chege and Byterbier (2005) studied structure of four small forest fragments, Kichuchenyi, Macha, Ndiwenyi and Yale. The forest was characterized by very large trees and no intermediates, which indicated poor or no regeneration. The basal area for Kchuchenyi was greatly influenced by a large Ficus thonningii Blume tree. Yale had the highest tree density. However, the bulk belonged to the small diameter size class (<10 cm diameter). The average height of trees was highest in Ndiwenyi (19 m) followed by Kichuchenyi whereas Macha and Yale had approximately the same average height of upper canopy trees.

Wattenberg and Breckle (1995) studied tree species diversity of a premontane rain forest in the Cordillera De Tilaran, Costa Rica. The study plot consisted of 25 squares of 20×20 m, located at an altitude of about 1000 m. Dominance and abundance of tree species was critically discussed. About 94 species of trees (DBH≥ 10 cm) from 40 families of

Angiosperms were recorded. The canopy of the study-plot reached a height of 40m. The mightiest canopy layer was formed at medium height between 10 to 20m by 55% of all trees. More than a third of all trees had height of between 5 and 10 m while 10% reached 5m. A more striking distribution had been found at the measured DBH's of all trees, which ranged between 10 and 210cm. 85% of all trees measured between 10 and 30 cm DBH. 8% of trees still remained between 30 and 50 cm DBH, and the upper range between 50 and 210 cm DBH was represented altogether by only 7%. Valencia et al., (2004) mapped and studied tree species distributions and local habitat variation in the Amazon. The largest number of species was mid –sized canopy trees with maximum height 10-20m and understrorey treelets with maximum height of 5-10m. There were no more than three distinct vegetation zones: valley, mid-slope, and upper ridge, and the latter two differed only slightly in species composition. Similarity species composition declined with distance even within a topographic habitat, to about the same degree as it defined between habitats. It suggested patchiness not related to topographic variations, and possibly due to dispersal limitation. They concluded that partioning of topographic niches did make a contribution to the alfa-diversity of Amazonian trees but only minor one. Total diversity was 1104 species, including 11 previously undescribed species, of which four were Lauraceae and two Burseraceae.

Materials and Methods

The study area was Melghat sanctuary, Melghat Tiger Reserve Maharashtra.The survey was carried out during study period to acquaint with the forest area, often visits were arranged of the place by taking help of forest guards, foresters, ranger, and collected first-hand information was collected. There are total 715 compartments or vegetation monitoring plots (VMP) in MTR. These plots have been monitored and observed, periodically. There is a presence of small water stream in the areas. Some part of the research area is having hilly, slopes and water stream at basal area.

In the present study especially the tree species were selected because the trees were economically and medicinally important and they show lot of diversity among them. The trees are perennial so the morphodiversity study can be carried out throughout the year. Moreover, flowering and fruiting period of the trees are different, and the morphological characters are visible with necked eyes. Study of diversity was done up to the family, genus and species level. The whole information was carried over further to computational study.The plant specimens such as flowering twig, bark samples, fruits etc. were collected; date and place of collection were noted. Plants were described according to Bentham and Hooker system of classification by considering parameters such as tree code, local name, family, genera, scientific name, habitat, habit, stem, leaf, flower, calyx, corolla, androecium, gynoecium, fruit, flowering and fruiting periods. Identification of the plants to the level of species, genus, and family was done with help of publish floras. Different sizes of the trees i.e. small, middle and large were also recorded. Photographs of complete tree, flowering twig, bark, fruit and herbarium sheets were taken and samples were preserved.

The biodiversity information was gathered and processed by applying bioinformatics tools. Trees were coded, tagged, and labeled with unique tree code. The height and girth data was important criteria for evaluation of research site in relation to number of tree species, genera, and families.The collected data was classified in different girth and height classintervals. The height and girthof distributedtrees was an important criteria for evaluating research area site quality, growth performance of the tree species and status of location.

Observations and Results

The current research study deals with the survey and distribution of trees species of Melghat Tiger Reserve. A field survey was carried out. During this survey, Melghat Sanctuary was found to be a suitable area for study. Research areawas showing maximum variability in vegetation type and topography.The distribution of the tree species in particular were studied. It was observed that, thisforest was of dry mixed deciduous type hence there was always fear of forest firing in summer. The number of trees showed leaf fall

during summer season and many of them had timber value. It was observed that the Teak (Tectona grandis Linn.)was the predominant species of the forest area. Present study was based on data recording, field survey and collection of specimens. Distribution of the trees species and their diversity appeared to be strongly related to environmental factors. Study trees species was completed by collecting all the required information available with respect to morphodiversity, e.g. specimen sample collection, photographs, description, illustrations, height and girth data and bark features.

The most common teak associatesin this forest area were Lagerstroemia parviflora, Lannea coromandelica, Phyllanthus emblica, Terminalia tomentosa, Anogeissus latifolia, Desmodium oojeinensis, Boswellia serrata, Wrightia tinctoria, Cassia fistula, Bauhinia racemosa, Butea monosperma and Mitragyna parviflora.Some trees were so notable that could catch the eye attention in hot dry deciduous summer by being lush green in otherwise dry deciduous leafless forest, the most prominent being Terminalia sp.,Madhuca sp.,Buchanania sp.,Diospyros sp., Lagerstroemia sp., Butea sp.and Ixora sp.The bark also showed variability from thin scaly, papery, smooth, greenish,to thick furrowed, and spiny; most of them showing vertical cracks, ridges and furrows and of various colours. Trees exhibiting different girths and heights; among the population of Tectona grandis L.f. Suppl., the oldest tree representedmaximum girth(170 cms) and youngest one representing minimum (19cms), likewise one individual measuring maximum height (58 feet)and another minimum (12 feet)were recorded in this research area.Occurrence of teak (Tectona grandis) in forest in huge number and a source of high quality timber, the teak was considered as a 'king' of Melghat. List of tree species was generated with its local and scientific names and their taxonomical identification to make data ready for computation study.

Ethnobotanical survey of the medicinal plants was conducted to collect the information regarding medicinally important plant species and its useon various human health problems such as bone fracture, acidity, injury,worm control, body power,blood impurity,antidote to snake poison,cough,dysentery, skin and fever**.**Information on medicinally important plant species and its traditional usage by the residents supported in understanding the value of forest species and its conservation.Bark samples were collected from the trees and morphological features were studied and recorded.Collected samples were carried to work place and properly identified, labeled and classified on the basis of external features. In present study the ethnobotanical information was gathered by communicating the local resident of MTR.It was observed that tree bark is protective and valuable even Tree bark was source of organic matter. In the present study it was noted that the tribal of Melghat villages often used the powder of the dried bark as the organic material by mixing it with the soil.The plants growing on such a soil showed improvement in the growth rate, flowering and fruiting. This indicated that bark powder was useful for nursery soils for rapid growth of plant species. It was because of bark having many more chemical features,resulting positively on the tree growth. So, this nutritive quality of the bark was the notable feature that could be properly utilized in the nursery practices. Biodiversity maintains the ecological balance necessary for human survival. Biodiversity maintains the ecological balance necessary for human survival. So, there is a great need for the storage and managing of this data to be protected and secure.

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SYNTHESIS OF 3-[(4-BROMO-6-METHOXY-1,3-BENZOTHIAZOL-2-YL)AMINO]-2-ARYL SUBSTITUTED-1,3-THIAZOLIDIN-4-ONE AND THEIR ANTIBACTERIAL ACTIVITY

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ABSTRACT

4-thiazolidinones are reported to possess significant antitubercular, antibacterial & antifungal activities. 4-bromo-6-methoxy aniline (1), which is aniline derivative have been found to be biologically interesting compound for many years. From this aniline derivative first we have synthesized 2-amino-4-bromo-6-methoxybenzothiazole (2) which is then treated with hydrazine hydrate to form 2-hydrazino-4-bromo-6-methoxybenzothiazole (3). Compound (3) condensed with o-vaniline,p-methoxybenzaldehyde, p-vaniline, o-hydroxybenzaldehyde, p-hydroxybenzaldehyde, p-dimethylaminobenzadehyde, (4a-4f). These hydrazone heated with mercapto acetic acid by using DMF as solvent and Pinch of anhydrous ZnCl2 for 5-6 hours,3-[(4-bromo-6-methoxy-1,3-benzothiazol-2-yl)-amino]-2-aryl-1,3-thiazolidin-4-one (5a-5h). These newly synthesized 4-thiazolidinone compoundsare screened for their antibacterical activity.

Keywords *:benzothiazole, hydrazone, thiazolidinone, antibacterial activity*

Introduction

A survey of literature reveals that large work has been carried out on the synthesis of 4-thiazolidinone and known to exhibits various biological activities as hypnotic[1], antitubercular[2], antiallergic[3]. and pharmacological application[4]. 4-thiazolidinone ring are reported to possess various biological activities, as antimicrobial, anti-nflammatory, antiviral, antiparasitic and antituberculosis[5-10]. These Schiff-bases can be prepared by the acid catalysedreaction of amine and aldehyde or ketone which shows good fungicidal acivity[11].
4-thiazolidinone give good pharmacological properties[12] are known to exhibits antitubercular[13], antibacterial[14], anticonvulsant[15], antifungal activity[16]. Large work has been carried out on 4-thiazolidinone but very less information is available about 4-thiazolidinone bearing substituted benzothiazolyl moiety.
The starting compound were prepared by the reaction of4-bromo-6-methoxy aniline and potassium thiocynate to obtained 2-amino-4-bromo-6-methoxy benzothiazole. 2-amino-4-bromo-6-methoxybenzothiazole treated with hydrazine hydrate which then condensed with aldehydes to obtain the hydrazones. These hydrazones then treated with thioglycolic acid to obtain the corresponding 4-thiazolidinone.

Experimental

All the melting points were determined in open capillary tube and may be uncorrected. The purity of compound was checked by TLC on silica gel coated glass plate. Infra-red spectra were monitored in KBr palates on Bomen 104 FT infra-red spectrophotometer. H1 NMR spectra were obtained on a Gemani 200 Mz spectrometer with tetra methyl silane as an internal standard.. Elemental analysis was performed on a Heraeus CHN-O rapid analyzer.

Synthesis of 2-amino-4-brmo-6-methoxybenzothiazole

2-bromo-4-methoxy aniline (10.2gm, 0.05M) and sodium thiocynate (4.8gm, 0.05 M) were dissolved in glacial acetic acid (150 ml). The solution was cooled in freezing mixture. Bromine (8gm, 5 ml, 0.05 M) in glacial acetic acid (25 ml) was added with stirring and maintaining temperature below 10°C. The mixture was allowed to stand for one hour at room temp. The resulting hydrobromide was dissolved in hot water and neutralized with 10 % NaOH to obtain base. The amine thus obtained was filtered, washed with water and recrystallized in aq. alcohol to get the product 2-amino-4-bromo-6-methoxybenzotiazole.
Yield:8.7gm,M.P: 160 °CI.R. (KBr) : 3440 cm^{-1}(Asymmetric stretching of -NH_2), 3340 cm^{-1}(N-H Symmetrical stretching of -NH_2), 3052 cm^{-1} (Ar-H stretching), 1630 cm^{-1} (-C=N stretching); PMR ($CDCl_3$)δ 6.0 (broad, 2H, NH_2), δ 7.0-7.5 (two singlet, 2H, Ar-H),

4-bromo-2-hydrazino-6-methoxybenzothiazole

Hydrazine hydrate (80%, 15 ml) was taken in a flask cooled to 5°C and concentrated HCl (11 ml) was added to it with stirring. The flask was kept at room temp. for few minutes and then 4-bromo-6-methoxy benzothiazole (8.6 gm) was added. Ethylene glycol (33 ml) was added into the flask. The contents of the flask were heated at 150°C on an oil bath for three hours. On cooling, the product 4-bromo 2-hydrazino-6-methoxyl benzothiazole crystallized out. It was filtered at pump, washed with cold water and recrystallized from ethyl alcohol,
Yield: 6.3gm, M.P: 80 °C I.R. (KBr) : 3452 cm^{-1} (asymmetric N-H stretching in $–NH_2$),3353 cm^{-1} (symmetric N-H stretching in $–NH_2$), 3052 cm^{-1} (Ar-H stretching), 1630 cm^{-1} (-C=N stretching)

General procedure for Synthesis of hydrazone of4-bromo-2-hydrazino-6-methoxy benzothiazole and substituted aromatic aldehyde (4a-4f)

4-bromo-2-hydrazino-6-methoxybenzothiazole(0.01 M) was taken in ethanol (30 ml). To this content, ethanolic solution of aromatic substituted aldehyde (0.01 M) was added. The mixture was refluxed on water bath for twohours, solid separated was allowed to cool. The solid was filtered at pump washed with ethanol and recrystallised from hot benzene.

4aYield: 2.5gm , M. P. : 150°C, IR(KBr) : 3185 cm-1 (-OH Stretch), 3160 (N-H) stretch), 1584 (C= N Stretch), 1290, (C-N Stretch),

4b. : Yield : 2.9 gm, M. P. : 130°C. IR (KBr) : 3200 cm-1 (-OH Stretch), 3167 cm-1 (N-HStretch),

4c. : Yield : 2.2gm , M. P. : 140°C. IR (KBr):3180 cm-1 (-OH Stretch), 3174 cm-1 (N-N Stretch).

4d. : Yield : 2.5gm, M. P. : 180°C. I.R. (KBr) : 3389 (N-H stretching) 3053 (= C-H stretch in aromatic ring), 3200 cm-1 (-OH Stretch), 1541 (C=N stretch), 1290 (C-N stretch),

4e. Yield : 2.0 gm , M. P. 138°C, IR (KBr):3423 cm-1 (O-H) stretching), 3209 cm-1 (N-H
stretching),

4f. Yield :1.5gm , M. P. : 172°C, IR (KBr) : 3302 (N-H stretching)

General Procedure for synthesis of3-[(4,6–dichloro-1,3-benzothiazol-2-yl)amino]-2-aryl substituted-1,3-thiazolidin-4-one: (5a-5f)

The hydrazone(0.0025M) (4a-4f) was refluxed with mercapto acetic acid (0.005M) by using DMF (10 ml) as solvent in 50 ml round bottom flsk containing Pinch of anhydrous $ZnCl_2$ for three hours. The reaction mixture was cooled and pours it on well crushed ice. The solid product obtained was Filtered and washed with cold water. The obtained product was recrystallized from methanol.

5a. : Yield : 0.9gm , M. P. : 172°C, I.R.(KBr) :3420 cm-1 (O-H stretching), 3160 cm-1 (N-H stretching), 1720 cm-1 (C=O) stretching); NMR : δ 3.7 (s, 3H, O-CH3), δ6.7 (s, 1H, -OH), δ 6.9 (s, 1H, -CH),δ 7.2- 7.6 (m, 3H, Ar-H), _ 8.2 (s, 1H, N-H), δ 9.6 (s, 1H, enolic O-H), Mass : 505 (M+) and 507 (M+2), base peak at 285.

5b. : Yield : 0.7gm , M. P. : 288°C, I.R. (KBr) : 3410 cm-1 (O-H stretching), 3150 cm-1 (N-H stretching), 1730 cm-1 (C=O) stretching

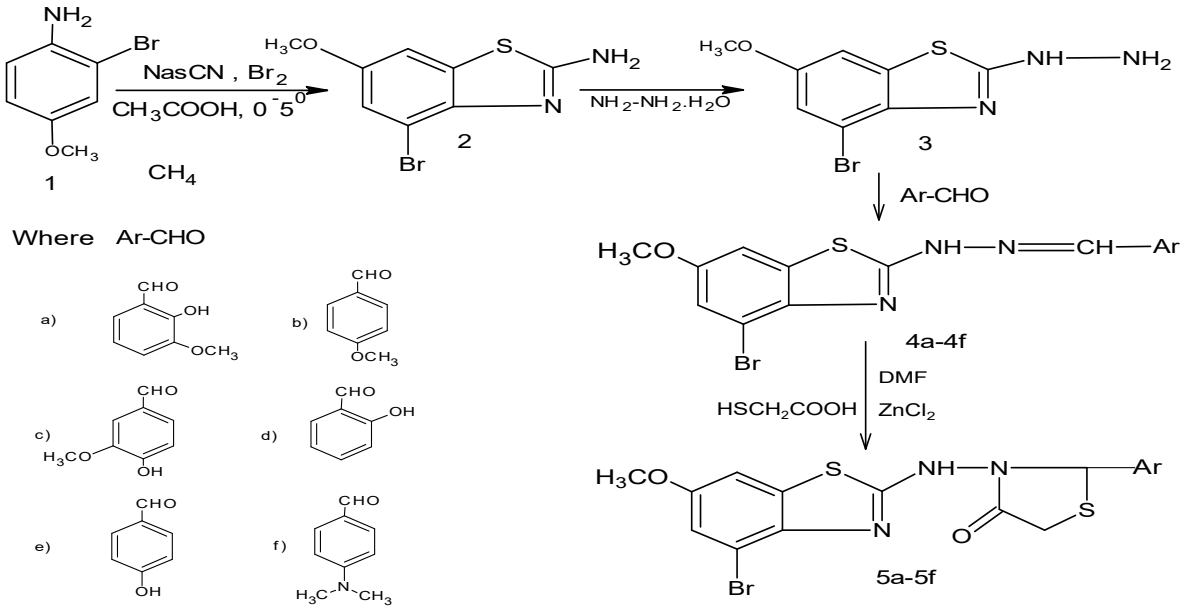
5c. : Yield : 0.8 gm, M. P. : 180°C, I.R. (KBr) : 3300-3100 cm-1 (broad) due to –OH and N-H stretching, 1710 (C=O stretching).

5d. :Yield : 1.0gm, M. P.: 198°C, I.R. (KBr) : 3220 cm-1 due to N-H stretching, 1710 cm-1 (C=O stretching).

5e. : Yield : 0.8 , M. P. : 140°C, I. R. (KBr) : 3415 cm-1 broad (O-H stretching), 3100 cm-1 (N-H stretching), 1710 cm-1 (C=O stretching).

5f. :Yield : 0.9gm , M. P. : 178°C, I. R. (KBr) : 3178 cm-1 (N-H stretching), 1710 cm-1 (C=Ostretching),

Scheme



Result and Discusion

Structures of the synthesizedcompounds have been confirmed by elemental analysis, IR, ^{1}HNMR and mass spectra.

I.R. Spectrum of compound (5a) in KBr shows absorption band 3163 cm^{-1} due N-H Stretching and at 1697 cm^{-1} to five membered cyclic C=O Stretching

PMR Spectrum of compound (5a) shows δ 2.3 due to $–COCH_2$- δ 3.8 due to OCH_3, δ 6.7 due to –OH, δ 7.0 due to -CH-, δ 7.2-7.6 (m) due to Ar-H and δ 9.5 due to -NH. Mass spectrum of the same compound (5a)shows peak at 481 (M^+.) which corresponds to its molecular weight.

Similarly I.R. spectra of compounds (5b-5f) exhibit bands in the region 3100-3400 cm^{-1} and 1600-1800 cm^{-1} due to N-H stretching and C=O stretching respectively.

Mass spectrum of the compound (5f) shows mass peak at 478 (M^+) which corresponds to its molecular weight.

The PMR spectrum exhibits two peaks for –NH proton (δ 8.4 and δ 9.5) which indicates that, compound (5a) may exists in tautomeric form

Antibacterial activity

Sr. No.	Comp.	Antimicrobial activity (zone of inhibition in mm)			
		E.coli	*Erwiniacartovara*	*Bacillus subtilis*	*Xanthom-onascitri*
1	5a	14	10	08	10
2	5b	12	12	08	10
3	5c	10	08	09	12
4	5d	12	06	08	07
5	5e	10	06	06	08
6	5f	08	06	04	06
Ampicillin		16	18	17	15
Streptomycin		20	18	22	18
Penicillin		15	20	18	17
Control		00	00	00	00

The compound 5a to 5g were tested for their antimicrobial actrivity by cup plate agar diffusion method against *E. Coli*, *Erwiniacarotovara,* *Bacillus subtilis*and*Xanthomonascitri* species using ampicilin, streptomycin penicillin as a standard compound (positive control) for comparison. The antibacterial screening data of the compound are presented in table---.

From the results it is also clear that the compounds tested showed variable toxicity against different bacteria. This variation in toxicity can be attributed to different structures and functional groups attached to the basic nucleus. It is also clear from the results presented in table that phenolic –OH and aryl substituted $–OCH_3$ groups in the basic nucleus, the antibacterial activity was increased. This was observed with bacteria that the subsequent addition of phenolic (-OH) and aryl substituted $–OCH_3$ groups antibacterial activity was enhanced.

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UTILIZATION OF PHARMACEUTICAL CHEMISTRY IN DRUG DISCOVERY

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ABSTRACT

The origin and advancement of pharmacy, medical chemistry and drug discovery are interwoven in nature. Medicinal chemistry provides understanding drug mechanisms of action, structure activity relationship (SAR). The pharmaceutical industry has a number of unusual characteristics of process of bringing new pharmaceuticals to the patient. The development of new pharmaceutical is very time consuming, extremely costly and high risk with very little chance of a successful outcome. The process of research and development is described, together with all its challenges, including environment ones. The field of pharmaceutical chemistry is diverse and involves many areas of expertise. The commercial realities and constraints of the business, together with its current problems are discussed followed by as exploration of some of the likely future commercial and technical development.

Sub themes :- *Pharmaceutical industry and Future of Drug Development.*
Keywords :- *Drug designs, pharmaceutical drugs, drug Synthesis, pre-clinical researches Drug discovery.*

Introduction

Pharmaceutical chemistry is concerned with the drug design and synthesis of biologically active molecules. The aim is to gain new chemical molecules that could enable the discovery of new Pharmaceutical or optimize already known drug Structures, thereby to expand the portfolio of chemical drugs. Although organic chemistry plays crucial roles, Only Knowledgeable Pharmaceutical chemists are able to work effectively in a highly interdisciplinary environment and interact with scientists in other disciplines, such as molecular biology, structural biology, pharmacology, physical chemistry, biochemistry,pharmacokinetics, pharmaceutical technology, toxicology or with experts from the field of translational medicine etc.

In the years of follow, the development of new drugs has been remarkably accelerated by radioactive drugs and metabolite labeling, which in turn enables scientist to identify new therapeutic targets pharmaceutical chemistry involves cures and remedies for diseases, analytical techniques, pharmacology, metabolism, quality assurance and drug chemistry. It is also an industry replete with contradictions, for example, despite the undisputed fact that for over a century the industry has made a major contribution to human wellbeing and the reaction of ill health and suffering, its is still regularly identified by the public in opinion surveys as one of the least trusted industries, often being compared unfavorably.

Drug Discovery and Drug Delivery Impact

Drug discovery is the fundamental of pharmaceutical chemistry, the drug discovery process includes all the stages of drug development, from targeting a disease or medical condition to toxicity studies in animals or ever, by some definitions, testing the drugs on human subjects, typically, conditions that affect subjects percentage of the population receive more attention and more research funding antiulcer drugs and cholesterol reducing agents are currently the therapeutic areas of greatest emphasis.

To develop a drug to target a specific disease, researchers try to understand the biological mechanism responsible for that condition, the field of drug delivery is highly interdisciplinary, covering aspects from biophysics to cellular biology and so collaborations have often had a key role in success. Drug discovery can be described as the process of identifying chemical entities that have the potential to become therapeutic agents. A key goal of drug discovery campaigns is the recognition of new molecular entities that may be of value in the treatment of disease that qualify as presenting unmet medicinal needs.

Pharmaceutical chemistry in clinical Trials

Once scientists and government regulatory agencies have determined the drug candidate to be relatively safe, it can enter into clinical trials. The clinical stages involves four phases of testing on human volunteers. Animal studies and In vitro testing continue during clinical investigations of a drugs. Drug therapy evaluation is very costly and time consuming.

Phase I Clinical trials evaluate drug tolerance and safety in a small group of healthy adult volunteers.

Phase II trials continue to assess the drug safety and effectiveness in a large population. Trials are made aware of the medication and any know side effects.

Phase III and IV clinical trials involve larger populations. Drugs phase III trials, which can last two to eight years, a drug is often brought to market phase IV studies continue after the drug is being marketed.

Result and Discussion

Drug discovery is the care of pharmaceutical chemistry. The drug discovery process includes all the stages of drug development, from targeting a disease or medical condition to toxicity studies in animal, or even, by some definition, testing the drug on human subjects the field of pharmaceutical chemistry is diverse and involves many areas of expertise. By discovering and structurally characterizing compound with medicinal activity, chemists are able to design new drugs adverse effect. Drug design is a creative act of adverse side effects one often due to interaction of the drug with biological molecules other that the desired target. It is very rare that a drug Interact with any one type of molecule in a living system. Drug selectively refers to the ability of the compound to interact with target not with other proteins or enzymes in the system. So investigate drug toxicity, animals studied are perform.

Conclusion

The field of pharmaceutical chemistry is diverse and involves many areas of expertise Nature product and analytical chemists isolate and identify active compounds from plants and other natural sources. Theoretical chemists construct molecular models o existing drugs to evaluate their properties. These computational studies help medicinal chemists and bioengineer design and synthesize compound with enhanced biological activity, pharmaceutical chemistry evaluate the bioactivity of drugs and drug metabolite. Toxicologists assess drug safety and potential adverse effects of drug therapy. When a drug has been approved for human studies, clinicians and physicians monitors patients response to treatment with the new drug. The impact of pharmaceutical chemistry on the normal human life span and on the quality of life enjoyed by most people is hard to overestimate.

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SYNTHESIS, SPECTRAL, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF CO(II), CU(II) COMPLEXES OF SUBSTITUTED A-BENZOINOXIME

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ABSTRACT

Recently, the synthesis of α-hydroxybenzoinoxime, with hydroxylamine hydrochloride, hydrazine hydrate, in presence of aqueous sodium hydroxide in DMF-water (80%) medium respectively. They were characterized by elemental and spectral analysis. The physico-chemical data suggest octahedral geometry for Co(II) and Cu(II) complexes. The synthesized complexes were screened for antimicrobial3activity at a concentration of 1000µgm/ml which was serially diluted to determine their MIC values .

Keywords:- *Metal complexes, Antimicrobial activity sodium hydroxide, DMF-water (80%) α-Benzoinoxime*

Introduction

synthesis of Fe(III) benzoin complexes and there characterization were carried out by El-agaily1. Luo2 synthesized oximes from different carbonyl compounds in a novel ionic liquid or water biphasic system synthesis of Co (II) , Ni (II) Zn (II), Fe (III), Cu (II) complexes with oxime amido and thioamido groups and their characterization were briefly studied. Synthesis Fe(III) complexes of O-Vanillin oxime and their characterisation by different physico-chemical techniques was carried out by kurup3.synthesis of mononuclear and binuclear Cr (III) complexes of α-benzoinoxime and their characterization was studied in detailed4. by El-Asmy5. complexes of Cr(III) and Mn(II) with oximes such as 2-hydroxyacetatophenone oxime, 2-hyroxynaphthaldehyde oxime and salicylaldehyde oxime were synthesized and characterized by Chandra6.Benzoinoxime are well known for their biological activity, co-ordination compounds containing O,N,S. as donor atoms are reported to possess antimicrobial activity7. synthesis characterization and thermall degradation studies of coordination polymers of ethanone oxime were carried out by wanjari8.Day9 ,synthesized a large number of Cr (III) complexes and reported the magnetic moment values in the range 3.78-3.99 .Rahangadale 10.synthesized the Schiff base and its complexes were screened for their antimicrobial activities various against bacteria and fungi.

Experimental

The benzoinoxime were prepared by refluxing substituted benzoin with hydroxylamine hydrochloride in alkaline medium for 3-4 hours, the reaction mixtures were kept overnight the solid products formed were isolated and wash several times with water alcohol mixture. The purity was checked by TLC paper. Their structural detail were confirmed on the basis of elemental and spectral analysis In order to synthesize the complexes, the equimolar mixture of each of the ligand (o.o1M) and metal salts was refluxed on a water bath for 6-8 hours in presence of sodium acetate in ethanol . The reaction mixture was kept overnight. The product formed were isolated ,washed several times with cold water ethanol mixture the characterization of synthesized complexes was made by elemental analysis, IR and UV-VIS spectra.

Results and discussion

IR spectral data of ligands and their complexes are given in table -1

Ligand and its complexes	(O-H)	(C=N)	(C-O)	(M-O)	(M-N)
[α-(L2)(H2O)]	3412	1666	1463	-	-
[Mn(L)2(H2O)2]	3343	1602	1458	465	583
[Co(L)2(H2O)2]	3369	1607	1459	479	589
[Cu(L)2(H2O)2]	3386	1610	1462	484	593

In these complexes α-HBO-Co(II), υ(O-H) is observed at 3369 cm-1 υ(C=N) at 1607 cm-1. Are indicative of linking of oxygen without loss of Hand linking of N to the metal ion respectively.These lower values of bands in hydroxyl and oximino stretching as compared to ligand clearly indicates that the coordinate bonding through hydroxyl oxygen and oximino nitrogen atom to the metal ion.In the complexes of α-HBO-Cu(II), υ(O-H) at 3386 cm-1 which shoes linking of metal oxygen atom without loss of proton similarly,(C=N) is observed at 1610 cm-1 which shows decrease in (C=N) stretching frequency during complexation and hence give clue about linkage

.Magnetic moment and electronic spectral data (cm-1) of the metal complexes as given table-2

Complexes	μeff(BM)	λmax(cm-1)	Dq(cm-1)	B1 (cm-1)	B	%Covalency
[Mn(L)2(H2O)2]	4.49	14075,18867,22892	1535	673	0.70	29
[Co(L)2(H2O)2]	5.19	13333,19417,22471	1461	694	0,71	28
[Cu(L)2(H2O)2]	1.88	13605,19230,22727	1461	694	0.71	28

The electronic spectrum of α-HBO-Co(II) complexes exhibits three transition in the range,1333,19417,22471cm-1.These spectral bands may be assigned to the following transition4A2g(F)→4T2g(F),4A2g(F) →4A2g(F),4T1g(F)→4T1g(P)characteristic to an octahedral geometry.The magnetic moment of 5.19 BM for Cu(II) complexes is consistent with octahedral geometry around central metal ion α-HBO-Cu(III) complexes exhibit absorption bands at 13605,19230,22727 cm-1.Which may be consign to 6A1g → 4T1g (F),6A1g→ 4T2g(F), 6A1g→4 Egtrasition respectively suggesting on octahedral geometry around a Cu(II) ion in the complexes under study,further more the magnetic moment measurement recorded at room temperature lies at 1.88 BM.This values is indicates of an octahedral geometry of these complexes the calculated values is of ligand field splitting energy(10Dq),Racah interelectronic repulsion parameter (β) and % Covalency as shown in above table.

On the basic of elemental analysis the complexes were assigned the composition as shown in table-3

Complexes	Colour	M. Wt.	Decomposition Tempoc
[Mn(L)2(H2O)2]	Browinsh red	592	323
[Co(L)2(H2O)2]	Yellow	596	286
[Cu(L)2(H2O)2]	Dark grey	601	276

Elemental analysis :-Table-4

Complexes	Elemental analysis found/(calculated)%			
	C	H	N	M
[Mn(L)2 (H2O)2]	55.71 (56.66)	4.13 (5.05)	4.72 (4.72)	8.94 (9.26)
[Co (L)2 (H2O)2]	55.34 (56.28)	4.10 (5.02)	4.69 (4.69)	8.91 (9.93)
[Cu(L)2 (H2O)2]	54.93 (55.85)	4.00 (4,98)	4.65 (4.65)	9,93 (10.56)

Thermogravimetric Analysis

An analysis of TG curve of α-HBO and its metal complexes . The decomposition ligand α-HBO start at comparatively lower temperature of around 120oC where as in most of the complexes decomposition start at higher temperature. Which indicates that the complexes of Co(II) and Mn(II) complexes decompose in three stages,while ligand and its complexes of Cr(III) and Fe(III) in two steps. The Co(II),Mn(II) and Cu(II) complexes are stable upto 130oC .The elimination of one water molecule from Co(II), Mn(II) and two water molecule from Cu(II) complerxesupto 150oC have been observed [% wt. loss obs. /calcd : Co(II) : 3.02 /3.00 ,Mn(II) :5.68 /5.66

,Cu(II) : 5.98/5.93]. In the some complexes i.e. Co(II) and Mn(II) there is further weight loss upto 230oC indicating the presence of two coordinated water molecule in the each complex24 [% wt. loss obs. /calcd: Co(II) : 9.06/ 9.00 ,Mn(II) :8.54 /8.53]. There is no weight loss upto 550-650oC indicating the absence of the any other water molecules (lattice / co-ordinated) in all these complexes33.Finally level beyond 650oC indicates the formation of final decomposition products corresponding to Cr2O3, CoO,MnO2, Fe2O3and CuO respectively. The half decomposition temperature and basic parameter calculated for the compounds.The relative thermal stability of half decomposition temperature is found to be

Co(II) < Mn(II) < Cu(II) < 2-HBO

Antimicrobial activity

The compounds were assayed for their antimicrobial activities12 .Against for test organisms. E. Coli S.aureus, P.aeruginosa and B.subtilis, at a concentration of 1000 µgm/ml by agar well technique13. Further their MIC value against these. Organisms were determined by serial dilution method using DMF as a solvent, the results obtained are given in the following table.

MIC Values in µgm/ml of compounds

Complex	E. coil	S. aureus	P. aeruginosa	B. subtilis
[Mn (L)2(H2O)2]	63	63	125	125
[Co(L)2(H2O)2]	125	125	63	63
[Cu (L)2(H2O)2]	125	125	125	125

On the basis of MIC Values, the complexes α-HBO-Cu(II), is found to be most effective antimicrobial agent followed by ,Co (II) and Mn(II). The enhance antimicrobial activity in case of the compounds 2HBO-Cu (II) may be attributed to the presence of amino group.

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