Heterocyclic chemistry represents a vast and important area of research which is of interest to a wide spectrum of chemists. This is amply documented by the fact that various journals, societies and interest groups have sprung up entirely devoted to the pursuit of heterocyclic chemistry.

Heterocyclic compounds arose on our planet long before the first living creatures. Together with other classes of organic compounds, heterocyclic compounds promoted the formation of life on earth. Nature selected the heterocycles as the basis of the most essential biological systems. It is proud past for India that, it contains the highest biodiversity.

Since rapid industrialization and increasing other human activities, forests are being depleted and the medicinal plants are disappearing. As an ever increasing demand of drugs and to fill up the scarcity of medicines originated from natural resources, it is necessary to develop, bioactive heterocyclic compounds in laboratory and research field.

Research in the field of synthetic heterocyclic chemistry has most important task in the development of new more potent and less toxic drugs. Their successful introduction into clinical practice is centralized to these efforts in search for pharmaceutical substances; such advantages may lead qualitative or quantitative improvement in undesirable side effects, improved stability and decreased cost. So, the chemistry of heterocyclic compounds is a vast increasing field of organic chemistry, because it fulfills one of our basic needs.
There was a time when all our pain relievers and other drugs came from natural sources like plants and animals, but around 1800 scientist began to put around in their laboratory and make new drug. This was useful when plant and animal sources are too hard to use or don't produce enough of the medicine, once a man figured out how to duplicate nature, he began to work at the molecules that are found in the natural world. Some times a plant would give us a medicine that had unpleasant side effects, so scientists would alter their molecular structure of the natural molecule until they had made a drug that worked like the natural drug, but without the side effect. Aspirin was one of the first natural inspired synthetic drug.

The last fifty years were an exhilarating period of chemical synthesis. Medicinal chemistry, particularly the discovery of sulpha drugs and antibiotics, the systematic research in pharmaceutical laboratories had led to the introduction of more and more synthetic drugs in the modern times. Synthetic drugs are obtained by simple on more involved modification of the structure of naturally occurring drugs or by pure synthesis.

The vegetable drugs have obvious limitations like non availability through out the year and hard work involved in their cultivation, collection, extraction, purification and characterization. Therefore scientists have been inspired to find synthetic alternatives. Francois megendie laid down the foundation of modern pharmacology (i.e.) the science dealing with the action of drugs, by introducing the scientific method of studying the
effects of drugs on guinea pig. Fighting disease with drug is the timeless struggle, its beginning echoed out of the primitive jungle.

Considerable diversity in the ring system is possible. The number of atoms in the heterocyclic ring can range from three to many. There is no prior limitation to the size of the ring. The ring may contain only single bonds or it may possess the aromatic unsaturation, character of benzene.

The era of synthetic drugs had to wait till the technique of synthetic organic chemistry became well advanced and physiology of human organism became well known. Most of the earliest efforts to find synthetic drugs were concentrated on anesthetics, hypnotics and analgesics. Chloralhydrate was synthesized in 1819, paraldehyde in 1882, sulphones in 1888, phenacetin in 1889, aspirin in 1899 etc. Synthetic drugs with long histories of illicit use include amphetanines and lysergic acid diethyl oxide (LSD).

**Heterocyclic Compounds:**

A cyclic organic compound containing all the carbon atoms in ring formation is referred to as a carbocyclic compound. If it is having at least one atom other than carbon, forms a part of the ring system than it is designated as a heterocyclic compound.

Heterocyclic compounds are organic compounds, containing carbon and at least one element other than carbon, such as nitrogen, oxygen or sulphur with in a ring structure.

The chemistry of heterocyclic compounds is a rapidly growing branch of organic chemistry. Heterocycles have constituted one of the
largest areas of research in organic chemistry. Almost 80% of the drugs
in clinical use are based on heterocyclic constitution, heterocycles play
on important role in biochemistry processes because the side groups of
the most typical and essential constituents of living cells, DNA and RNA
are based on aromatics heterocycles. The investigations of chemistry of
heterocyclic compounds have not only been an essential element in
man's endeavors to unravel the mysteries of living world, but at the
same time the studies have constantly stimulating new directions in
which the subject may grow in organic pharmaceutical and medicinal
chemistry. The strength of heterocyclic compounds lies in its rich
diversity.

Heterocyclic compounds are widely spread in nature and
have significant position, because a large variety of physiological
activities are associated with these compounds. In recent years the
I.U.P.A.C. have made efforts to systemize the nomenclature of
heterocyclic compound. The cell is generally thought to be the unit of
human body and is a great chemical factory. This is surprising because
nature has chosen heterocyclic substances for some of the most
important functions in the living cell as vitamins, co-enzymes and
component of nucleic acids. These contents in specific concentration in
living cell give the characteristics of life.

The most commonly found elements in these rings are nitrogen,
oxygen and sulfur. The development of heterocyclic chemistry has done
hand in hand with an investigation of great variety of natural products.
Many plant pigments such as catechins and tannins are derived from benzopyron; indigo is derived from indole.

The "Golden Period" of new discovery was from 1930 to 1960 a very large number of important drugs had been introduced during that period. Such as,

<table>
<thead>
<tr>
<th>Name of Drugs</th>
<th>Years</th>
<th>Usages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfa drugs</td>
<td>1933</td>
<td>First antibacterial drug</td>
</tr>
<tr>
<td>Penicillin</td>
<td>1940</td>
<td>Antibiotic</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>1945</td>
<td>Anti malarial</td>
</tr>
<tr>
<td>Methyldopa</td>
<td>1950</td>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Chlorothiazide</td>
<td>1957</td>
<td>Diuretic</td>
</tr>
<tr>
<td>Adrenergic beta blockers</td>
<td>1958</td>
<td>Coronary vasodilatory</td>
</tr>
<tr>
<td>Semi synthetic Panicillin</td>
<td>1960</td>
<td>Antibacterial</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>1965</td>
<td>Antimicrobial</td>
</tr>
<tr>
<td>Disodium Chromoglycolate</td>
<td>1970</td>
<td>Anti allergic</td>
</tr>
</tbody>
</table>

**Significance of heterocyclic compounds:**

Everything of this creation has its importance and nothing is meaningless. However, some of them have more importance than others and also these important things are produced in large amount with varieties. Heterocyclic compounds are such type of important things of the creation. There are also a larger number of heterocyclic compounds with other practical applications as dyestuffed, copolymers, solvents photographic sensitizers and developers; some are used as antioxidant and valuable intermediate in synthesis. Some typical areas where heterocycles are of large importance are summarized below.
**Heterocycles in life and society:**

The role of heterocycles in science technology, medicine and agriculture provides an introduction to complex chemistry of heterocycles and an overview of the many and varied applications of this versatile class of compounds, it features descriptions of the impact of heterocyclic compounds in living organism, in the structure of DNA, enzyme and proteins, vitamins and antibodies and their role in plants and animals. The use of the compounds in the chemical industry is also covered. 

**Heterocycles in drugs:**

Heterocyclic compounds exhibit a wide range of biological activities, quinoline derivatives are well known drugs for the treatment of malaria. Introduction of amino group in the ring of quinolines found to be associated with a number of activities viz, antidepressant, hypoglycemic, gastric secretion inhibitors, antihepatic, gastric ulcer inhibitors, psychoanaleptic, and also active against HIV-I integrase. Acridine based antimalarial and antibacterial compound (mepacrine, azacrine, protlavine and aminocrine are known. Ansacrine has a wide spread clinical use as antitumor agent. These compounds are also used for lessening of memory impairment and potent anticonflict activity ex.- Benzothieno - pyridines. Besides these, heterocycles compounds posses various other activities like anaesthetic, antidiabatic, diuertic, cardiovascular agents, antiviral, antiparkinsonian, African sleeping sickness, anticonvulsant, muscle relaxant, antineoplastics, antimicrobial, antihypertensive, antihistamine, antispasmodic, tranquillizers, antiulcerc, etc. Retenoids are a group of synthetic
compounds designed to refine the numerous biological activities of retinoic acid into pharmaceutical for several disease including cancer. Designs that confirmationally restricted the rotation of the structure resulted in crotinoids that were biologically active, but with increased toxicity. Incorporation of hetero atom in one cyclic ring of the crotinoid structures drastically reduced the toxicity, while retaining biological activity. A large number of benzo-diazepines, are now in clinical practice. For example chlorodiazepoxide, flurazepam, torazepam, nitrazepam, oxazepam estazdam, triazolam, quazepam and temazepam.

**Heterocycles in dyes:**

Many of the heterocyclic compounds are used as dyes, menveine, acridine, methylene blue, soffraniae, nile blue and rhodamine are a few of them. In dye stuff industry heterocyclic compounds are encountered in all the fields of colouring matters. Azodyes, for example, contain heterocycles such as pyrazolones, thiazoles, indoles, imidazoles and triazoles. Besides these heterocyclic systems such as azine, oxazine, xanthineacridine, thiazone, quinoline amino thiazone and aminobenzothiazole, amino thiophene, 3-amino-1, 2, 4 triazole, and amino benzoisothiazole.

**Heterocycles in agrochemicals:**

1,2,4-triazoles were found to have broad applications as herbicides, fungicides and antibacterial agents. Trizoles and their derivatives have been detected only in the last decade to posses a significant biological activity which makes them of interest in the area of agrochemicals.
Heterocycles in nature:

Heterocyclic compounds are widely spread in nature. The plants are green and blood is red due to presence of chlorophyll and haemin respectively and also the life of plants and animals is stored in them. Tannis and amino acids are derived from heterocyclic origin. The physiologically active substances like heteroauxin, serotoxin, adenine, biotin, vitamin B$_{12}$ family, tocopherol, histamine, purine and pyrimidine bases like adenine, guanine, cytocene, thiamine, breakdown products of metabolism like uric acid alloxane, essential amino acids like histidine, tryptophan and proline alkaloids such as strychnine, reserpine and morphine, antibiotics like penicillin and cephalosporin, energy storing units like, A.D.P. and A.T.P. electro transport system, like cytochrome ‘a’ and ‘b’ etc. also contain heterocyclic nucleus.

Heterocycles in industry:

Heterocycles like benzofuran polymerises to give useful plastic and resins, Heterocycles like 2-mercapto benzothiazole, piperidine and phenothiazines are used as antioxidants and vulcanizing accelerators in rubber industry. Some of the heterocyclic compounds are used in agro industry as insecticides and fungicides, 2-phenanthroline, 8-hydroxy quinoline and dipyridyl have their use in analytical chemistry for estimating different metals in solution.

Heterocyclic chemistry in computer age:

Powerful computer techniques are used in organic chemistry. QSAR has been used for the discovery and development of new drugs to achieve objectives like quantitative prediction of biological efficiency of a
compound, classification of compounds into various classes, optimization of a lead compound and refinement of synthetic drug. The biological activity assayed thiazolidinones are anti HIV\(^{50-51}\) agents and antioxidant\(^{52}\) activity proved them as potential insecticides.\(^{53}\)

**Heterocycles in photo stabilizers:**

Thiazoles and benzotriazoles were successfully used as photo stabilizers for fibers, plastics or dyestuffs and also used for the protection of human skin from harmful U.V. radiations.

**Heterocycles in human diet:**

Cooking of protein rich foods may include the formation of a series of heterocyclic compounds that have been found to be mutagens and carcinogens. Despite very potent mutagenic activity found in salmonella/micros oral assay, this test cannot predict carcinogenic potency\(^{54}\) of heterocyclic compounds in rodents and monkeys. Doses used in feeding studies with animals exceeded by several orders of magnitude. The level of heterocycles found in human diet, being approximately 5,00,000-3,000,000 fold higher than the human dietary levels. A comparison of these levels and their relevance for human is presented. Differences in metabolic fate of different heterocyclic compounds due to species and sex of animals are discussed. The influence of trace levels of heterocyclic compounds on human health remains to be confirmed.

**Methods of Chemical Analysis:**

During last few years’ enormous development in the field of synthetic organic chemistry has taken place due to the availability of
powerful analytical techniques. The spectral methods have been of immense help in collection of valuable information about individual compounds. Ultraviolet, infrared, nuclear magnetic resonance spectroscopy and mass spectrometry are among the most important spectroscopic techniques that the organic chemists now use routinely to gain information about a particular substance\textsuperscript{55-56}. In the present study I.R. and \textsuperscript{1}HNMR techniques are used to characterize the synthesized compounds. Thin layer chromatography is used to check the purity of the synthesized compounds.

**Infrared spectroscopy:**

In the structure elucidation of various organic compounds especially for the presence of functional groups, I.R. spectral technique is very reliable. This technique depends on the vibration and rotation of atoms of molecules. Bellamy\textsuperscript{57} and Rao\textsuperscript{58} reviewed the application of I.R. spectroscopy. This technique is widely used for the identification of all kinds of organic compounds.\textsuperscript{59-60}

The infrared absorption spectroscopy is based on the absorption of infrared radiation by molecules; it has been observed that all chemical compounds show marked selective absorption in the infrared region. However infrared spectroscopy is most widely used for the identification of organic compounds. The infrared absorption spectrum of an organic compound represents one of its truly unique physical property. IR spectrum of a chemical substance is a finger print for its identification, organic applications of infrared spectroscopy are almost entirely concerned with the range 650–4000 cm\textsuperscript{-1}. The region of frequencies lower
than 650\(^{-1}\) is called the far infrared and that of frequencies higher than 4000 cm\(^{-1}\) is called near infrared.

In structure determination the infrared spectra can at once indicate the presence of various atomic groupings and can give some information about the size of the ring. This technique is useful for identification of functional groups, study of tautomerism and for finding out hydrogen bonding in the molecule. Many scientists have applied I.R. spectroscopy for the structural interpretation of terpenes, glycosides, carbohydrates and all kinds of natural and synthetic compounds. Dhar and Singh\(^{61}\) have studied the I.R. spectra of some new chalcones. Advance studies have been done in this field and are illustrated by many workers.\(^{62}\)

**Nuclear magnetic resonance spectroscopy:**

Nuclear magnetic resonance spectroscopy serves as a powerful tool for the structural elucidation of organic compounds. \(^{1}\)HNMR and \(^{13}\)C-NMR techniques gave configurational and conformational nature of compound. This technique is used in observing each and every proton and carbon atom separately in the compounds, as well as natural compounds\(^{63-64}\), have been studied by NMR spectroscopy. The subject have developed very rapidly in recent years and today it has extended so much that it is of equal importance with the other established vibrational and electronic branches of spectroscopy.

Nuclear magnetic resonance involves the interaction between an oscillating magnetic field of electromagnetic radiation and the magnetic energy at the hydrogen nucleus or some other type of nuclei when these
are placed in an external static magnetic field. The sample absorbs electro magnetic radiations in radio wave region at different frequencies and absorption depend on type of protons or certain nuclei contained in the sample. Radio waves are regarded as the lowest energy form of electromagnetic radiations that find valid application in analytical chemistry. It is powerful tool for investigating nuclear structure. It has been used to determine the molar ratio of the components in a mixture. It is extensively used in pharmaceutical and polymer industry. Their applications have been extensively reviewed in standard works.65

**Chromatographic techniques:**

Chromatography is the most useful technique for separating and identifying a mixture of substances in to its components. This technique is based upon the difference in the rate of mobility of various constituents of substances through a porous medium (called stationery phase) under the influence of some solvent or gas (called moving phase). There are different types of chromatographic techniques like paper, thin layer, column and gas chromatography.

In the present work thin layer chromatography was used to check the purity of the compounds. Thin layer chromatography also serves as a great tool for the separation of various complex organic mixtures. In this technique, stationery phase is made by coating a slurry of absorbent on a glass plate as a thin and uniform layer. It is a rapid technique and separation is very sharp. Its sensitivity of detection is very high. This technique successfully separates the heterocyclic compounds, alkaloids, flavonoides and amino acids.
Biological assay studies:

To evaluate the pharmacological importance, the new synthesized heterocycles are tested for their curative properties against various diseases. So it was thought worth while to study thiazolidinone, benzo-oxazole and coumarin derivatives, for their biological assay. Studies carried out are antimicrobial, anthelmintic and insecticides and antitubercular activity.

Antimicrobial activity:

The invention of microscope in the 17\textsuperscript{th} century gave vision to the hitherto unknown world of micro-organism. These organisms are closely associated with the health and welfare of human beings and plants. Some are beneficial and others cause disease to human and plants.\textsuperscript{66} The theory of the spontaneous generation of disease, was finally buried by Pasteur and Koch in 1876, when they convinced one and all that the anthrax disease was incited by bacterium. This had wide implications in related fields of study.

In 1878 Burrill of Illinois reported that the fire blight disease of pear and apple was caused by bacterium. Arthur (1885) proved that the disease could be incited by the bacterium obtained from a pure culture. The common disease of human and animals which are caused by fungi include actinomycosis, sporotrichosis and epidemophytosis. Joseph Hinsten in 1875 was the first scientists who developed pure culture technique to the germs outside the body and proved by experiments that the germs can grow outside the body are also susceptible to produce
same symptoms, when it is inoculated into the body in the same pattern. Fungi and bacteria are grown using the suitable culture media and a number of chemicals can be tested in vitro for their activity on microbes.

The microbial activity\(^{67}\) is measured in vitro in order to determine.

I. The potency of antimicrobial agent.

II. Sensitivity of the germ micro organism to the known concentration of the drug.

**Anthelmintic Activity:**

The anthelmintics are the drugs, which are used to kill or expel the parasitic worms known as helminths from the infected host. These drugs are of great importance because helminthiasis is the most common disease in the world. All the clinical anthelmintics are toxic to earthworm. Therefore earthworms can be used to have an idea, whether the test substance has any anthelmintic activity and to compare its relative activity with the standard drug like piperazine hydrochloride, etc. A number of workers\(^{68-70}\) have used earthworms for the preliminary in vitro evaluation of anthelmintic activity of new substance.

**Insecticidal activity:**

Without doubt insects occupy a dominant position in the animal world, out numbering all other inhabitants and they are very successful animals. Of the estimated 1.35 million living species of animals, more than 9,00,000 are insects. They eat human crop and some of his other possessions and transmit diseases, such as malaria, trypanosomiasis,
onchocerociasis and other disease. The above losses results in the enormous wealth damages and that is the reason why, a number of chemicals have been introduced for insect control. The chemicals used for control of insects are termed as insecticides.71

Eliot72 in 1977, suggested that the synthetic insecticides should have low mammalian toxicity and controlled environmental stability.

**Scope of Heterocyclic Compounds:**

The chemistry of heterocyclic compounds is challenging but at the same time a handsomely rewarding field for study. Each year, we witness the inclusion of thousands of heterocyclic compounds in literature, both on account of their intrinsic chemical interest and on the basis of their therapeutic, biological and industrial potential.

Heterocyclic compounds have a wide range of applications; they are predominant among the types of compounds used as pharmaceuticals, as agrochemicals and as veterinary products. They are used as optical brightening agents, as antioxidants, as corrosion inhibitors and as additives with a variety of other functions. Many dyestuff and pigments, drugs and natural products have heterocyclic moiety in their structures.

Heterocyclic compounds are also find an increasing use, as intermediates in organic synthesis. One of the reason for the widespread application of heterocyclic compounds is that their structures can be subtly manipulated to achieve a required modification in function. Many heterocycles can be fitted into one of a few broad groups of structures that have overall similarities in their properties but significant
variations with in the groups. Such variations can include differences in acidity or basicity, different susceptibility to attack by electrophiles or nucleophiles, different polarity and the possible structure variation may lead to the development of novel heterocyclic compounds with different properties and significance.
References


