

**EVALUATION AND SYNTHESIS OF SOME HETEROCYCLIC DERIVATIVES AS  
PHARMACOLOGICAL AGENTS**

**NITIN KUMAR**

Research Scholar  
Sunrise University  
Alwar, Rajasthan

**DR. ANIL AHUJA**

Supervisor  
Sunrise University  
Alwar, Rajasthan

**ABSTRACT**

The title of the paper clearly reflects the importance of nitrogen heterocyclic compounds: in fact they are extremely pivotal structural motifs responsible for eliciting various biological activities in natural products and synthetic medicines. This has attracted the medicinal chemists towards the synthesis of various compounds having nitrogen heterocyclic as useful medicines to treat various diseases. Heterocyclic derivative is important structures present in numerous natural and synthetic compounds and have application in medicinal chemistry. Heterocyclic compounds are reported to have broad pharmacological activities. The diversity of the structures encountered, as well as their biological and pharmaceutical relevance.

**KEY WORDS:** Heterocyclic derivative, pharmaceutical

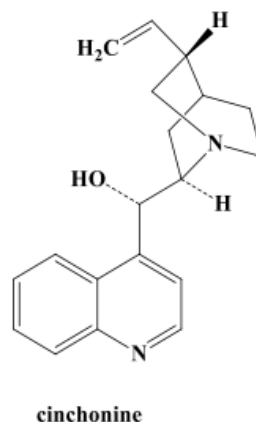
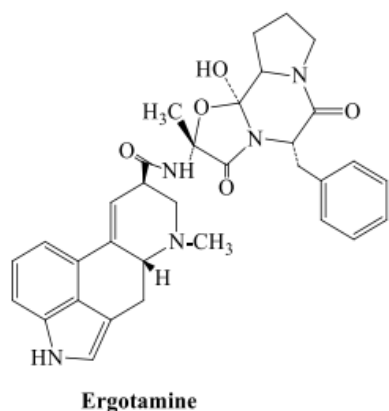
**INTRODUCTION**

Heterocyclic chemistry is a very important branch of organic chemistry accounting for nearly one-third of modern publications. In fact two thirds of organic compounds are heterocyclic compounds. A cyclic organic compound containing all carbon atoms in ring formation is referred to as a carbocyclic compound. If at least one atom other than carbon forms a part of the ring system then it is designated as a heterocyclic compound<sup>1</sup>. Nitrogen, oxygen and sulfur are the most common heteroatoms but heterocyclic rings containing other hetero atoms are also widely known. An enormous number of heterocyclic compounds are known and this number is increasing rapidly. Accordingly the literature on the subject is very vast. Heterocyclic compounds may be classified into aliphatic and aromatic. The aliphatic heterocyclics are the cyclic analogues of amines, ethers, thio ethers, amides, etc. Their properties are particularly influenced by the presence of strain in the ring. These compounds generally consist of small (3- and 4-membered) and common (5 to 7 membered) ring systems. The aromatic heterocyclic compounds, in contrast, are those which have a heteroatom in the ring and behave in a manner similar to benzene in some of their properties. Furthermore, these compounds also comply with the general rule proposed by Huckel. Besides the vast distribution of heterocycles in natural products, they are also the major components of biological molecules such as DNA and RNA. DNA is without doubt the most important macromolecule of life. Nucleotides, the building blocks of our genes are derivatives of pyrimidine and purine ring structures. Chlorophyll and heme, the oxygen carriers in plants and animals respectively are derivatives of large porphyrin rings. Heterocycles are an important class of compounds, making up more than half of all known organic compounds. Heterocycles are present in a wide variety of drugs, most vitamins, many natural products, biomolecules, and biologically active compounds, including antitumor, antibiotic, anti-inflammatory, antidepressant, antimalarial, anti-HIV, antimicrobial, antibacterial, antifungal, antiviral, antidiabetic, herbicidal, fungicidal, and insecticidal agents. Also, they have been frequently found as a key structural unit in synthetic pharmaceuticals and agrochemicals. Some of these compounds exhibit a significant solvatochromic, photochromic, and biochemi-luminescence properties.

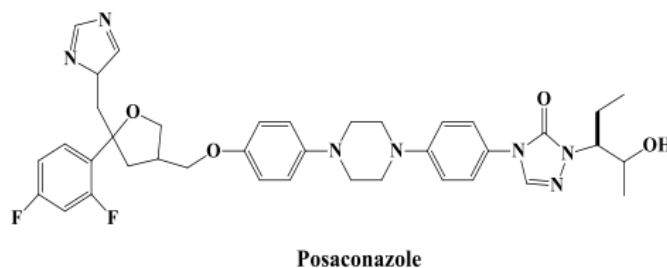
Most of the heterocycles possess important applications in materials science such as dyestuff, fluorescent sensor, brightening agents, information storage, plastics, and analytical reagents. In addition, they have applications in supra molecular and polymer chemistry, especially in conjugated polymers. Moreover, they act as organic conductors, semiconductors, molecular wires, photovoltaic cells, and organic light-emitting diodes (OLEDs), light harvesting systems, optical data carriers, chemically controllable

switches, and liquid crystalline compounds. Heterocycles are also of considerable interest because of their synthetic utility as synthetic intermediates, protecting groups, chiral auxiliaries, organocatalysts, and metal ligands in asymmetric catalysis inorganic synthesis. Therefore, substantial attention has been paid to develop efficient new methods to synthesize heterocycles.

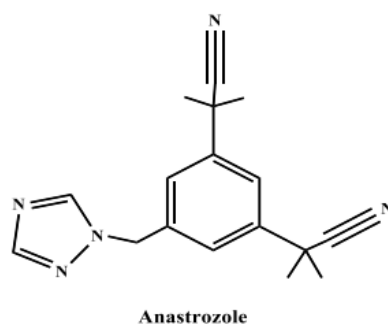
The alkaloids form a major group of naturally occurring heterocyclic compounds having varied biological activity. Most alkaloids contain basic nitrogen atoms. Ergotamine, the indole based alkaloid exhibits antimigraine activity. Cinchonine, a quinolone class of alkaloid shows antimalarial activity.



Posaconazole is a triazole antifungal drug<sup>4</sup>. It is active against the following microorganism candida, asperigillus, Zygomycetes.



Anastrozole is an aromatase-inhibiting drug approved for the treatment of breast cancer after surgery, as well as for metastasis in both pre and postmenopausal women. The severity of breast cancer is increased by estrogen, as sex hormones cause hyperplasia, and differentiation at estrogen receptor sites<sup>5,6</sup>. Anastrozole works by inhibiting the synthesis of estrogen.



Three out of twenty natural amino acids are heterocyclic, as are many essential vitamins. The range of application of heterocyclic compounds is very wide. They are of specific importance as they are associated with a wide variety of physiological activities. Significant number of compounds synthesized in the industrial sector is heterocyclic in nature. A large number of synthetic heterocyclic compounds are

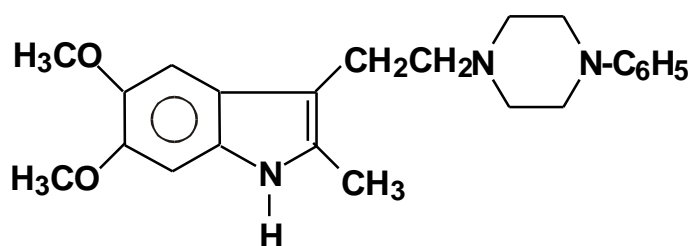
predominant among all types of pharmaceuticals, agrochemicals veterinary products. Some of the synthetic heterocyclics are used in photography and as rocket propellants.

## REVIEW OF LITERATURE

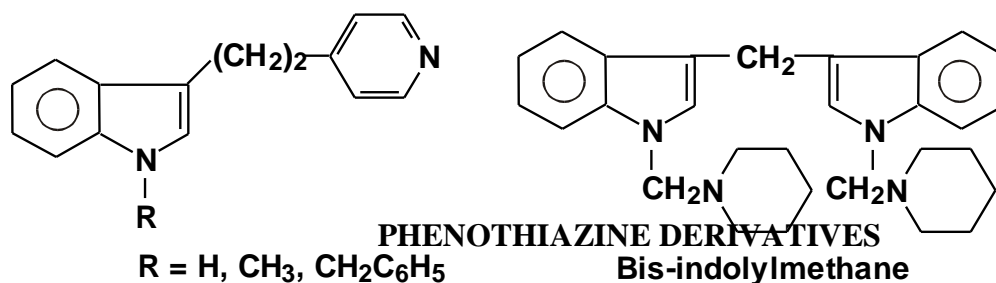
Globally more than 10-15% of the prescriptions are written for the patients suffering from mental disorders. Drugs which are used for the treatment of mental disorders are psychotropic agents. Psychotropic agents can be placed into 4 major categories. Antianxiety-sedative agents particularly benzodiazepines are those used for the drug therapy of anxiety disorders. Anti-depressant (mood-elevating agents) and antimanic particularly Lithium salts and certain anticonvulsants and are used to treat affective or mood disorders and relative conditions. Antipsychotic or neuroleptic drugs are those which are used to treat very severe psychiatric illness the psychosis and mania. They have beneficial effect on mood and thought but many standard neuroleptic agents carrying the risk of producing characteristic side effects that mimic neuroleptic diseases, whereas modern antipsychotics are associated with weight gain and adverse metabolic effects such as diabetes.

About 10 to 15% of world population is suffering from psychiatric disorders. However changes in socioeconomic pattern of modern society with concomitant increase in stress and strain have greatly increased the frequency and the intensity of these problems which underline the need of effective therapy of psychiatric diseases. The therapeutic agents, commonly known as psychotropic agents effect specifically the CNS and bring about changes in mood, behaviour and performance with or without causing disturbance of autonomic nervous system or any other serious disability. The drugs meant for successful treatment of anxiety, insomnia and mood disorders are the antipsychotic which are a group of heterogenous organic compounds and these are as follows:

### INDOLE DERIVATIVES

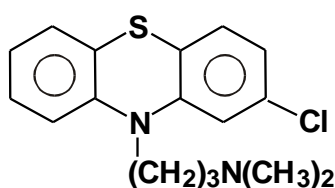


Oxypertine

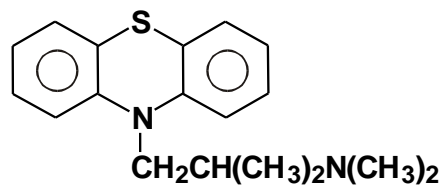


### PHENOTHIAZINE DERIVATIVES

Bis-indolylmethane



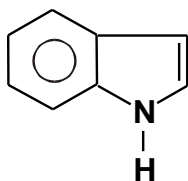
Chlorpromazine



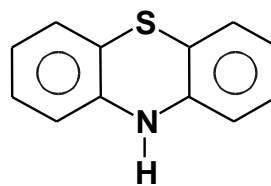
Promethazine

In spite of considerable development in the field of psychotropic drugs which are used as antipsychotic drugs, there is no single drug available which could be considered as ideal. Besides this, these compounds

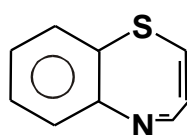
either possess nonanticonvulsive activity or are proconvulsants. Since epilepsy is very often associated with psychiatric disorders, a drug with both antipsychotic as well as antiepileptic activity will be more beneficial. The search for the better drugs for the treatment of CNS psychiatric disorders associated with or without epilepsy with minimum side effects and maximum efficacy is therefore, the need of the day. Some of the compounds which possess potent psychotropic activity are the derivatives of following heterocyclic nuclei.



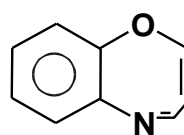
**Indole**



**10H-Phenothiazine**



**1, 5-Benzothiazepine**



**1,5-Benzooxazepine**

The different derivatives of the above mentioned heterocyclic system will be synthesized and screened for their antipsychotic, antiepileptic activity and toxicity studies. There are several reports in the literature, which have shown promising psychotropic activity in indole phenothiazine benzothiazepine and benzooxazepine. It is therefore our contention to develop potent psychotropic agents, therefore we propose to synthesize and screen for their psychotropic activity of some newer indole, phenothiazine, benzothiazepine & benzooxazepine derivatives.

## REFERENCES

- Jaiswal N., Jaiswal R.K., Barthwal J.P., Kishor K.; Synthesis and biological activity of some new 10-[(3,5-diaryl-2-pyrazolin-1-yl)acetyl]phenothiazines; *Indian J. Chem.* 20 8(1981)252.
- Liegeois J.F.F., Register F.A., Bruhwylar J., Damas J., Nguyen T.P., Inarejos. M.O., Chleide E.M.G., Mercier M.G.A., Delarge J.E.; Pyridobenzoxazepine and pyridobenzothiazepine derivatives as Potential central nervous system agents: Synthesis and neurochemical study; *J. Med. Chem.* 37 (1994) 519.
- Nakanishi M., Oe Takanori, Seki T.; Psychotropic 1-piperazinylalkyl-substituted phenothiazine and dibenz [b, f]azepines ; *Chem. Abstr.* 78 (1973) 29823s.
- Orzalesi G., Selleri R., Landi V.R., Innocenti H., Grandolini G.; Potential Psychotropic agents. 7-chloro-9-phenyl-3,3-diethyl-3H-pyrazolo [5,1 -b]quinazolin-10-ium-2-olate and 9-chloro-2,3,4,5-tetrahydro-1-methyl -3,3-diethyl-7-phenyl-1H-benzo-1,5,6-triazonine-2,4-dione; *J. Heterocycl. Chem.* 14 (1977) 733.
- Postovskii I.Y., Chupakhin O.N., Pilicheva T.L., Kurilenko V.M., Vysokovskii T.M., Mekhova G.M.; 3,4-Dihydro-4-(2-methylindolyl)-2-quinazolinone crystallasolvate with DMF with psychotropic activity ; *Chem. Abstr.* 86 (1977) 101147j.
- Blondel J.C.R.G., Fouche J.C.L.; Psychotropic esters of 3- (dimethylsulfomoyl)-10-[3-[4-(hydroxyethyl)piperidino]propyl]phenothiazine with alkanedioic acids; *Chem. Abstr.* 75 (1971) 49100v.
- Diaz J.A., Vega S., Exposito M.A., Sanchez M.C.C., Darias V.; Synthesis and antidepressant evaluation of new hetero[2,1]benzothiazepine derivatives; *Arch Pharm.* 329 (1996)352.
- Sudarsham K., Prem C.D., Hoshyari L.S.; Mass spectrometry of some New 2- substituted 10-N-(Aminoacyl)phenothiazines ; *Org. Mass Sped.* 17(1982) 309.
- Vierfond J.M., Lehuède J., Miocque M.; Aminomethylation of phenothiazine and phenoxazine. Chemical and pharmacological studies ; *Chem. Abstr.* 98 (1983) 198168a.