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A Study the overview of Heterocyclic Composites Compounds in Nitrogen

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Abstract- Heterocycles are integral to all aspects of organic chemistry and the processes of life. Their work is enhancing our knowledge of living processes, which in turn helps us better our quality of life, and it is also advancing society from an industrial and biological perspective. Every organic substance contains heterocycles, which are essential in many scientific disciplines, including pharmacy, agriculture, biochemistry, and biology. As medicinal agents, heterocyclic compounds have shown to be both widely and economically beneficial due to their structural diversity. This study delves into the intricate realm of heterocyclic composite compounds with a specific focus on those containing nitrogen. the importance of nitrogen-containing heterocyclic composites in drug discovery, where they often serve as core structures for pharmaceutical agents.

Keywords- Heterocycles, Heterocyclic Compounds, Nitrogen, Organic Chemistry

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INTRODUCTION

Heterocycles are integral to all aspects of organic chemistry & processes of life. Their work is enhancing our knowledge of living processes, which in turn helps us better our quality of life, and it is also advancing society from an industrial and biological perspective. Every organic substance contains heterocycles, which are essential in many scientific disciplines, including pharmacy, agriculture, biochemistry, and biology. Organic compounds that contain carbon, nitrogen, oxygen, and sulphur atoms in at least one ring, or more than one heteroatom in the ring, are known as heterocyclic compounds.1 This heteroatom is not like carbon or hydrogen in any way. Heteroatoms are responsible for the heterocyclic system's increased polarity, water solubility, or reactivity. As medicinal agents, heterocyclic compounds have shown to be both widely and economically beneficial due to their structural diversity. Heterocyclic chemistry encompasses many well-known subfields that have far-reaching effects on practically every practical area of organic chemistry, biochemistry, medicinal chemistry, etc. Throughout the evolution of organic synthesis, chemists have placed a premium on thousands of 4, 5, or 6-membered heterocyclic molecules containing nitrogen and sulphur.2 In addition to oxygen, phosphorous, selenium, and additional heteroatoms, many natural medicines also contain heterocycles with other heteroatoms.

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 heterocycles3. 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.4-10 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,

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

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 dysestuffed, 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.11

Heterocycles in drugs: Among the many biological actions displayed by heterocyclic compounds, quinoline derivatives have gained notoriety as effective medications in the fight against malaria. Antidepressants, hypoglycemics, gastric secretion inhibitors, antihepatics, gastric ulcer inhibitors, psychoanaleptics, or active against HIV-I integrate are all linked to quinolines that have an amino group added to their ring. Other quinoline-based antimalarial or antibacterial compounds include aminocrine, azacrine, protlavine, and mepacrine. There is extensive medical application of ansacrine as an anticancer agent. Examples of these chemicals include benzothieno pyridines, which have strong anticonflict properties and are used to reduce memory impairment. In addition to these, heterocycle compounds have a wide range of additional activities, such as anaesthetic, antiidiabetic, diuretic, cardiovascular agent, antiviral, antiparkinsoman, anticonvulsant, muscle relaxant, antineoplastic, antimicrobial, antihypertensive, antihistamine, antispasmodic, tranqulizers, antiulcer, etc. With the goal of developing retinoic acid into a medicine for a variety of diseases, including cancer, retinoids12 are a class of synthetic chemicals with a wide range of biological actions. Biologically active crotinoids with higher toxicity were produced by designs that confirmationally restricted the structure's rotation. The toxicity was significantly lowered without losing biological activity when hetero atoms were added to one cyclic ring of crotinoid molecules. Lots of benzo-diazepines.Methods 13-19 are now being used in clinical practice. For instance, triazolam, quazepam, temazepam, oxazepam, nitrazepam, torazepam, and chlorodiaszepoxide are some examples.

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, thiazine, quinoline amino thiazole20 and aminobenzothiazole21, amino thiophene22, 3-amino– 1, 2, 4 triazole23, 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 gained interest in the field of agrochemicals due to their remarkable biological activity, which has only been discovered in the past ten years.

Heterocycles in nature: Heterocyclic compounds are abundant in the natural world. Chlorophyll gives plants their green colour & haemin makes blood red; both substances store energy for plants and animals. The heterocyclic origin is the source of both tannins and amino acids. Heterocyclic nuclei are found in a wide variety of biologically active substances, including: biotin, heteroauxin, serotoxin, adenine, biotin, vitamin B12, tocopherol, histamine, purine or pyrimidine bases, uric acid alloxane,

histidine, tryptophan, proline alkaloids, penicillin, cephalosporin, energy storage units, cytochrome 'a' and 'b', and electrotransport systems.

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 & dipyridyl have their utilize in analytic 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 [24-25] agents and antioxidant26 activity proved them as potential insecticides.27

Heterocycles in photo stabilizers: Benzotriazoles & thiazoles have found successful applications as photostabilizers for fibres, plastics, and dyestuffs, as well as for shielding human skin from damaging ultraviolet light.

Heterocycles in human diet: It is possible for a class of heterocyclic compounds with carcinogenic & mutagen properties to be formed during the cooking of protein-rich foods. This test cannot predict the carcinogenic potency28 of heterocyclic chemicals in rodents and monkeys, despite the fact that the salmonella/micros oral assay has extremely strong mutagenic activity. A number of orders of magnitude higher than the doses utilised in animal feeding trials. There are over 5,000–3,000,000 times more heterocycles in the average human diet than in the average human blood. We offer a comparison of these tiers together with the human-relevant information they contain. We talk about how species and sex affect the metabolic destiny of certain heterocyclic molecules. Confirmation of the impact of trace amounts of heterocyclic chemicals on human health is still pending.29

Methods of Chemical Analysis: The availability of strong analytical tools in recent years has led to tremendous advancement in synthetic organic chemistry. For the purpose of gathering useful information on specific substances, spectral approaches have shown to be extremely useful. Organic chemists nowadays frequently employ a number of essential spectroscopic techniques, such as mass spectrometry, nuclear magnetic resonance spectroscopy, infrared spectroscopy, and ultraviolet spectroscopy, to learn more about a substance30-32. The synthesised chemicals are characterised in this study using I.R. and 1HNMR methods. The synthesised chemicals are tested for purity using thin layer chromatography.

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. Bellamy31 and Rao32 reviewed the application of I.R. spectroscopy. This technique is widely used for the identification of all kinds of organic compounds.33-34 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-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 terpens, glycosides, carbohydrates and all kinds of natural and synthetic compounds. Dhar and Singh35 have studied the I.R. spectra of some new chalcones. Advance studies have been done in this field and are illustrated by many workers.36

NITROGEN CONTAINING HETEROCYCLES

Nitrogen containing heterocyclic compounds are very common in nature as structural subunits of various biomolecules such as vitamins, heme, chlorophyll, bile, alkaloids, and nucleotides (Balaban 2004)37. Nucleotides, which are essential components of RNA & DNA and are created by combining purine & pyrimidine bases, contain these elements (Pozharskii 1987)38. The nitrogenous bases of nucleotides containing the purine ring are as shown in (Figure 1).

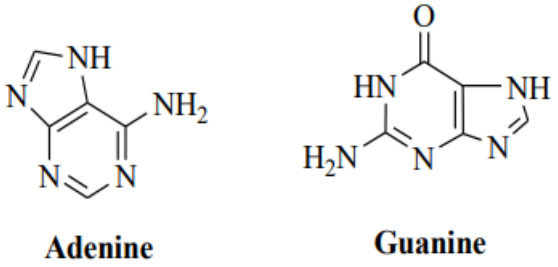

Figure 1: Nitrogen-containing Purines

Coffee beans contain caffeine, tea leaves contain theophylline, & cocoa fruits contain theobromine, three more significant purines found in nature. You may see the chemical blueprints of these substances in (Figure 2).

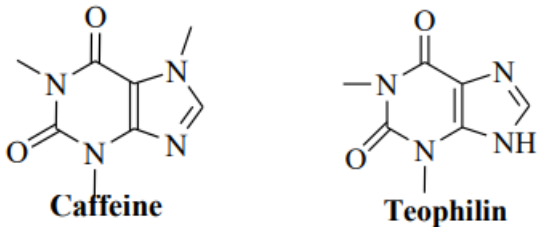

Figure 2: Examples of naturally occurring Purines

Chlorophyll and heme are two examples of naturally occurring & significant oxygen-transporting molecules that contain pyrrole subunits in their enormous porphyrin rings. For life on Earth to persist, these substances are crucial (Moan 2008, Chem 2009, Bucci 2009)39–41 (Figure 3).

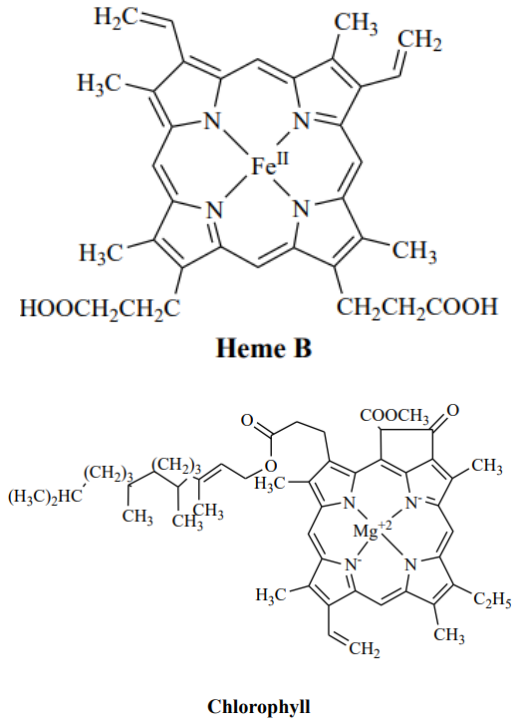

Figure 3: Heme B and Chlorophyll

Thiamine (B1), Nicotinamide (B3), Pyridoxol (B6), Ascorbic acid (C), and Riboflavin (B2) are nitrogenous heterocyclic moiety subunits of compounds; this is also true of many vitamins (Kesse-Guyot 2009, Christensen 2005). 42–43 (Figure 4).

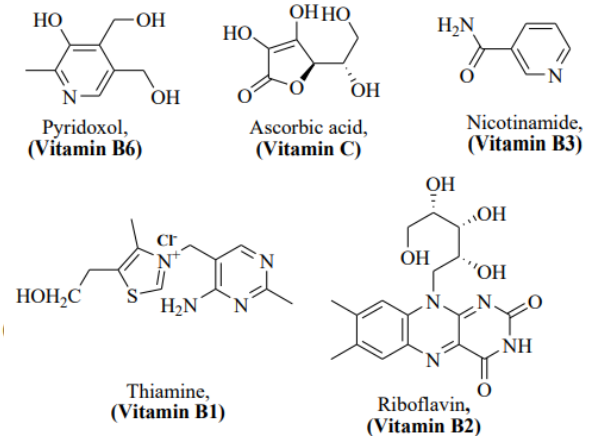

Figure 4: Structures of important vitamins

Many alkaloids having nitrogenous-heterocyclic ring systems exhibit varying degrees of biological performance. e.g, Ergotamine possesses anti-migraine activity (TfeltHansen 2008)44. Cinchonine exhibited antimalarial activity (Raynes 1999)45. Prior to its addictive qualities being discovered, morphine was employed as an analgesic in the early eighteenth century (Figure 5).

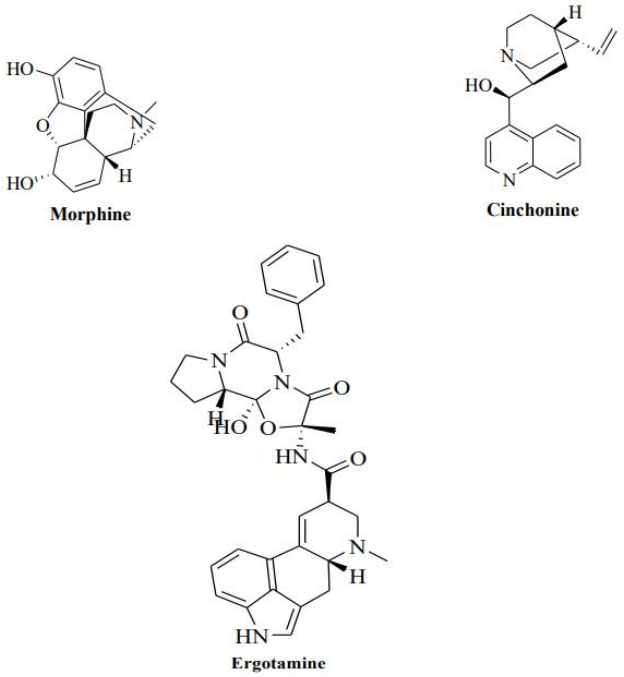

Figure 5: Nitrogen-containing naturally hetero alkaloids

Nitrogen-containing heterocyclic moieties are also found in coloring agents. The heterocyclic dye such as indigo blue is a naturally occurring molecule that can be obtained from Indigofera (Figure 6) (Shakoori 2015)46.

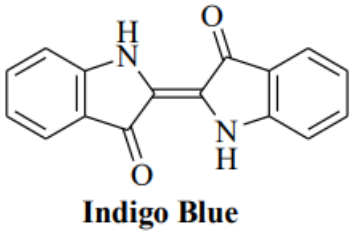

Figure 6: Indigo blue is a naturally occurring heterocyclic dye

Nitrogen heterocycles are crucial building blocks of numerous commercially significant synthetic chemicals, including medicinal drugs, pharmaceutical intermediates, dyes, polymer compounds, optical brightening agents, photographic material, and insecticides. For example, 5-amino tetrazole compounds were utilised in an automobile's airbag system, and some of these chemicals have also found utility as rocket propellant (Akutsu 1993). Some pyrrole and pyrrolidine derivatives (Scott 1960)47 have demonstrated suitability as a component of rocket propellants (Figure 7).

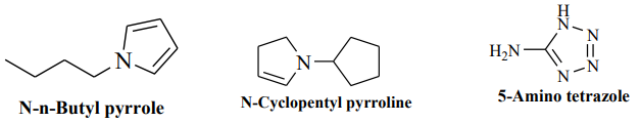

Figure 7: Nitrogen-containing Heterocycles

Nitrogenous heterocyclic compounds have also found applications in the agriculture sector as pesticides. The structure of the most widely used insecticide Imidacloprid (Li 2006, Raslan 2001)48 is given in Figure 8.

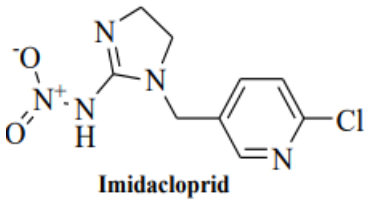

Figure 8: Heterocyclic compounds as a pesticide

A large number of the best-selling medications also contain heterocyclic molecules that contain nitrogen. For instance, tenofovir, the first medicine to effectively combat HIV, and Ibrutinib, a blood cancer treatment that has sold quite well (Deeks 2017; Deeks 2018)49. Figure 9

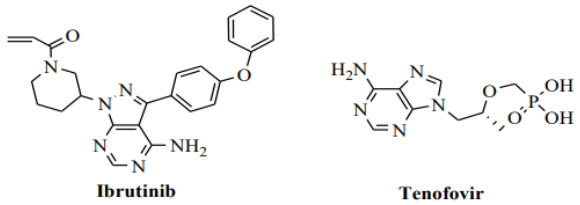

Figure 9: Heterocyclic anticancer and anti-HIV drug

The topmost selling drugs in the USA in the current year have a nitrogen-containing heterocycle as a structural subunit (Martins 2015)50. Below mentioned three drugs (Figure 10) account for almost 75% of the pharmaceutical business.

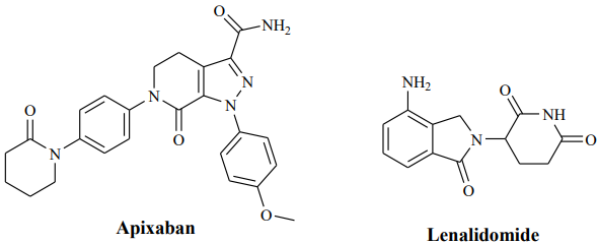

Figure 10: Top selling nitrogen-containing heterocyclic drug structures

Figure 11 shows USFDA-approved anticancer medicines from 2010–2015.

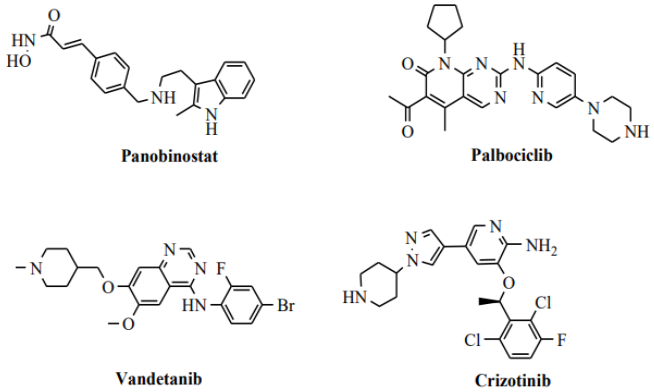

Figure 11: Heterocyclic drugs approved by the US Food and Drug Administration between 2010 and 2015.

CONCLUSION

Heterocyclic compounds play a crucial role in various fields, including medicinal chemistry, materials science, and agriculture. Nitrogen-containing heterocycles, in particular, exhibit diverse and valuable properties that make them essential building blocks in the synthesis of bioactive molecules and functional materials. this study contributes to the collective knowledge in the field, serving as a valuable resource for researchers, scientists, and practitioners interested in the synthesis and applications of nitrogen-containing heterocyclic composites. The intricate interplay between nitrogen and heterocyclic structures unveiled in this study not only enriches our understanding of these compounds but also paves the way for future breakthroughs that hold promise for diverse scientific and industrial applications.

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