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A STUDY ON THE SIGNIFICANCE OF SOME FUSED HETEROCYCLES AND USE OF AMMONIUM ACETATE IN THE SYNTHESIS OF FUSED HETEROCYCLES

1. Dhirendra Kumar
2. Rahul Kumar E-mail: dhirendra.kmr10@ gmail.com

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Abstract: ***In this study we have discussed about the Heterocyclic chemistry in which firstly we discuss about the drug discovery and development, significance of some fused heterocycles, biological significance of imidazole[1,2-A] pyridine, use of ammonium acetate in the synthesis of fused heterocycles. Which conclude that derivatives of these heterocycles constitute a major component of many bio-active compounds. These heterocycles are explored for their significant activity against several targets and thus has emerged as a promising area of analysis in the area of medical chemistry and materials science.***

Key words-Fused heterocycles, Ammonium acetate, Imidazole.

The biggest category of organic chemicals is heterocyclic. For a wide range of industrial, medical and traditional uses they are essential. Novel and effective methods of combining new heterocyclics are becoming required. The creation of green technology and environmentally-friendly and competitive solutions is an essential test for the plastic network. Probably the biggest and diverse category of organic chemicals is the delegated heterocyclic compounds. Each carbocyclic compound, with its structure and utility little consideration, may be transformed into a heterocyclic range of analogues at the fundamental level by replacing at least one of the ring carbon molecules with an alternative component. Regardless of whether we limit our thinking to oxygen, nitrogen and Sulfur (the best-known heterocyclic components), there are particular alterations and combinations. Heterocyclic chemistry is an endless source of new molecules, and almost unlimited carbon, hydrogen and heteroatomic combinations may be designed[1]. These make it very easy to understand the enormous dispersion and significance of heterocyclic substances that are composites with the most diverse physical, synthetic and organic characteristics [2]. A study of the preferred natural compounds shows an impressive preference in the formation not of carbon bonds but of carbon heteroatom bonds, certainly not a surprise, because carbon dioxide is the beginning material for nature and most of the reactions occur in water. Condensation polymers of the tiny subunit stitched together by a carbon heteroatom link include nucleic acids, protein and polysaccharides [3].

Heterocyclic compounds are commonly used scaffolds on which pharmacophores are arranged to provide potent and selective drugs [4-5]. This is especially true for five membered ring heterocyclic compounds, which serve as the core compounds of a large number of substances that possess a wide range of interesting biological activities. Among them oxygen, sulfur and nitrogen containing five membered heterocyclic compounds have maintained the interest of researchers through decades of historical development of organic synthesis. The grounds of this interest were their biological activities and unique structures that led to several applications in different areas of pharmaceutical and agrichemical research or more recently in material sciences.

Heterocyclic chemistry: Heterocyclic compounds are the cyclic compounds that contain two or more distinct types of atoms integrated into the ring. There are virtually no limits to the number of potential heterocyclic systems. There are a large number of heterocyclic compounds, and this number is growing fast. There are similarly many literatures in this topic and the latter studies are considerably greater among the three main categories of organic, carbocyclic and heterocyclic chemistry. In Chemical Abstracts, over six million compounds have been documented and almost half are heterocyclic. The heterocyclic molecules, which play a major part in the metabolism of all living cells, are extremely widespread and necessary for existence. A variety of heterocyclic compounds are pharmacologically active, several are regularly used in clinics. Some of them are natural compounds like penicillin and cephalosporin, alkaloids like vinblastine, ellipticine, morphine and reserpine and cardiac glycosides such as digitalis. These are also natural products. However, the vast majority of synthetic heterocyclics, such as anti-carcer, analgesics, analeptics, hypnotic and

Department of Chemistry, ShriVenkateshwara University, Gajraula, Amroha (UP) India

Corresponding Author/Joint Authors

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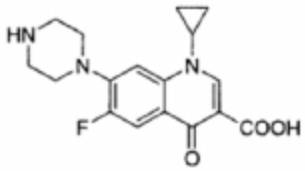
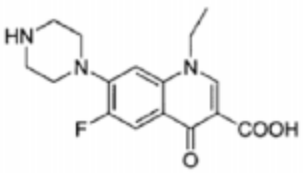
vasopressin agent and pesticides, insecticides, weedkillers, and rodenticides, have been widely used.

There are numerous synthetic, heterocyclic compounds that are essential for various practical uses, such as dyestuffs, copolymers, solvents, sensitizers of photographs and developments as antioxidants and rubber-industrial vulcanization accelerators. Heterocycles, to the delight of environmentalists, are also discovered in fossil fuels. The current fluoroquinolone antibacterial available for widespread usage both at the community level and in the hospital are Ciprofloxacin and Norfloxacin.



Ciprofloxacin



Norfloxacin

The work comprehended in this thesis is based on the nitrogen heterocycles which are exceptionally fruitful.

DRUG DISCOVERY AND DEVELOPMENT- Most cures and elixirs consisted of medicines before the 21st century and only in the mid-19th century tried to isolate and cleanse the various treatment needs the first time (e.g., pure chemicals essential for restorative properties). Other common compounds have been discovered and their shapes established from that point forward (for example, opioid heroin, cocaine since coca leaves, and quinine from the cinchonas tree bark). Such ordinary things began a vast synthetic effort, in which scientists had just created a large number of analogues to improve nature. The findings showed many basic principles underlying drug creation, although many of these activities were done on a foundation of trial and error.

Recently, medicinal chemistry has experienced a revolutionary change. Fast improvement in organic field has contributed to a vastly improved knowledge of the ability of the body at cell and sub-atomic stages. As a consequence, much work in pharmaceutical trade is now beginning to recognize an acceptable goal within the body and to prepare the product to be aligned with that objective. The interpretation of the concept and aspect of the goal is essential to this method and is therefore discussed in the now-target-oriented sense. Of eg, drug metabolism suggests, lethality checking and enhancement of a vast group are generally done on an equal footing. Most equivalent to, the launch and development of another product growing take 10 years or longer, include a combination of more than 10 000 compounds and a local expense of $360 million. We shall now look at each stage in turn.

1. Drug discovery and development - The present- The last several years have seen dramatic changes in pharmaceutical chemistry. Quick advancements in biology have led to a much better knowledge on the cellular and molecular levels of the body's functioning. As a consequence, most pharmaceutical research initiatives start today by finding an adequate target in the organism and developing a medication to interact with it. To this strategy, it is important to know the structure and mechanism of the goal and thus to aim for study.

In general, in drug discovery and drug manufacturing, the following stages may be recognized:

* Select an illness!
* Select a medicine goal
* Determine a bioassay
* Search for a 'lead substance'
* Isolate and cleanse if required the lead compound
* Identify the lead compound structure
* Identify structure - connections of activities (SARs)
* Determine pharmacopoeia
* Enhancing target interactions
* Enhance pharmaceutical properties
* Patent the medication
* Metabolism of the drug study
* Toxicity testing
* Design of a production process
* Conduct clinical studies
* Market the medication
* Make cash!

Many of these stages are concurrently conducted and interdependent. For example, medicaments are usually randomized for drug metabolism, toxicity testing and large-scale synthesis development. However, for the discovery and development of new drugs a synthesis of over 10000 molecules with a total cost of $360 million may need 10 years or more. We turn to each step now.

2. Discovering drug targets- Only if a medication or poison had a biological impact,

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which demonstrated that there is a molecular target could the presence of a medicament target be proven in the past. Consequently, it was first necessary that the identification of pharmacological targets was discovered. Natural compounds from plants were many early medicines. Nevertheless, natural compounds of the plant aren't produced for interacting with a receptor or the enzyme in the human body. Thus, it was a hit and a miss affair to identify pharmacological objectives in this manner. Subsequently, the body's own chemical messengers were found, and the fingers pointed to specific goals.

Nevertheless, very few messengers were found, either because they were in such little quantities because they were too short to be divided. In reality, there still remain many chemical messengers undiscovered. This also resulted in the disguise of many possible goals in body medicine. All of this has changed in molecular genetic development. Different genome studies that map human and micro-organism DNA show a growing number of novel receptors and enzymes that may be future therapeutic targets. Since these targets are also unaware of their natural chemical messengers, medical chemistry faces novel targets for the first time but no leading compounds to interact with them. Since these targets are still concealed. The task now is to discover a chemical that interacts with these objectives, to see what their functions are and whether they are appropriate as pharmacological objectives.

SIGNIFICANCE OF SOME FUSED HETEROCYCLES- Heterocyclic compounds, especially nitrogen heterocycles represent an important class of compounds having a unique identity in area of pharmaceutical research and drug discovery [4]. These are present in many natural products and number of biologically vigorous substances (Figure 1).

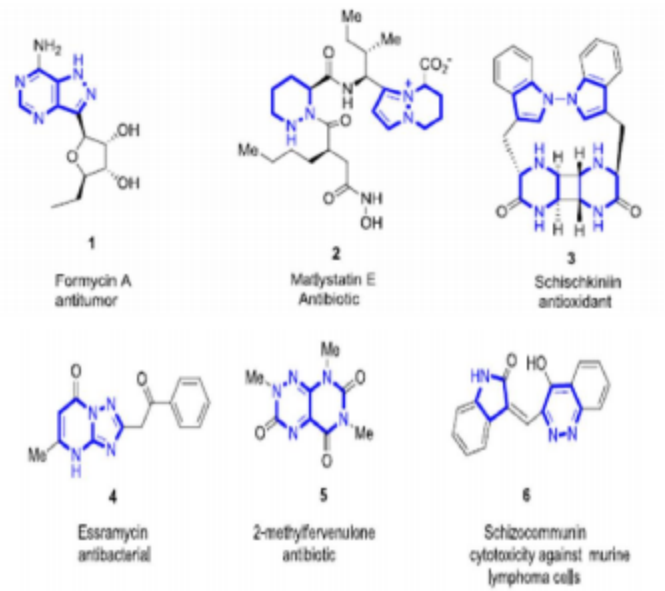

Figure 1: Natural products bearing N-heterocyclic skeletons

Presence of more than one nitrogen atoms in the ring makes the system more stable. In particular, five and six membered fused heterocycles containing more than one nitrogen atom have received considerable attention. These fused aza-heterocycles act as an active core scaffold and has attracted a tremendous attention for their synthesis. Derivatives of these heterocycles constitute a major component of many bio-active compounds. These heterocycles are explore for their significant activity against several targets and thus has emerged as a promising area of analysis in the area of medical chemistry and materials science [5]. A few selected, block buster, marketed aza-heterocyclic drugs are shown in Figure 2

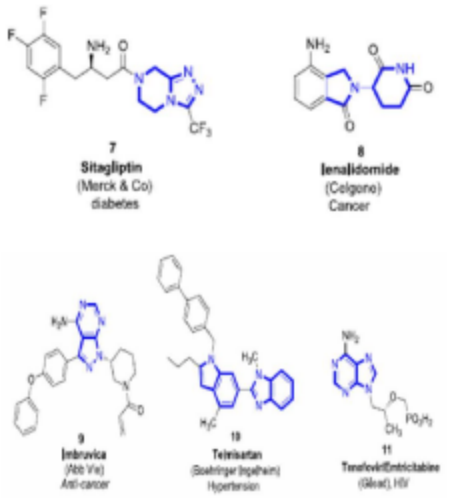

Figure 2: Top-selling marketed AZA-heterocyclic drugs

Owing to the biological significance of fused heterocyclic compounds, we attempted to develop newer synthetic routes to synthesis of imidazopyridine derivatives such as 2-arylamides [1,2-a] pyridines and 2-aroyl-3-arylimidazo[1,2-a] pyridine for their anticancer screening. To get an access to these moieties, Orto leva-King approach has been followed. In this regard, I2-NH4OAc and heterogeneous carbo-catalyst, Graphene

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Vol.-14, No.-III, Issues-21, YEAR- Sept.-2021

oxides were recognized to be the most efficient mediators to achieve their synthesis. Also, the synthesis of 2-amino-3-cyano tetrahydroquinolines and 3-nitro hexahydroquinolin-2(1H)-ones as C-5 curcuminoid analogues for anti-cancer evaluation was successfully achieved.

IMIDAZO [1,2-A] PYRIDINE: INTRODUCTION AND SIGNIFICANCE- The identification and design of novel heterocycles was one of the most important areas of explore in the area of medicinal chemistry. In spite of this, the nitrogen bridgehead fused heterocycles comprising the imidazole ring constitute an important group of molecules known as azaindoles, which has shown to show a broad variety of activities[6].One of the most significant class of heterocyclic systems from AZ indolizines is the imidazole[1,2-a]pyridine which consist of an imidazole ring fused to the pyridine moiety with bridgehead nitrogen atom (Figure 3) [7]. The imidazopyridines 20 and 21have been extensively analysis during to their presence in various pharmacologically important compounds.

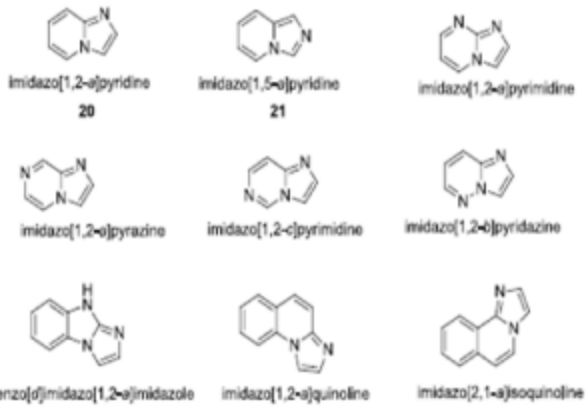
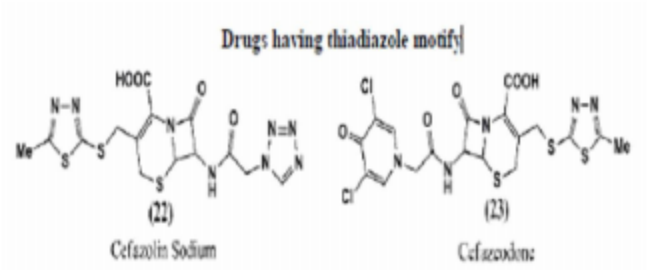
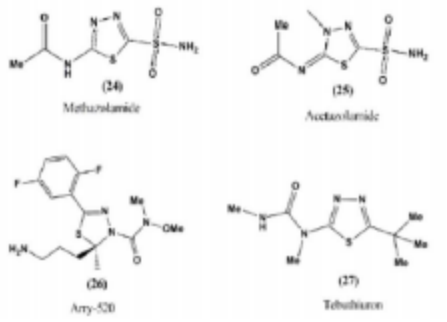
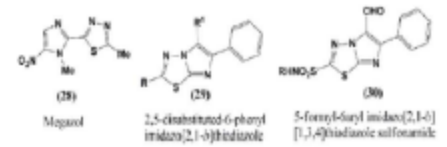


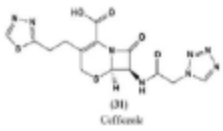
Figure 3: A few imidazole fused heterocyclic systems with bridgehead nitrogen

1. Imidazole [2,1- b] [1,3,4] thiadiazols- From the past few decades, interests of chemists have been on imidazothiadiazole scaffolds and their derivatives as well as with their applications in the chemical and pharmaceutical fields. Some of the drugs available in the market which contains core moiety as thiadiazol and imidazole23-26 are as follows.

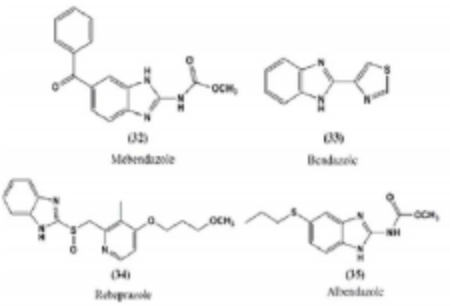




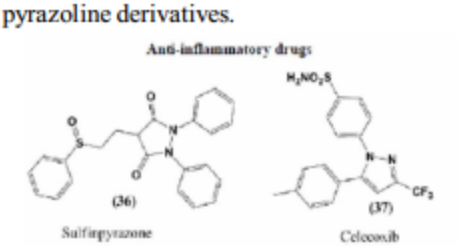




Drugs containing imidazole moiety.



2. Pyrazolines- 2-Pyrazolines are most frequently studied due to their useful synthons in the organic synthesis.27 They display a wide range of pharmacological properties and are present in therapeutically active molecules such as sulfinpyrazone(36), celecoxib(37), famprofazone(38), morazone(39), phenylbutazone(40) oxyphenbutazone(41) (anti-inflammatory), anturane(42) (uricosuric), muzolimine(43) (diuretic), antipyrine (44), aminopyrine (45), dipyrone (46) (antipyretic) etc., attracted the researchers to synthesis of pyrazoline derivatives.



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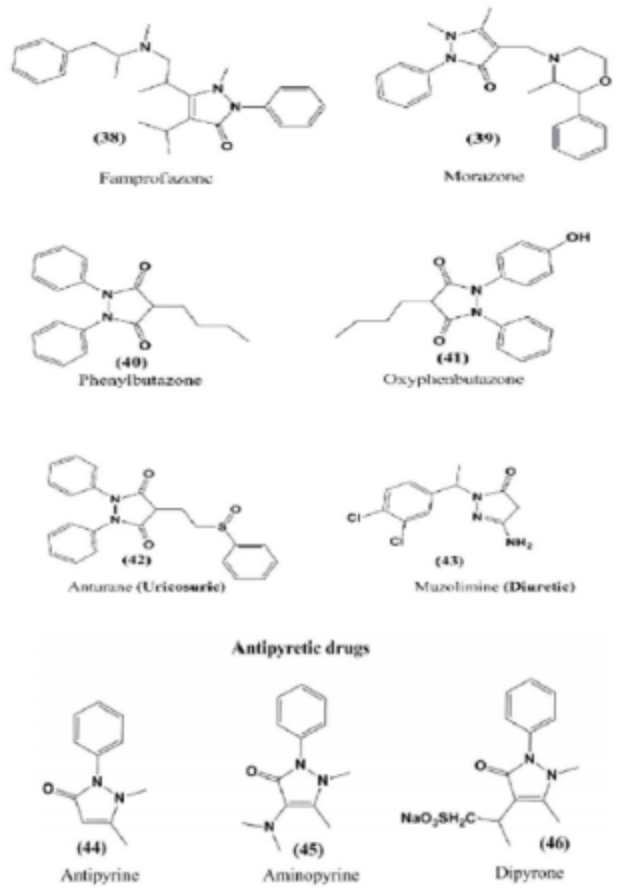

BIOLOGICAL SIGNIFICANCE OF IMIDAZO[1,2-A] PYRIDINE- These heterocyclic scaffolds are now becoming popular among organic and medicinal chemists during its extensive spectrum of pharmacological and biological activities [8] such as antibacterial [9], CDK2 inhibitor[10], anti-inflammatory [11], antineoplastic[12],molluscicide, kinase inhibitor, anti-tubercular, and antiviral activity. The basic unit also exist in mGlu2 receptors GSK812397 (HIV infection) TNF-? inhibitors displays insecticidal activity against pea aphids and also act as PI3K? inhibitors (Figure 4).

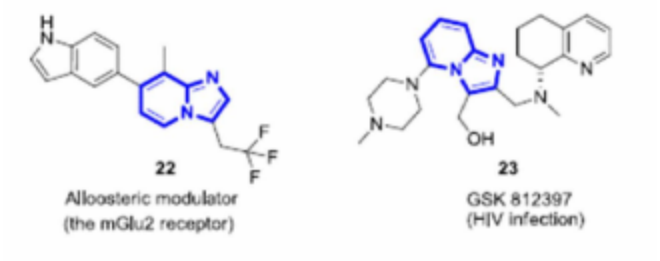

Figure 4: TNF-? inhibitors displays insecticidal activity against pea aphids

USE OF AMMONIUM ACETATE IN THE SYNTHESIS OF FUSED HETEROCYCLES- Ammonium acetate (NH4OAc) is an efficient multi-purpose reagent and displays its versatility in a variety of synthetic organic transformations. It is easily available and biodegradable chemical substance. It plays a promising role in various organic reactions such as Knoevenagel condensation, Hantzsch pyridine synthesis, Krohnke pyridine synthesis, Mannich, 100 etc. Moreover, it has widely been used in the synthesis of N-heterocyclic compounds [12-15].

CONCLUSION- In this study We've studied about Heterocyclic Chemistry, and also, we've discussed about drug discovery and development, the importance of certain fused heterocycles, the biological relevance of imidazole[1,2-A] pyridine, and the usage of ammonium acetate in fused heterocycle synthesis. As a result, derivatives of these heterocycles are found in a wide range of bioactive chemicals. These heterocycles are being investigated for their potent action against a variety of targets, and have therefore emerged as a potential topic of research in medicinal chemistry and materials science.

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