



FUSED HETEROCYCLE COMPOUND OF PYRIDINE: - RECENT ADVANCES IN BIOACTIVE ANTI-INFLAMMATORY DRUG DISCOVERY

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Abstract: -

Heterocyclic compounds are basically cyclic compounds which are also called as ring structural compounds. These compounds contain ring with carbon and atoms of atleast two different or more than two elements. Compound may also include oxygen, nitrogen, and sulphur. Heterocyclic is one of the major branches of chemistry mainly organic chemistry. Which deals with the synthesis properties of their heterocycles. Some or all the atoms in their molecules are joined in ring, The most common cycles contain five or six atoms. Some are 3- membered, 4 membered, 5 membered, 6membered heterocyclic compounds. Some are condensed or fused

heterocyclic compounds. As per their primary classification they are saturated and unsaturated in nature. These heterocycle compounds include many of the biochemical material essential for life. The best known of the simple heterocyclic 5 compound include Pyridine, Pyrrole, Furan, and thiophene. In this present paper we will focus on the structure synthesis, role properties and application of fused on the structure synthesis role properties and application of fused pyridine compound and its advances in anti-inflammatory.

Keywords: - Heterocyclic, Pyridine, Ring, Chemistry, Pyrrole, Furan

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Introduction: -

Heterocyclic compounds play an important and very chief role in medical chemistry. A six membered heterocyclic compound, Pyridine, Possess various application which prove to be very fruit full in agrochemicals and Pharmaceuticals¹.

Pyridine is basic heterocyclic organic compound with the chemical formula C₅H₅N. It is considered highly flammable and miscible liquid. Pyridine easily dissolves in other substances. So it is used in products like dyes medicine food flavouring and various insecticides and pesticides. Common name of pyridine is replaced by a nitrogen action. The newly studies showed that pyridine show anti-inflammatory properties².

Inflammation occurs due to injury of any tissue in body or any infections (Bacterial, Viral, Allergies etc). This risk of inflammation poses a great challenge to the medicinal chemists to search for effective anti-inflammatory agents. Various Pyridines containing anti-inflammatory agents are being reported it produces a slight fall in the tension of directly stimulated muscles. It enhances the muscle response to neurotransmitter i.e., acetylcholine with nucleophiles pyridine reacts at position 2 and 4 and thus behaves similar to imines and carbonyls. The reaction with many Lewis acids results in the addition to the nitrogen atom of pyridine. Pyridine acts as nucleophile for the carbonyl group due to its lone pair of electrons on nitrogen atoms which can be delocalized in its rings³⁻⁶. So, it acts as a catalyst. Pyridine is a nucleophile for carbonyl groups and is often used as a catalyst in acylation reaction.

Properties of Pyridine: -

Its Physical Properties include: -

1. It is a diamagnetic with diamagnetic susceptibility.
2. It has a thermal conductivity.
3. Pyridine is conventionally detected by the gas chromatography and mass spectrometry method.

Pyridine based ring system are one of the most extensively used heterocycle in the field of drug design. The remarkable therapeutic applications have encouraged researchers to prepare a larger number of biologically active compounds decorated with pyridine. The present of pyridine have a substantial impact on pharmacological profiles of drugs and bioactive molecules. Its applications are very vast it acts as a bioactive compound⁷⁻¹⁰.

Pharmacology of Pyridine: -

Pyridine has nicotine like properties it is a depressant of many tissues and it is also depress the central nervous system. Pyridine and its derivatives have both medicinal and non-medicinal uses. Pyridine and its derivatives also have increasing important for modern medicinal application¹¹. There are lot of medicines which consists of pyridine ring system compounds which contain Pyridine are mostly calcium channel blockers. Heterocyclic compounds waves into basic processes of life and play a crucial role in pharmaceutical and agrochemical industries¹². In pharmaceutical targets pyridine and its various precursor have a prevalent and important structural unit¹³.

In recent synthetic chemist have been focusing on developing new analogues that employ pyridine. A pyridine in a drug improves its biochemical potency as well as metabolic stability pyridine contain tosemide which it an FDA approved drug that promotes diuresis and present in Lowering the BP of the patient. It also contains beta – adrenergic blockers which help in managing hypertension and save the patient from heart attack¹⁴⁻¹⁸.

Mostly Pyridine possesses antimicrobial, antiviral, anticancer, antioxidant, antihypertensive, antimalarial, and anti-inflammatory activity. When a pyridine reacts as a base or a nucleophile if forms a pyridinium cation in which the aromatic sextet is retained and the nitrogen acquires a formal positive charge. Acetaldehyde and formaldehyde are combined with ammonia to make pyridine with a chemical formula C₅H₅, Pyridine is a colourless to yellow liquid heterocyclic compounds. Pyridine is the hydrogen derivative of this ring. Pyridine nitrogen pairs are delocalized so they are more basic than dimethylamines¹⁹⁻²⁰.

The invitro anti-inflammatory activity of this compounds and its derivatives was evaluated by denaturation of the bovine serum albumin method and showed inhibition in the range of IC₅₀ values. A detailed synthetic process for the target compound is given below²¹.

Initially 3-cyanopyridine was converted to pyridine 3-carbothiamide by treating with P4S10 compound. Inflammation is a biological response that take place when any healthy tissue gets injured by any means (either pathogen are accidentally). The leading cause of inflammation is the alteration of the native states of the tissue proteins. In in-vivo studies the denaturation of proteins takes place because of the synthesis of autoantigens and a compound which inhibit denaturation are potentially useful for the discovery of an anti-inflammatory drug²².

All the thiazole synthesized hydrazide derivatives were tested and evaluated for their in vitro anti-inflammatory activity by inhibiting protein denaturation methods. The compound containing heterocyclic rings showed better inhibition as compared to other compounds²³. So pyridine and its compounds exhibit good inhibition of the bovine albumin. Pharmacokinetic study also evaluate that the active compound of heterocyclic are better absorption distribution metabolism and eliminating profile (especially Pyridine)²⁴.

Pyridine and its derivatives possess tremendous application in various field are discussed previously. The molecules of pyridine are planer in nature and follows Huckle criteria for aromaticity. The pyridine derivatives give different bands of characters. Which make them unique and effective in curing and treating various health issues²⁵.

The pyridine containing benzo-thiazolyl amino group substituted at position 2 and carboxylic functionality are synthetic derivatives and have been checked for their various biological activities²⁶.

Structural Characteristics of Pyridine: -

Pyridine is considered as an aromatic compound have five carbon atoms and one is nitrogen atom. Pyridine is basic in nature as it consists a nitrogens lone pair of electrons. Pyridine can be represented well as a resonance hybrid of the following structure²⁷.

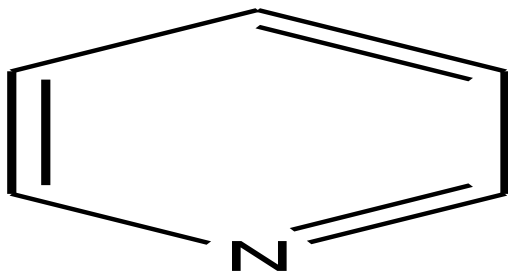


Fig:-1

Some of the chemical activities of pyridine are explained below: -

1. It Show reaction with oxide of sulphur with the participation of heteroatom.
2. Reaction with electrophilic substitution for the hydrogen atoms of pyridine ring.
3. It also show reaction with Nucleophilic substitution. Example of this is animation of pyridine with sodium of amide on chy chybabyne
4. It undergo reduction as well as oxidation²⁸.

Synthesis of Pyridine and its derivatives: -

Pyridine was very firstly synthesized by William Ramsay in 1876 by combing acetylene and hydrogen cyanide, A furnace tube (iron) was used

to take out this procedure. Now a day several methods are there for its synthesis:

Some of these includes:-

1. Synthesis DMPA²⁹
2. Synthesis of Pyridine- Quinoline hybrid etc.

Uses of Pyridine³⁰: -

1. It act as a best solvent.
2. It act as a catalyst
3. It is helpful in denaturing alcohol
4. It is helpful in preparing various drugs

Medicinal compounds³¹⁻³²: - Various medicinal compounds possess by pyridine heterocyclic ring system.

1. Isoniazid
2. Nikethamide
3. Nicotinic acid
4. Mepyramine
5. Benzhexol

1. Isoniazid: - It is an antitubercular drug. It is effective against pulmonary and extrapulmonary tuberculosis.

2. Nikethamide: - It is used in the treatment of central nervous system depression caused by drugs.

3. Nicotinic acid: - It is available as biologically active amide derivative. Nicotinamic exist in human and animals tissues as coenzyme NAD and NADP.

4. Mepyramine: - It is used for symptomatic relief of hypersensitive reactions.

5. Benzhexol: - Used in treatment of Parkinson's.

Basicity of Pyridine³³: -

Pyridine behaves as a base, It reacts with acid to form stable salts. It reasons behind its basic character is lone pair of electron being in SP² hybrid orbital is not involved in the formation of the delocalized π molecular orbital. It is readily available for the formation of the new N-H bond with proton.

Inflammation:- It is response to stimulation by pathogens or any internal signal of body like damage tissue/cells that are in need of repairs. Each tissue exhibits distinct characteristics of inflammation due to general and local molecule processes. Inflammation is essential for efficient immunity. Physiological inflammation is self-limiting and self-regulated. It is considered as the first response of living tissue³⁴.

Inflammation is referred to didactically as acute when it lasts 2 days or 3 weeks and as chronic when more prolonged acute inflammation on is characterized by vasodilation. The immune response obtains partially by the synthesis of small

cytokines called chemokines with chemokine receptors without which the cells would never respond. As it can be dangerous if occur for more than weeks so there should be a need of the development of anti-inflammatory drugs. Thus, we need to apply natural anti-inflammatory factors with in medication therapy to achieve good response with lower degree of unwanted side effects. So pyridine as its derivatives were considered a good source of this which act as a P38a/ MAPK14 inhibitor as it is a intracellular signalling regulator involved in biosynthesis of inflammatory mediator cytokines. Which include the production of inflammatory proteins. Pyridine were efficiently prepared under microwave irradiation in one pot reaction and their anti-inflammatory activities were evaluated³⁵. Fused pyridine heterocyclic ring derivatives are mostly used in drug research due to their vastness of the chemical space and fused pyridine derivatives its imidazopyridine rings isomers expressed several positive modulations of receptor, Positive glutamate receptor 2as anti-inflammatory activity. Pyrazolo Pyridines was reported firstly by Englert and Mc Elvain were considered as anti-inflammatory agents. So, it is not wrong to say that fused five membered pyridine hetero aromatic rings are privileged in medicinal chemistry with lot of activities including anti-inflammatory activity. There are several drugs containing those heteroaromatic rings on the market and several phase trails were going on various other compounds with similar chemical similarities³⁵.

Conclusion:-

Pyridines are very important in medicinal chemistry and play a key role in biological field because of its various properties. Pyridine as well as its derivatives are very important there compounds share on important part. In recent as well as in previous years. Pyridine and its derivatives have been developed based on structural modification with other compound for attractive properties and biological activities. A deep look in the structural analysis of pyridines give us a base for all the building blocks derived from it and its applications. It is found in various natural products such as vitamins, alkaloids, Drug etc. Drugs containing pyridine have wide spectrum of application in pharmaceutical field which are pharmacologically as well as biologically active in nature and is used in treatment of various diseases. On the basis of above studies. Pyridine derivatives show various activities like anti-cancer, anti-microbial, anti-viral, anti-inflammatory and the possible improvement in its activity can be further

modified. Thus Pyridine has been long focused and chosen for research purpose in the field of Pharmacology/ medicine due to its tremendous activities exhibited by its derivatives.

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