A Review on PYRIDINE Derivatives "Potential for Analgesic & Anti-inflammatory Activity"

[1]Preeti Avasthi, [2]Rishu Yadav,[3]Arvind Kumar,[4]Monika Rana

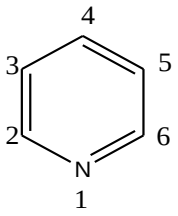
Assistant Professor
School of Pharmacy
Maharja Agrasen University
Baddi, Solan, H.P. India.

Abstract- **Pyridine derivative are shown to be having good biological activities for the prevention, treatment and cure of humans or animal diseases. Pyridine derivatives have good activity as analgesic and anti-inflammatory agents. Pyridine reacts with different compound and produced new products that give different activity. Therapeutically usage of these clinically useful drugs in the treatment of pain and inflammation encouraged the development of some more potent and significant compound. Pyridine derivative gives biological activity such as Analgesic, anti-inflammatory, anticancer, anticonvulsant, antiviral, antimicrobial, antifungal, antiulcer etc. Honoor et al. synthesized a compound pyridine-2-ethyl-(3-carboxylideneamino)-3-(2-phenyl),-1, 2-dihydroquinazolin-4-one and shown it to be having good analgesic activity. Reetu and Vipin Kumar *et al*. synthesized fifteen 2-(arlyimino)-5-(pyridine-2-yl methyl)-1, 3-thiazolidine-4-one derivatives as anti-inflammatory activity. These are some of the examples included in this review.**

Index terms: **Pyridine, Analgesic, Anti-Inflammatory**

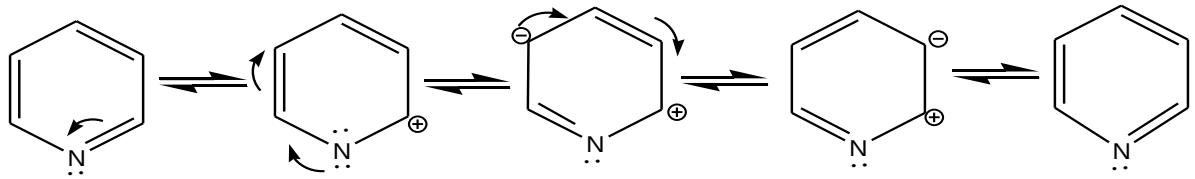
I. INTRODUCTION

Pyridine ring is having six-membered heterocyclic ring consisting of five carbon atom and one nitrogen atom. Pyridine was first isolated and characterized by Anderson (1846). It was obtained from bone oil and coal tar. The cyclic nature of pyridine was given by Dewar and Korner in the year of 1869.(1-2). The hybridization of pyridine is sp^2. The third sp^2 orbital on each carbon atom overlaps with s-orbital from hydrogen to form the C-H sigma bond ; the third sp^2 orbital on nitrogen is occupied by the nitrogen lone pair electrons.(3-4) All sigma bonds in pyridine lie in one plane.The chemistry of pyridine can be divided into two category: reactions at the ring-atomic centres, and reaction at substituent attached to the ring-atomic centre.(5)



PYRIDINE

Pyridine shows some aromatic properties because the resulting molecule orbital satisfies the Huckel's rule (n= 1in 4n+2), according to the resonance theory pyridine is considered to be hybrid of the following five contributing structure.(6)



The nitrogen atom on pyridine features a basic lone pair of electrons. Because this lone pair is not delocalized into the aromatic pie system, pyridine is basic with chemical properties similar to tertiary amines.(7-8) Pyridine is protonated by reaction with acids and forms a positively charged aromatic polyatomic atom called pyridinium.(9) In organic reaction pyridine behaves both as a tertiary amine undergoing protonation, alkylation, acylation and N-oxidation at nitrogen and as an aromatic compound undergoing nucliophillic substitution .It is easily susceptible to alkylating agents to give N-alkylpyridinium salts.(10-11)

Physically pyridine is organic base; flammable, soluble in water, alcohol, benzene, and ether; burning taste; boils at 116^0C . In many enzymes, the prosthetic pyridine nucleotide (NADP) is involved in various reduction-oxidation reactions.(12-13)
Pyridine derivatives continue to attract great interest due to the wide variety of interesting biological activities observed for pyridine derivative, such as anticancer, analgesic, antimicrobial, and antidepressant, activities. Pyridine is used in the pharmaceutical industry as a raw material for various drugs, vitamins, and fungicides (14-15)

Pyridine is a heterocyclic organic compound with the chemical formula C_5H_5N. It is structurally related to benzene, with one CH group replaced by a nitrogen atom. It is used as a precursor to agrochemicals and pharmaceuticals and is also an important solvent and reagent. Pyridine was first isolated and characterized by Anderson in 1846. It was obtained from bone oil and from coal tar. The cyclic nature of pyridine was recognized by korner and dewar in 1869[2]. In many enzymes of living organisms it is the prosthetic pyridine nucleotide (NADP) that is involved in various oxidation-reduction processes. Other evidence of the potent activity of pyridine in biological system is its presence in the important vitamins niacin and pyridoxine and also in highly toxic alkaloids such as nicotine.(16)

The present work is to design and synthesize some new pyridine derivative bearing pyridine moiety at main position, evaluate their biopotentialmand also perform docking studies against COX-2 receptor.(17)

Non-steroidal anti-inflammatory drugs(NSAID's) are the most widely used therapeutic agents , for the treatment of pain and inflammation for decades(18). In general, long term clinical usage of NSAID's is associated with significant side effect of gastrointestinal lesions, bleeding and nephrotoxicity . Therefore the discovery of new safer analgesic and anti-inflammatory agents represents a challenging goals for such a research area.(19)

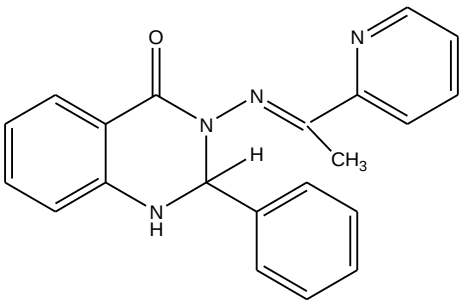
II. USES OF PYRIDINE

It have been widely used as solvents in organic chemistry and with increasing frequency, in industrial practice.(20)Pyridine itself is a good solvent that is rather unreactive. The basic nature of pyridine makes them ideal acid scavengers.(21) Typically pyridine is the solvent of choice for acylations. Furthermore dehydrochlorination reactions and extraction of antibiotics, pyridine is an excellent solvent. Large amount of pyridine are used as the starting material for agrochemical and pharmaceutical. For example, pyridine is a precursor for herbicides and antifungal agents such as zinc salts of pyrithione.(22)

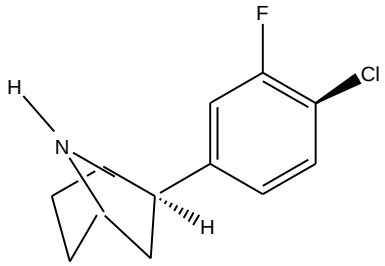
III. PHARMACOLOGICAL AND BIOLOGICAL EVALUATION

A. ANALGESIC ACTIVITY:

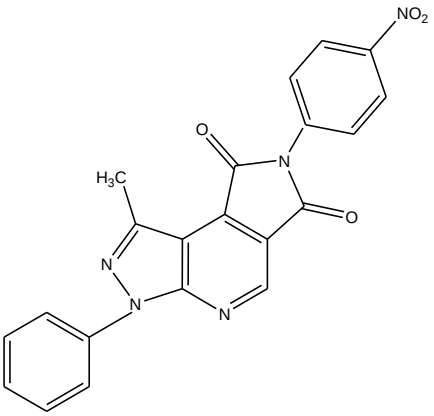
- Hoonoor *et al* synthesized a compound pyridine-2-ethyl-(3-carboxylideneamino)-3-(2-phenyl),-1,2-dihydroquinazolin-4-one coordinated metal complex, and characterized by single crystal X-ray diffraction. The analgesic activity was determined by acetic acid-induced writhing test in mice. They demonstrated the copper complex showed significant dose-dependent inhibition mediate by inhibition of peripheral mechanism of nociception.(23)



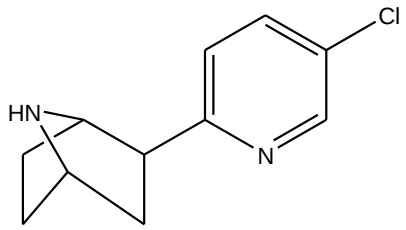
- Galya *et al* performed pharmacologically screened the selectivity and efficacy of 3-fluro substitution in the pyridine ring of epibatidine, which confirmed an increased efficacy and selectivity.(24)



- Menegatti *et al* synthesized four pyrazolo[3,4] pyrrolo[3,4-d] pyridine derivatives from the lead compound zolpidem. The potent cetral acting analgesic archetype compound LASS BIO-873 was obtained by isosteric modulation on the lead and the activity of resulted compound was reliant on the modulation of opioid receptors.(25)



- Baraznenok *et al* synthesized some new compounds analogous to epibetidine (1)and tebanicline (2), and evaluated the analgesic activity in mouse. The R-isomer of compound 3 gave useful results indicating that R-5 have favorable analgesic activity.



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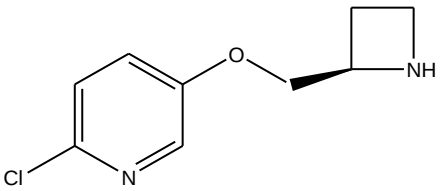

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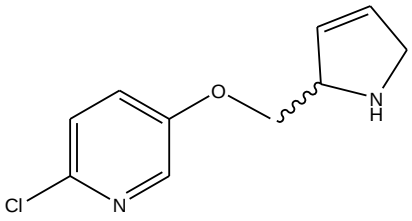

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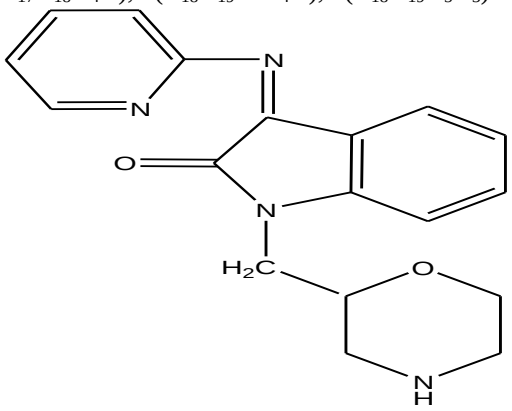
- Ajit kumar chaubey *et al* synthesized a series of some new pyridine containing compound were screened for analgesic activity. These synthesized pyridine containing compounds show activity against using both central analgesic and peripheral analgesic assays. these compounds are 1($C_{17}H_{18}N_4O$), 2($C_{18}H_{19}BrN_4O$), 3($C_{18}H_{19}N_5O_3$):



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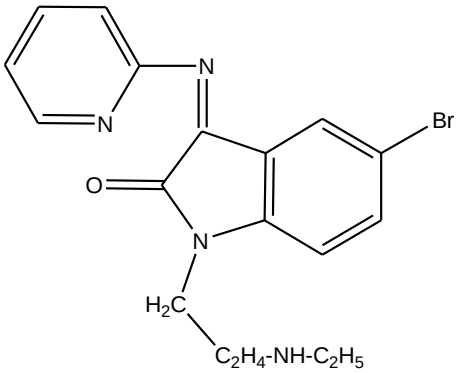

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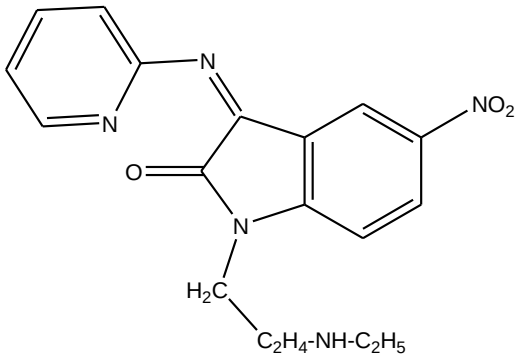

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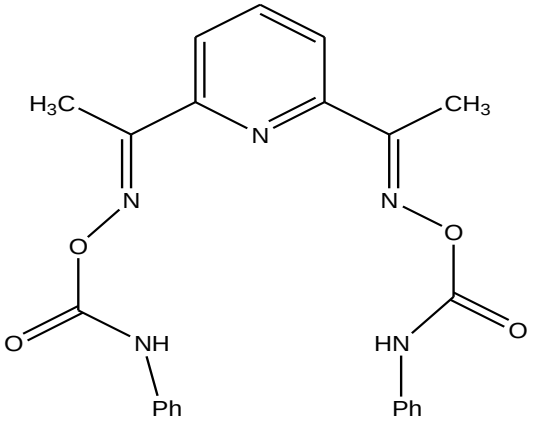
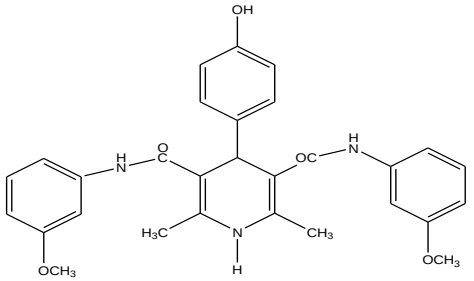
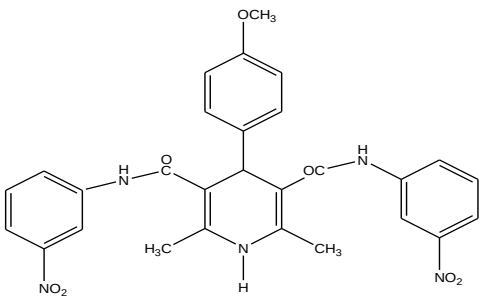
- Abdel-Galil E. Amr *et al* synthesized some chiral macrocyclic pyridine derivatives and performed the analgesic activity. The synthesized product 2,6-bis-(phenylcarbazide) pyridine and other derivatives shows the analgesic activity:



- S Venkataraman *et al* synthesized various new compound containing pyridine moiety to give analgesic activity. Compound names 4-(4-hydroxy phenyl)-1,4-dihydro-2,6-dimethyl N,N,bis(4-methoxyphenyl)pyridine-3,5-dicarboxamide (PAH) and other is 4-(4-methoxy phenyl)-1,4-dihydro-2,6-dimethyl N3,N5, bis(m-nitro phenyl)pyridine-3,5-dicarboxamide(MNA) were prepared. The derivative shows analgesic activity and that are:



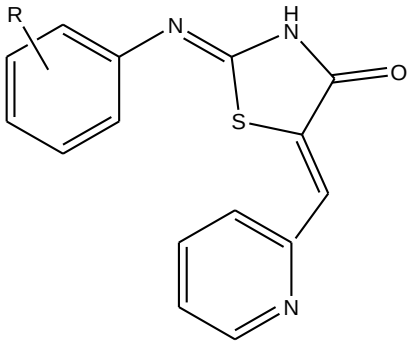
PAH



MNA

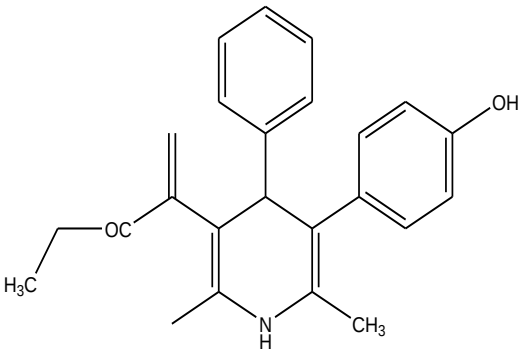
B. ANTI-INFLAMMATORY ACTIVITY (26-27)

- Reetu and Vipin kumar *et al* synthesized several of pyridine containing compound that showed analgesic activity. In this synthesis some new thiazolidin-4-one derivatives bearing pyridine moiety at position -5,evaluated for their biopotential and were performed docking studies against COX-2 receptor that leads to inflammation. They gives 15 new 2-(arylimino)-5-(pyridine-2-yl methyl)-1,3-thiazolidine-4-one derivatives as anti-inflammatory activity and they are:



R= Aniline, o-toluidine, 2-bromoaniline, 2-chloroaniline, o-nitroaniline, 4-fluroaniline, m-nitroaniline. These compound shows analgesic and Anti-inflammatory.

- G.Swarnalatha *et al* synthesized some new compound pyridine moiety with 1,4-dihydropyridine a multifunctional molecule. These 1,4-dihydropyridine derivativeswere found to possess analgesic and anti-inflammatory activity and the compound have almost equipotent activity. That compound are:



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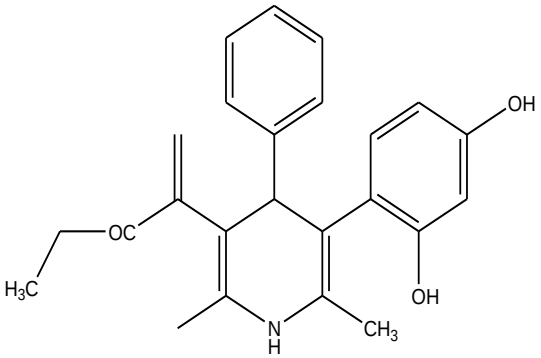
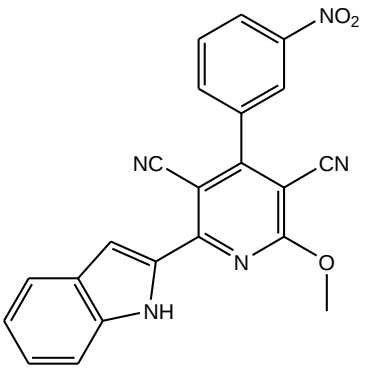


2

- Prakasam Thirumurugan *et al* synthesized several of compound containing pyridine moiety and that were 3-indolyl pyridine derivative in better yields via one pot multi-component reaction. These compounds showed good anti-inflammatory activity in comparison with the standard drug. These synthesized product name nidol-3-yl-pyridine and 2,2'bipyridine derivative(1 to 4) and these are as follows:



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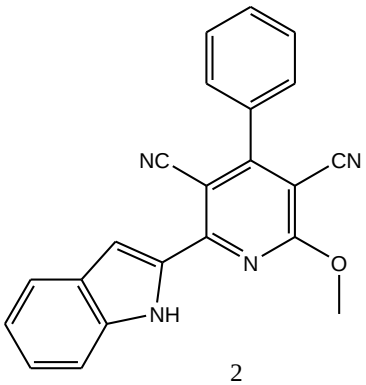

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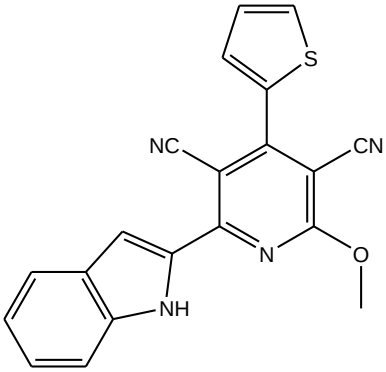

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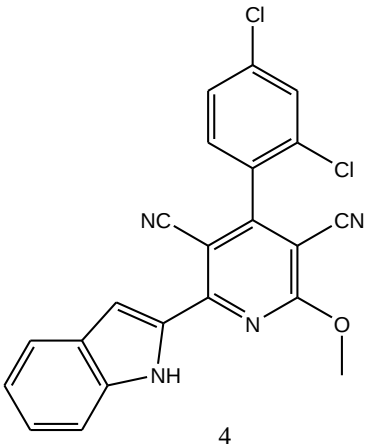
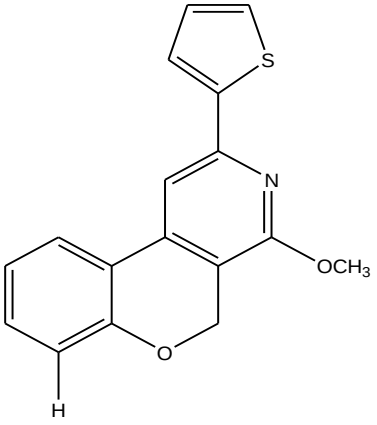


4

- Hanaa M. Hosni *et al* synthesized various of compound for shows its anti-inflammatory activity. These compounds are having pyridine moiety and compounds are pyridinedicarbonitrile and benzopyranopyridine derivative(1 to 6). A number of compound synthesized for these activity contain pyridine moiety. These compounds are:



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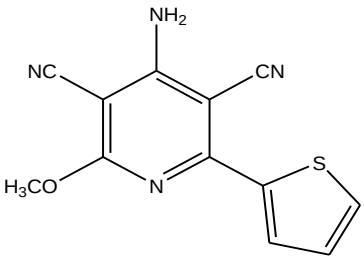

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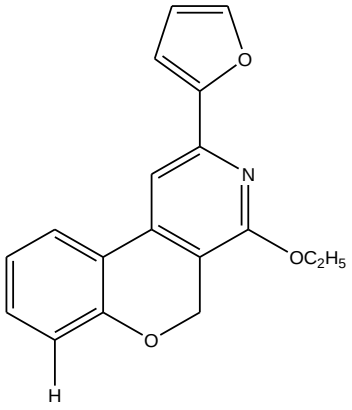

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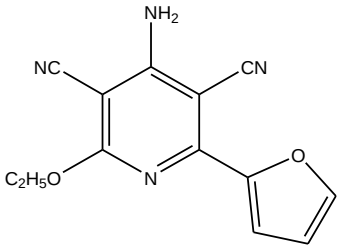

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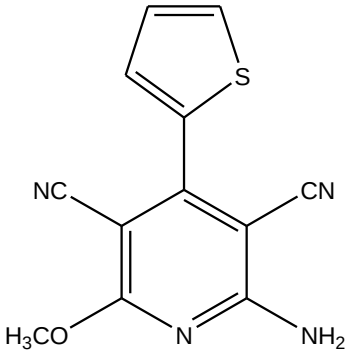

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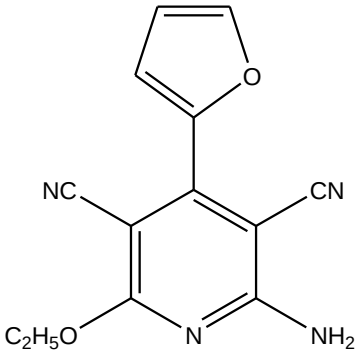

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Conclusion:

Pyridine is a six membered compound that associated with several of pharmacological and biological activities. This review highlight the work of many researchers regarding pharmacological activities on pyridine derivatives. The review has presented comprehensive details of pyridine and its analgesic activity and anti-inflammatory activity has reported.

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