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PHARMACOLOGICAL ACTIVITIES OF ISOXAZOLE DERIVATIVES

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ABSTRACT:

The substituted isoxazoles are well developed in literature to posses significant biological activities .The Di – substituted and tri- substituted isoxazoles have been reported to exhibit broad range of biological activities such as Anti-oxidant, Antimicrobial, Immunological, Anti-Nosciceptive, Anti-Cancer, Anti platelet Analgesic and Miscellaneous activities like acts on human β-Adrenergic receptor etc. The present review explains substituted isoxazoles with potent biological activity.

KEY WORDS: Isoxazoles, Pharmacological activities, Antioxidant, Antimicrobial, Anticancer.

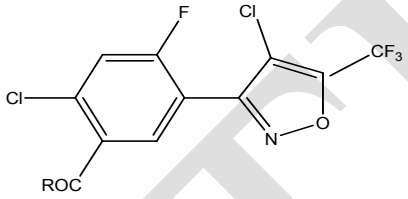
INTRODUCTION:

Isoxazole is an azole with an oxygen atom next to nitrogen. Isoxazole rings are found in natural products like ibotonic acid .These are also forms the basis for a number of drugs like cox-2 inhibitor, nitric oxide donor – furaxan etc.A highly appreciable number of five membered heterocycles containing nitrogen atom and oxygen atoms obtained by laboratory synthesis. Which are having potential therapeutic and pharmaco tharapeutic activities. Some of useful synthetic analogues with improved therapeutic activity can be obtained from single lead compound by structural modifications .A lot of modifications have been done during the last few years on Isoxazole nucleous . A survey of literature revealed that substituted isoxazolesposses different types of potent biological activities.

HERBICIDAL ACTIVITY[1-4]:

Yuttanzhou et al synthesized some new three (substituted phenyl) isoxazole derivatives and subjected them for herbicidal activities which are having property of inhibiting the porphyrinogen oxidase. Many researchers have studied on three compounds having high bioactivities and reported. And some of them have been commercialized such as JU-485 and KPP-314 which are substituted phenyl isoxazoline derivatives.

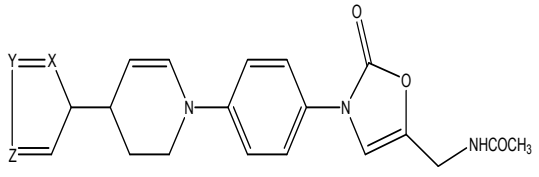
In this several novel-3(substituted phenyl) isoxazole derivatives are synthesized and exists herbicidal activities towards various weeds like Echinochloa, Crusgalli, Setaria Viridis, Abutilon theoprastil.



R - OCH_3
-OC2H_5
-NHC_6H_5
-$N(C_2H_5)_2$

ANTIOXIDANT ACTIVITY, ANTI BACTERIAL AND ANTI MICROBIAL ACTIVITY[4-7]:

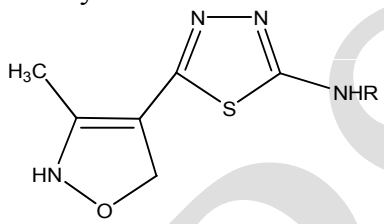
P.Manoj kumar Et.al synthesized some new series of 1-isonicotinyl 3,5 dimethyl-4-arylazo isoxazoles which shows Antioxidant Antibacterial and Antimicrobial activities against staphylococcus aureus and E.coli and antifungal against candida albicans. The antioxidant activity is compared with standard drug ascorbic acid and the activity is done by DPPH method.



X- C or O
Y- N or O
Z- C or N

IMMUNOLOGICAL ACTIVITY:

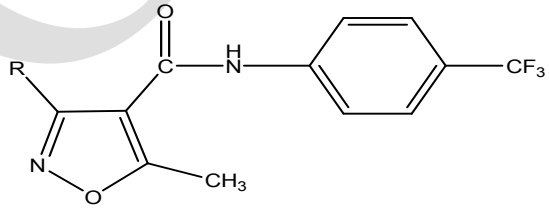
Stanislaw ryng and Michael zimeki synthesized some new derivatives of isoxazoles including 4-substituted 3(5 amino 3 methyl 4 isoxazole) 1, 2, 4-triazoline-5-tione and 5-substituted 2(5 amino 3 methyl 4 isoxazole). 1, 3, 4 tridiazole derivatives which shows immuno modulatory activity. The compounds were tested for their ability to affect the proliferative response of moule sphlenocytes to conconavalin (A) and secondary humoral immune response of sphlenocytes to sheep red blood cells measured as the number of antibody forming cells and Cyclosporine A served as a reference compound



R- Aliphatic,Aromatic

INVITRO METABOLISM STUDIES ON ISOXAZOLE RING SCISSION[8-10]:

Amit S.kalgutkar, Hang T.Nguyen et.al suggested that the lack of isoxazole ring opening in 3-methyl leflunamide strongly suggested that the hydrogen at 3-leflunamide is essential for ring opening. In an attempt provide further evidence for P-450 mediated deprotanation of the C-3 hydrogen in the leflunamide. So they examined the possibility of C-3 hydrogen/deuterium exchange in leflunamide/recombinant P-450/A_2 incubated in phosphate buffer. The P-450 mediated isoxazole ring opening in a leflunamide is also catalyzed by the Fe (11) form of the enzyme, recombinant P450A/A_2 incubations conducted in the presence of NADPH. Under anaerobic conditions and also in the presence of carbon monoxide. The presence of molecular oxygen in the incubation mixture greatly inhibited the formation of A77172.

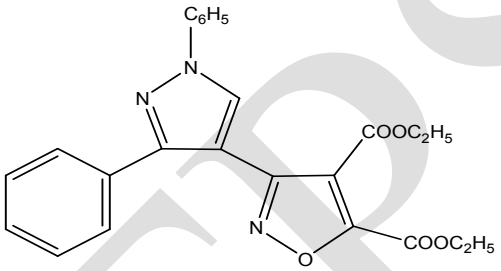


R - H Leflunamide
R -CH_3 Methyl Leflunamide

ANTI NOCICEPTIVE ACTIVITY OF PYRAZOLYL ISXAZOLES[11-13]:

K.Karthikeyan, T.veenuseelan et.al was developed a systematic procedure for the synthesis of pyrazolyl isoxazole and they performed the activity of anti nociceptive action by using various animal tissues.

The lead molecule was synthesized by using 1, 3 dipolar cyclo addition of pyrazole derived nitric oxide with various dipolarophiles such as N-substituted maleimide, diethyl acetylene dicarboxylate and phenyl acetylene. The given structure of synthesized pyrazolyl isoxazoles shows maximum anti nociceptive activity.

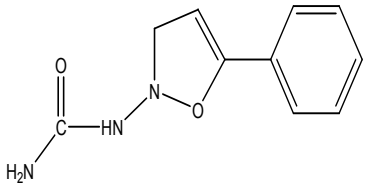


ANTI CANCER ACTIVITY[14-16]:

The novel compound (5, R) 3-phenyl 4,5 dihydro 5 oxazole acetic acid-nitric oxide shows anti cancer properties, *Invitro* and in *Invivo*. The preclinical studies revealed that nitric oxide donating NSAIDs also possess the anticancer properties.The nitric oxide scavenges hemoglobin completely prevented GIT-27NO induces death indicating that 'NO' released mediated the humoricidal effect of the compound increased in intracellular NO upon the treatment was associated with infantilized production of reactive oxygen species. The antihumoral activity of drug was mediated by the selective activation of nitrogen-activated protein kinase in a cell specific manner and neutralized by the specific inhibitors. In vitro treatment with GIT-27NO significantly reduces the B-16 melanoma growth in syngenic C57BC16 mice. The compound was synthesized by Daniela Maksimovic-Ivanic et.al. Some of the 1, 2 benzisoxazole phosphorodiamidalis are also acts as anticancer drugs which are novel and require prodrugs for the bio reductive activation.

ANTIBACTERIAL ACTIVITY[17]:

The isoxazolyl tetrahydropyridinyl oxazolidinones and their substituents show the antibacterial activity. The in vitro antibacterial activity of synthesized compound was evaluated by using several gram positive stains include staphylococcus and enterococcus and vancomycin, linezolid are reference compounds. Some of the isoxazole derivatives of ampicillin like 5-arylisxazole-7-carboxamide also show antibacterial activity which acts against gram negative bacteria and pseudomonas bacteria. This character is due to having hydrophobicity.



ANTIPLATELET ACTIVITY[19]:

Xue CB, Roderick J synthesized the novel isoxazole derivatives which show Antiplatelet activity. The Antiplatelet activity of labeled isoxazole derivative is due to glycoprotein 2b/3a antagonistic mechanism. The synthesized isoxazole derivative show high antiplatelet activity in dogs

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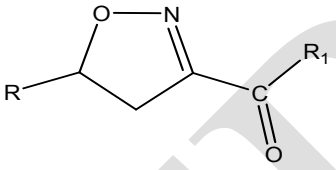
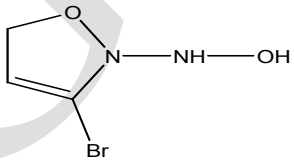


R - Aryl or Alkyl
R_1 - Alkyl or Benzyl

ACTIVITY ON HUMAN B-ADRENERGIC RECEPTORS[20-21]:

The three pairs of stereo isomeric 3-bromo isoxazolyl amino alcohols (S,R), -(-)-7a, (R,R)-(+)7b, S,R-(_)-8a, (R,R)-(+)-8b and S,R-(-) 9a/-(+)-9b were synthesized by clelia Dallonoce, Fabiofregerio and the labeled compounds shows the effect on B_1,B_2,B_3 adrenergic receptors. They possess high affinity and efficacy towards the adrenergic receptors. The activity was performed by using Chinese hamster ovary.

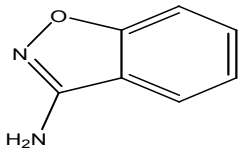


ANALGESIC AND ANTIMICROBACTERIAL ACTIVITY[22]:

The labeled compound of 4-(5^1 substituted- aryl-4^1, 5^1 dihydro-isooxazole-3^1-4^1 amino) phenols have the property of both analgesic and antimicrobial activity. The analgesic activity of synthesized compound was observed with the reference compound paracetamol where as antimicrobial activity was done by using reference standard ciproflaxin and antifungal activity was done by using clotrimaxazole as reference. The 4-chloro phenyl substitution at 5 position of isoxazole ring was found to be most potent compound.The activity of drug is done by using bacteria B. Cirroflagiellusus and E.coli and P.putida and the fungi C.albicans A Niger and Wamari. The compound was synthesized by SK.Sahu M.Banerjee et.al.

MISSCELLANEOUS ACTIVITY[14-18]:

3 amino Benz (d) isoxazoles acts as multi targeted inhibitors of receptor tyrosine kinase. SAR studies lead to identification of labeled compound and that potently inhibits both vascular endothelial growth factor receptor and platelet derived growth factor receptor families of RTK'S. The synthesized compound also demonstrated by in vivo studies also. The activity was done by Jiz, Ahmed AA Et.al – Global pharmaceutical research and development.



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