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Therapeutic Approaches of Some Novel Glyoxaline Derivatives

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Abstract
Gloxaline have occupied a unique position in heterocyclic chemistry, and its derivatives have attracted considerable interests in recent years for their versatile properties in chemistry and pharmacology. Gloxaline is nitrogen-containing heterocyclic ring which possesses biological and pharmaceutical importance. Thus, Gloxaline compounds have been an interesting source for researchers for more than a century.

The Gloxaline ring is a constituent of several important natural products, including purine, histamine, histidine, and nucleic acid. Being a polar and ionisable aromatic compound, it improves pharmacokinetic characteristics of lead molecules and thus is used as a remedy to optimize solubility and bioavailability parameters of proposed poorly soluble lead molecules. There are several methods used for the synthesis of gloxaline -containing compounds, and also their various structure reactions offer enormous scope in the field of medicinal chemistry. The Gloxaline derivatives possess extensive spectrum of biological activities such as antibacterial, anticancer, antitubercular, antifungal, analgesic, and anti-HIV activities. This paper aims to review the biological activities of gloxaline during the past years.

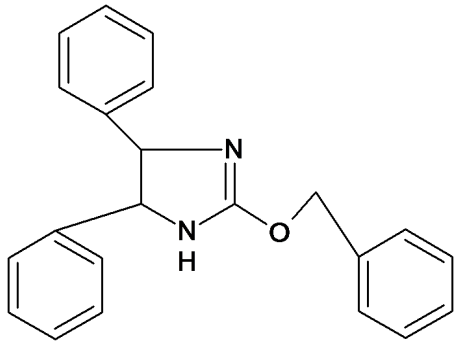
Introduction

Gloxaline nucleus forms the main structure of some well-known components of human organisms, that is, the amino acid histidine, Vit-B12, a component of DNA base structure and purines, histamine, and biotin. It is also present in the structure of many natural or synthetic drug molecules, that is, cimetidine, azomycin, and metronidazole[1]. Gloxaline - containing drugs have a broaden scope in remedying various dispositions in clinical medicine [2]. Gloxaline was first synthesized by Heinrich Debus in 1858, but various Gloxaline derivatives had been discovered as early as the 1840s.

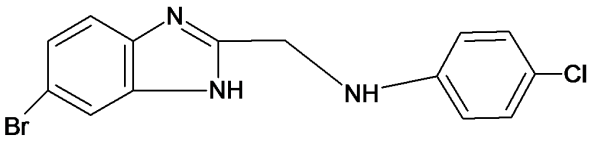
On the basis of various literature surveys Gloxaline derivatives shows various pharmacological activities

Anti -inflammatory and analgesic activity

Puratchikody A.et al studies on 2-substituted-4, 5-diphenyl-1H- Gloxaline and checked the anti-inflammatory activity based on Carrageenan-induced paw edema method. This compound shows maximum activity and indomethacin used as reference drug[3].

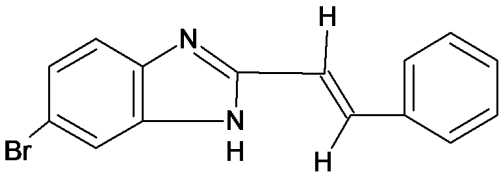


Kavitha C.S.et al has synthesized a series of 2-methylaminibenzgloxaline derivatives and newly synthesized compounds were screened for analgesic and anti-inflammatory activities. This compound shows analgesic activity and compared with standard nimesulide drug. [4]

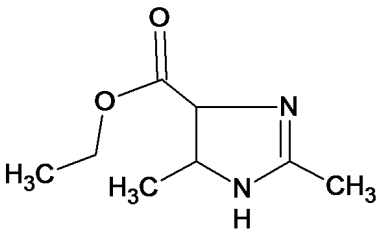


Antitubercular activity

Ramya V et al synthesized series of novel 5-(nitro/bromo)-styryl-2-benzgloxaline (1–12)derivatives and screened for in vitro anti-tubercular activity against *Mycobacterium tuberculosis* ,and these compounds showed good antitubercular activities. Streptomycin was used as reference drug [5].

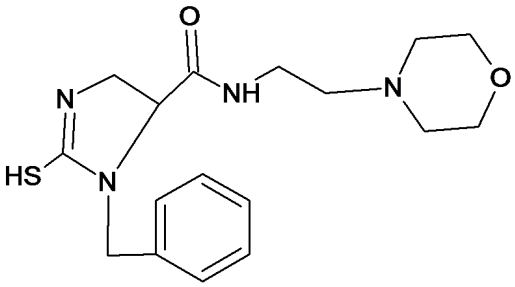


Preeti Gupta et al describe anti-mycobacterium tuberculosis activities of ring substituted -1H Gloxaline -4-carboxylic acid derivatives and 3-(2-alkyl-1H-imidazole-4-yl)-propionic acid derivatives against durg-sensetive and durg-resistent *M. tuberculosis* strains. [6]



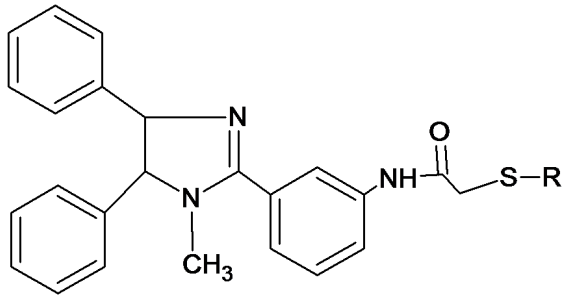
Antidepressant activity

Farzin Hadizadeh et al synthesized moclobemide analogues by replacing moclobemide phenylring with substituted Gloxaline and studied for the antidepressant activity using forced swimming test which was found to be more potent than moclobemide. [7]

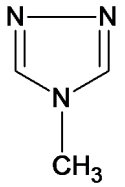


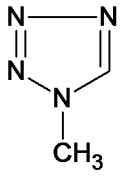
Anticancer activity

Yusuf Ozkay et al synthesized many novel Gloxaline -(Benz) azole and Gloxaline epiperazine derivatives in order to investigate the anticancer activity. Anticancer activity screening results revealed that these were the most active compounds in the series. Cisplatin was used as reference drug. [8]



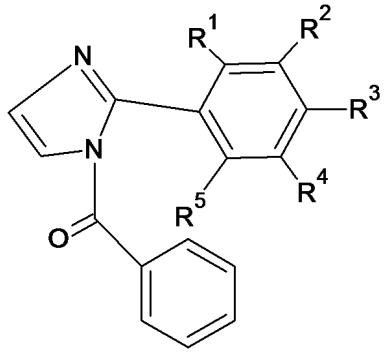
R=





Antiviral activity

Deepika Sharma et al synthesized Gloxaline derivatives and the antiviral screening of(substituted phenyl)-[2-(substituted phenyl)- gloxal -1-yl]-methanones against viral strains indicated that compounds A and B selected as the most potent antiviral agents. Ribavi in was used as standard drug. [9]

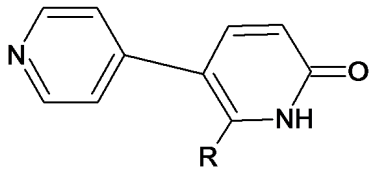


For compound A, R_1=H ,R_2=H, R_3=Cl, R_4=H,R_5=H

B ,R_1=R_2=R_4=R_5=H And R_3=NO_2

Cardiotonic agents

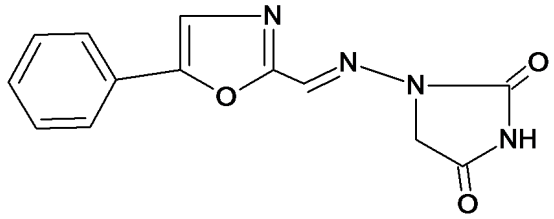
For some 200 years, digitalis and its constituent cardiac glycosides such as digitoxin and digoxin have been used as positive ionotropic agents for the treatment of congestive heart failure.[10] Although these drugs are selective in their ionotropic effects and exhibit no significant direct effects on the vasculature but their potential for producing cadiac arrythmia leads to undesirably low therapeutic ratios [11]. This problem and increasingly high death rate from congestive heart failure have spurred attempts to find an orally available digitalis replacement. The discovery of amrinone has led to the synthesis of a number of agents that show varying promise for congestive heart failure treatment.[12] A few compounds have shown



R=H,Me

Muscle relaxant

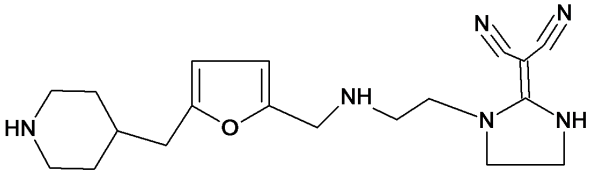
In the research for compounds for the treatment of skeleton muscular disorders, a series designed to be direct skeletal muscle relaxants was synthesized and pharmacologically evaluated. Dantrolene sodium and other similar 1-[[[5-(substituted phenyl)2-furanyl] methylene] amino] 2,4imidazolidinediones have been found to exhibit direct skeletal muscle relaxant activity.[13]



Gastrointestinal motility promoter

Alterations in the motility of the alimentary canal are associated with many symptoms of gastrointestinal disease. Examples of the digestive systems diseases that are manifested by a disturbance in motor activity are *dysphagia*, *gastric stasis, vomiting, abdominal pain, paralytic ileus and constipation.*

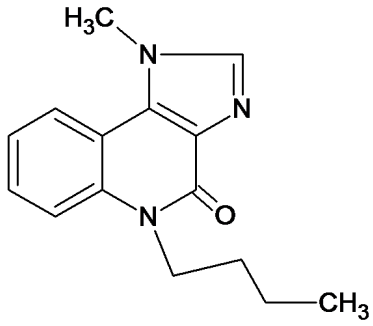
Ranitidine the histamine H2 receptor antagonists, has been previously reported to increase gastric emptying and gastric motility by inhibition of acetyl cholinestrase (AchE) and enhancement of Acetylcholine (Ach) release. In order to obtain potent gastro-prokinetic agents, a new series of ranitidine derivatives possessing a nitrogen atom instead of a sulfur atom was synthesized and their AchE inhibitory activity and potentiating action on electrically evoked contractions of guinea pig ileum were evaluated.[14]



New bronchodilator

Bronchial asthma is chronic debilitating disease, which in its severe forms can threaten life. Efforts have been done to develop new xanthine derivatives, which relax the bronchial smooth muscle in a fashion similar to that of theophylline

but without its CNS and cardiovascular side effects. A series of novel xanthine-based tricyclic hetero-cycles in 1H-imdazo[4,5-c]quinolin-4(5H)- ones was designed, synthesized and tested as potential active bronchodilators.[15]



Stimulators of insulin secretion

Jakoben et al31 synthesized a series of gloxalines with glucose dependent effects on insulin exocytosis from pancreatic -cells. Regioisomers and enantiomers were found to exhibit marked differences in exocytotic effects as well as different activities on the K ATP-Channel.

CONCLUSION

Vast number of gloxaline containing compounds have been synthesized and evaluated for their biological activity. On the basis of various literature survey gloxaline derivatives show various activity against antimicrobial, anti-inflammatory, analgesic, antitubercular, anticancer etc. The possible improvements in the activity can be further achieved by slight modifications in the substituentson the basic gloxaline nucleus. Having structural similarity with histidine gloxaline compound can bind with protein molecules with ease compared to the some other heterocyclic moieties.Thus gloxaline offers better pharmacodynamic characteristics. Furthermore, some gloxaline drugs, at high concentrations, could exert direct inhibitory effects on membranes, without interference with sterols and sterol esters. Various recent new drugs developments in gloxaline derivatives show better effect and less toxicity.

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