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PHAMARCOLOGICAL EFFECTS PRODUCED BY THE MODIFICATIONS IN ISOXAZOLE MOEITIES

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ABSTRACT

Isoxazole and its derivatives are an important class of heterocyclic compound displaying a broad spectrum of biological activities which have made them privileged structures. In the present work, attempts were made to identify leading isoxazole moieties as candidate drugs against many diseases. For example, isoxazole substituted 9-anilino acridine derivatives was found to have increased antioxidant activities. The molecular docking studies show a good correlation between their biological activities screened and auto dock binding free energy. These derivatives will encourage helping to design future anti cancer agents with higher therapeutic potential. Another example is isoxazole incorporated 2-quinolones to show increased antimicrobial and anti inflammatory activities. More importantly, various isoxazole derivatives greatly increase biological properties of the structure like anti-infective action, anticancer properties, anti-protozoal and mutagenic properties. A modification in their structures has offered a high degree of diversity that has proven useful for the development of new therapeutic agents having improved potency and lesser toxicity. In the present study of concise review, is provided on the activities of isoxazole and its derivatives which involve history, chemistry, different methods of synthesis of isoxazole with biological activities and docking studies. Thus large number of pharmacologically active molecules with a wide variety of biological activities shows the importance of isoxazole moieties for the development of new therapeutic agents.

KEYWORDS

Docking studies and Isoxazole moieties.

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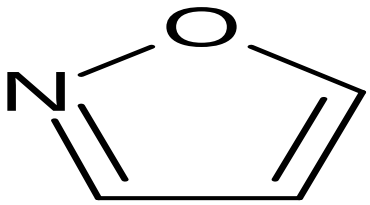
INTRODUCTION

Nitrogen containing heterocycles with an oxygen atom are considered as an important class of compounds in medicinal chemistry because of their diversified biological applications. The exploitation of a simple molecule with different functionalities for the synthesis of heterocycles is a worthwhile

contribution in the chemistry of heterocycles. Isoxazole[1-3] is a five membered heterocyclic compound containing oxygen and nitrogen atoms in the 1, 2 positions, its partially saturated analogs are called is oxazolines and completely saturated analog is oxazolidine. Isoxazoles are an important class of heterocycles, which are largely employed in the area of pharmaceuticals and therapeutics such as insecticidal, antibacterial, antibiotic, antitumour, antifungal, antituberculosis, anticancer and ulcerogenic activities[4,5].

ISOXAZOLE DERIVATIVES[6-9]

Isoxazole derivatives are used in the market as COX-2inhibitor and anti-inflammatory drugs. Isoxazole derivatives such as sulfamethoxazole, sulfisoxazole, oxacillin, cycloserine and acivicin have been in commercial use for many years.



Cycloserine is the best known antibiotic drug that possess antitubercular, antibacterial activities and in treatment of leprosy. Acivicin is an antitumour, antileishmania drug, while isoxaflutole is used as herbicidal drug. Isoxazoles have illustrious history; their chemistry is associated with Ludwig Claisen, who first recognized the cyclic structure of 3- methyl-5-phenylisoxazole in 1888 and was shown to possess typical properties of an aromatic system under certain reaction conditions; particularly in basic media, it is very highly labile. Dunstan and Dymond were the first to synthesize the isoxazole ring1. They isolated a liquid base by heating nitro ethane with aqueous alkalies to obtain 3,4,5- trimethyl isoxazole. A very significant contribution to the development of isoxazole chemistry came between 1930–1946 from Quilico's studies on the synthesis of ring system from nitrile oxides and unsaturated In recent years, there has been increased attention towards the synthesis of isoxazole derivatives, since they possess a broad spectrum of biological activities. Isoxazoles are one of the key oxygen and nitrogen containing five-membered ring heterocycles that possess significant roles in the medicinal chemistry. Considerable attention has been focused on isoxazoline derivatives due to their interesting biological activities.

The synthesis of novel isoxazoline derivatives remains the main focus due to their diverse pharmacological activities. Owing to their versatile chemotherapeutic importance, a significant amount of research effort has been focused on preparing new derivatives of isoxazole compounds. Isoxazole derivatives are a promising structural moiety for drug designing, which are reported to possess antibacterial, anticonvulsant, antipsychotic, anti-inflammatory, antitumor, analgesic, insecticidal, antioxidant and antimicrobial activities.

ISOXAZOLE MODIFICATIONS

Isoxazolerings[10-12] is found in some natural products, such as ibotenic acid. Isoxazoles also form the basis for a number of drugs, including the COX-2 inhibitor valdecoxib (Bextra). A derivative, furoxan, is a nitric oxide donor. An isoxazolyl group is found in many beta-lactamase-resistant antibiotics, such as cloxacillin, dicloxacillin and flucloxacillin. The synthetic androgenic steroid danazol also has an isoxazole ring. In addition, isoxazoline derivatives have played a crucial role as intermediates in the organic synthesis of a number of hetero-cyclic pharmacologically active compounds. Encouraged by the diverse biological activities of isoxazoline compounds, it was decided to prepare a new compound, 5-(3-dimethylane-p-tolylsulfonyl) -propyl-3- (4-

flurophenyl) -isoxazole. The need to reduce the amount of toxic waste and byproducts arising from chemical processes requires increasing emphasis on the use of less toxic and environmentally compatible materials in the design of new synthetic methods. One of the most promising approaches is the use of water as the reaction medium. Compared to organic solvents the aqueous medium is less expensive, less dangerous, and more environmentally friendly. In recent years, there has been increasing recognition that water is an attractive medium for many organic reactions. Many important types of heterocycles, such as furans, pyridines, quinolines, indoles, triazines, acridines, pyrazines, and pyrimidines have been synthesized in aqueous media. The synthesis of new and other important type of heterocyclic compounds in water continues to attract wide attention among synthetic chemists.

Nitrogen-containing heterocyclic building blocks[13-15] is of great importance to both medical and organic chemists, and their synthesis continues to represent a challenge from both academic and industrial perspectives. Isoxazole derivatives are an important class of heterocyclic pharmaceuticals and bioactive natural products because of their significant and wide spectrum of biological activities, including potent and selective antagonism of the NMDA receptor and anti-HIV activity.

Many syntheses of isoxazoles have been developed. However, these syntheses are usually carried out in organic solvents. As part of our current studies on the development of new routes to heterocyclic systems in aqueous media, we now report an efficient and clean synthetic route to isoxazole derivatives via the reaction of 3-(dimethylamino) -1-arylprop-2-en-1-ones with hydroxylamine hydrochloride in aqueous media.

CONCLUSION

Isoxazole is a five membered heterocyclic compound having various pharmacological actions. The great interest associated with isoxazoles and their derivatives is based on their versatility as synthetic building blocks. This review paper comprises of up to date information of isoxazole analogs. More emphasis was given to critical discussion on the synthetic strategy of isoxazole derivative, their utility as building blocks in their transformation to more biologically potent molecules. Results of isoxazole derivatives and their substitutions effect on diverse biological activities are also presented. These derivatives will encourage helping to design future anti cancer agents with higher therapeutic potential. Another example is isoxazole incorporated 2-quinolones to show increased antimicrobial and anti-inflammatory activities. More importantly, various isoxazole derivatives greatly increase biological properties of the structure like anti-infective action, anticancer properties, anti- protozoal and mutagenic properties. The present study of concise review shows that modifications in their structures has offered a high degree of diversity that has proven useful for the development of newer therapeutic agents having improved potency and lesser toxicity.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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