IN SILICO DESIGN AND BIOLOGICAL IMPORTANCE OF OXAZOLE DERIVATIVES

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ABSTRACT

The heterocyclic molecules have immense biological significance in pharmaceutical field. Oxazole is considered as a crucial moiety in heterocyclic chemistry and a privileged nucleus in medicinal chemistry due to its wide range of biological activity. Oxazole is composed of an unsaturated 5-membered ring having one oxygen atom at position one and a nitrogen at position three separated by a carbon in-between. In the present research work, novel oxazole derivatives were designed using *in silico* molecular modelling techniques. From different journals gone through, 15 schemes were selected, and 150 oxazole derivatives were prepared from those 15 schemes. MolSoft, PreADMET and PASS Online data of 150 derivatives were collected. From those 150 derivatives, 12 compounds passed MolSoft and 6 compounds passed PreADMET. After completing the PASS Online studies of these 6 compounds, the compound 1-[5-bromo-2-(4-hydroxyphenyl)-1,3-oxazole-4-yl] propan-1-one (OB10) was found to have antifungal activity and its docking was done using AutoDock 4.0. A binding score of -6.88 Kcal/mol for OB10 revealed good interaction between protein and ligand. The project revealed the potential of oxazole as lead compounds for further research and drug development. This study may be used for further research to develop novel and cost-effective antifungal activity. There is a need for new antifungal agents, mainly due to increased incidence of invasive fungal infections (IFI), high frequency of associated morbidity and mortality and limitations of the current antifungal agents (e.g., toxicity, drug-drug interactions, and resistance). The clinically available antifungals for IFI are restricted to four main classes: polyenes, flucytosine, triazoles and echinocandins. Several antifungals are hampered by multiple resistance mechanisms being present in Consequently, novel antifungal agents with new target's and modified chemical structures are required to combat fungal infections.

KEYWORDS: Oxazole, *In silico*, Antifungal, Docking, MolSoft

INTRODUCTION

Medicinal chemistry is the branch of science concerned with the discovery and development of new medicinal compounds, as well as their transformation into usable medicines. IUPAC defines Medicinal chemistry as "it concerns the discovery, the development, the identification and the interpretation of the mode of action of biologically active compounds at the molecular level" In other words, Medicinal chemistry is an interdisciplinary science at the interface of chemical, biology, pharmacology and medicine, playing a crucial role in drug discovery. The main objectives of medicinal chemistry are to discover chemical probes and lead compounds for understudied biological targets and to demonstrate target drug ability and to address issues that determine drug success or failure. [1-3]

Heterocyclic compounds are of very much interest in our daily life. Heterocyclic compounds have one or more hetero atoms in their structure. They are the cyclic organic compounds which contain at least one hetero atom, the most common heteroatoms are the nitrogen, oxygen and sulphur but heterocyclic rings containing other hetero atoms are also widely known. Heterocyclic compounds are considered as one of the vital classes of organic compounds, which are used in many biological fields, due to it is activity in multiple illnesses. They are frequently found in large percent in biomolecules such as enzyme, vitamins, natural products and biological active compounds including antifungal, anti-inflammatory, antibacterial, antioxidant, anticonvulsant, antiallergic, enzyme inhibitors, herbicidal activity, anti-HIV, antidiabetic, anticancer activity and insecticidal agents.[4]

Many heterocyclic compounds are employed in the treatment of infectious diseases due to their specific antimicrobial activity. Heterocyclic systems are a part of large number of drugs and biologically relevant molecules. Often the presence of hetero atoms or groupings imparts preferential specificities in their biological responses. The chemistry and biological study of heterocyclic compounds has been interesting field for a long time and oxazole is one such moiety which has gained attention in recent times due to its increasing importance in the field of medicinal chemistry. Oxazole is a doubly unsaturated 5-membered ring having one oxygen atom at position 1 and a nitrogen at position 3 separated by a carbon in-between. It was first prepared in 1947, has a boiling point of 69 °C and is a stable liquid at room temperature. Substitution pattern in oxazole derivatives play a pivotal role in delineating the biological activities like antimicrobial and antifungal, anticancer, antitubercular, anti-inflammatory,

antidiabetic, anti-obesity and antioxidant etc. Oxazole and its derivatives are a part of number of medicinal compounds (Fig.1) which includes Aleglitazar (**1**, antidiabetic), Ditazole (**2**, platelets aggregation inhibitor), Mubritinib (**3**, tyrosine kinase inhibitor), Oxaprozin (**4**, COX-2 inhibitor) [5].

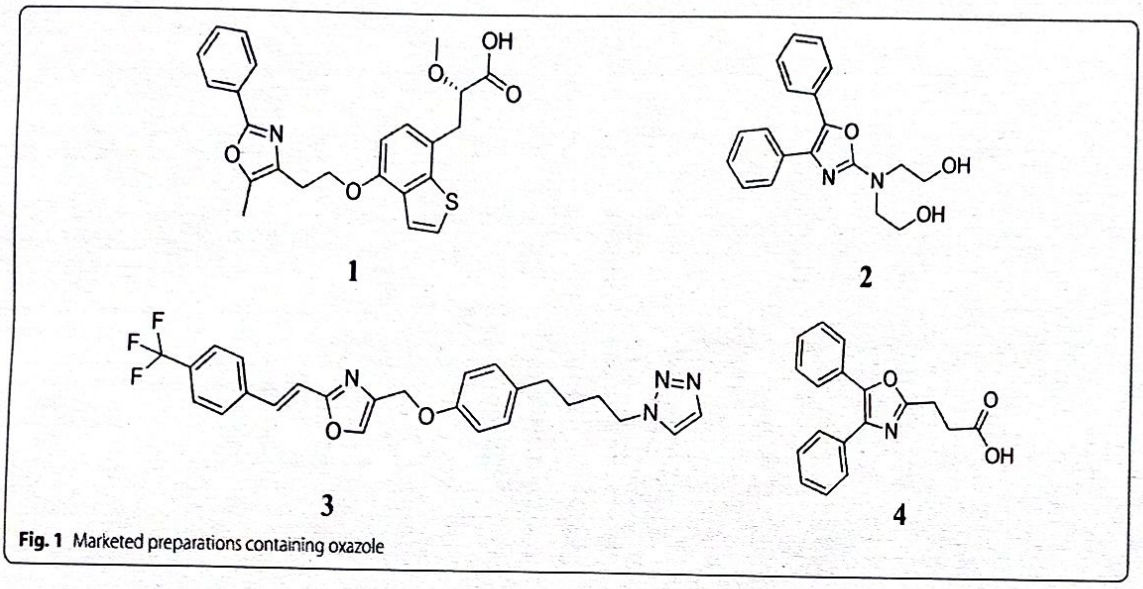

Fig. 1 Marketed preparations containing oxazole

Oxazole is an important heterocyclic nucleus having a wide spectrum of biological activities which drew the attention of researchers around the globe to synthesize various oxazole derivatives and screen them for their various biological activities. Therefore, utility of oxazole as intermediates for the synthesis of new chemical entities in medicinal chemistry have been increased in the past few years. In spite of these studies there are many uses of oxazole derivatives to be discovered.[6]