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Recent Medicinal Attributes of 1,2,3-Triazoles

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Abstract

1,2,3-Triazoles are imperative five-membered heterocyclic scaffold due to their widespread biological activities. This scaffold is capable of readily obtained in excellent yields through click chemistry via reaction of aryl/alkyl halides, alkynes and NaN3 at room temperature. Owing to its biological importance it has been a potential area of curiosity for many researchers throughout the world. 1,2,3-triazole serves as a bioisosteres for the unstable bonds such as amide and disulphide. Applications of click chemistry are increasingly found in all aspects of drug discovery ranging from lead finding through combinatorial chemistry. The triazole products are more than just passive linkers; they readily associate with biological targets, through hydrogen-bonding and dipole interactions. The present work aims to review the medicinal significance of these architectures in particular on use of the 1,2,3-triazole moiety as pharmacophore.

Keywords: 1,2,3-Triazoles; Scaffold; Anticancer; Antifungal; Anti tuberculosis; Antibacterial; Antiprotozoal activity; HIV protease inhibitors; Drug molecules; Azide-alkynes cycloaddition

Introduction

The foremost intention of medicinal chemist is to synthesize libraries of compounds during the process of drug discovery or lead optimization, and for this reason, click chemistry is particularly attracted synthetic methodologies that allow rapid edifice of molecules [1-2]. The recognition of such quick synthetic strategies allows the medicinal chemist to assemble many biologically active compounds in an exceptionally short period of time speeding up the practice of discovery and lead optimization [3-5]. One of the motifs is triazole, which have been explored widely and still its scope is predictable. Triazoles are heterocyclic organic compounds containing five-membered ring with three nitrogen and two carbon atoms [6-10]. A very important advantage of azide-alkynes cycloaddition is undeniably because of their lofty chemoselectivity. This feature makes these reactions particularly attractive for modifying highly functional biomolecules. Triazole linkages can be considered as a motivating peptide mimics exhibiting H-bonds capability, aromaticity and rigidity [11-13]. 1,2,3-Triazole moieties are attractive connecting units because they are stable to metabolic degradation and capable of hydrogen bonding, which can be encouraging in the binding of biomolecular targets and can improve the solubility. The importance of triazolic compounds in medicinal chemistry is unquestionable. Contrary to other aza heterocycles, the 1,2,3-triazole ring is not protonated at physiological pH because of its poor basicity. The 1,2,3-triazoles are having different biological activities such as Anticancer, HIV protease, Anti tuberculosis, Antifungal, Antibacterial, Antiprotozoal activity and inhibiting serine hydrolases enzymes (Obesity, Diabetes, Alzheimer's disease). The triazole group displays structural similarity with the amide bond, mimicking a Z- or an E-amide bond depending on its substitution pattern [14-16]. Thus, the 1,4-disubstituted triazole moiety shows similarity with a Z-amide bond: the lone pair of the 3-nitrogen mimics the one of the carbonyl oxygen of the amide bond, the polarized C(5)-H bond can act as a hydrogen bonding donor, just like the amide N–H bond, and the electrophilic and polarized 4-carbon is electronically similar to the carbonyl carbon. Since the overall dipolar moment of the triazole system is larger than that of the amide bond, its hydrogen bonding donor and acceptor properties are more marked than those of an amide bond, with enhanced peptide mimicry. The major structural difference between a triazole and a Z-amide is the distance between the substituent's, linked by two atoms in the amide, and by three atoms in the triazole ring, with an overall increase of about 1.1A°. On the other hand, the 1,5- substitution pattern mimics the E-amide bond. In this case, the link between the substituent's is identical in terms of the atoms occupied and the relative position of the hydrogen bonding donor and acceptor sites is also similar [17-21]. Yet, there are some differences in atom polarization, as the electrophilic carbonyl carbon is now replaced by a negatively polarized nitrogen atom. Besides the potential of triazoles in mimicking the amide of the peptide bond, it has also been predicted that triazoles might act as bioisosteres of the acyl-phosphate and trans-olefinic moieties.

Conclusion

The triazole nucleus especially 1,2,3-triazole ring has been tried as a linker in various bioconjugates and thus, can be utilized in targeted drug delivery systems as well. Thus, this five-membered aromatic heterocyclic ring structure, with three nitrogen atoms and rich electron density, endow the mammoth variety of its scaffolds in flourishing research and progress leading to a good therapeutic effect, low toxicity as well as superior pharmacokinetic properties making wonderful contributions in the treatment of human diseases. The rich array of functionality display by these products can provide opportunities for the creation of unique combinatorial libraries.

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