

RESEARCH ARTICLE

STUDY OF SOME 1,2,4-TRIAZOLES DERIVATIVES AND THEIR BIOLOGICAL ACTIVITIES

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Abstract:

It is well established that various derivatives of triazole exhibit broad spectrum of pharmacological properties. The 1,2,4-triazole moiety present in the various natural products and the synthesis of compounds. This moiety has attracted attention of chemists as well as biologists. The compounds containing different heterocyclic moiety would be tested for antimicrobial activity against different strains of pathogenic organisms. Similarly few of the compounds would also be screened for anti-inflammatory and analgesic activities.

Keywords: Antimicrobial, heterocyclic, triazole, pharmacological properties.

Introduction

The chemistry of N-bridged heterocycles derived from 1,2,4-triazole has received considerable attention in recent year due to their usefulness in different areas of biological activities and as industrial intermediates. 1,2,4-triazole moiety appears frequently in the structure of various natural products¹ and the synthesis of compounds incorporating this moiety has attracted widespread attention of chemists as well as biologists, mainly due to their diverse biological activities in pharmaceutical and agrochemical fields. A large variety of 1,2,4-triazole derivatives possess antibacterial^{2,3}, antifungal⁴, antimycobacterial⁵, antiviral⁶, anti-inflammatory^{7,8}, anticonvulsant⁹, antidepressant¹⁰, antitubercular¹¹, antitumoral¹², antihypertensive, analgesic¹³, enzyme inhibitor¹⁴, hypoglycemic¹⁵, sedative, hypnotic¹⁶, antiparasitic, herbicidal, insecticidal and plant growth activities.

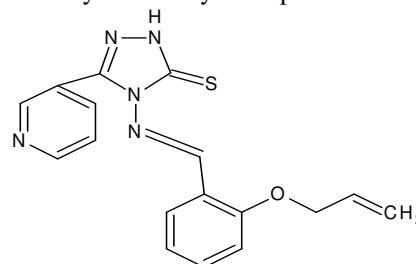
Thus several potent drugs possessing triazole nucleus have been applied in medicine like, alprazolam (anxiolytic, tranquilizer), anastrozole, letrozole, vorozole (antineoplastics, non-steroidal competitive aromatase inhibitors), estazolam (hypnotic, sedative, tranquilizer), etoperidone (antidepressant), fluconazole, itraconazole, terconazole (antifungal agents), ribavirin (antiviral agent), benatradin (diuretic), rilmazafon (hypnotic, anxiolytic, used in the case of neurotic insomnia), nefazodone (antidepressant, 5-HT₂ A-antagonist), rizatriptan (antimigrain agent), trapidil (hypotensive), prazodone (antidepressant, anxiolytic, selectively inhibits central serotonin uptake) and triazolam (sedative and hypnotic).

Other heterocyclic moiety with triazole ring: Schiff bases are considered as a very important class of organic compounds which have wide applications in many biological aspects¹⁷. Many Schiff bases containing 1,2,4-triazole moiety exhibit antibacterial, antifungal¹⁸ and antitumoral activities¹⁹. The substituted nicotinic acid is among the various heterocycles that have received most attention during last three decades as potential biomolecules. Nicotinic acid derivatives exhibit antibacterial, antioxidant, anti-inflammatory and anticarcinogenic activities. It is seen from the current literature that pyridine congeners are associated with different biological properties like pesticidal^{20,21}, insecticidal and antifungal activities. A large number of antibiotics contain amide linkage. Several derivatives of amides were prepared and found to possess antimicrobial activities. Literature survey reveals that various drugs e.g. penicillin (antibacterial), pyrazinamide (antitubercular), indinavir, ritonavir. (Protease inhibitors as anti-AIDS) etc contain their particular activities due to the amide linkage present in their structure.

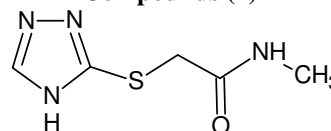
Biological activity of 1,2,4-triazole derivatives:

Various work are available with regard to the study of 1,2,4-triazoles. The literature revealed that the compound containing 1,2,4-triazole are reported to possess diverse biological activities. Some 1,2,4-triazole fused acyclic and 21-28 membered macro cyclic compounds (1) with potential antimicrobial activity²². The 1,2,4-triazoles derivative (2) with antibacterial activity against *Staphylococcus aureus*, *Klebsiella pneumonia*, *Escherichia coli* and *Pseudomonas aeruginosa* using cup-plate method²³. Some 1,2,4-triazole analogues (3) for evaluation of their antifungal activity against *C. albicans*, *A. niger*²⁴. Some new 1,2,4-triazoles and their Mannich and Schiff bases (4) and screened for their antimicrobial activity against *E. coli*, *Y. pseudotuberculosis*, *P. aeruginosa*, *Enterococcus faecalis*, *S. aureus*, *B. cereus*, *C. tropicalis* and *C. albicans*²⁵. Some 1,2,4-triazole derivatives (5) and have shown the activity against *E. Coli*, *klebsiella pneumonia*, *Yersinia pseudotuberculosis*, *Enterobacter aerogenes*, *P. aeruginosa*, *staphylococcus aureus*, *E. faecalis*, *Bacillus cereus*, *Candida tropicalis*, *C. glabrata*²⁶. Some new 1,2,4-triazole derivatives (6) and screened for their biological activity in vitro against *Gibberella zeae*, *Alternaria solani*²⁷. Some 1-acylthiosemicarbazides, 1,3,4-oxadiazoles, 1,3,4-thiadiazoles and 1,2,4-triazole-3-thiones (7) has described activity as anti-inflammatory by carrageenan Paw Edema Test (CPE) method²⁸. Some 1,2,4-triazoles (8) starting from isonicotinic acid hydrazide and evaluation of their antimicrobial activities against *E. coli*, *Y. pseudotuberculosis*, *P. aeruginosa*, *Enterococcus aureus*, *Bacillus cereus*, *C. tropicalis* and

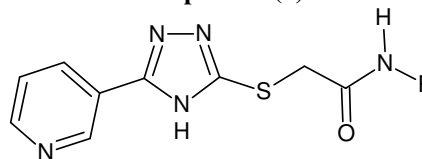
The 5-aryl-3-alkylthio-1,2,4-triazoles (9) and sulfones with anti-inflammatory activity by Carrageenan-induced edema test in mice and also analgesic activity³⁰. The 1-acylthiosemicarbazides, 1,2,4-triazole-5(4H)-thiones (10), 1,3,4-thiadiazoles and hydrazones containing 5-methyl-2-benzoxazolinones and evaluation for their analgesic activity by acetic acid-induced writhing test and hot plate test in mice and anti-inflammatory activity by carrageenan-induced hind paw oedema model in mice and also antimicrobial activity against *Candida krusei*, *Candida albicans* and *Candida parapsilosis*³¹. The 4H-1,2,4-triazole derivatives (11) which have shown analgesic activity with Eddy's hot plate method³².



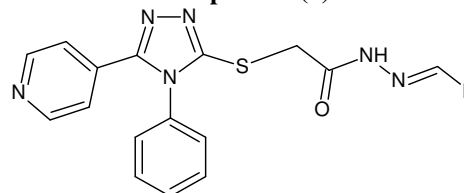
Compounds (1)



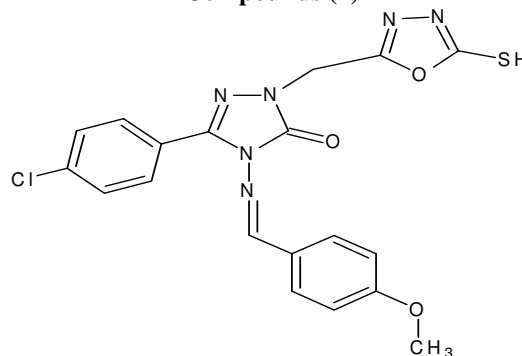
Compounds (2)



Compounds (3)

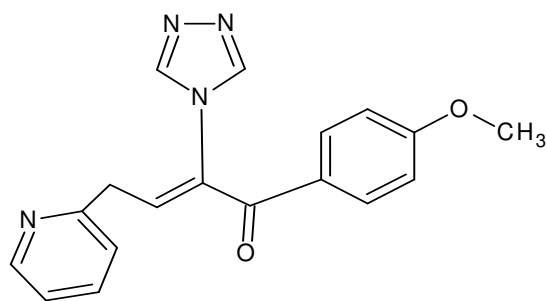


Compounds (4)

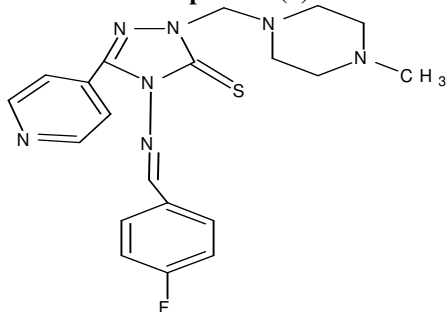


Compounds (5)

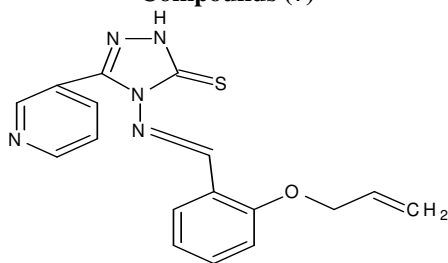
C. albicans, by Agar-well diffusion method²⁹.



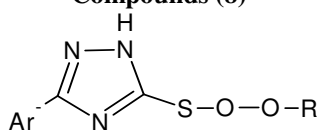
Compounds (6)



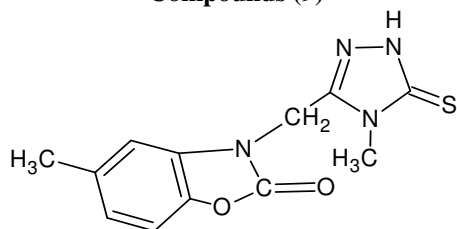
Compounds (7)



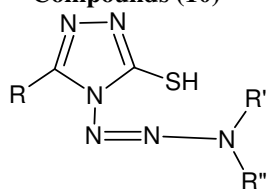
Compounds (8)



Compounds (9)



Compounds (10)



Compounds (11)

Conclusion: Many of the available therapeutically important medicines such as ketoconazole, itraconazole, voriconazole and fluconazole contain this heterocyclic nucleus. In view of the above mentioned facts and in continuation of interest in the heterocycles containing 1,2,4-triazole moiety to identify as new molecule that may be value in designing new, potent, selective and less toxic antimicrobial agents. This combination is thought in an attempt to investigate the influence of structure variation on the anticipated biological activities, hoping to add some synergistic biological significance to the target molecules.

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Figure 1. Structure of some 1,2,4-triazole derivatives.

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