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Synthesis And Characterization Of Heterocyclic Compounds Containing 1,2,4–Triazole

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Abstract:

Heterocycles are at the forefront of research because of their wide range of applications. Because of their diverse biological activity and clinical uses, the triazole ring system is of considerable interest in the field of medicinal chemistry. A variety of triazole compounds have biological and pharmacological properties such as antibacterial, anti-inflammatory, antihypertensive, antifungal, anticancer, and antitumor action. Fused heterocyclic triazoles have clinical applications as well. In addition to its vital biological applications, 1,2,4-triazoles are valuable in preparative organic chemistry, agriculture, and the polymer industry. The most significant goal of pharmaceutical research is the discovery of new, better pharmaceuticals and their successful introduction into clinical practise, which is complicated by bacterial resistance to previous drugs and other side effects. Because triazole compounds have such features, we have been able to synthesise novel derivatives and test their antibacterial activities.

Key words: Synthesis, Characterization, Biological activity, Antibacterial, 1,2,4-Triazole.

1. Introduction:

The emergence of resistant microorganisms has reached an alarming level around the world, and the development of new anti-infective chemicals has become a pressing necessity for microbial illness therapy. The 1,2,4-triazole nucleus has been incorporated into a wide range of therapeutically useful compounds, with antibacterial properties being the most common.Organic compounds with heterocyclic ring structures continue to pique researchers' interest due to their diverse biological properties. The structural properties of many bioactive chemicals include 1,2,4-triazoles and 1,3,4-thiadiazoles and their derivatives, which are among the diverse five-membered heterocyclic systems. Triazole and thiadiazole rings are known to be included in the structures of a variety of medications. Because of various biological properties such as antibacterial, antifungal, antitubercular, antiviral,

antioxidant, antitumoral, antiinflammatory, anticonvulsant, the synthesis of new derivatives of 1,2,4-triazole-3-thiones and 2-amino-1,3,4-thiadiazoles has attracted considerable attention from these classes of heterocyclic compounds. We designed and synthesisedtriazole system as antibacterial agents in light of these facts and as a continuation of our research on the biological characteristics of 1,2,4-triazole and 1,3,4-thiadiazole containing derivatives.

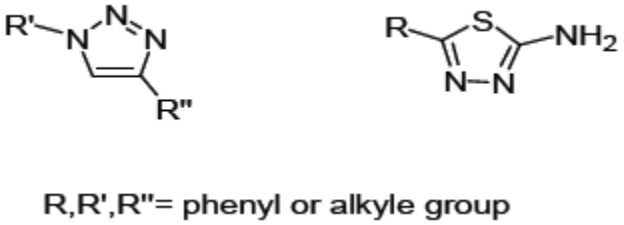

Fig. 1 : General structure of triazole and thiadiazole ring system

Thus, the synthesis and study of new 1,4-disubstituted 1,2,3-triazole and 2-amino-1,3, 4-thiadiazole derivatives have been attracting the chemists over the recent years.

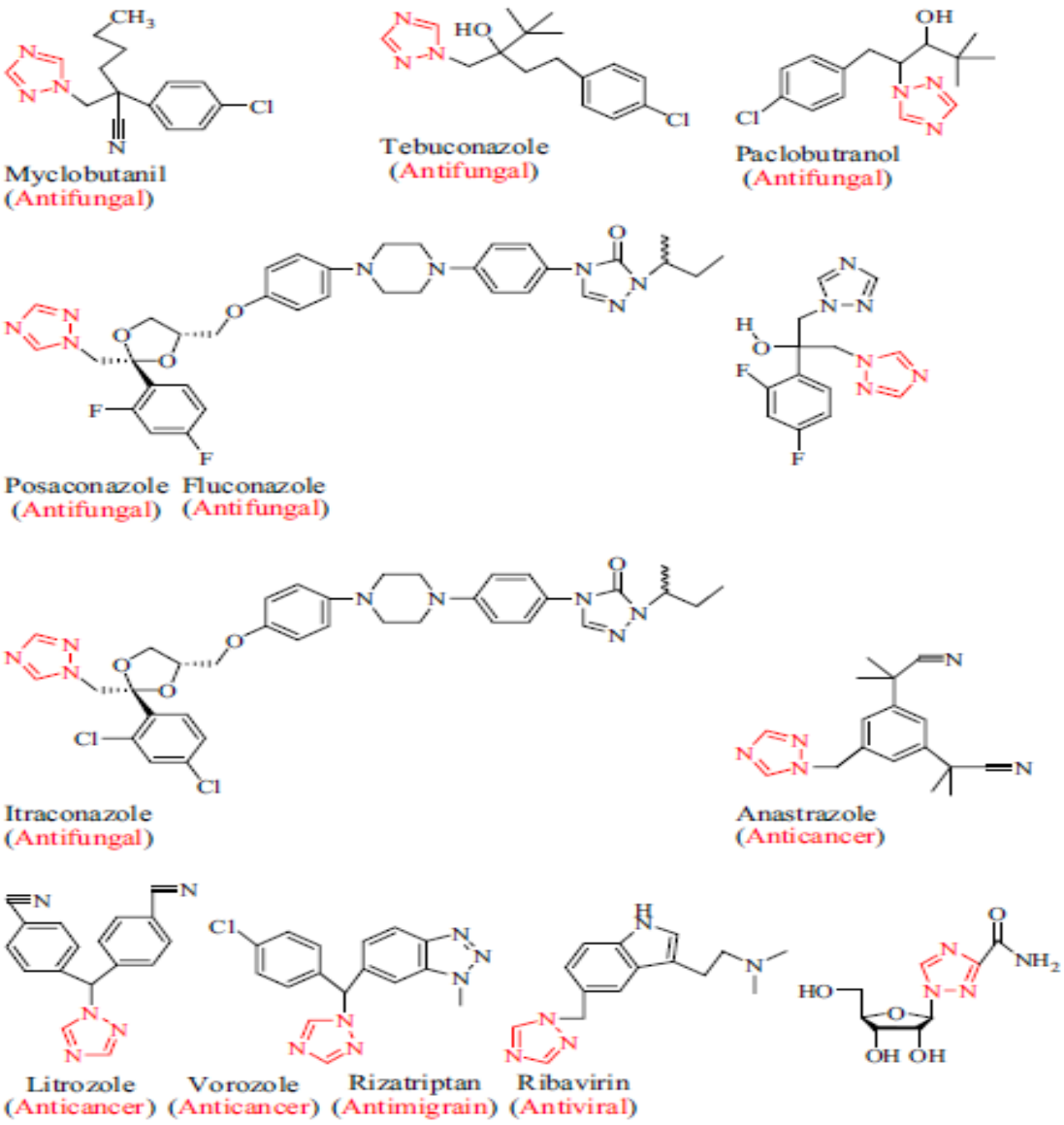

Fig. 2 :Applications of Heterocycles

Antimicrobial resistance is a concern in our medical sector right now, affecting a wide range of microbial types. As a result, as highlighted by various health organisations, there is a need for the discovery or development of novel antimicrobial agents with broad spectrum action and high efficacy against Gram positive, Gram negative, and fungal strains that are extremely resistant.

2. Experimental

All of the necessary starting ingredients and solvents for the synthesis of the target compounds were acquired from readily available sources and used without further purification.

2.1: Synthesis of 1,2,3-Triazoles through 1,3-DCRs

The 1,2,3-triazole core, which is frequently found in heterocyclic compounds with biological activity, serves as a disubstitutedbioisostere (usually in the 1,4-positions), a linker between two physiologically active molecules, or a core buried in a polycyclic skeleton. Catalytic or non-catalytic synthetic methods can be used to synthesise the triazole core via 1,3-DCRs. DFT calculations can be used to obtain structural and energetic features of a 1,3-DCR reaction process.

2.2: Synthesis of 1-(4-methoxyphenyl)-1H-[1,2,3]-triazolyl-4-carboxylic acid 6

Compound 1 (4.47 g, 30.0 mmole): Yield (5.0 g, 75 percent) as a brown solid was used to make it. 3293-2500 (OH, COOH), 3151 (CH-aromatic), 2930 (CH-aliphatic), 1730 (C=O), 1610 (C=C, triazole), 1564 (C=C, Ar) and 1437 (N=N) FT-IR (KBr disc, cm-1) 3.8 (s, 3H, OCH3), 7.1-7.8 (m, 4H, Ar-H), and 9.2 (s, 1H, C=CH, triazole ring) 1H-NMR (500 MHz, DMSO-d6) Calc. for C10H9N3O3 = 219.0, Found = 219.1. HPMS-EI+ (m/z): Calc. for C10H9N3O3 = 219.0, Found = 219.1.

2.3 : Synthesis of 1-(4-methylphenyl)-1H-[1,2,3]-triazol-4-yl carboxylic acid 7

Compound 2 (3.9 g, 30.0 mmole) was used to make a pale brown solid yielding 3.5 g (50 percent). 3332-2560 (-OH, COOH), 3134 (CH-aromatic), 2883 (CH-aliphatic), 1720 (C=O), 1640 (C=C, triazole), 1606 (C=C, Ar), 1471 (N=N, triazole) FT-IR (KBr disc, cm-1) 2.3 (s, 3H, CH3), 7.3-7.7 (m, 4H, Ar-H), and 8.7 (s, 1H, C=CH triazole) 1H-NMR (500 MHz, DMSO-d6) (m/z) HPMS-EI+: Calc. = 203.2, Found = 203.0 for C10H9N3O2.

2.4 : Synthesis of 2,5-dimercapto-1,3,4-thiadiazole

Refluxed for 5 hours was a combination of (80%) hydrazine hydrate (0.1 mol, 5g, 4.5 ml) and carbon disulfide (0.2 mol, 15g, 20ml) with dry pyridine (30 mL). The surplus solvent was then distilled off, and the solid was separated by adding (25 mL) water and (5 mL) hydrochloric acid to the mixture. The solid was then recrystallized from ethanol after the mixture was filtered. yield=77.6 percent, m.p = (162-164) C

2.5 : Synthesis of diethyl 2,2`-(1,3,4-thiadiazole-2,5-diyl)bis(sulfanediyl)diacetate

Potassium hydroxide (0.2 mol, 12 g) was added to a solution of 2,5-dimercapto-1,3,4-thiadiazole (0.1 mol, 15 g) in 20 ml 100% ethanol. After 30 minutes of stirring, ethyl chloroacetate (0.2mol, 25ml) was added drop by drop to the solution. For 4-5 hours, the reaction mixture was refluxed. After allowing it

cool to room temperature, add 100 mL of ice water. The precipitated ethanol was filtered out, washed with water, and recrystallized. (47-48) C° m.p., yield 79 percent

2.6: Synthesis of5,5'-(1,3,4-thiadiazole-2,5 diyl)bis(sulfanediyl)bis(methylene)bis(4-amino-4H-1,2,4-triazole-3 thiol)

Refluxed for 18– 20 hours was a suspension of compound (4) (3mmol,1.56g) in water (4 mL) and hydrazine hydrate (80%, 9 mmol,0.45ml). With a little tremor. With the formation of hydrogen sulphide gas, the colour of the reaction mixture changed to green. During the procedure, a homogenous reaction mixture was obtained. After cooling to room temperature, the reaction mixture was diluted with cold water (5mL). The necessary triazole was precipitated out after acidification with Conc. HCl, and it was recrystallized from a DMF–water combination. Yield= 52 percent, m.p= (198-200) C

3. Biological study

"The antibacterial test was performed according to the disc diffusion method. Compounds were assayed for their antimicrobial activity in vitro against four strains of bacteria (two of them were gram negative (Escherichia coli, Klebsiellapneumoniae) and the other were gram positive (staphylococcus aureus, Enterococcus faecalis)). Prepared agar and petri dishes were sterilized by autoclaving for15min at 121C°. The agar plates were surface inoculated uniformly from the broth culture of the tested microorganisms. In the solidified medium suitably spaced apart holes were made all 6mm in diameter". [1][2]

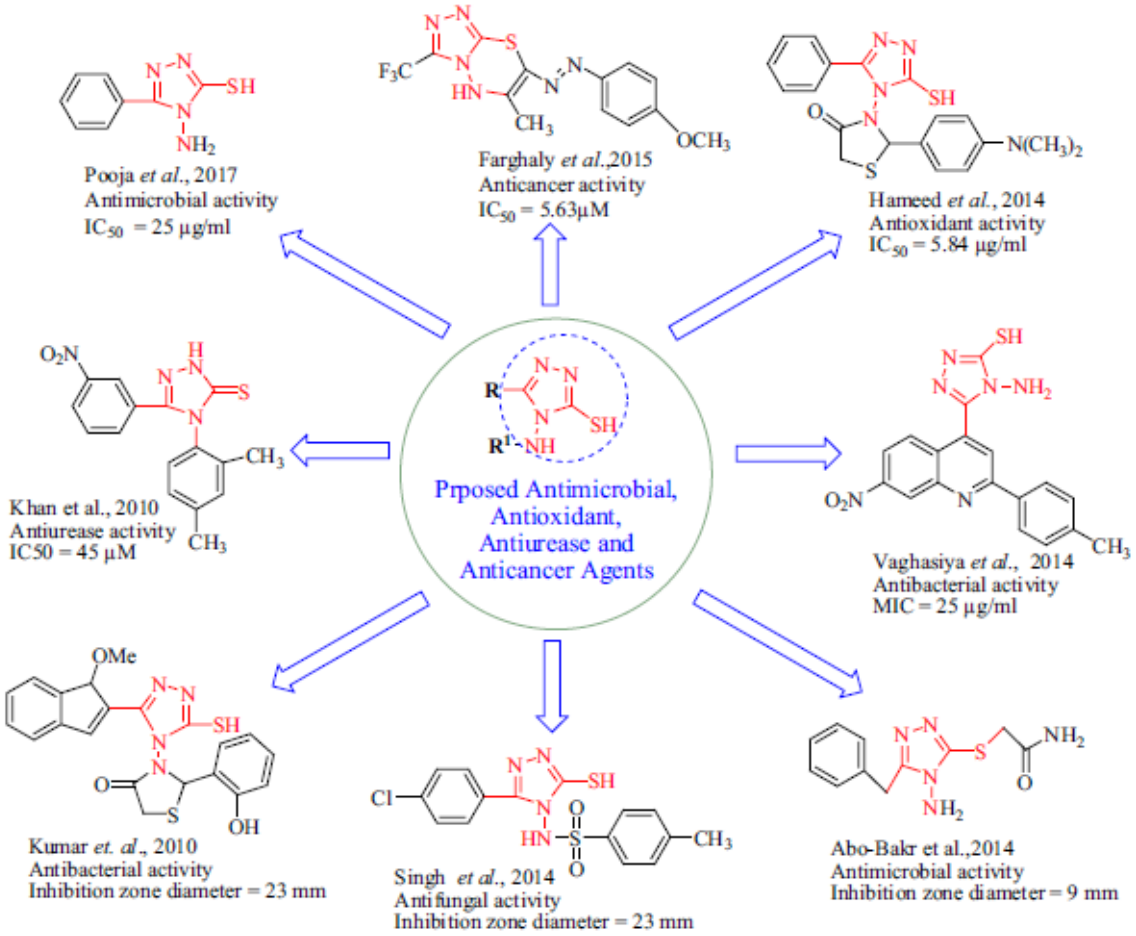

Fig. 3 :1,2,4-triazole analogues for antimicrobial, antioxidant, antiurease and anticancer activities

These holes were filled with 0.1ml of the produced compounds, with four concentrations (25, 50, 100, and 200 g/ml) for each compound. Amoxicillin and ceftriaxone were utilised as antibiotic reference medications, while fluconazole was employed as an antifungal reference drug. The solvent utilised was DMSO. One of these holes was filled with DMSO as a control, and the plates were incubated at 37°C for 24 hours to see how the solvent affected the results. The experiment was then repeated with all chemicals at a constant dose of 25 g/ml.

Conclusion

Finally, under click reaction circumstances, all poor-rich electron phenyl azide compounds were effectively reacted with propiolic acid. Because the produced compounds possess a carboxyl functional group, they were used as a starting point for the development of a series of novel heterocyclic compounds having both 1,2,4-triazole and 1,3,4-thiadiazole rings in a single molecule. Furthermore, all of the heterocyclic compounds that were produced had a good thermal stability.

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