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Review Article

Synthesis, Characterization, and Biological Evaluation of [1, 2, 4]-Triazole-3yl] Sulfanyl Acetamide Derivative

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Article History	Abstract
Received on: 27-01-2022 Revised on: 14-02-2023 Accepted on: 11-03-2023	A significant portion of recent papers is in the field of Mercapto substituted Triazole moiety received considerable attention in the literature. Characterization and Antibacterial activity against important medically Gram positive Bacteria likely Actinomyces, Clostridium, Mycobacterium, Strptococci, Staphylococci and Nocardia. Triazole is a class of N-Bridged Heterocyclic compounds especially in Chemotherapy. Triazole moiety seems to be very small but 1, 2, 4-Triazole derivatives have wide range of potential antibacterial activities against drug-resistant pathogens. Hybridization shows a high potential to develop novel drugs, reduce toxicity, and improve Pharmacokinetic profiles. More effective antibacterial studies might be obtained by the hybridization of 1,2,4-Triazole mercapto moiety. A number of clinically effective antibacterial drugs become more effective. Therefore, we shed, herein, more light on novel synthetic drug and its antibacterial activity.
Keywords: N-Bridged Heterocyclic compounds, 1, 2, 4-Triazole derivatives, Sulfanyl Moiety, Antibacterial Activity.	
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INTRODUCTION (BACKGROUND OF THE STUDY)

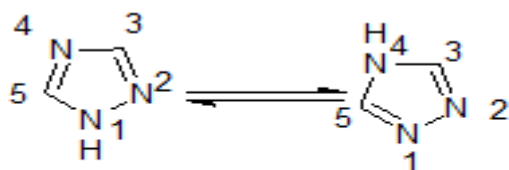
Heterocyclic ring present in a small organic molecule received considerable attention in the literature, mainly due to a broad range of biological properties and a detailed history as important medicinal pharmacophore. Among these heterocycles, nitrogen containing ring compound is an expanding area of research in medicinal chemistry, exhibit a wide range of biological activities including anti-depressive, analgesic, antipsychotic, antihistaminic, and antimuscarinic, anticancer, antitumor activity. Literature Review shows that 1,2,4-Triazole core has been incorporated into a wide variety of thera-

apeutically important agents available in clinical therapy, such as Itraconazole, posaconazole, voriconazole (Antifungal), Ribavirin (Antiviral). Rizatriptan (antimigraine), Alprazolam (anxiolytic) Trazodone (antidepressant), Letrozole, anastrozole (antitumour), and their fused heterocyclic derivatives shows a wide spectrum of A significant portion of recent papers is in the field of Mercapto substituted Triazole moiety received considerable attention in the literature. Characterization and Antibacterial activity against important medically Gram positive Bacteria likely Actinomyces, Clostridium, Mycobacterium, Strptococci, Staphylococci and Nocardia. Triazole is a class of N-Bridged Heterocyclic compounds especially in Chemotherapy. Triazole moiety seems to be very small but 1,2,4-Triazole derivatives have wide range of potential antibacterial activi-

ties against drug-resistant pathogens. Hybridization shows a high potential to develop novel drugs, reduce toxicity, and improve Pharmacokinetic profiles. More effective antibacterial studies might be obtained by the hybridization of 1,2,4-Triazole mercapto moiety and Structure activity Relationship also discussed. A number of clinically effective antibacterial drugs become more effective. Therefore, we shed, herein, more light on novel synthetic drug and its antibacterial activity. Sulphur containing Heterocycles represents important group in Practical applications and among these Heterocycles the Mercapto and Thione substituted 1,2,4-triazole ring system have been well studied.

Recent research Acetamide derivatives are reported to exhibit antibacterial effects substitution including alkyl thio and alkenyl thio derivatives have been carried out primarily at 3rd position of the nucleus ring as potential antibacterial activity.

The Five-member ring system containing three nitrogen atoms defines an interesting class of compounds, the triazole. This may be of two Tautomeric forms the 1H-1,2,4-triazoles (**1**) and the 4H-1,2,4- triazoles



1H - tautomer

4H - tautomer

Theoretical studies favor the 1H-structure (1a) for triazole rather than the more symmetrical 4H-structure (1b) and very difficult to separate them due to their rapid interconversion. By affecting the Hydrogen Bonding ability, Solubility, Lipophilicity, of the 1H-1,2,4-Triazole moiety can improve the physicochemical properties ,Toxicology, Pharmacokinetics and Pharmacology of the compounds.

Triazole melts at 120-121 °C and boils at 260 °C. It has a Density of 1.132 and a specific conductivity of about 10⁻¹⁰ Ω⁻¹ cm⁻¹, of the same order as imidazole. Triazole dissolves readily in water and ethanol but is only slightly soluble in ether. Substitution on N (1) usually lowers the melting point this effect is usually much smaller for substitution at N(4), although 4-aminotriazole has a melting point of 84-86 °C. 3-Amino triazole has a melting point of 159 °C

and the 3-thiol derivatives of 221-224 °C, both of which probably reflects substantial hydrogen bonding in the crystal.

Theoretical studies favor the 1H-structure (1a) for triazole rather than the more symmetrical 4H-structure (1b). Calculation suggest that destabilization of (1b) is due to the contiguous hetero atoms of the same hybridization type .1,2,4-triazole has also been called s-triazole, to distinguish it from the isomeric 1,2,3-triazole, termed v-triazole. Except for those containing exocyclic double bonds, which maintain the potential aromatic character of the parent triazole ring, partially or fully reduced triazoles are relatively unstable and have not piqued the curiosity of researchers.

Statement of The Problem

Acetanilide derivatives are reported to exhibit number of biological activities including anaesthetic, anti-inflammatory, antibacterial effects substitution including alkyl thio and alkenyl thio derivatives have been carried out primarily at 3rd position of the nucleus ring as potential antimicrobial activity. Moreover Rational Design and Development of the novel antibacterial agents incorporating 1,2,4-triazole can help in dealing with the escalating problems of Microbial Resistance.

Scheme of Work

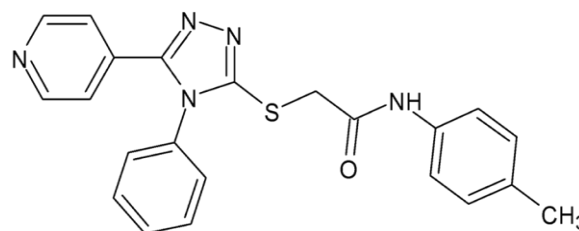
1,2,4-triazoles hybrids ,the two Novel compounds were synthesized and synthesized compounds studied as potential Antibacterial activity against important medically Gram positive Bacteria. In this Review only elemental analysis and activity was covered by novel compound (Scheme1) & (Scheme2)

SCHEME 1:

4 [N-(4-aryl amine)-2-[[4-phenyl-5-(pyridin-4-yl)-4H-1,2,4-triazol-3-yl] sulfanyl] acetamide] .

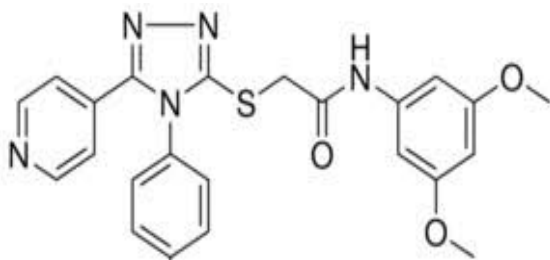
SCHEME 2 [N-[4-(3-Oxo-3-phenyl-propenyl)-phenyl]-2-(4-phenyl-5-pyridin-4-yl-4H- [1,2,4] triazol-3-yl sulfanyl)-acetamide]

SCHEME 1: STRUCTURE



SCHEME 2

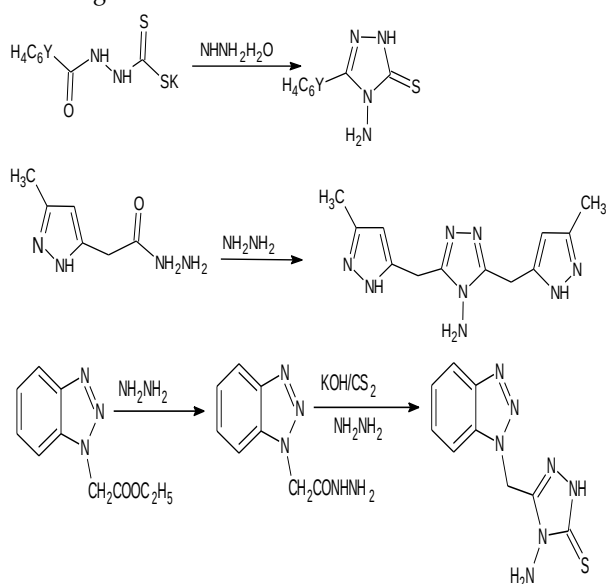
[N-[4-(3-Oxo-3-phenyl-propenyl)-phenyl]-2-(4-phenyl-5-pyridin-4-yl-4H- [1,2,4] triazol-3-yl sulfanyl)-acetamide]



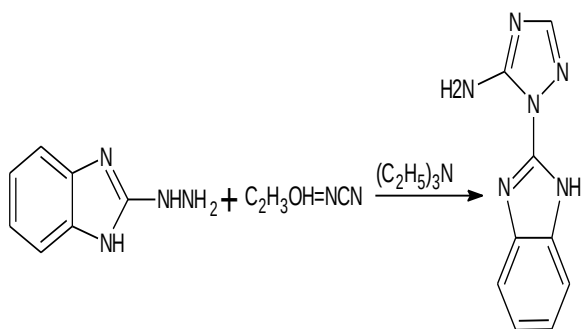
Literature Review

Methods of preparing triazole

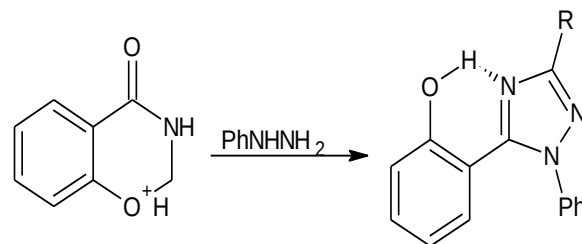
The reaction of hydrazine or substituted hydrazine with suitable electrophiles remains the most common method of preparing triazoles. The Hydrazine will usually form N (1) and N(2), but there are numerous examples of it becoming NH₂-N.⁸⁴⁻⁸⁷ Example where hydrazine provides all nitrogen has been described.⁸⁸⁻⁹⁰



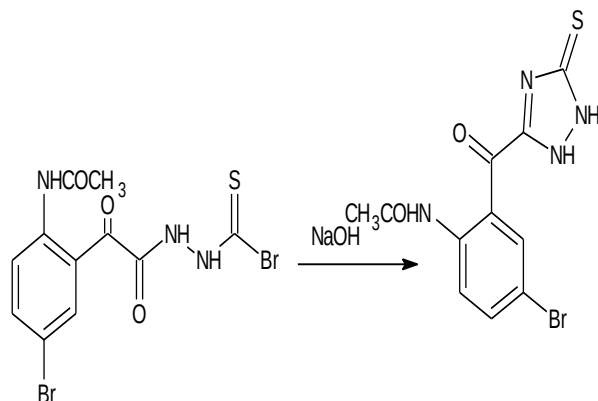
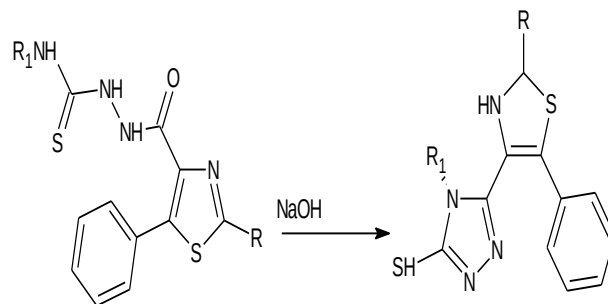
Treatment of ethyl-N-cyanoformimidate with a hydrazine hydrate in triethylamine gives the corresponding 5-aminotriazole.



The oxonium salt reacts with phenylhydrazine to give the 1-phenyltriazole the X-ray structure of which shows intramolecular hydrogen bonding between the phenol hydrogen and N(4).



The thiosemicarbazide cyclises to the triazole on treatment with Sodium Hydroxide and undergoes similar reaction to give 1,2,4-triazole.



Synthetic approaches towards 1,2,4-triazoles

The early methods of preparation of 1,2,4-triazoles were simple and low yields were obtained but they made the nucleus available for study within a year of the original discovery by Bladin. These have now been replaced by later modifications and by more efficient methods.⁹⁷⁻⁹⁸

From semicarbazides

A method of practical importance involves synthesis of 1-aryltriazoles from 1-arylsenicarbazides. This is illustrated by the formation of 3-hydroxy-1-phenyl-1,2,4-1H-triazole from 1-phenylsemicarbazide and boiling anhydrous formic acid. By heating to over 200°C with phosphorus pentasulfide, 1-phenyl-1,2,4-1H-triazole is obtained in 80% yield.

From triazine

The reaction of s-triazine with a substituted hydrazine salt¹⁰⁰ gives substituted 1,2,4-triazoles. For example, from phenyl hydrazine hydrochloride 1-phenyl-1,2,4-1H-triazole is obtained in 83% yield. The reaction proceeds by the formation of a substituted formamidrazone as a

result of ring cleavage of s-triazine, which reacts immediately with another molecule of triazine to yield the substituted triazole.

From thiosemicarbazides

Usually, 1,2,4-triazoles are formed by the cyclization of a preformed nucleus of the following types: The former type of ring closure is the most efficient method of synthesis of C-mono-substituted triazoles. In this way, a triazole containing amercapto or hydroxyl group is obtained which then may be removed by oxidation. Thus, the cyclization of 1-acetylthiosemicarbazide with sodiummethoxide in methanol results in the formation of 5-mercapto-3-methyl-1,2,4-triazole which readily loses the mercapto group on oxidation with nitric acid to form 3-methyl-1,2,4-triazole. It is interesting that 4-benzoyl-1-carbamoyl-3-thiosemicarbazide under various reaction conditions forms different products: with 20% sodiumhydroxide it yields 5-mercapto-3-phenyl-1,2,4-triazole that is normal cyclization product of 4-acylthiosemicarbazides with alkali; with concentrated-sulfuric acid at room temperature it forms 3-benzamido-5-hydroxy-1,2,4-triazole by the elimination of hydrogen sulfide; and a hot acetic anhydride-acetic acid mixture results in the formation of 3-benzamido-5-methyl-1,2,4-triazole.¹⁰⁴ Dimova *et al.* synthesized a series of 4-substituted 5-aryl-1,2,4-triazoles by cyclization of the corresponding substituted thiosemicarbazides.¹⁰⁵

From benzalsemicarbazones with ferric chloride

Oxidation of benzalsemicarbazone with ferric chloride solution readily gives 3-aryl-5-hydroxy-1,2,4-triazole which is also obtained by the oxidation of a mixture of benzaldehyde and azodicarbamide. The hydroxyl group is removed on fusion of hydroxyl triazole with phosphorus pentasulphide forming 3 (or 5)-substituted triazole.¹⁰⁶

From carboxylic acid hydrazides

The condensation of carboxylic acid hydrazides with carbon disulphide in ethanolic potassium hydroxide yields potassium 3-aryldithiocarbazates that is directly converted to 4-amino-4H-1,2,4-triazole-3-thione with an excess of hydrazine. The methylation of with methyl iodide provided the S-alkylated derivatives that also cyclize to with hydrazine.

From 1,3,4-oxadiazol-5-thione

1,3,4-Oxadiazol-5-thiones are converted into 4-amino-1,2,4-triazol-5-thiones with hydrazine hydrate.¹⁰⁸⁻¹¹¹ Thus, Reid and Heindel¹¹⁴ indicated that the 5-aryl-2-1,3,4-oxadiazol-5-thione recycled to form 4-amino-1,2,4-triazole-3-thione with hydrazine hydrate.

From thiosemicarbazides and carbonyl compounds

The cyclocondensation of 2,4-disubstituted thiosemicarbazides with carbonyl functions forms triazoles¹¹². Reaction of 4-(2-methylallyl)-2-phenylthiosemicarbazide with ketones in the presence of catalytic amount of sulfuric acid afforded 3,3-dimethyl-4-(2-methylallyl)-1-phenyl-1,2,4-triazolidin-5-thione.

From thiocarbohydrazides and carbohydrazides

The condensation of thiocarbohydrazides with aliphatic and aromatic carboxylic acids is the choicest method for the preparation of 3-alkyl/aryl-4-amino- Δ^2 -5-mercapto-1,2,4-triazoline.¹¹³⁻¹¹⁵ The reaction is improved by using carboxylic acids at their melting points, resulting in the preparation of 3-alkyl/aryl-4-amino-5-mercapto-1,2,4-triazole. The carbohydrazide on treatment with acid forms 4-amino-3-methyl- Δ^2 -1,2,4-triazolin-5-one.

From thiosemicarbazides with benzoyl chloride

Thiosemicarbazide with benzoyl chloride in boiling pyridine or alkali undergo benzylation and cyclization resulting in the formation of 4-benzoyl-3-phenyl- Δ^2 -5-mercapto-1,2,4-triazoline.¹¹⁶

From phenylthiosemicarbazide with ethylphenylimidate

Hydrochloride

The reactions of 4-phenylthiosemicarbazide with ethylphenylimidate hydrochloride illustrated the formation of 3,4-diphenyl- Δ^2 -1,2,4-triazoline-5-thione.¹¹⁷

From condensation of a nitrile and a hydrazide

3,5-Disubstituted 1,2,4-triazoles are synthesized from the condensation of a nitrile and a hydrazide in a convenient and efficient one step base catalyzed synthesis described by Kap-Sun Yeung and co-workers from Bristol-Myers Squibb.¹¹⁸ Under the reaction conditions, a diverse range of functionality and heterocycles are tolerated.

From isothiocyanates

Isothiocyanates on condensation with acylhydrazide affords hydrazinecarbothioamides which are cyclized to 3-mercapto-1,2,4-triazoles under basic conditions.¹¹⁹ The hydrazide derivatives on refluxing with phenylisothiocyanate in absolute ethanol yield the corresponding phenylthiosemicarbazides, which may be cyclized¹²⁰ in the presence of NaOH.

From aromatic nitriles

Aromatic nitriles on reaction with hydrazine dihydrochloride in the presence of hydrazine hydrate under microwave irradiation give 3, 5-disubstituted-4-amino-(4H)-1,2,4-triazoles.¹²¹⁻¹²²

Solid phase synthesis of triazoles

So far, only a few investigations on the solid-phase synthesis of substituted 1,2,4-triazoles have been reported. Katritzky described the synthesis of trisubstituted 1,2,4-triazoles on a solid substrate by the condensation reaction of an acyl hydrazide and substituted amidines¹³⁰. The yields ranged from 37 to 90 percent, and the purities were determined by the triazole core substituents.

This method allows for the alkylation of the 1-position, yielding trisubstituted 1,2,4-triazoles, however it suffers from the reaction sequence's nontraceability. As a result, the 1,2,4-triazoles produced include the 4-hydroxyphenyl linker of the starting Wang resin. On solid supports, 3,4,5-trisubstituted 1,2,4-triazoles were also synthesised.

On polymeric supports¹³², a traceless synthesis of 3,5-disubstituted 1,2,4-triazoles was devised, employing immobilised mesoionic 1,3-oxazolium 5-oxides (münchnones) as essential intermediates in the 1,3-dipolarcycloaddition process, as illustrated below.

Synthesis of 1,2,4-triazoles under microwave irradiation

Microwave irradiation has become a popular approach for quickly synthesising several important organic compounds with great selectivity and yields. Many relevant research only propose a thermal basis of microwave action, which implies that microwaves are thought to be a way of rapidly heating chemical reagents without overheating. Other papers identify particular non-thermal effects, which are likely to exist. Sometimes the impacts are assumed to be limited to certain types of heat effects, however this is not always the case. In the meanwhile, Molteni and Ellis, examined the work done since 1994 in the field of microwave-assisted synthesis of heterocyclic compounds and processes in which a heteroatom is directly participating in the bond formation process that gives rise to a heterocyclic core. The reaction of chalcones with bis(1,2,4-triazolyl) sulfoxide resulted in an unique one-step synthesis of thiazolo-[3,2-b]-1,2,4-triazoles. Symmetrical 3,5-substituted 4-amino-1,2,4-triazoles are synthesised swiftly from aromatic aldehydes via nitriles in two steps with no separation under microwave irradiation for several minutes each. Under microwave irradiation, acid hydrazide condensed with S-methylisothioamide hydroiodide and ammonium acetate on the surface of silica gel to produce 1,2,4-triazoles. Using substituted primary amines, an effective microwave-assisted one-pot and three-component synthesis of substituted 1,2,4-triazoles was obtained. Kidwai et al. used microwave irradiation to

manufacture novel antifungal azoles, including 1,2,4-triazole derivatives, from substituted hydrazide. A straightforward and quick synthesis of 6-aryl-3-substituted 5H-[1,2,4]-triazolo-[4,3-b] [1,2,4] Microwave aided heterocyclization of N-(3-methylthio-5-substituted 4H-1,2,4-triazol-4-yl)benzene-carboximidates resulted in high quantities of -triazolesmin.

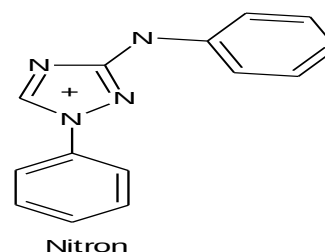
Important compounds and application

The interest in triazole largely derives from their biological effects in both medicine and agriculture, but there is also an interest in 3-nitro triazole and its derivatives as explosives. In many cases the biological properties of triazole are found in many related heterocycles but the triazoles are often the most potent derivatives. There has also been a considerable interest in triazoles as ligands in organometallic compounds and as functional groups on macrocyclic rings for selective complexation of ions.

Analytical and Synthetic application.

Analytical uses

Triazole have been used extensively in analytical chemistry. Nitron have been used for the determination of Boron, rhenium, and tungsten. Nitron have been bonded to a polymer and used for the removal of nitrate from the water.¹³³ Other triazole have been used for the spectrophotometric assay of cobalt, rhodium, and platinum.¹³⁴⁻¹³⁵ Hydroxyphenylazotriazoles from brilliant lakes with number of metal ions.¹³⁶



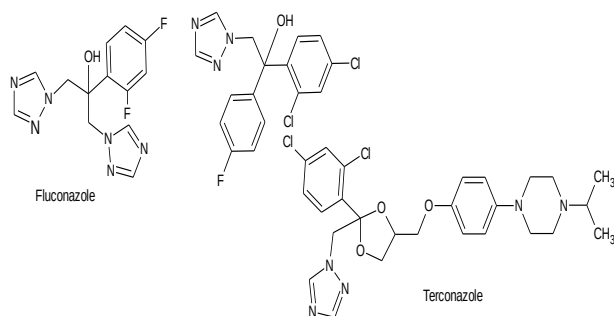
Synthetic uses.

Halotriazole can act as halogenating agent and N-acyltriazole can act as acyl transfer reagents. Triazole can be used for the synthesis of peptide bonds and is superior to imidazole in that less racemization is observed. It can also be used for transfer the t-butyloxycarbonyl (t-Boc) protecting group to the nitrogen of amino acids.¹³⁷ Diwakar and Reese have been used triazole as a reagent having good nucleophile and leaving group properties for both the conversion of uridine into cytosine and for conversion of the corresponding arabinose derivatives. This reaction has found further used in the conversion of other nucleotide and nucleoside derivatives. In an interesting modification, the triazole ring has been constructed from the amine group of

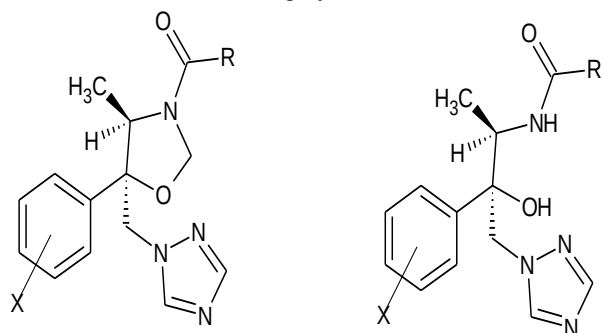
an adenine derivative and displaced by other nucleophiles, other example of triazole as leaving groups are known. PTAD has been used as protecting groups for dienes.

Biological uses

3-aminotriazole has been used as a herbicide and defoliant and also as a histidine analogue. It is reported to inhibit intracellular catalase and to block certain ethanol-induced behavioral effects. 3-Nitrotriazole and derivatives has found use as radio sensitizers of hypoxic cancer cells. Simple 5-oxo-and 5-thio-3-aryltriazole derivatives have anticonvulsant activity. A precursor of paclobutrazole, an agrochemical, crystallizes from the racemic mixture as pure crystal of one enantiomer.¹⁴⁷ A variety of compound related to fluconazole have been prepared as potential antifungal agents, including terconazole.¹⁴⁹ These compounds inhibits the biosynthesis of ergosterol, the major steroid in fungal membrane,

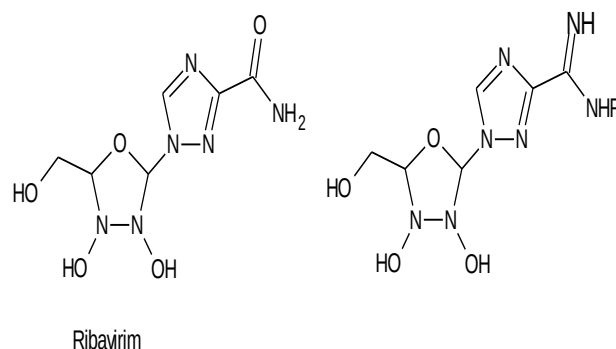


A number of compound which control *Candida albicans* infections in mice have been prepared which contain 4,5-dihydrooxazole rings. It has been shown that only certain enantiomers are highly active.

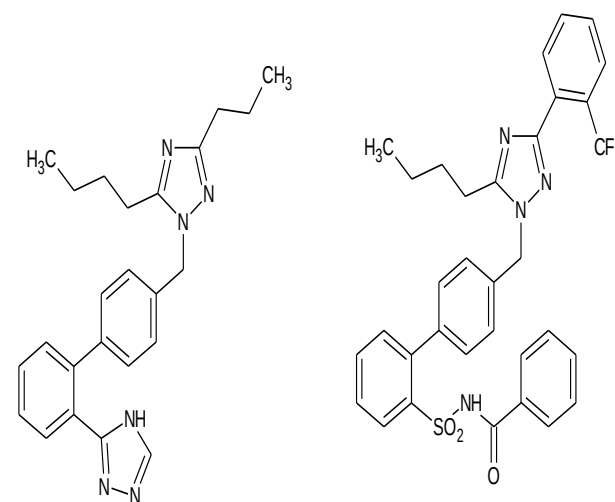


Ribavirin is abroad spectrum antiviral agent consisting of 3-amino triazole as the N-glycoside of ribose. It is active against both RNA and DNA viruses and is used in an aerosol for lower respiratory tract viral diseases. It is also used in a treatment of influenza, Lassa fever and Hantaan virus. A number of 3-sulfonamide derivatives has been prepared but these were devoid of antiviral or antitumor activity. a number of amide and guanidine derivatives has been prepared, some of the guanidine

derivatives also exhibiting broad spectrum antiviral activity.



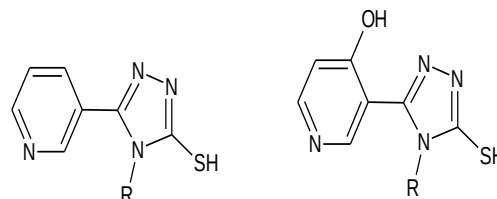
A number of triazole derivatives are angiotensin II receptor antagonist.¹⁵⁴⁻¹⁵⁸ Proceeding of a symposium on this subject have been appeared. The compound act at the AT1 receptor to mediate the action of angiotensin II to increase blood pressure.



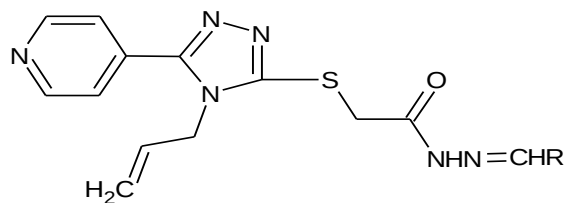
Some substituted 3-thiomethyltriazole derivatives show anti-thyroid activity¹⁶⁰ and some N-1-methylcarboxylate mimic the action of penicillins.

Reported synthesis strategies

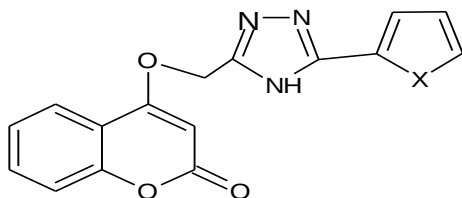
- **Suresh CH¹** and his co-workers have been synthesized 4-methyl-5-(pyridin-3-yl)-4H-1,2,4-triazole-3-thiol and 2-(4-methyl-5-sulfany-1,2,4-triazol-3-yl) phenol and tested it for possible antimicrobiological activity. (2010)



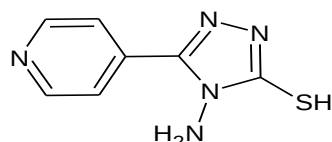
- **Akbar Mobinikhaledi et. al.** have synthesized some novel Schiff bases containing 1,2,4-triazole ring.



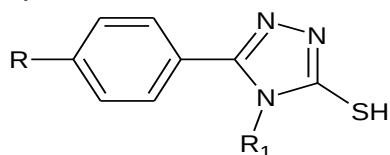
- **Panda S. S et.al.** have been synthesized 4-(5-Aryl-4H-[1,2,4] triazol-3-ylmethoxy)-2H-chromen-2-ones have been synthesized by the one pot cyclo condensation reaction of 2-(2-oxo-2H-chromen-4-yl-oxy) acetohydrazide with aromatic/heterocyclic aldehydes in the presence of ammonium acetate in acetic acid. These compounds were also evaluated for their anti-bacterial and antifungal activity against various strains of bacteria and fungi and some are found to possess significant antimicrobial activity.



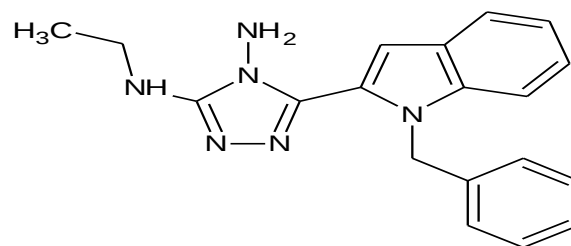
- **Murthi Y.** and his co-workers have been synthesized some substituted 1,2,3- and 1,2,4-triazole and screened it for pharmacological action.



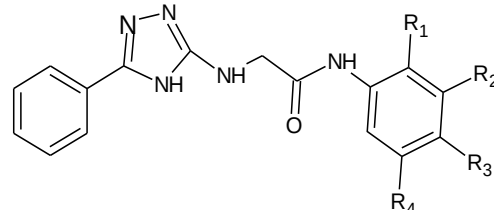
Parmar Kokila A. et.al. have been synthesized 4-Aryl triazoles and its derivatives 4-aryl triazoles were obtained by cyclization reaction of the potassium salt of substituted dithiocarbazinic acids with aromatic amines. Compounds have been screened for their antibacterial activity.



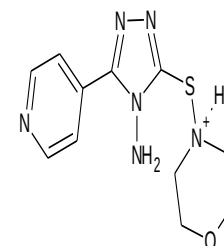
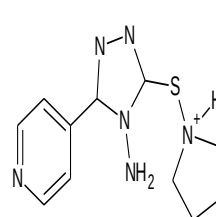
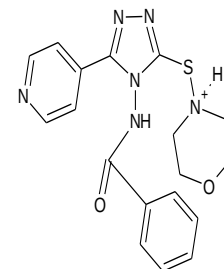
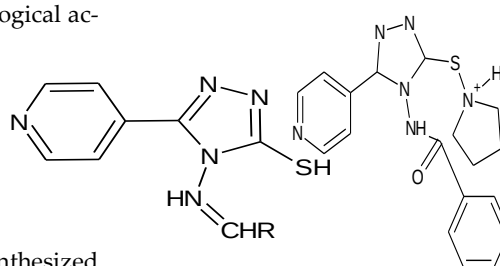
- **Ghareb N. et. al.** have been novel Indole-3-Carbinol and (Benzimidazolylmethyl) Triazole-3, 4- Diamine Derivatives.



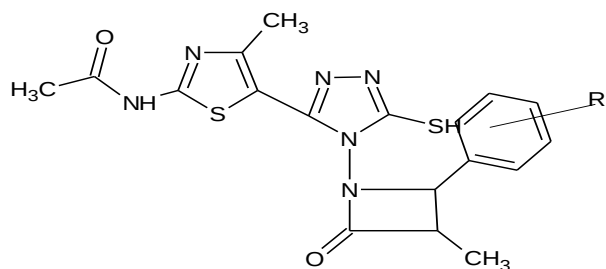
- **Kadadevar D.** and his co-workers have synthesized five N-(substituted phenyl)-2-[5-phenyl-2H-1, 2, 4-triazol-3-ylamino] acetamide and tested for anticonvulsant activity by MES method. Cyclocondensation of benzamidoguanidine in sodium ethoxide gives 5-amino-3-phenyl-1, 2, 4-triazole. This on reaction with 2-chloro-N-substituted phenylacetamide gives the title compounds.



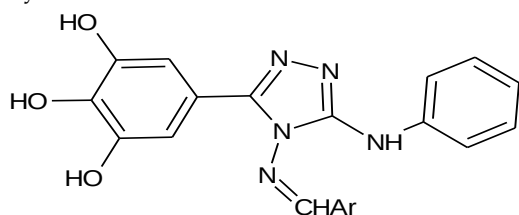
- **Khatale et.al.** have been synthesized of 4-(N-substituted)-3-pyridyl- 5- mercapto-5-triazole with secondary amines and evaluated it for anti-microbial activity.



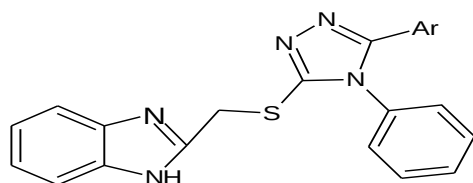
- **Bhaviskar B.A. et. al.** synthesized triazolyltriazole substituted azetidinone as microbial agents.



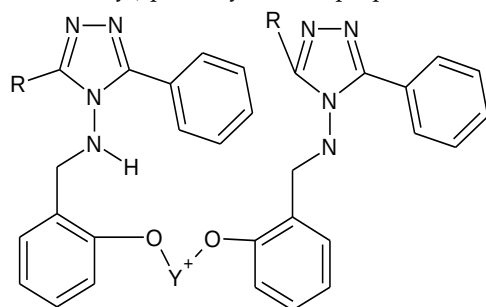
- **Jain V. K** and his co-workers have been synthesized some triazole derivatives of propyl gallate and evaluated for anti-tubercular activity.



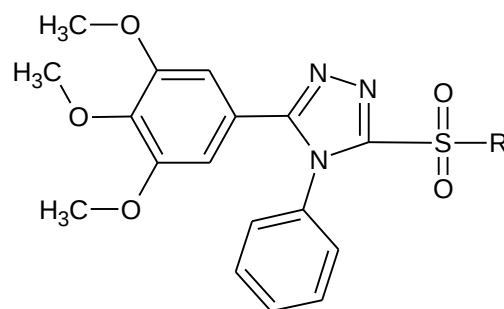
- **Badr S.M** et.al have synthesized certain 1,2,4-triazole based Benzimidazole and fused Benzimidazole derivatives



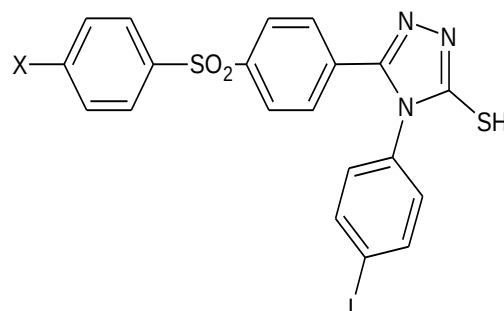
- **Olca Bekircan and Hakan Bektas** have synthesized a series of new 1,2/1,3-bis[o-(N-methylidenamino-3-aryl-5-phenyl-4H-1,2,4-triazole-4-yl) phenoxy] ethane/propane.



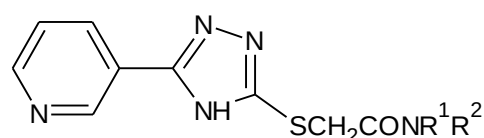
- **Baoan Song** have synthesized and derived crystal structure of novel Sulfone derivatives containing 1,2,4-Triazole moieties.



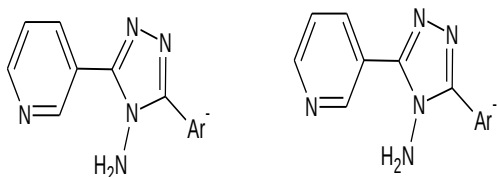
- **Stefania F. arbuceanu et.al** have reported new heterocyclic compounds from the class of 1,2,4-triazole-3-thione which were obtained by intramolecular cyclization, in basic media of some acylthiosemicarbazides containing diphenyl sulfone moieties. The new 1-(4-(4-X-phenylsulfonyl)benzoyl)-4-(4-iodophenyl)-3-thiosemicarbazides were obtained by the reaction of 4-(4-X-phenylsulfonyl)-benzoic acid hydrazides with iodophenylisothiocyanate. The cyclization of the acylthiosemicarbazides in the presence of an 8 % NaOH solution resulted in the formation of the new 5-(4-(4-X-phenylsulfonyl)phenyl)-4-(4-iodophenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thiones.



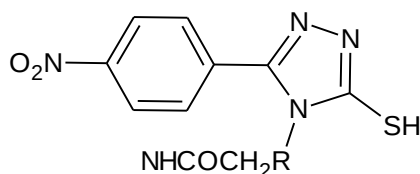
- **Somani R.R.** have been prepared 3-(3'-pyridyl)-1, 2, 4-triazole-5-thiol (2) with appropriately N-substituted-α-chloroacetanilides in aq. potassium hydroxide yielded corresponding 5-(N-substituted carboxamidomethylthio)-3-(3'-pyridyl) - 1, 2, 4-Triazoles. Anti-fungal activity was carried out against *C. albicans* and *A.niger* at the concentrations of 50 and 100 µg/mL using Fluconazole as the standard and in-vitro anti-tubercular activity was done at 50 µg/mL against *Mycobacterium tuberculosis* H37 Rv.



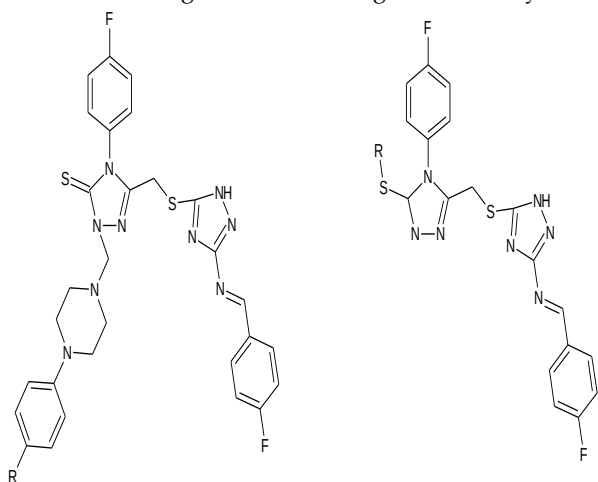
- **Muthal N.** and his co-workers have been synthesized some 5-substituted-3-pyridine-1, 2, 4-Triazoles and evaluated it for anti-bacterial and anti-tubercular biological activity.



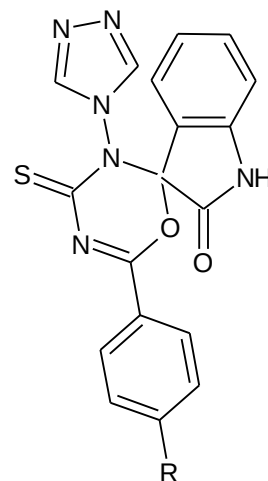
- **Upmanyu N.** have synthesized a series of 4-(substituted ethanoyl) amino-3-mercapto-5-(4-nitro) phenyl-1,2,4-triazoles as novel antimicrobial agents starting from 4 nitrobenzoic acid. Their antimicrobial activities against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Bacillus subtilis*, *Candida albicans*, *Aspergillus niger* and *Fusarium oxysporum*) were investigated.



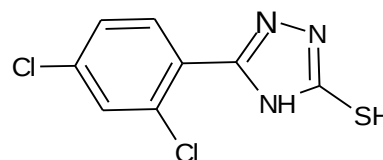
- **Laila A. Abou-zeid** have been synthesized A novel family of 3,5-disubstituted triazoles was developed and tested for antifungal and antibacterial activities in vitro. When compared to the commercial fungicide clotrimazol, all substances examined demonstrated considerable antifungal effectiveness against micromycetes.



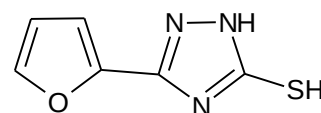
- **Patel H.S,** and his co-workers have been synthesized 6'-Phenyl-4'-thioxo-3'-(4H-1,2,4- triazole-4-yl)-3',4'-dihydrospiro [Indoline-3,2'- [1,3,5] oxadiazine]-2-one and compounds have been screened for their anti-microbial activity.



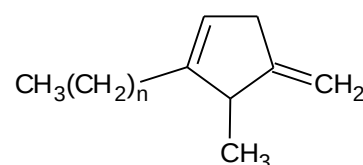
- **Goswami *et.al.*** reported that the oxidative cyclization of 1-(2,4-dichloro-benzoyl) thiosemicarbazide gives the 3-(2,4-dichlorophenyl)-1H-1,2,4-triazole-5-thiol Compound exhibited antimicrobial activities against *B. Cereus*, *Esch. Coli* and *P. Salanarium*.



- **Koapirr et al** 5-Furan-2-yl-4*H*-1,2,4-triazole-3-thiol was prepared by the reaction of the appropriate 2-furoyl-thiosemicarbazide and potassium hydroxide in ethanol for 3 hours under reflux, followed by acidification with acetic acid.

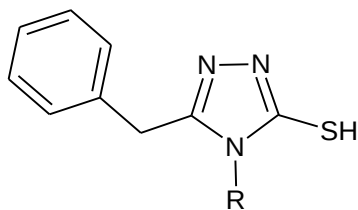


- **Katica C. R** have reported 4-alkyl/aryl-5-nonanoyl/octadecanoyl-2,4-dihydro-3H-1,2,4-triazoline-3-thiones were synthesized as potential antimicrobial agents. The course of synthesis included the reaction of nonanoyl/octadecanoyl hydrazine with selected alkyl/aryl isothiocyanates. The prepared thiosemicarbazides gave by cyclization the required 1,2,4-triazoles.

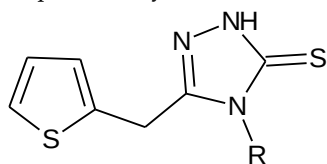


- **Koparir M.** The 1-(phenyl acetyl)-4-substituted thiosemicarbazides 47 on refluxing with 2N NaOH solution were cyclized into the corres-

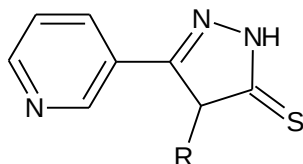
ponding 5-benzyl-4-aryl-4H-1,2,4-triazole-3-thiol.



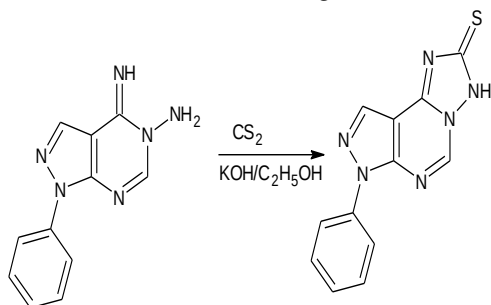
- **Wujec, M.;** have been prepared 1,2,4-triazoline-5-thiones were synthesized by the cyclization of the corresponding thiosemicarbazide derivatives in NaOH solution. Compounds showed antifungal activity against some species belonging to *Trichophyton spp.* known as the causative agents of superficial mycoses.



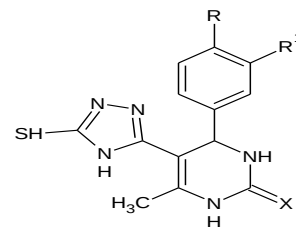
- **Zamani, K** reported the isomeric substituted thiosemicarbazides when subjected to react with 4N NaOH, underwent intra molecular dehydrate cyclization to furnish the corresponding 4-alkyl/aryl-5-(isomeric pyridoyl)-1,2,4-triazole-3-thioles. Compound exhibit moderate inhibitory activities at 32 µg/mL against *S. aureus*.



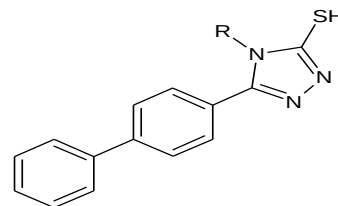
- **Baraldi, P. G** were prepared compound shown below and evaluated for biological action



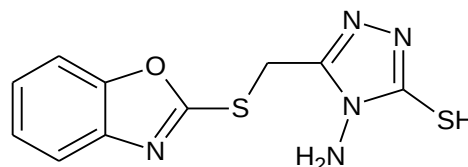
- **Andrews B. and Ahmed M.** have been synthesized a series of pyrimidine bearing 1,2,4-triazole derivatives and evaluated for antifungal activity.



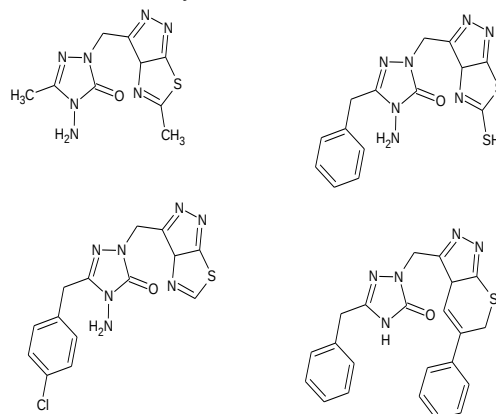
- **Rakesh Kumar** and his co-workers have been synthesized novel 1,2,4-triazole derivatives as potent antibacterial and anti-inflammatory agents.



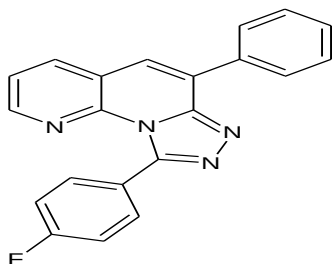
- **Sarangapani et al.** have been synthesized some new 4-substituted -5-[(2-benzoxazolyl thio)methyl]-3-mercapto-4H-1,2,4-triazoles and screened them for antibacterial activity.



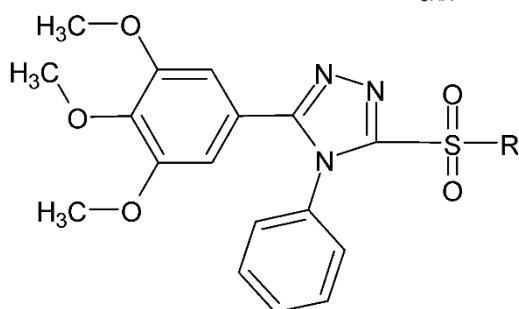
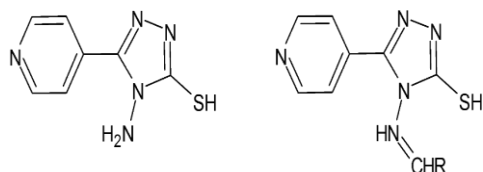
- **Neslihan Demirbas et al.** have been synthesized some new [1,2,4]-triazolo-[3,4-b], [1,3,4]-thiadiazoles and [1,2,4]-triazolo-[3,4-b], [1,3,4]-thiadiazines] and screened them for antimicrobial activity.



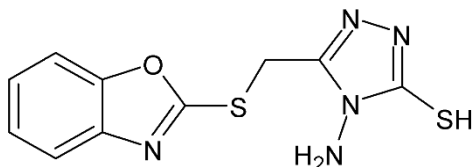
- **Mogilaiah³¹ et al.** have synthesized some 6-aryl-9-(p-fluorophenyl)-1,2,4-Triazolo[4,3-a][1,8]Naphthyridines and screened them for antibacterial activity.



- **Murthi Y** and his co-workers have been synthesized some substituted 1,2,3- and 1,2,4-triazole and screened it for pharmacological action.



- **Sarangapan32 et al.** have been synthesized some new 4- substituted -5- [(2-benzoxazolyl thio) methyl] -3-mercapto -4H-1, 2, 4-triazole



les and screened them for antibacterial activity.

- **Haitham Husein Al-Sa'doni 33** have been synthesized a series of 1,2,4-triazole-3-carbohydrazone derivatives and compounds of 1,2,4-triazole-3-(4H)-thione and its antibacterial activity in the European Journal of Chemistry 2020.
- **Jie Li et al.34** synthesized the Antibacterial activity of 1,2,3-triazole -and 1,2,4-triazole-containing Hybrids against *Staphylococcus aureus* in the journal of National Library of Medicine, 2020

Research Gap

Till date there has also been a dearth of literature focusing on potent antibacterial activity on 1,2,4-triazole-3-yl)sulfanyl acetamide derivative. Drug resistance pa-

thogens emerging globally and morbidity and mortality gives high rate. So to conduct the novel drug explore highly in the market the emergency and reemergence of multi drug resistance (MDR) bacteria, the appearance of MDR pathogens, the currently used antibiotics remains insufficient and the development of antibacterials are merely slow. Thus the development of active antibacterial Activity call of the day.

Research Questions:

RQ1:

Is 1,2,4-Triazole having Therapeutic actions ?

RQ2:

How far the Drug is good for Antibacterial actions ?

Research Objectives:

Heterocyclic compounds are widely used in Therapeutic agents taking this important concept in consideration I have chosen 1,2,4-triazole Heterocyclic compounds for the synthesis of Novel 1,2,4-triazole-3-yl)sulfanyl} Acetamide derivatives and for Evaluation of its Pharmacological Properties. Triazole are important class of the Heterocyclic compounds containing Triazole nucleus is very effectively and successful Drugs in the market, so synthesized compounds containing Triazole nucleus with Effective Biological Activity as mine main Focus.

Significance of Study

The Global Spread of Drug Resistance in Bacteria requires new potent and safe antibacterial agents. Compounds containing the 1,2,4-Triazole ring in their structure are characterized by multidirectional biological activity a large volume of Research on 1,2,4-triazole and their 3-yl)sulfanyl} Acetamide Derivatives has been carried out, proving Significant potent Antibacterial Activity of this heterocyclic core.

Scope of The Study

Novel 1,2,4-Triazole -3-yl)sulfanyl} Acetamide Derivatives will provide definite scope for researchers for the Advancement of Novel potential drug candidates having better efficacy and Selectivity.

Research Methodology:

- Synthesis of 1,2,4-Triazole Nucleus.
- Synthesis of Novel 1,2,4-Triazole -3-yl)sulfanyl} Acetamide Derivatives.
- Spectral Characterization of The Synthesized Compounds (TLC, IR, MASS, NMR)
- Structural Activity Relationship (SAR) Studies of Novel compounds.
- Antibacterial Evaluation of the Synthesized Compounds.
- Computational Studies and Virtual Drug Screening with the Auto Dock suite.

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