A Review: Triazole and their derivatives

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Abstract: This article aims to highlight the work reported, chemistry and biological activities of Triazole and their derivative which were synthesized during past years and recently.The importance of triazole derivatives lies in the field that these have occupied a unique position in heterocyclic chemistry due to it's various biological activities.The derivation of triazole ring is based on the phenomenon of bioisoterism in which replacement of oxygen of oxadiazole nucleus with nitrogen analogous. Out of the two triazole 1,2,4- triazole has wide variety of activities. This article highlighted research work of many researchers reported in literature has different pharmacological activities on triazole compounds synthesized as well as their characterization. This review paper has comprehensive details of triazoles analogous, potent compounds reported for particular pharmacological activities like Antimicrobial, Anti-inflammatry, Antimalarial and Anticancer agents.

Keywords:

Heterocyclic,Triazole,Biological,Bioisoterism,Pharmacological,Antimicrobial,Anticancer,Anti-Infalammatary

Introduction

In chemistry of heterocyclic compound continuous to be an explore field in organic or pharmaceutical chemistry.The importance of triazole derivatives lies in the field that these have occupied a unique position in heterocyclic chemistry due to it's biological activities.[1] TThe derivation of triazole ring is based on phenomenon of bioisoterism in which replacement of oxygen of oxadiazole nucleus with nitrogen analogous.Out of the two triazole 1,2,4-triazole has wide variety of activities.[2] Triazole and its derivatives represent an important class of heterocycles. They are of biological importance and are used in the synthesis of drugs. Triazole derivatives are also used in the synthesis of antibiotics, fungicides, herbicides, and plant growth hormone insulators and are potentially good corrosion inhibitions[3-5]The incorporation of various substituent into the 1,2,4-triazole ring and its fusion with various heterocyclic systems yield compounds with enhanced biological activities. The arrangement of 3 basic nitrogen atoms in the triazole ring induces the antiviral activities in the compounds containing this ring.[6] The 1,2,4-triazolenucleus has been incorporated into a wide variety of therapeutically interesting drug candidates including H_1/H_2 histamine receptor blockers, cholinesterase active agents, CNS stimulants, ant anxiety and sedatives[7] and those Synthesis, characterization, and antioxidant activities of..., K. SANCAK, et al. with antimycotic activity such as fluconazole, itraconazole, and voriconazole. Moreover, there are some known drugs containing 1,2,4-triazole moiety, e.g., triazolam, alprazalam, etizolam, furacylin, and ribavirin.[8]

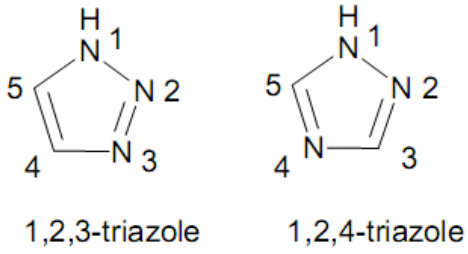
In the present study, prompted by these observations, the synthesis and antioxidant screening of new trisubstituted1,2,4-triazole derivatives and as hybrid molecules including different pharmacophores were examined. Triazole derivatives are showing very promising and excellent therapeutic effectiveness. The major activities exhibited by these derivatives include insecticidal, antifungal, antiviral, antibacterial, sedative, hypnotic, anticonvulsant and anti-inflammatory action. Either as single heterocyclic derivatives or in fusion with the other cycles, these heterocycle is emerging as the most explored center to obtain clinically significant compounds. The highly explored isomers of triazole being the 1H-1, 2,4-triazoles.

There are number of triazoles derivatives reported in this review possessing different biological activity comparable to clinically synthetic compounds. Excellent anticonvulsant activity is shown by 3-[4-(substituted

phenyl)-1,3-thiazol-2-ylamino]-4-(substituted phenyl)-4,5-dihydro-1H-1,2,4-triazol-5-thione and 8-chloro-6-(2-fluorophenyl)1-(aryl)-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine comparable to standard drug.

Substituted coumarin 1,2,4- triazol and sulphanilamide derived 1,2,3 triazol compounds displayed stronger antibacterial action. Potent anticancer activity was demonstrated by heterocycle fused 1,2,3 triazole and 3,6-disubstituted triazolo[3,4-b]thiadiazole derivatives. Compounds having pharmacophore such as methyl, methoxy, chloro, cyno, chloro, fluoro, and bromo groups have exhibited best anticonvulsants, anti-inflammatory, anticancer, antitubercular and antimicrobial activity. From the above discussions it may be concluded that the modifications in triazole moiety displayed valuable biological activities and these modifications can be utilized to develop potentially active agents for future investigations.

Triazole is one of the class of heterocyclic compounds with composition $C_2H_3N_3$ having five membered di unsaturated ring system containing three nitrogen and two carbon atoms. There are two types of Triazoles which are presenting below

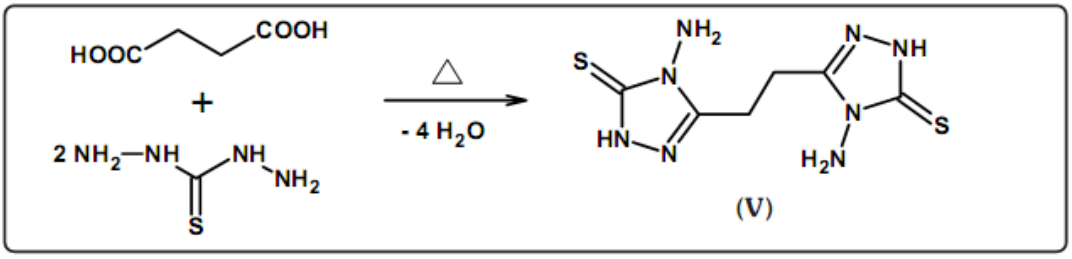


Types of Triazole

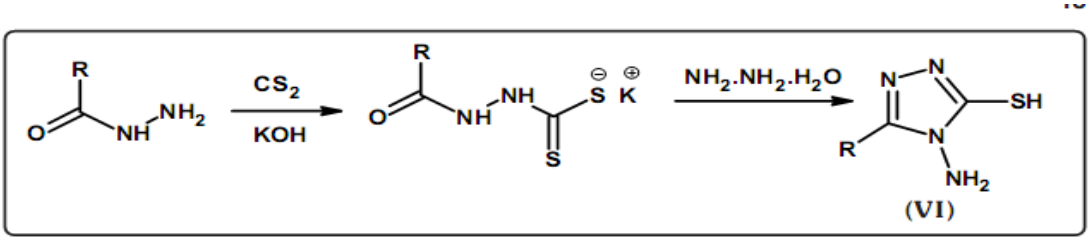
SYNTHETIC ASPECTS OF TRIAZOLE DERIVATIVES:

Several methods have been reported in the literature for the preparation Of 1,2,4-triazoles. The procedure for synthesizing 1,2,4-triazoles have been described as under.

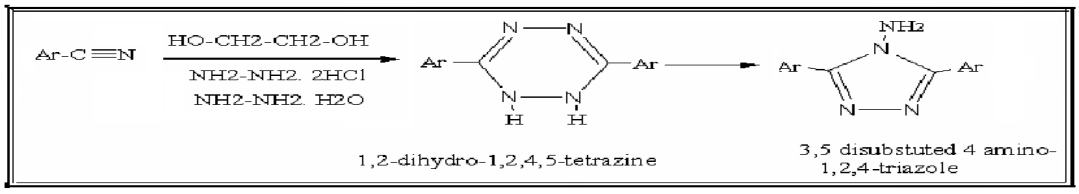
1. Ahmad S. Shawali et. Al[9] synthesised 1,2-bis (4-amino-5-mercapto-4H-1,2,4-triazol-3-yl) ethane by heating succinic acid with two molar equivalents of carbonothioic dihydrazide in an oil bath at 170°C



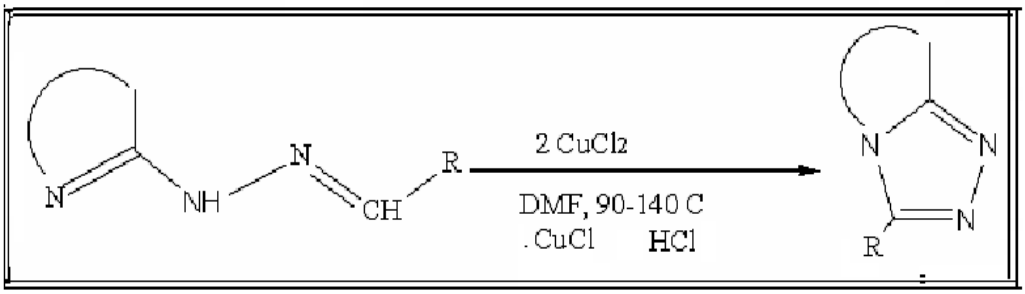
2. Reid and Heinde[10] reported that the reaction of aryl acid hydrazide with CS_2 / KOH and hydrazine hydrate furnished triazoles.



3. Bentiss et al.[11] in 2000 reported the reaction of aromatic nitriles with hydrazine dihydrochloride in the presence of hydrazine hydrate in ethylene glycol under microwave irradiation, give 3,5- disubstituted 4-amino-1,2,4-triazoles.



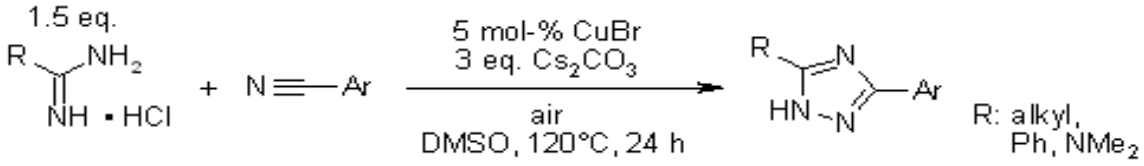
4. **Ciesielski et al.**[12] in 2005 described a novel copper- oxidative heterocyclization of hydrazones yielding the corresponding 1,2,4-triazoles.



Synthesis Reviews on 1,2,4- Triazole:

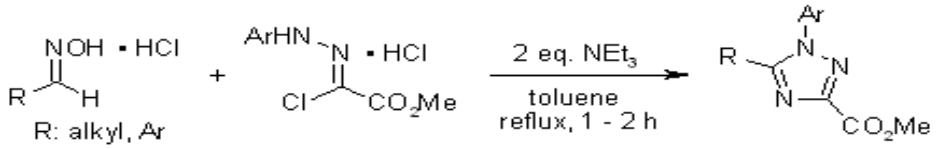
A copper-catalyzed reaction

A copper-catalyzed reaction under an atmosphere of air provides 1,2,4-triazole derivatives by sequential N-C and N-N bond-forming oxidative coupling reactions. Starting materials and the copper catalyst are readily available and inexpensive.A wide range of functional groups are tolerated.[13]



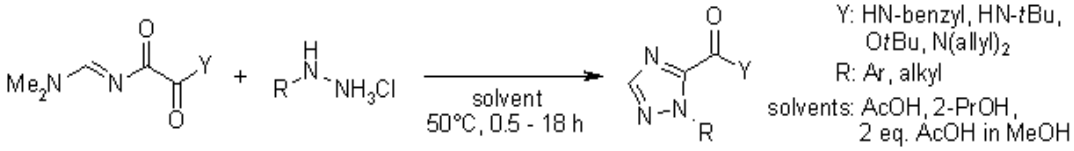
Dipolar cycloaddition

An effective 1,3-dipolar cycloaddition for the synthesis of 1,3,5-trisubstituted 1,2,4-triazole derivatives by reaction of oximes with hydrazonoyl hydrochlorides using triethylamine as a base gave the desired 1,3,5-trisubstituted 1,2,4-triazoles in good yields. The reaction was applicable to aliphatic, cyclic aliphatic, aromatic and heterocyclic oxime substrates.[14]



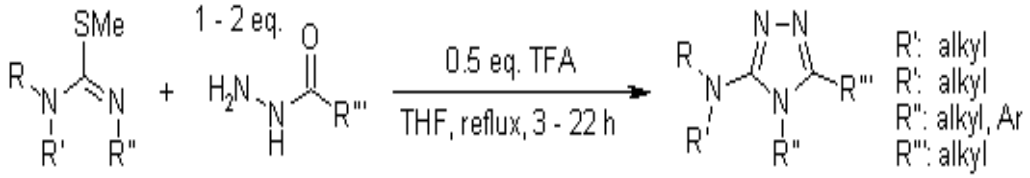
Reaction of oxamide

A series of new oxamide-derived amidine reagents can be accessed in excellent yield with minimal purification necessary. A subsequent reaction of these reagents with various hydrazine hydrochloride salts efficiently generates 1,5-disubstituted-1,2,4-triazole compounds in good yields. Both aromatic and aliphatic hydrazines react readily with the amidine reagents under very mild reaction conditions.[15]



Preparation from dialkylamino 1,2,4-Triazole

3-*N,N*-Dialkylamino-1,2,4-triazoles can be prepared from *S*-methylisothioureas and acyl hydrazides in good yields. The reaction conditions are relatively mild and tolerate a broad range of functional groups.[16]

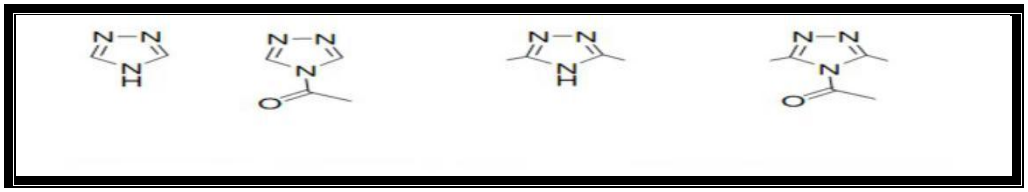


Characterization OF 1,2,4-Triazole:

Ultraviolet, infrared and nuclear magnetic resonance spectroscopic studies are very informative about the structure of 1,2,4-triazoles and their derivatives.

i) Ultraviolet spectroscopy:

The unsubstituted 1,2,4-triazole shows a very weak absorption at 205 nm in the ultraviolet absorption spectrum. Bathochromic shift occurs in N-acetyl-1,2,4-triazole , with the absorption band being located at 221.5 nm[53]. A similar shift in the absorption maximum of 3,5-dimethyl-1,2,4-triazole appears on conversion into N-acetyl-3,5-dimethyl-1,2,4-triazole (14)[17]



Several 1,2,4-Triazole with different UV absorption

Cyclopentadiene has an absorption maximum at 238.5 nm and by replacing carbon-carbon unsaturation with carbon-nitrogen unsaturation, a known hypsochromic shift occurs, therefore, the lower value obtained for 1,2,4-triazoles is understandable.[18] A large hyperchromic effect occurs on the acetylation of triazole and its derivatives which may be compared qualitatively to the similar effect observed in passing from benzene to acetophenone. In case of 5-substituted-3-mercapto-1,2,4-triazoles, the thione-thiol tautomeric forms can also be differentiated by UV spectroscopy.

The ultraviolet spectra of an ethanolic solution of 5-aryl-3-mercapto-1,2,4-triazoles usually show two absorption maxima at 252-256 nm and 288-298 nm. The absorption at 288-298 nm is due to the presence of the chromophoric C=S group.

ii) Infrared spectroscopy:

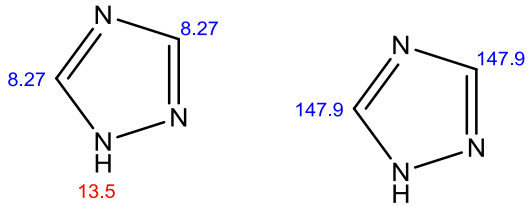
The infrared spectroscopy is also very useful in characterization of triazole ring. The absorptions in the region of 1570-1550 cm^{-1} due to N=N and in the region of 1640-1560 cm^{-1} due to C=N functions[19] are the diagnostic features. 4-Amino-1,2,4-triazoles show the characteristic strong N–H stretching of a primary amine at 3400-3200 cm^{-1}.

In 5-substituted-3-mercapto-1,2,4-triazoles, the thione-thiol tautomeric forms can also be differentiated in the IR spectra by the presence of C=S absorption band at about 1325-1300 cm^{1} for thione and by characteristic

SH absorption band at about 2600-2550 cm^{-1} for thiol forms[20]The N–H stretching vibrations at 3165 cm^{-1} and 3450 cm^{-1} have also been found supportive of thione-thiol equilibrium. 4-Amino-1,2,4-triazoles have been characterized by the appearance of N–H bands in the regions of 3200-3100 cm^{-1}. For NH_2 group, the absorption bands appear at about 3400-3300 cm^{-1}

iii) NMR and Mass spectrometry:

^{13}C NMR is a powerful tool to characterize 1,2,4-triazol-3-ones. In the spectrum of 1,2,4-triazol-3-ones two values for chemical shifts are obtained, one at about 164-173 ppm for imine (C=N) and the other at 150-160 ppm for carbonyl (C=O) carbon[21-22]. In EIMS of 1,2,4-triazoles, a strong molecular ion peak is always observed and the cleavage of bonds between N_1–N_2 and N_4–C_5 has been observed usually. The triazole ring also undergoes N_1–N_2 and C_3–N_4 cleavage.[23-24]



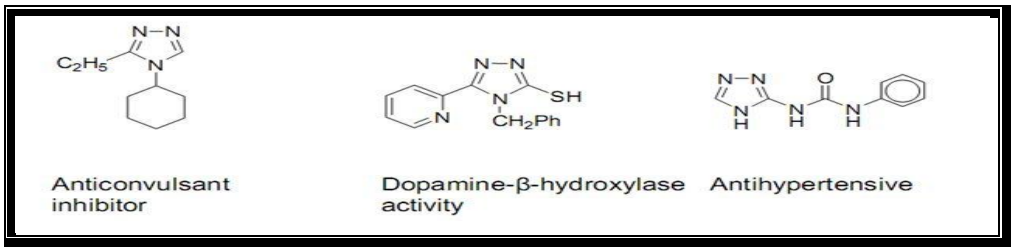
1,2,4-triazole:{^{1}H-NMR: NH=13.5ppm; CH=8.27 ppm; CH=8.27}.

1,2,4-triazole:{^{13}C-NMR: CH=147.9ppm; CH=147.9 ppm;}.

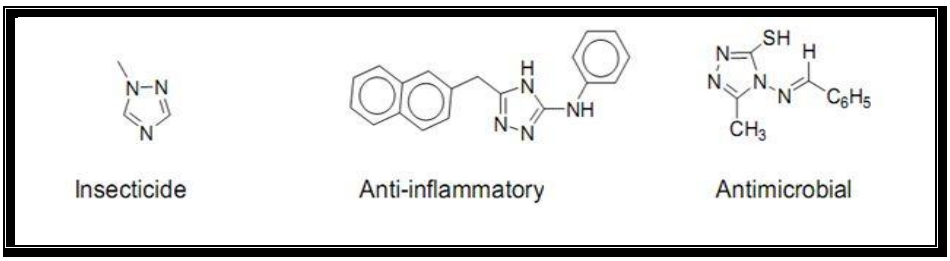
Application:

i) Biological activities:

1,2,4-Triazole and its derivatives are an important class of compounds which possess diverse agricultural, industrial and biological activities, including anti-microbial , sedative, anticonvulsant, anticancer , anti-inflammatory, diuretic, antibacterial , hypoglycemic , antitubercular and antifungal. In recent years, the synthesis of these heterocyclic compounds has received considerable attention. This wide range of applications has been covered by more than sixty papers in the literature, many in the form of patents.



applications of 1,2,4-Triazole



Several 1,2,4-Triazole derivatives shows different types of biological properties

ii) Agricultural applications:

In the plant protection technology, the research has been promoted to discover more efficient pesticides to tackle new challenging problems.[25] In order to selectively control the growth of weeds, a whole range of azole

herbicides has been developed exhibiting high levels of activity, application flexibility, crop tolerance and low levels of toxicity to mammals. Triazoles play an important role among this classes of heterocycles. A series of 1,2,4-triazole derivatives have been patented and extensively employed. One example of a herbicidal and pesticidal 1,2,4-triazole is given below.[26-28]

Example of herbicidal and pesticidal 1,2,4-Triazole

iii) Pharmacological applications:

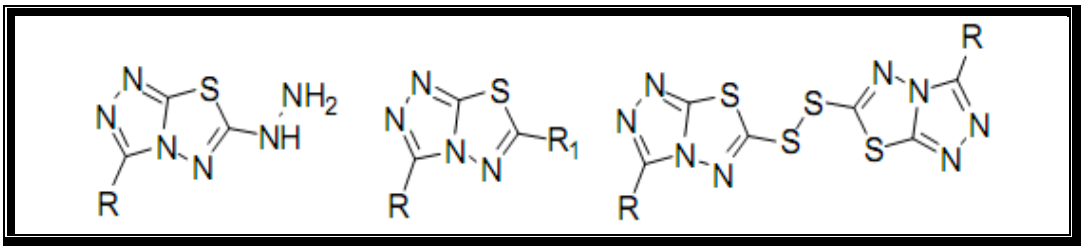
Over the last few decades, the biological and pharmaceutical properties of 1,2,4-triazoles have created considerable interest in their synthesis and chacterization[29-34]. 1,2,4-Triazole and its derivatives possess widely differing activities e.g., bacteriostate , bactericide , antifungal sedative , anti-carcinogen, tuberculostatic, anti-inflammatory, diuretic, antiviral, muscle relaxant and antihuman immunodeficiency virus (HIV). The pathogenic fungi cause life threatening infections that have become increasingly common during the past two decades. Fungal infections are common in individuals with immune-compromised hosts, such as patients undergoing anticancer chemotherapy or organ transplants and patients with AIDS.

Three major fungal infections in immuno-compromised individuals are candidosis, aspergillosis and cryptococcosis.Whereas the most widespread human superficial and coetaneous fungal infections are dermatomycoses such as, toenails and tinea pedis. The common antifungal agents currently used in clinic are azoles (such as fluconazole, ketoconazole, and itraconazole), polyenes (such as amphotericin B) nystatin, echinocandins (such as caspofungin and micafungin) and ally amines (such as naftifine and terbinafine). In antifungal chemotherapy, azoles having fungi static and broad-spectrum activities are used widely against most yeasts and filamentous fungi. Flouconazole is preferred as first line antifungal chemotherapy with relatively low toxicity but is not effective against invasive aspergillosis and has suffered severe drug resistance.

An improvement of fluconazole is itraconazole, having a broader antifungal spectrum and better tolerance but its variable oral absorption and low bioavailability has hampered its use. The second generation of azoles such as voriconazole, posaconazole and ravuconazole, have been developed with improved profiles. They are noted for their broad antifungal spectrum, low toxicity, and improved pharmacodynamic profiles.

Glycosylated triazole derivatives like 1-β-D-ribofuranosyl-[1H]-1,2,4-triazole-3-carboxamide (Virazol) belong to the highly potent drugs against DNA- and RNA-viruses . Moreover, this compound shows antitumor activity just as the anomeric 1-(2,3,4,6-tetra-O-acetyl-D-glucopyranosyl)-5-nitro-[1H]-1,2,4-triazole. The therapeutic use of non-steroidal anti-inflammatory drugs (NSAIDs) which are used in treatment of a number of arthritic diseases such as rheumatoid arthritis and osteoarthritis is limited because of their side effects, such as, gastrointestinal hemorrhage and ulceration. So, new drugs having potent anti-inflammatory activity with minimum side effects have been developed.

A new series of 3,6-disubstituted triazolo[3,4-b] thiadiazole derivatives has been synthesized by simple, high yielding routes .The newly synthesized compounds were evaluated for their cytotoxic activity against a panel of 60 human cancer cell lines by the National Cancer Institute (NCI) and some of them demonstrated inhibitory effects on the growth of a wide range of cancer cell lines generally at 10−5 M level and in some cases at 10−7 M concentrations. In this assay, the anti-tumor activity of the newly synthesized compounds could not be interpreted in terms of tyrosine kinase inactivation but more likely as a relatively broad specificity for the ATP-binding domain of other kinases.



Compound 3,6-disubstituted triazolo[3,4-b] thiadiazole

Some triazole-pyrazoline derivatives have been synthesized and screened using both modified forced swimming and tail suspension test. Rota- rod test was also performed for the examination of probable neurological deficits due to the test compounds .Among the series compound were more effective than the reference drugs fluoxetine with respect to antidepressant activity. 3-[(2-Methyl-1H-3-indolyl) methyl]-4-aryl-4,5-dihydro-1H-1,2,4-triazole-5-thiones and their respective N-{5-[(2-methyl-1H-3-indolyl) methyl]-1,3,4-thiadiazol-2-yl}-N-aryl amines have been prepared .

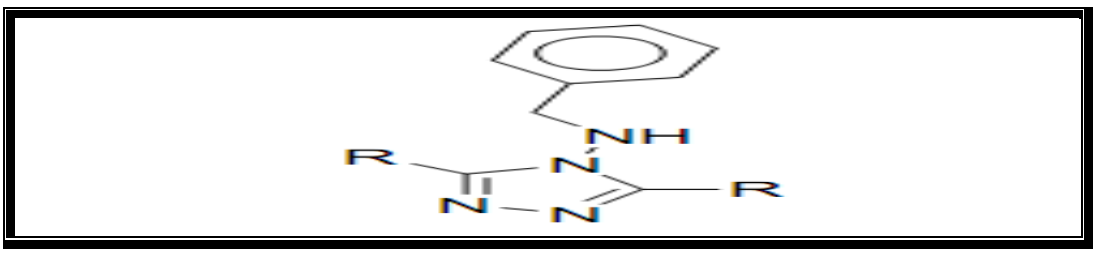
The antidepressant profile of the compounds was studied on mice with respect to that of the analogous 3-(1H-1-indolylmethyl)-4-aryl-4,5-dihydro-1H-1,2,4-triazole-5-thiones and the respective N-15{(2-methyl-1H-3-indolyl)methyl]-1,3,4-thiadiazol-2-yl}-N-arylamines, the synthesis and antimicrobial potency of which have been reported. Behavioral effects, induced by the members of both series, in conjunction with their activity in some specific tests (forced swim, pentetrazole convulsions) on mice, showed that these derivatives cross the blood-brain barrier and could develop an antidepressant activity. comparable to that of imipramine. Blood-brain barrier penetration is also supported by the lipophilicity data obtained for all analogs.

Synthesis of a series of 3 - (2,4 - dichlorophenoxy) methyl)-1,2,4 -triazolo (thiadiazoles and thiadiazines) and screened for their anti-inflammatory activity .Among the synthesized compound, 3 -((2, 4 - dichlorophenoxy) methyl) -6-(4- methoxyphenyl)- [1,2,4] triozolo (1,3,4) thiadiazole , 3,6 -Bis ((2,4-dichlorophenoxy) methyl) - [1,2,4] triazolo [[1,3,4] thiadiazole , 3-((2,4-Dichlorophenoxy) methyl)-6-phenyl-7H - [1,2,4] triazole [[1,3,4] thiadiazine and 3-((2,4- Dichlorophenoxy methyl) -7-((3-benzofuran-2-yl) -1-phenyl-1H-pyrazol-4-yl) methylene)-6-(benznofuran-3-yl) -7H-[1,2,4] triazolo [3,4-b] [1,3,4] thiadiazine , showed potent anti inflammatory activity.

iv) Industrial Applications:

a. *Chemical Industry*: Some selected triazoles have been used as light emitting diodes (Electroluminescent devices). Some triazole systems have extensive use in the separation of silver from other metal cations in liquid membrane systems. In addition, these compounds are used as synthetic dyes and bleaching agents. Moreover, the inks having smooth writing properties also contain triazole derivatives e.g., 3-amino-5-mercapto-1,2,4-triazole. These compounds have also been reported as inhibitors of corrosion of copper, brass, aluminum and steel in marine environment and inhibit fog formation in photographic emulsions, plant growth inhibitors and herbicides.[35-37]

b. *Textile Industry*: The triazole derivatives have many applications in textile industry e.g, sodium salt of a sulphonated triazole derivative possesses good detergent action and N-benzylated aminotriazoles have useful properties in inhibiting the acid fading of dyestuff.[38]



N-benzylated aminotriazoles

c. *Cotton industry*: In the cotton industry,3-amino-1,2,4-triazole under its trade name Amizol, has been used as a commercial defoliant for a number of years.[39]

d. *Antioxidant activity*: DPPH assay: T Radical scavenging activity of synthesized compounds against stable free radical 2,2-diphenyl-2-picrylhydrazyl hydrate (DPPH, Sigma-Aldrich Chemie, Steinheim, Germany) was determined spectropho-tometrically. When DPPH reacts with an antioxidant compound, which can donate hydrogen, it is reduced. Following the reduction, its deep violet color in methanol bleaches to yellow, showing a significant absorption decrease at 517 nm. Fifty milliliters of various concentrations of the compounds dissolved in methanol was added to 5 mL of a 0.004% methanol solution of DPPH. After a 30 min incubation period at room temperature,the absorbance was read against a blank at 517 nm (ATI-Unicam UV-2 UV–Vis spectrophotometer, Cambridge,UK).

Free radical DPPH inhibition as a percentage (I%) was calculated as follows: I% = (A blank –As ample /A blank)× 100, where A blank is the absorbance of the control reaction (contain-ing all reagents except the test compound), and As ample is the absorbance of the test compound. Compounds' concentration providing 50% inhibition (IC50 was calculated from the graph plotted as inhibition percent-age against compound concentration.

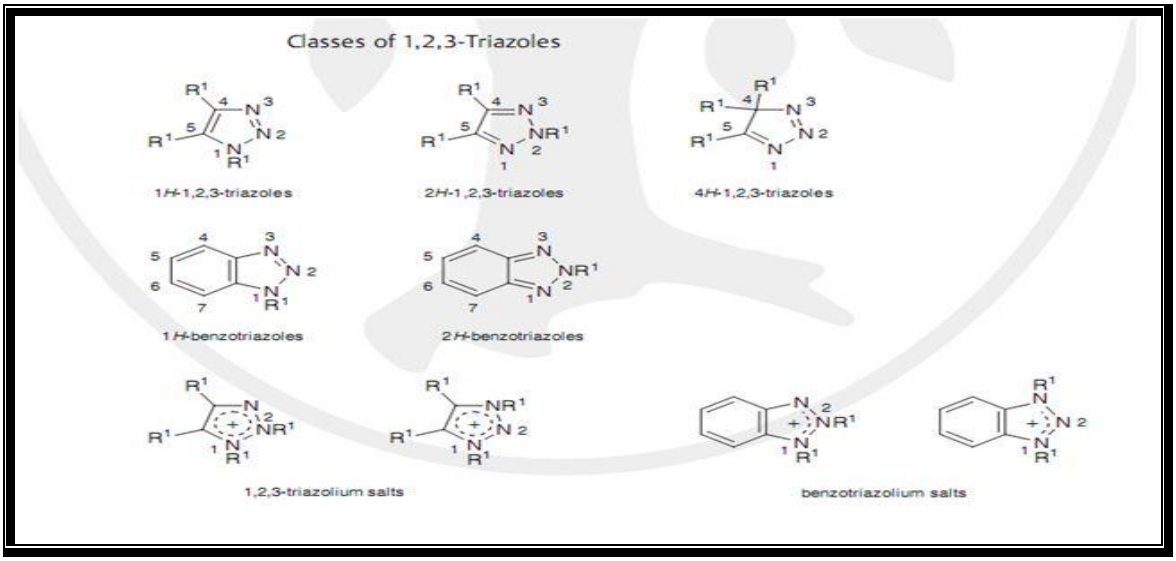
1,2,3- Triazole:

1,2,3-Triazole is one of a pair of isomeric chemical compounds with molecular formula $C_2H_3N_3$, called triazoles, which have a five-membered ring of two carbon atoms and three nitrogen atoms.1,2,3-Triazole is a basic aromatic heterocycle. Substituted 1,2,3-triazoles can be produced using the azide alkyne Huisgen cycloaddition in which an azide and an alkyne undergo a 1,3-dipolar cycloaddition reaction. It is a surprisingly stable structure compared to other organic compounds with three adjacent nitrogen atoms.

However, flash vacuum pyrolysis at 500°C leads to loss of molecular nitrogen (N_2) to produce aziridine. Certain triazoles are relatively easy to cleave due to so-called ring-chain tautomerism. One manifestation is found in the Dimroth rearrangement.1,2,3-Triazole finds use in research as a building block for more complex chemical compounds, including pharmaceutical drugs such as tazobactam.

1,2,3-Triazoles are important types of heterocyclic compounds. They find numerous applications in industry, namely as dyestuffs, fluorescent whiteners,photostabilizers of polymers, optical brightening agents, corrosion inhibitors and as photographic photoreceptors.[40-41]Also, due to their extensive biological activities, they find successful application in medicine and as agrochemicals. Beyond this, these com-pounds are intensively studied by many research groups due to their theoretical interest and synthetic usefulness.

The 1,2,3-triazoles can be divided in three main groups: monocyclic 1,2,3-triazoles,benzotriazoles, and 1,2,3-triazolium salts. As indicated in Scheme 1, for monocyclic1,2,3-triazoles three subclasses can be recognized, depending on the position of the substituent's in the ring. While 1H- and 2H-1,2,3-triazoles are aromatic compounds their 4H-isomers are not. This fact is reflected in the abundance of examples of 1H- and 2H-1,2,3-triazoles and the rarity of 4H-1,2,3-triazoles.[42]In the literature, the 1,2,3-triazole systemissometimes named as "v-triazole" in order to distinguish it from "s-triazole", the 1,2,4-tri-azole system. Also, due to their extensive biological activities, they find successful application in medicine and as agrochemicals· Beyond this, these com-pounds are intensively studied by many research groups due to their theoretical interest and synthetic usefulness. The 1,2,3-triazoles can be divided in three main groups: monocyclic 1,2,3-triazoles,benzotriazoles, and 1,2,3-triazolium salts. As indicated in figure 1, for monocyclic1,2,3-triazoles three subclasses can be recognized, depending on the position of the substituent's in the ring. While 1H- and 2H-1,2,3-triazoles are aromatic compounds their 4H-isomers are not. This fact is reflected in the abundance of examples of 1H- and 2H-1,2,3-triazoles and the rarity of 4H-1,2,3-triazoles. In the literature, the 1,2,3-triazole system is sometimes named as "v-triazole" in order to distinguish it from "s-triazole", the 1,2,4-tri-azole system.

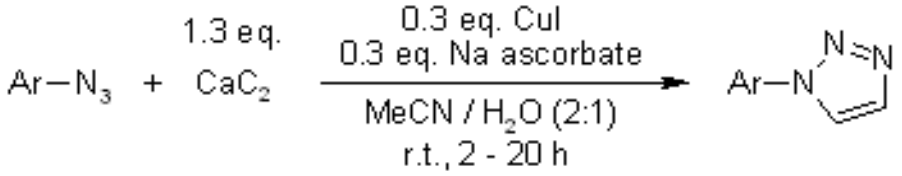


Classes of 1,2,3-Triazoles

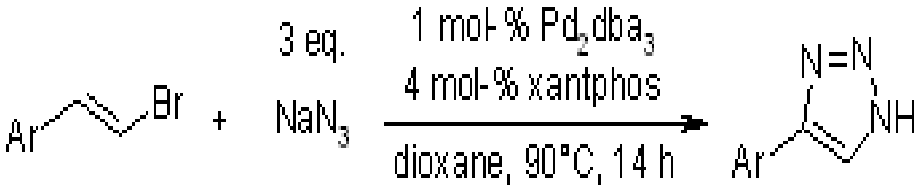
Synthesis of 1,2,3-Triazole:

Many new H-1,2,3-triazoles (**T**) were readily synthesized by nucleophilic attack of sodium azide on activated acetylenes in dimethylformamide. Typical activating groups were COR, COOR, $O_2NC_6H_4$ $PO(OC_2H_5$, CO**T**, and $(C_6H_5)_3P^+$. Propynyl 4-triazolyl ketone or phenylethynyl 4-triazolyl ketone may be converted to acylic adducts (triazolylketoenamines), biheteroaromatic systems (isoxazolytriazoles, pyrazolytriazoles), as well as to ditriazolyl ketones. Certain **T** properties were examined in detail. The apparent p*K*'s for our group of *ca* 30 triazoles were in the range 4·95–9·45 in ethanol-water (v/v 1/1) at 25°. The Hammett correlation for five 4-aryl-**T** was log K_a = 0·89σ⁻ −9·21 and for seven 4-aryl-5-carbethoxy-**T** was log K_a = 1·45σ−6·95. The UV spectra of **T** are similar to those of other heteroaromatic and phenyl compounds: interesting analogies between triazolyl and phenyl, e.g., "ortho" crowding effects, appear to be indicated in the spectra of compounds related to biphenyl, stilhene and benzophenone. With regard to structure assignment on the basis of spectra, characteristic features of UV and IR spectra of the H-1,2,3-triazoles are discussed.

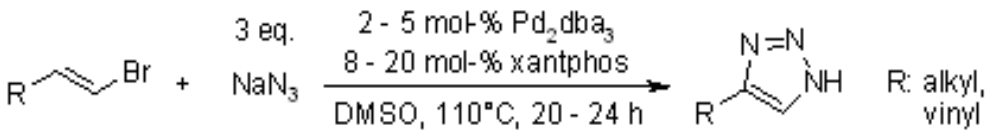
1. The synthesis of 1-monosubstituted aryl 1,2,3-triazoles was achieved in good yields using calcium carbide as a source of acetylene. The copper-catalyzed 1,3-dipolar cycloaddition reactions were carried out without nitrogen protection and in a MeCN-H_2O mixture.[43]



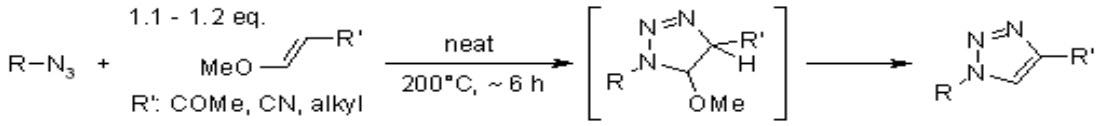
2. A Pd-catalyzed synthesis of 1*H*-triazoles from alkenyl halides and sodium azide represents a completely new reactivity pattern in the context of Pd chemistry.[44]



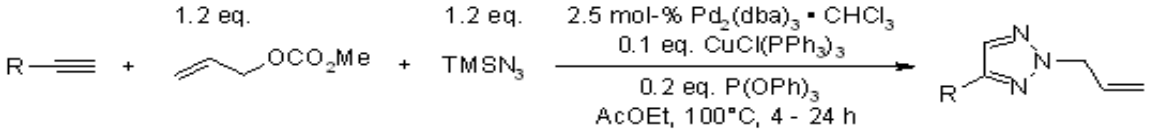
3. Synthesis of 1,2,3-Triazole by dimethyl sulfoxide[45]



4 . 1,2,3-Triazoles were prepared in good to modest yields by cycloaddition of alkyl azides onto enol ethers under solvent less conditions. The reaction can access ring-fused triazoles that are unavailable by azide-alkyne cycloadditions and is easily scalable. The 1,2,3-triazole products bear functionality that may be readily derivatized.[46]

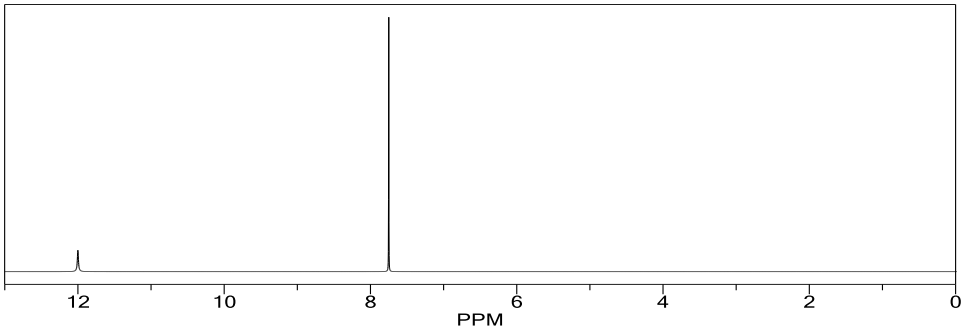


5. Triazoles have been synthesized via a three-component coupling reaction of inactivated terminal alkynes, allyl carbonate, and trimethylsiyl azide under Pd(0)-Cu(I) bimetallic catalysis. The deallylation of the resulting allyltriazoles is described.[47]

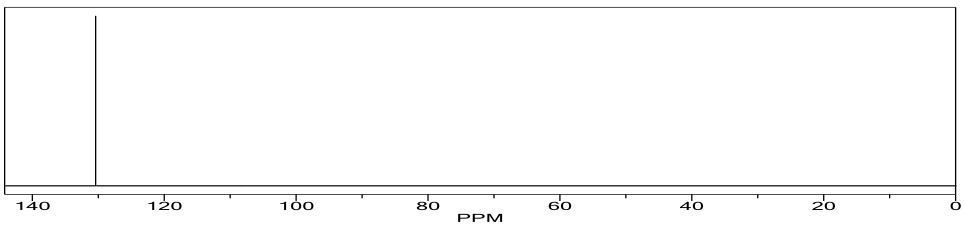


A. Characterization:

^{1}H-NMR of 1,2,3-Triazole:



^{13}C-NMRof 1,2,3-Triazole

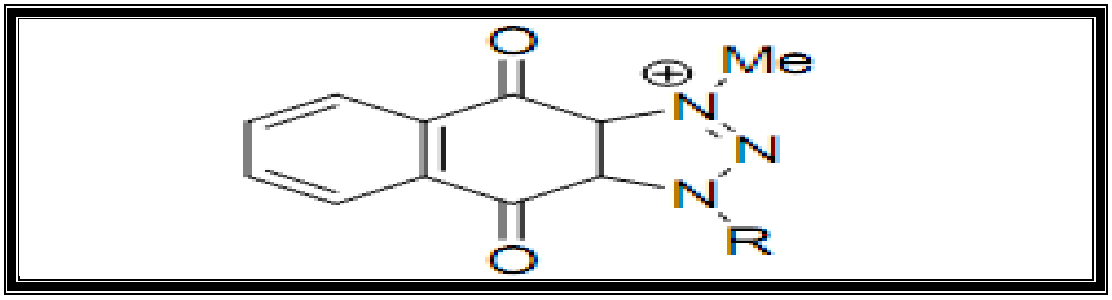


APPLICATIONS:

A. Pharmacological activities:

i) Antimicrobial activity

A novel class of cationic anthraquinone analogs has been synthesized .Among these compounds synthesized showed high potency (MIC<1ug/ml) and selectivity against gram positive pathogens including methicillin resistant staphylococcus aurous (MRSA), while modest activity against gram negative bacteria. Compound and exhibit broad antibacterial activity including MRSA and vancomycin- resistant Enterococcus faecalis (VRE), which is comparable to other commercially available cationic antiseptic chemicals. As compound given below:



Compound for antimicrobial activity

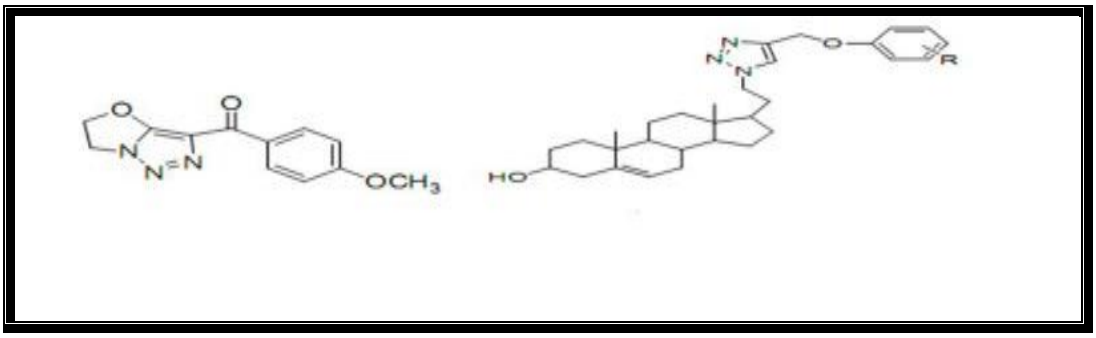
A series of novel sulphanilamide derived 1,2,3 triazol compounds has been synthesized and screened in vitro for their antibacterial and antifungal activities . Compounds 4-amino-N-((1-dodecyl-1H-1,2,3-trizol-4-yl) methyl) benzene sulfonamide , 4 amino-N-((1-(2,4-dichlorobenzyl)-1H-1,2,3triazol-4-yl)methyl)-4- aminobenzenesulfonamide and 4-amino-N-((1-(2,4-diflurobenzyl)-1H-1,2,3-triazol-4-yl) methyl) benzene sulfonamide 16c were found to be most potent compounds against all the tested strain except Candida albicans and Candida mycoderma.

Bay synthesized six new series of N,N bis (1,2,4 triazol-1-yl methyl) amines and evaluated for their antifungal activity against the budding yeast Saccharomyces cerevisiae and antibacterial activity against Escherichia coli. Compounds 2,6-bis (bis(1H-1,2,4-triazol-1-yl) methyl) amino) hexanoic acid N,N (bis ((1H-1,2,4-triazol-1-yl) methyl) - 2 methyl propane-amine showed strong antifungal and antibacterial activity.

ii) Anticancer activity

Synthesis of a series of heterocycle-fused 1,2,3 triazoles by 1, 3 -dipolar cycloaddition of heterocyclic ketene aminals or N, O-acetals with sodium azide and polyhalo isopthalonitriles has been carried out and evaluated in vitro against a panel of human tumor cell lines .Compound 4-Methoxy-phenyl substituted 1,3, -oxazoheterocycle fused 1,2,3 triazole was found to be most potent derivative against A 431 and K 562 human tumor cell lines.

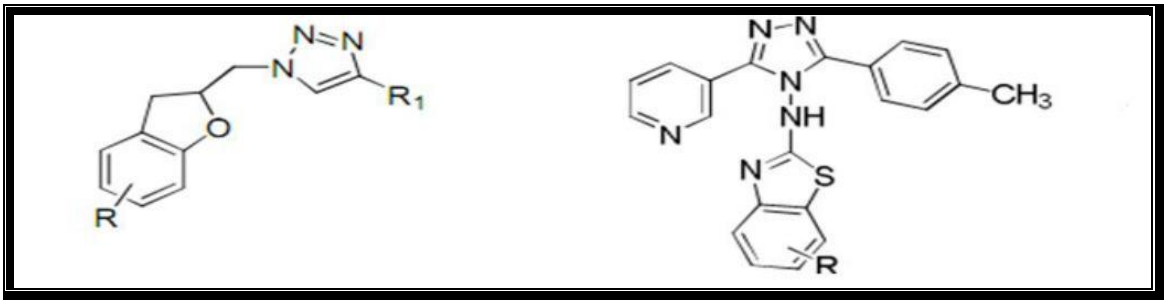
Synthesis of 21- triazolyl derivatives of pregnenolone has been performed with transformation of pregnenolone acetate which is used as starting material, using 'click chemistry' approach. Compound showed most active anticancer activity when screened for their anticancer activity against seven human cancer cell lines.



Fused 1,2,3-Triazole and Pregnenolone

iii) Antimycobacterial activity

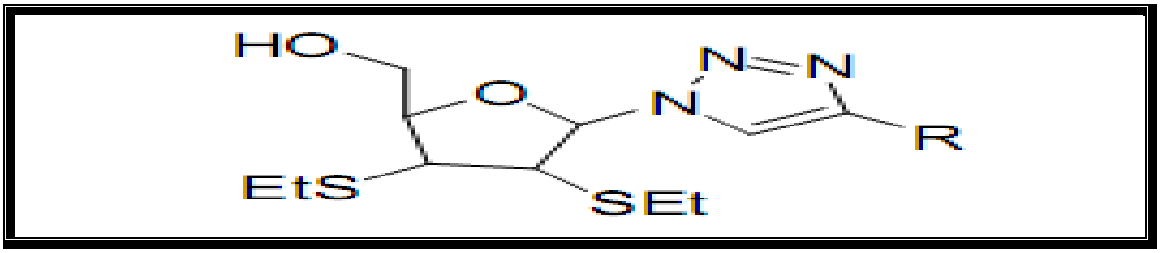
Different 1,4-Disubstituted -1,2,3-triazoles has been developed and screened for antitubercular activity against Mycobacterium tuberculosis H37Rv and exihibited antitubercular activities with MIC ranging from 12.5 to 3.12 ug/ml.. Newly 1,2,4 triazoles analogs has been synthesized and carried in vitro antitubercular activity against Mycobacterium tuberculosis H37Rv strain. Compound 3-(3-pyridyl)-5-(4-methylphenyl)-4-(N-4-chloro-1,3-benzo thiazol-2-amino)-4H-1,2,4 triazole showed better antitubercular activity compound to rifampicin.



Compound containing Antimycobacterial activity

iv) Antiviral activity

A series of novel 2',3'-dideoxy-2',3'-di-ethanethioribonucleosides has been reported which is modified into a triazole ring and evaluated for their antitumor activity. Nucleosides with a triazole ring shared significantly improved activity towards broad range of tumor cell line.

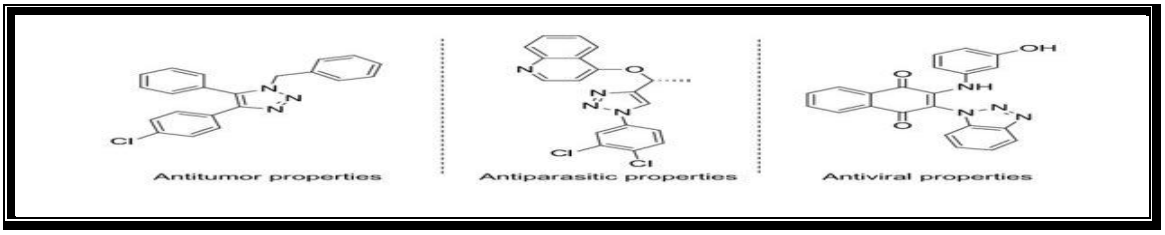


Compound Containing antitumor activity

v) Antimalarial activity

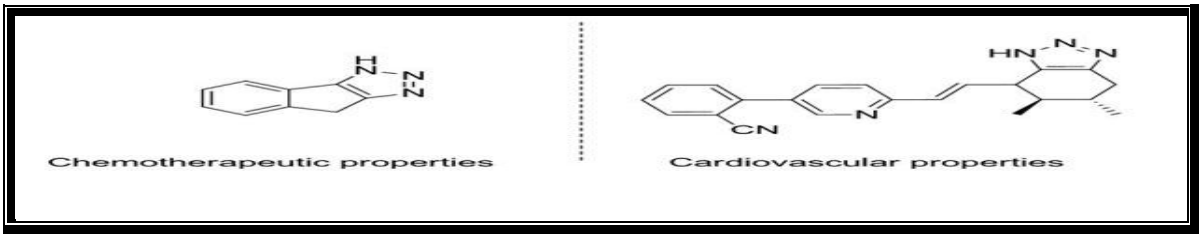
A series of triazole- linked chalcone and die none hybrid compounds has been synthesized and evaluated for in vitro anti- malarial activity. Several chalcone-chloroquinoline hybrid compound were found to be active, with compound 3-{4-[1-(7-chloro-quinoline-4- yl) 1H-[1,2,3] triazol-4-yl methoxy]-3-methoxy phenyl} -1-(2,4-dimethoxyphenyl)-propenone 53 the most active against D10, Dd2 and W2 strains of plasmodium falciparum. Synthesis of a series of triazolium salts has been carried out and found to be

highly potent with active conc. in the nanomolar range in plasmodium falciparum cultures. It is hypothesized as electron deficient cores that are essential to interact with negatively charged moiety on the parasites merozoite which determine both the potency and selectivity of the compound. Compounds containing 1,2,3-triazoles have been shown to exhibit a wide range of biological activity, including anticancer, antiparstic and antiviral.



Biological Properties of different 1,2,3 Triazoles

In addition to substituted 1,2,3-triazoles, fused 1,2,3-triazoles have also demonstrated relevance in the pharmaceutical industry. As compounds containing fused 1,2,3-triazoles become increasingly common in pharmaceutical targets and biologically active substances, such as chemotherapeutic and cardiovascular agents (Figure 51), new strategies to synthesize this class of molecules are highly desirable.[48-49]



Chemotherapeutic and cardiovascular Properties

CONCLUSIONS

This Article aims to present the chemistry and significance of triazole and their derivatives.Triazole is a unique template that is associated with several biological activities. This review article presents whole criteria of Triazole derivatives with respect to their synthesis,characetrization and biological activities. This article highlightened research work of many researchers reported in literature for different pharmacological activities on triazole compounds synthesized. This review study has presented comprehensive details of triazole analogues, potent compounds reported for particular pharmacological activity and the method or technique involved in evaluation process.

More investigations must be carried out to evaluate more activities of triazole for many diseases whose treatment are difficult in the medical sciences. This study also presented triazole derivatives which are so useful in many biological activities.

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