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A Review on Diverse Role of Heterocyclic Moieties Containing Aminoquinoline and Azoles

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Abstract

Over past few decades, the problems posed by multi-drug resistant microbes have reached an alarming level in many countries around the world. The use of most antimicrobial agents is limited not only by rapidly developing drug resistance but also by the unsatisfactory treatment of microbial infections. In pursuit of this goal, our research efforts are focused on the development of novel structural moieties with diverse activities. Literature survey revealed that various heterocyclic members such as pyrazole, imidazole, triazole, thiadiazole, thiazole are predominantly imperative antibacterial and antifungal agents including azoles derivatives like tazobactam, cefatrizine, rufinamide, fluconazole, itraconazole, voriconazole, posaconazole and ketoconazole. 1,2,4 triazole derivatives is five membered heterocyclic ring among various heterocycles that have received most attention during last two decades as potential antimicrobial, antifungal, analgesic, anticonvulsant, diuretic, antimalarial. Synthesis of benzothiazole derivatives have long been focused for interest of research in the field of medicine, especially 2-substituted benzothiazole derivatives with fluoride functional group as substituent. After extensive literature survey it was observed that not enough efforts are made to combine these two moieties as a single molecule to identify the new *Candida*te that may be value in designing new, potent, selective and less toxic drug. Quinoline derivatives have also demonstrated a variety of biological properties that includes antimalarial, antibacterial, anti-inflammatory, anti-tubercular etc. The biconjugation aimed as ligation of two or more compounds to form new complex with combined properties of their individual components.

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Keywords

Aminoquinoline; Triazole; Benzothiazole; Antibacterial; Anticonvulsant; Antimalarial.

Introduction

The development of diminutive molecules therapeutic agents for the cure and prevention of disease has played a crucial role in the practice of medicine for several years. Amongst the beginning of modern scientific methodology, various plant medicines come under chemical scrutiny, ultimately prominent to the isolation of active beliefs since early. In 19th century biological research followed by pharmacological evaluation leads to development of modern medicine. The infectious caused by microbes such as bacteria, viruses and parasites have been treated by drugs known as antimicrobial agents. Most drugs available currently at the market for treatment are heterocyclic compounds, i.e. compounds in which ring structure with one or more atoms different other than carbon atom inside the ring. Some of the natural products e.g. antibiotics such as penicillin's, cephalosporin; alkaloids such as vinblastine, morphine, reserpine even the compounds like pyrimidine

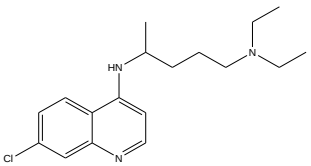
and purine are basis of genetic material DNA have heterocyclic moiety due to which they played a crucial role in the metabolism of all living cells. Amongst heterocyclic compounds the five and six membered heterocycles represent an extensive and differentiated group with broad range of biological activity [1].

More than 90% of new drugs contain heterocycles and the interface between chemistry and biology, at which so much new scientific insight, discovery, and application is taking place is crossed by heterocyclic compounds. Most of them are five and six membered compounds containing one to three heteroatoms in their nucleus. These heterocyclic compounds may be present as isolated or fused heterocyclic systems. Towards this region we would like to analyse the edifices of a large number of drugs. The ultimate artifact of a successful drug design effort [2]. The members of heterocyclic group such as pyrazole, imidazole, oxazole, triazole, thiadiazole, oxadiazole, and thiazole are predominantly imperative antibacterial and antifungal agents also including azoles derivatives like tazobactam, cefatrizine, rufinamide, fluconazole, itraconazole, voriconazole, posaconazole and ketoconazole [3]. Heterocycles also embraces quinolines and their derivatives which present in numerous natural products and many of them acquire remarkable physiological and biological properties. It was eminent that the quinoline nucleus and its derivatives play an imperative role in the search on wide antibacterial activity spectrum [4]. Compounds from this class are found in nature as constituents of nucleic acids, some vital amino acids, alkaloids and hormones. The aim of this investigation will draw an important role in shaping our on existing and imminent ventures. Besides the enormous distribution of heterocycles in natural products, they are also present as major components occur in natural molecules such as DNA and RNA. Which are without doubt the most significant macromolecule of life. These Nucleotides, the edifice blocks of our genes are derivatives of pyrimidine and purine ring structures. Now a day's investigation is altered towards the overture of new and safe therapeutic agents having quantifiable importance. The nitrogen containing heterocycles are found in profusion in most of the medicinal compounds. Triazoles are used for the synthesis of active ingredients for pharmaceutical and veterinary products and also they are used for Photographic products. Imidazole appears as important moiety in number of medicinal agents led to introduction of the triazoles. The triazoles are known be the isosters of imidazole in which one of the carbon atoms of imidazole is iso-sterically replaced by nitrogen [5]. Quinoline family is widely used as a parent compound to make drugs, alkaloids, dye, rubber chemicals and flavoring agents. It is also used in manufacturing of oil soluble dyes, food, colorants, pharmaceuticals, pH indicator and other organic compounds. The quinoline was first introduced for the treatment of urinary tract infections in 1963, the drugs which are containing quinolone nucleus includes oxolinic acid, norfloxacin, ciprofloxacin etc [6]. Benzothiazole moieties are major component of compounds screening numerous biological activities such as antimicrobial [7] anthelmintic [8], anti-inflammatory activities [9]. They are also having abundant utility in industry as anti-oxidants, vulcanisation accelerators. Various benzothiazoles such as 2-aryl benzothiazole received a great deal of consideration due to distinctive arrangement and its uses as radioactive amyloid imagining agents and anticancer agents [10] Benzothiazoles are bicycle ring system with multiple applications. In the 1950s, huge quantity of 2-aminobenzothiazoles were intensively deliberated, as the 2-amino benzothiazole scaffold is one of the important structures in medicinal chemistry and reported cytotoxic on cancer cells [11]. It was acknowledged that combination of 2-aminobenzothiazoles with other heterocyclic compounds was well known approach to design new drugs like molecules, which permits achieving new pharmacological profile, action, toxicity lowering. The 2-(4-aminophenyl) benzothiazoles are new class of effective and selective antitumor agents and exhibit specific contour of cytotoxic reaction across the cell lines. Benzothiazole ring is also present in different marine or terrestrial natural compounds, which include valuable biological characteristics. In previous few years it was reported that benzothiazole, its bioisosters derivatives had antimicrobial activities against Gram-negative, Gram positive bacteria's such as *Enterobacter*, *Pseudomonas aeruginosa, Escherichia Coli,* and *Staphylococcus epidermidis* etc.) and the yeast (e.g., *Candida albicans*) [12]. In this review article the main focus on exploration of heterocyclic compounds containing aminoquinoline, Triazole and Benzothiazole derivatives.

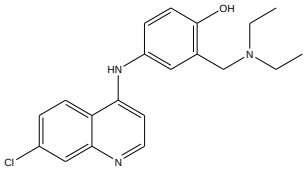
Amino quinoline

Donatella *et al.,* (2001) have reported the Inhibition of Intramacrophage Growth of *Penicillium marneffei* by 4-Aminoquinolines, The antimicrobial activities of chloroquine (CQ) and several 4-aminoquinoline drugs were tested against *Penicillium marneffei,* an opportunistic fungus that invades and grows inside macrophages and causes disseminated infection in AIDS

patients. Human THP1 and mouse J774 macrophages were infected in vitro with *P. marneffei* conidia and treated with different doses of drugs for 24 to 48 hrs followed by cell lysis and the counting of *P. marneffei* CFU. CQ and amodiaquine exerted a dose-dependent inhibition of fungal growth, whereas quinine and artemisinin were fungistatic and not fungicidal.

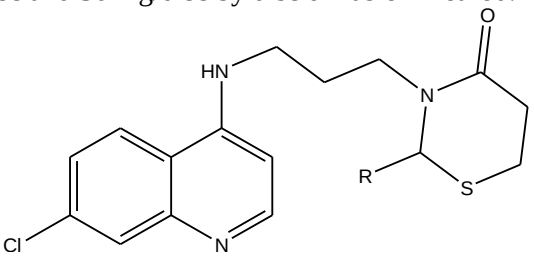


Chloroquine

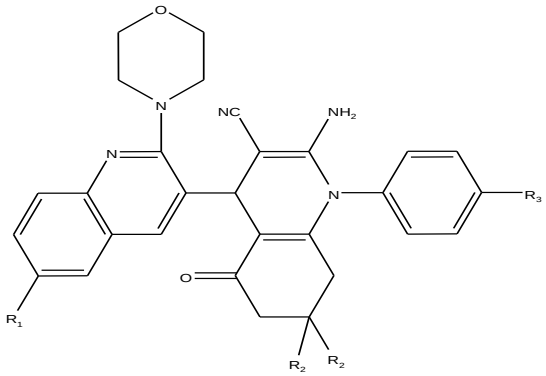


Amodiaquine

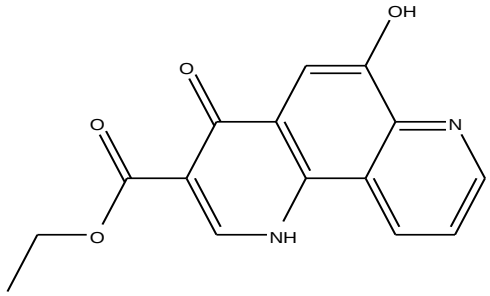
Rudrapal *et al.,* (2010) have reported the synthesis and antibacterial activity evaluation of some novel 7-chloro-4- aminoquinoline derivatives. 7-chloro-4-aminoquinoline derivatives were prepared by modification at C-2 position of six membered 1,3-thiazinan-4-one ring system attached at the terminal propyl side chain of 7-chloro-4-aminoquinoline nucleus. The synthesized compounds were evaluated for antibacterial activity against six different strains of Gram positive (*Bacillus subtilis*, *Bacillus cereus*, *Staphylococcus aureus*) and Gram negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*) at two different tested doses viz. 25 mg/disc and 50 mg/disc by disc diffusion method.



Makawana *et al.,* (2011) have reported synthesis and *in vitro* antimicrobial activity of new 3-(2-morpholinoquinolin-3-yl) substituted acrylonitrile and propane nitrile derivatives, series of new 3-(2-morpholino quinolin-3-yl) acrylonitrile derivatives (IVa–IVf) has been synthesised by the base-catalysed condensation reaction of 2 morpholino qionoline-3-carboxaldehydes (IIa–IIc) and 2-cyanomethyl benzimidazoles (IIIa–IIIb). Subsequent regiospecific reduction of the C——C double bond in acrylonitrile moiety afforded 3-(2-morpholinoquinolin-3-yl) propanenitrile derivatives (Va–Vf). All the compounds synthesised were subjected to in vitro antimicrobial screening against representatives of bacteria and fungi. The majority of the compounds were found to be active against Gram-positive bacteria *Bacillus subtilis* and *Clostridium tetani* as well as against the fungal pathogen *Candida albicans.*

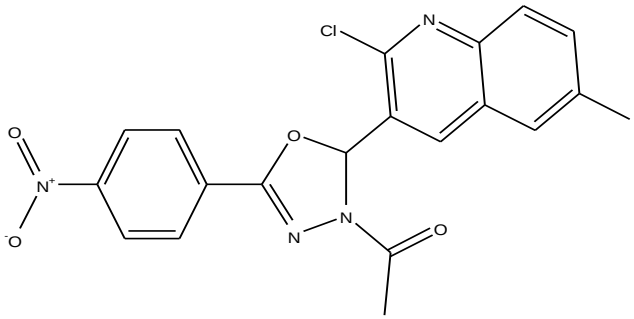


Patel *et al.,* (2011) have reported Synthesis and *in vitro* microbial activities of amides of pyridoquinolone, they report the antimicrobial evaluation of newly synthesized amides of pyridoquinolones from substituted aniline, substituted phenyl thiourease and 4-amino-N-(substituted phenyl) benzenesulfonamide. Structures of selected compounds have been established by IR and 1H NMR spectra and elemental analysis. The structure– activity relationships have been studied by screening of antimicrobial activity over *S. aureus, B. subtilis, E. coli, P. aeruginosa* and *C. albicans* using cup–plate method.

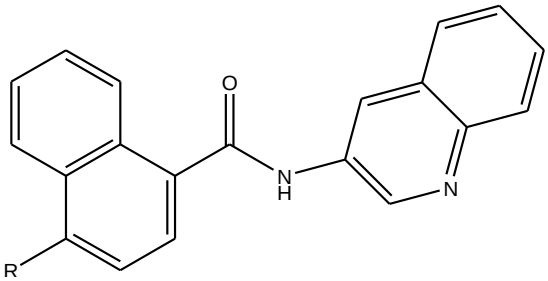


Desai *et al.,* (2011) have reported Conventional and microwave techniques for synthesis and antimicrobial studies of novel 1-[2-(2-chloro(3-quinolyl))-5-(4-nitrophenyl)-(1,3,4-oxadiazolin-3-yl)]-3-(aryl)prop-2-en-1-ones,they described the conventional and microwave method for the synthesis of 1-[2-(2-chloro(3-quinolyl))-5-(4 nitrophenyl) (1,3,4-oxadiazolin-3-yl)]-3-(aryl)prop-2-en-1-ones (4a–l). Through this method, we have achieved reduction in reaction time and better yield than the previously described conventional method. The application of microwave irradiation (MWI) is used for carrying out chemical transformations which are pollution free and eco-friendly. The structure of the compounds was characterized by spectral data. These

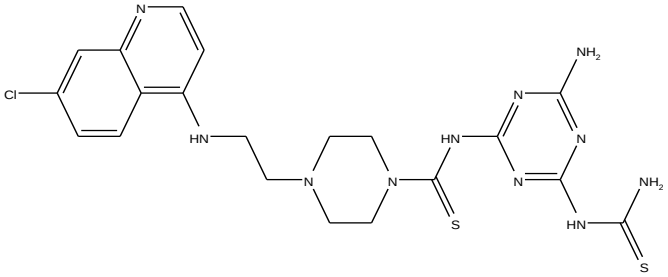
compounds (4a–l) were evaluated for their in vitro antimicrobial screening on different strains of bacteria and fungi.



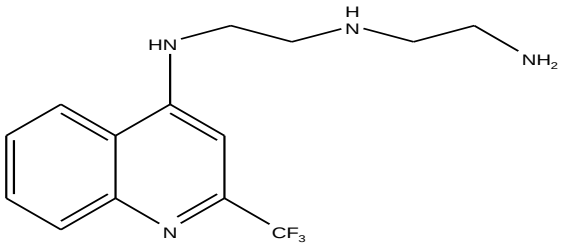
Zhang *et al.,* (2008) have reported the Synthesis and characterization of 3-aminoquinoline derivatives and studies of photo physicochemical behaviour and antimicrobial activities, The quinoline ring core, typical of amino-quinolines, and a naphthalene group was combined to devise (4-alkyl-1-naphthyl)-quinolin-3-ylamide derivatives. These derivatives were designed and synthesized in light of the chemical and biological profiles of these important subunits. All the compounds were evaluated for their *in vitro* antibacterial and antifungal activities by the paper disc diffusion method with Gram-positive *Bacillus subtilis, Bacillus megaterium and Staphylococcus aureus*, Gram-negative *Enterobacter aerogenes*, *Escherichia coli*, *Klebsiella pneumoniae and Pseudomonas aeruginosa* and yeasts *Candida albicans*, *Saccharomyces cerevisiae* and *Yarrovia lipolytica*.



Bhat *et al.,* (2015) have reported Synthesis, antimalarial activity and molecular docking of hybrid 4-aminoquinoline-1,3,5-triazine derivatives, a series of novel hybrid 4-aminoquinoline 1,3,5-triazine derivatives was synthesized in a five-steps reaction and evaluated for their *in vitro* antimalarial activity against chloroquine-sensitive (3D7) and chloroquine-resistant (RKL-2) strains of *Plasmodium falciparum*. Entire synthetic derivatives showed higher antimalarial activity on the sensitive strain while two compounds, *viz*., **9a** and **9c** displayed good activity against both the strains of *P. falciparum*.

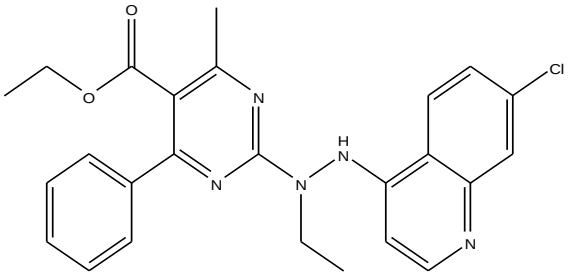


De-Meneses *et al.,* (2015) reported Synthesis and evaluation of the anti-nociceptive and anti-inflammatory activity of 4-aminoquinoline derivatives, The compounds were characterised and tested in models of pain and inflammation, using the writhing test with acetic acid, formalin test, peritonitis test by zymosan and arthritis test with Freund's adjuvant complete assay. The results revealed that all of the 4-aminoquinolines that were prepared promoted anti-nociceptive activity as well as acute and chronic anti-inflammatory effects, with marked activity in the derivates labelled with BAQ and 7-CF_3-MAQ. After 7 days of treatment, 7-CF_3-MAQ did not induce significant hepatotoxicity, gastrotoxicity or nephrotoxicity.

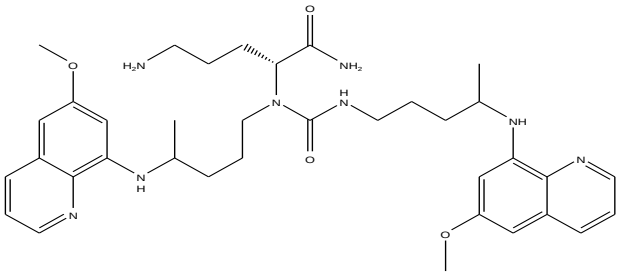


Singh *et al.,* (2012) have reported the 2-Aminopyrimidine based 4-aminoquinoline anti-plasmodial agents. Synthesis, biological activity, structure–activity relationship and mode of action studies, the compounds showed *in vitro* anti-plasmodial activity against drug-sensitive CQS (3D7) and drug-resistant CQR (K1) strains of Plasmodium falciparum in the nM range. In particular, 5-isopropyloxycarbonyl-6-methyl-4-(2-nitrophenyl)-2-[(7-chloroquinolin-4-ylamino) butylamino] pyrimidine depicted the lowest IC50 (3.6 nM) value (56-fold less than CQ) against CQR strain. Structure–activity profile and binding with heme, μ-oxo-heme have been studied. Binding assays with DNA revealed better binding with target parasite type AT rich pUC18 DNA. Most compounds were somewhat cytotoxic, but especially cytostatic. Molecular docking

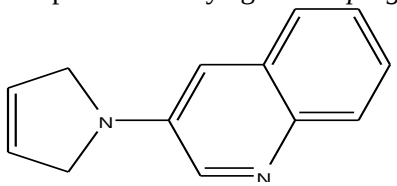
analysis with Pf DHFR allowed identification of stabilizing interactions.



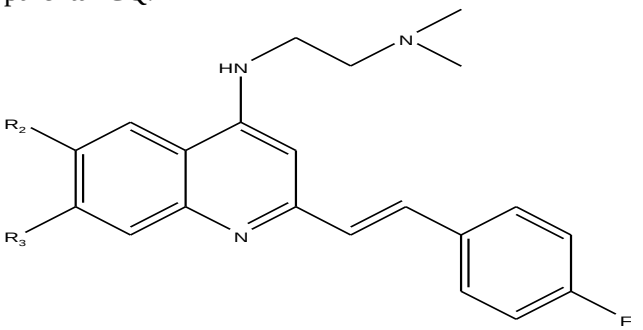
Kaur *et al.*, (2011) have reported the Synthesis, antiprotozoal, antimicrobial, β-hematin inhibition, cytotoxicity and methemoglobin (MetHb) formation activities of bis (8-aminoquinolines), The bisquinolines were evaluated for in vitro antimalarial (Plasmodium *falciparum*), antileishmanial (Leishmania donovani), antimicrobial (a panel of pathogenic bacteria and fungi), cytotoxicity, β-hematin inhibitory and methemoglobin (MetHb) formation activities. Several compounds exhibited superior antimalarial activities compared to parent drug primaquine. Selected compounds (44, 61 and 79) when tested for in vivo blood-schizontocidal antimalarial activity (*Plasmodium berghei*) displayed potent blood-schizontocial activities. The bisquinolines showed negligible MetHb formation (0.2–1.2%) underlining their potential in the treatment of glucose-6-phosphate dehydrogenase deficient patients. The bisquinoline analogues (36, 73 and 79) also exhibited promising in vitro antileishmanial activity, and antimicrobial activities (43, 44 and 76) against a panel of pathogenic bacteria and fungi.



Vandekerckhovea *et al.*, (2014)[23]have reported the Synthesis of functionalized 3-, 5-, 6- and 8-aminoquinolines via intermediate (3-pyrrolin-1-yl)- and (2-oxopyrrolidin-1-yl)quinolines and evaluation of their antiplasmodial and antifungal activity,(3-Pyrrolin-1-yl)- and (2-oxopyrrolidin-1-yl)quinolines were prepared via cyclization of diallylaminoquinolines and 4-chloro-N-quinolinylbutanamides, respectively, as novel synthetic intermediates en route to N-functionalized 3-, 5-, 6- and 8-aminoquinolines with potential biological activity. (3-Pyrrolin-1-yl) quinolines were subjected to bromination reactions, and the reactivity of (2-oxopyrrolidin-1-yl) quinolines toward lithium aluminium hydride and methyllithium was assessed, providing an entry into a broad range of novel functionalized (pyrrolidin-1-yl)- and (hydroxyalkylamino) quinolines. Antiplasmodial evaluation of these novel quinolines and their functionalized derivatives revealed moderate micromolar potency against a chloroquine-sensitive strain of the malaria parasite Plasmodium falciparum, and the two most potent compounds also showed micromolar activity against a chloroquinine-resistant strain of *P. falciparum*. Antifungal assessment of (hydroxyalkylamino) quinolines revealed three compounds with promising MIC values against *Rhodotorula bogoriensis* and one compound with potent activity against *Aspergillus flavus*.

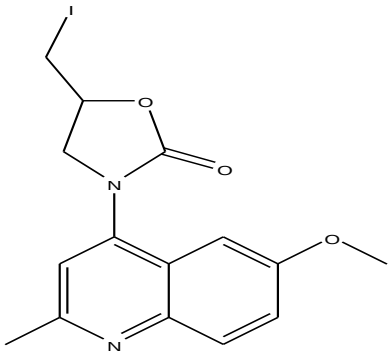


Srivastava *et al.*, (2015) have reported the synthesis of Chloroquine-based hybrid molecules as promising novel chemotherapeutic agents, Chloroquine (CQ) has a broad spectrum of pharmacological activities including anticancer and anti-inflammatory, in addition to its well-known antimalarial activity. This very useful property of CQ may be rendered through a variety of different molecular and cellular mechanisms, including the induction of apoptosis, necrosis and lysosomal dysfunction. CQ alone may not be as effective as many well-known anticancer drugs; however, it often shows synergistic when combined with other anticancer agents, without causing substantial ill-effects. To increase its pharmacological activity, scientists synthesized many different chloroquine derivatives by a repositioning approach, some of which show higher activities than the parental CQ.

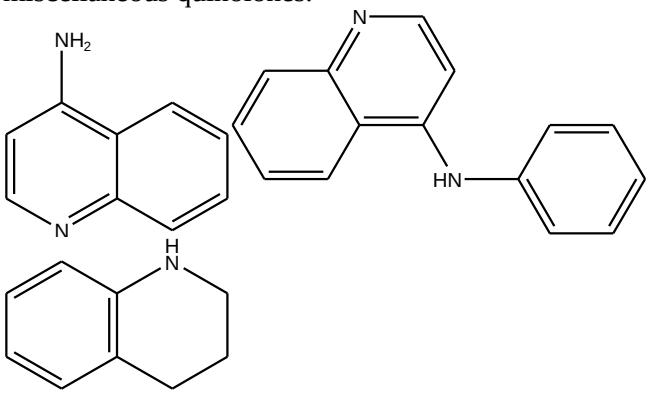


Thomas *et al.*, (2011) have reported the Design, synthesis and docking studies of quinoline-oxazolidinone

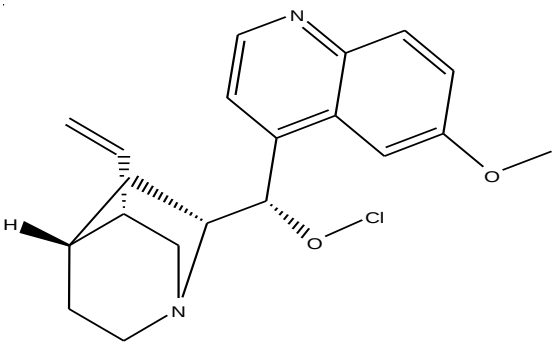
hybrid molecules and their antitubercular properties, New series of quinoline-oxazolidinone hybrid molecules were synthesized based on the preliminary docking studies. All the newly synthesized compounds were characterized by spectral analyses. The newly synthesized compounds were screened for their antimycobacterial properties based on the promising preliminary antibacterial screening results. Amongst tested compounds, compounds 8a, 8j and 13a were active at 0.65 µg/mL against Mycobacterium tuberculosis H37Rv strain. The mode of action of these active compounds was carried out by docking of receptor enoyl-ACP reductase with newly synthesized *Candida*te ligands 8a, 8j and 13a. These compounds exhibited well established bonds with one or more amino acids in the receptor active pocket. From the docking studies, compound 8j was considered to be the best inhibitor.



Kaur *et al.,* (2010) have reported the Quinolines and structurally related heterocycles as antimalarials. The quinoline scaffold is prevalent in a variety of pharmacologically active synthetic and natural compounds. The discovery of chloroquine, the most famous drug containing this scaffold resulted in control and eradication of malaria for decades. The other known antimalarial drugs from the quinoline family include: quinine, amodiaquine, piperaquine, primaquine, and mefloquine. The drugs from this group mostly act during the blood stages of the parasite's life cycle but some like primaquine targets the tissue stages. This review provides a comprehensive literature compilation concerning the study of quinolines and also other heterocycles structurally similar to quinoline scaffold in the treatment of malaria. This review covers advances made in the last ten years and it is subdivided into eight sub-headings. It consists of discussion on the biological activities, structure–activity relationship, and potential biochemical pathways of 4-aminoquinolines, 4-anilinoquinolines, 8-aminoquinolines, quinolines from nature, quinolones, isoquinolines and tetrahydroquinolines, ring-modified quinolines, and miscellaneous quinolones.

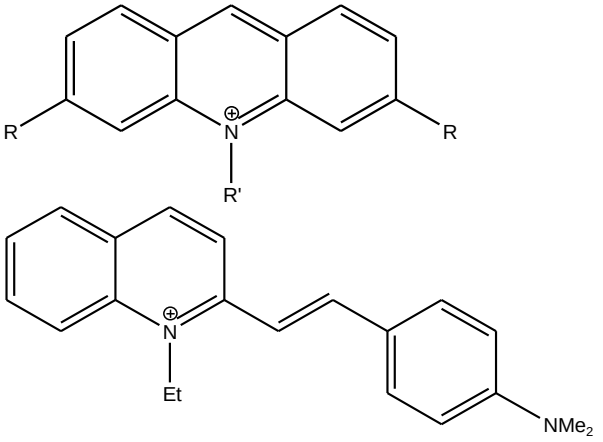


Geary *et al.,* (1987) have reported that Activity of quinoline-containing antimalarials against chloroquine-sensitive and -resistant strains of Plasmodium falciparum in vitro, quinoline-containing antimalarials and the phenanthrene methanol halofantrine were tested in vitro against 6 strains of Plasmodium falciparum with known sensitivity to chloroquinine. Sensitivity to chloroquine was not uniformly associated with sensitivity to mepacrine (quinacrine), halofantrine, SN-12108 or SN-6911 (3-methylchloroquine, sontochin). Amodiaquine was slightly less potent with chloroquine-resistant strains, whereas SN-12309 closely resembled chloroquine in the pattern of sensitivity. (Bis)desethylchloroquine was nearly as potent as chloroquine against chloroquine-sensitive strains but was about 10-fold less potent than the parent drug against chloroquine-resistant strains. 8-aminoquinolines, primaquine and pamaquine, were more potent against chloroquine-resistant than chloroquine-sensitive strains. The mutation(s) responsible for chloroquine resistance in P. falciparum greatly reduce(s) the sensitivity to a major metabolite of the drug but also generate(s) parasites which are more susceptible to a different class of drugs, the 8-aminoquinolines.

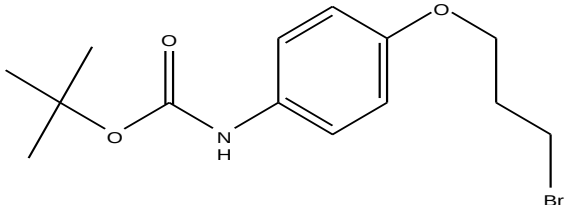


Wainwrighta *et al.,* (2003) have reported the Quinoline and cyanine dyes—putative anti-MRSA drugs,

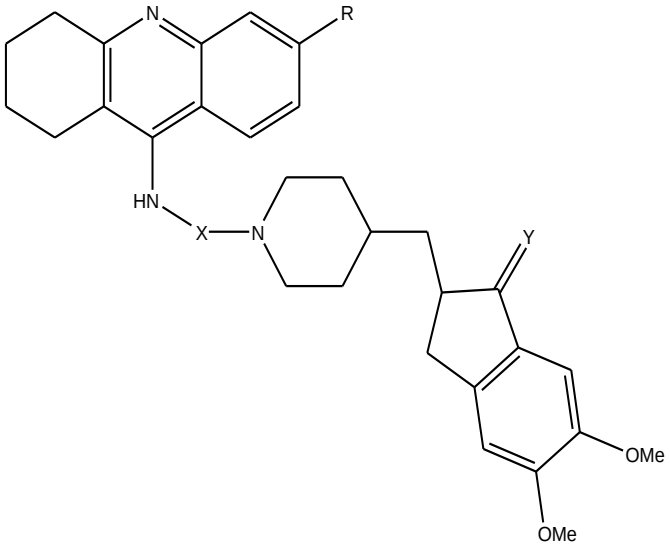
Quaternary quinoline compounds and dyes were studied by Carl Browning (1887–1972) and Julius Cohen (1859–1935). A remarkable part of Browning and Cohen's work was the early development of structure–activity relationships for their series of compounds. Thus cationic species were found generally to be more effective antibacterials than neutrals or anionics, and the testing of partial or deconstructed active molecules was also carried out. Much of this work underpinned the fuller understanding of e.g. aminoacridine action developed by Adrien Albert (1907–1989), himself also a collaborator of Browning. Analysis of the activity of a range of compounds developed by Browning and Cohen suggests that these might again be examined as topical antimicrobials in the fight against methicillin-resistant *S. aureus* (MRSA) and other resistant bacteria.



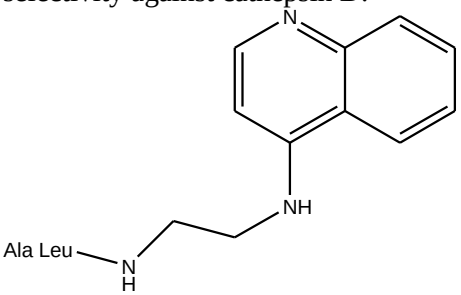
Medapi *et al.,* (2015) have reported the 4-Aminoquinoline derivatives as novel Mycobacterium tuberculosis GyrB inhibitors: Structural optimization, synthesis and biological evaluation, Mycobacterial DNA gyrase B subunit has been identified to be one of the potentially underexploited drug targets in the field of antitubercular drug discovery. In the present study, we employed structural optimization of the reported GyrB inhibitor resulting in synthesis of a series of 46 novel quinoline derivatives. The compounds were evaluated for their in vitro Mycobacterium smegmatis GyrB inhibitory ability and Mycobacterium tuberculosis DNA supercoiling inhibitory activity. The antitubercular activity of these compounds was tested over Mtb H37Rv strain and their safety profile was checked against mouse macrophage RAW 264.7 cell line. Among all, three compounds (23, 28, and 53) emerged to be active displaying IC50 values below 1 μM against Msm GyrB and were found to be non-cytotoxic at 50 μM concentration. Compound 53 was identified to be potent GyrB inhibitor with 0.86 ± 0.16 μM and an MIC (minimum inhibitory concentration) of 3.3 μM. The binding affinity of this compound towards GyrB protein was analysed by differential scanning fluorimetry which resulted in a positive shift of 3.3 °C in melting temperature (Tm) when compared to the native protein thereby re-acertaining the stabilization effect of the compound over protein.



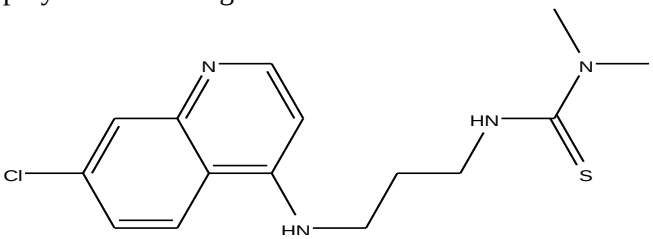
Sola *et al.,* (2015) have reported the Synthesis, biological profiling and mechanistic studies of 4-aminoquinoline-based heterodimeric compounds with dual trypanocidal–antiplasmodial activity, Dual submicromolar trypanocidal–antiplasmodial compounds have been identified by screening and chemical synthesis of 4-aminoquinoline-based heterodimeric compounds of three different structural classes. In *Trypanosoma brucei*, inhibition of the enzyme trypanothione reductase seems to be involved in the potent trypanocidal activity of these heterodimers, although it is probably not the main biological target. Regarding antiplasmodial activity, the heterodimers seem to share the mode of action of the antimalarial drug chloroquine, which involves inhibition of the haem detoxification process. Interestingly, all of these heterodimers display good brain permeabilities, thereby being potentially useful for late stage human African trypanosomiasis. Future optimization of these compounds should focus mainly on decreasing cytotoxicity and acetylcholinesterase inhibitory activity.



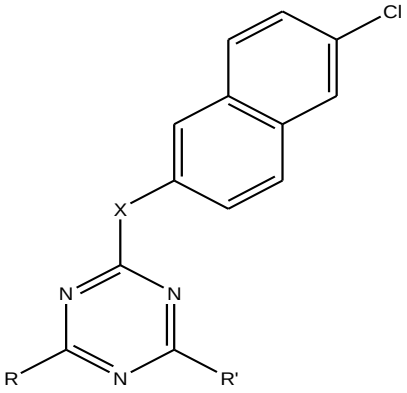
Vaiana *et al.*, (2012) have reported the Antiplasmodial activities of 4-aminoquinoline–statine compounds. These compounds were designed using the double drug approach by introducing a residue able to enhance the accumulation of plasmepsins inhibitors into the food vacuole. Some of the molecules were more active than CQ against CQ-resistant strain and showed good selectivity against cathepsin D.



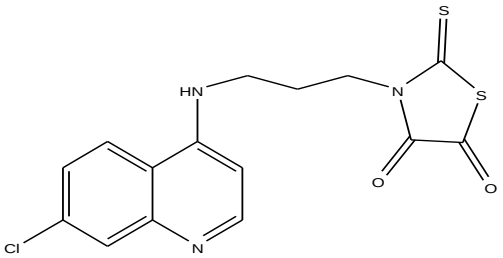
Solomon *et al.*, (2010) have reported the 4-Aminoquinoline derived antimalarials: Synthesis, antiplasmodial activity and heme polymerization inhibition studies, series of 4-aminoquinoline derivatives have been synthesized and found to be active against both susceptible and resistant strains of Plasmodium falciparum in vitro. Compound 1-[3-(7-chloro-quinolin-4-ylamino)-propyl]-3-cyclopropyl-thiourea (7) exhibited superior in vitro activity against resistant strains of P. falciparum as compared to chloroquine (CQ). All the compounds showed resistance factor between 0.59 and 4.31 as against 5.05 for CQ. Spectroscopic studies suggested that this class of compounds act on heme polymerization target.



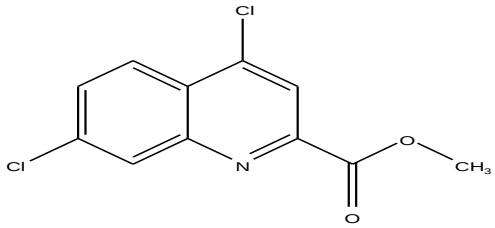
Manohar *et al.*, (2010) have reported the Synthesis, antimalarial activity and cytotoxicity of 4-aminoquinoline–triazine conjugates, series of 4-aminoquinoline–triazine conjugates with different substitution pattern have been synthesized and evaluated for their in vitro antimalarial activity against chloroquine-sensitive and resistant strains of Plasmodium falciparum. Compounds 16, 19, 28 and 35 exhibited promising antimalarial activity against both strains of P. falciparum. Cytotoxicity of these compounds was tested against three cell lines. Several compounds did not show any cytotoxicity up to a high concentration (48 μM), others exhibited mild toxicities but selective index for antimalarial activity was high for most of these conjugates.



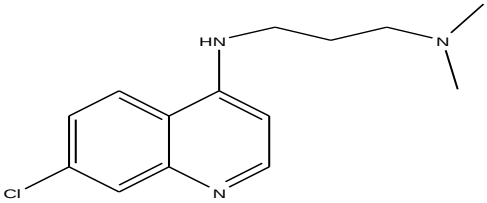
Sunduru *et al.*, (2009) have reported the Synthesis of novel thiourea, thiazolidinedione and thioparabanic acid derivatives of 4-aminoquinoline as potent antimalarials, new 4-aminoquinolines which are not recognized by CQR mechanism, thiourea, thiazolidinedione and thioparabanic acid derivatives of 4-aminoquinoline were synthesized and screened for their antimalarial activities. Thiourea derivative 3 found to be the most active against CQ sensitive strain 3D7 of Plasmodium falciparum in an in vitro model with an IC50 of 6.07 ng/mL and also showed an in vivo suppression of 99.27% on day 4 against CQ resistant strain N-67 of Plasmodium.



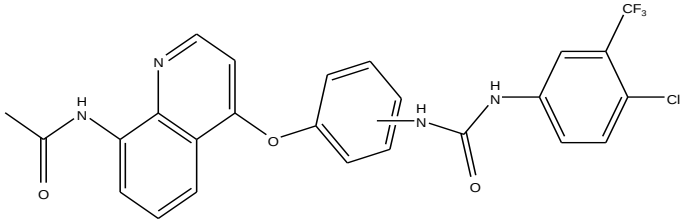
Adriana *et al.*, (2012) have reported the Synthesis and in vitro anticancer activity of ferrocenyl-aminoquinoline-carboxamide conjugates, aminoquinoline-carboxamides and their ferrocene derivatives are reported, as well as their cytotoxicity against human colon adenocarcinoma (Caco-2, HTB-37), human breast carcinoma (HTB-129) and a normal cell line as a control (human normal breast epithelial cells MCF-10A, CRL-10317). All tested compounds showed higher activity against HTB-129 cells than against Caco-2 cells. The ferrocenyl-chloroquine amide conjugates displayed higher activity against both cancer cells than did their parent organic compounds.



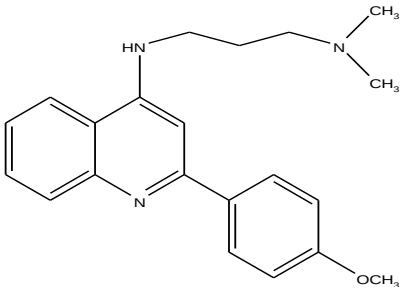
Zhang *et al.*, (2008) have reported the Synthesis and in vitro cytotoxicity evaluation of 4-aminoquinoline derivatives, series of 4-aminoquinoline derivatives were synthesized by the reaction of 4-chloro-7-substituted-quinolines with the corresponding mono/dialkyl amines. The structures of the synthesized compounds were confirmed by NMR and FAB-MS spectral and elemental analyses. Subsequently, the compounds were examined for their cytotoxic effects on two different human breast tumor cell lines: MCF7 and MDA-MB468. Although all compounds examined were quite effective on both cell lines, the compound N′-(7-chloro-quinolin-4-yl)-N,N-dimethyl-ethane-1,2-diamine emerged as the most active compound of the series. It was particularly potent against MDA-MB 468 cells when compared to chloroquine and amodiaquine. The compound butyl-(7-fluoro-quinolin-4-yl)-amine showed more potent effects on MCF-7 cells when compared to chloroquine. Therefore, 4-aminoquinoline can serve as the prototype molecule for further development of a new class of anticancer agents.'



Nam *et al.*, (2009) have reported the Aminoquinoline derivatives with antiproliferative activity against melanoma cell line, novel series of aminoquinoline derivatives 1a–p and their antiproliferative activities against A375 human melanoma cell line were described. Most compounds showed superior antiproliferative activities to Sorafenib as a reference compound. Among them, quinolinyl oxymethylphenyl compounds 1k and 1l exhibited potent activities (IC50 = 0.77 and 0.79 μM, respectively) and excellent selectivity against melanoma and fibroblast cell lines.

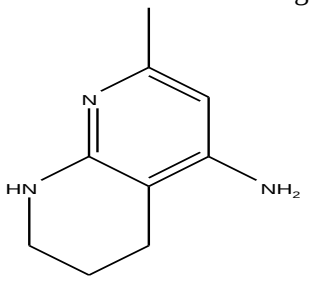


Joel *et al.*, (2012) have reported the Characterization of a series of 4-aminoquinolines that stimulate caspase-7 mediated cleavage of TDP-43 and inhibit its function, eries of 4-aminoquinolines with affinity for TDP-43 upon caspase-7-induced cleavage of TDP-43 and TDP-43 cellular function. These compounds were mixed inhibitors of biotinylated TG6 binding to TDP-43, binding to both free and occupied TDP-43. Incubation of TDP-43 and caspase-7 in the presence of these compounds stimulated caspase-7 mediated cleavage of TDP-43. This effect was antagonized by the oligonucleotide TG12, prevented by denaturing TDP-43, and exhibited a similar relation of structure to function as for the displacement of bt-TG6 binding to TDP-43. In addition, the compounds did not affect caspase-7 enzyme activity. In human neuroglioma H4 cells, these compounds lowered levels of TDP-43 and increased TDP-43 C-terminal fragments via a caspase-dependent mechanism. Subsequent experiments demonstrated that this was due to induction of caspases 3 and 7 leading to increased PARP cleavage in H4 cells with similar rank order of the potency among the compounds tests for displacement of bt-TG6 binding.

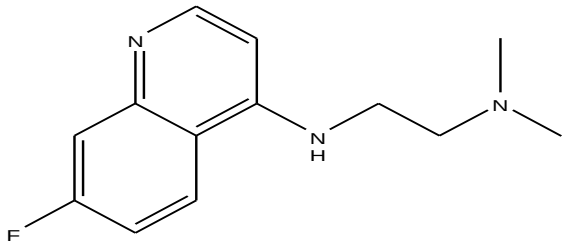


William *et al.*, (2010) have reported the Synthesis of aryl-heteroaryl urease (AHUs) based on 4-aminoquinoline and their evaluation against the insulin-like growth factor receptor (IGF-1R),The insulin-like growth factor receptor (IGF-1R) is a receptor tyrosine kinase (RTK) involved in all stages of the development and propagation of breast and other cancers. The inhibition of IGF-1R by small molecules remains a promising strategy to treat cancer. Herein, we explore SAR around previously characterized lead compound (1), which is an aryl-heteroaryl urea (AHU) consisting of 4-aminoquinaldine and a substituted aromatic ring system. A library of novel AHU compounds was prepared based on derivatives of the 4-aminoquinoline heterocycle (including various 2-substituted derivatives, and naphthyridines). The compounds were screened for in vitro inhibitory activity against IGF-1R, and several compounds with improved activity (3–5 μM) were

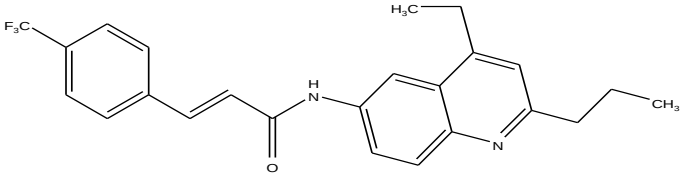
identified. Furthermore, a computational docking study was performed, which identifies a fairly consistent lowest energy mode of binding for the more-active set of inhibitors in this series, while the less-active inhibitors do not adopt a consistent mode of binding.



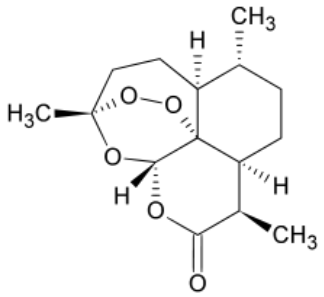
Hu *et al.*, (2010) have reported the 4-aminoquinoline derivative that markedly sensitizes tumour cell killing by Akt inhibitors with a minimum cytotoxicity to non-cancer cells, chloroquine analogues and Akt inhibitors are highly effective. In particular, the chloroquine analog N′-(7-fluoro-quinolin-4-yl)-N,N-dimethyl-ethane-1,2-diamine (compound 5) was highly effective in sensitizing cancer cell killing when combined with either Akt inhibitor 8 (1-{1-[4-(7-phenyl-1H-imidazo[4,5-g]quinoxalin-6-yl)-benzyl]-piperidin-4-yl}-1,3-dihydro-benzoimidazol-2-one) or 9 ([4-(2-chloro-4a,10a-dihydro-phenoxazin-10-yl)-butyl]-diethyl-amine hydrochloride). Importantly, the enhancement of chloroquine analogs 5 on cell killing by Akt inhibitors 8 and 9 was cancer-specific. Thus, this combinational approach is highly promising in controlling tumour with a minimum side effect. Structural analysis of effective and ineffective chloroquine analogs suggests that the 4-aminoquinoline scaffold and lateral side chain of dimethylamino functionality play an important role for the enhancement of cell killing by Akt inhibitors.



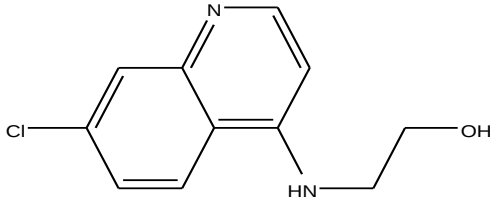
Jinlong *et al.*, (2006) have reported the 4-Aminoquinoline melanin-concentrating hormone 1-receptor (MCH1R) antagonists, Structure–activity relationships of a 4-aminoquinoline MCH1R antagonist lead series were explored by synthesis of analogs with modifications at the 2-, 4-, and 6-positions of the original HTS hit. Improvements to the original screening lead included lipophilic groups at the 2-position and biphenyl, cyclohexyl phenyl, and hydrocinnamyl carboxamides at the 6-position. Modifications of the 4-amino group were not well tolerated.



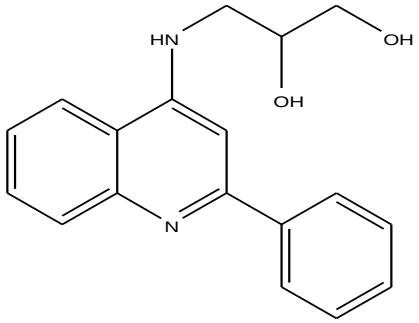
Lombard *et al.*, (2011) have reported the Synthesis, in vitro antimalarial and cytotoxicity of artemisinin-aminoquinoline hybrids, Dihydroartemisinin (DHA) was coupled to different aminoquinoline moieties forming hybrids 9–14, which were then treated with oxalic acid to form oxalate salts (9a–14a). Compounds 9a, 10a, 12, 12a, and 14a showed comparable potency in vitro to that of chloroquine (CQ) against the chloroquine sensitive (CQS) strain, and were found to be more potent against the chloroquine resistant CQR strain. Hybrids 12 and its oxalate salt 12a were the most active against CQR strain, being 9- and 7-fold more active than CQ, respectively (17.12 nM; 20.76 nM vs 157.9 nM). An optimum chain length was identified having 2 or 3 Cs with or without an extra methylene substituent.



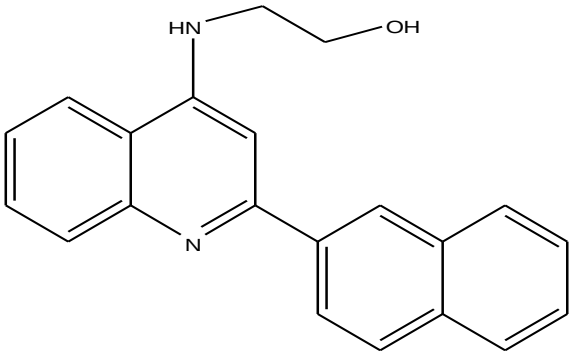
Artemisinin Macedo *et al.*, (2010) have reported the Synthesis and anti-prion activity evaluation of aminoquinoline analogues, antimalarial compounds, such as quinolines, possess antiscrapie activity. Here, we report the synthesis and evaluate the effect of aminoquinoline derivatives on the aggregation of a prion peptide. Our results show that 4-amino-7-chloroquinoline and N-(7-chloro-4-quinolinyl)-1, 2-ethanediamine inhibit the aggregation significantly. Therefore, such aminoquinolines might be considered as *Candida*tes for the further development of therapeutics to prevent the development of prior diseases.



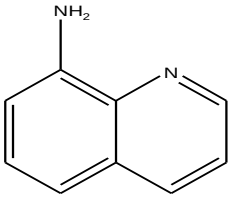
Emmanuel *et al.,* (2002) have reported the 4-Aminoquinolines as a novel class of NR1/2B subtype selective NMDA receptor antagonists, Screening of the Roche compound library led to the identification of 4-aminoquinoline 4 as structurally novel NR1/2B subtype selective NMDA receptor antagonist. The SAR which was developed in this series resulted in the discovery of highly potent and in vivo active blockers.



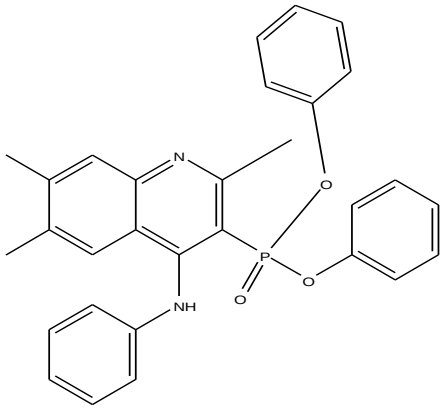
Lucjan *et al.,* (2003) have reported the Bis-4-aminoquinolines: novel triple-helix DNA intercalators and antagonists of immunostimulatory CpG oligodeoxy nucleotides, six dimeric 2-(2-naphthyl)quinolin-4-amines with a linker between the amino groups and eight dimeric 2-(4-anilino)quinolin-4-amines linked between the anilino groups were synthesized and evaluated for their interaction with duplex/triplex DNA's and as antagonists of immunostimulatory oligodeoxy nucleotides with a CpG-motif (CpG-ODN). The most powerful triple-helix DNA intercalator known to date, with high affinity toward T·A·T triplets and triplex/duplex selectivity, was found. The potent antagonism of immunostimulatory CpG-ODN by several bis-4-aminoquinolines is not related to their DNA interactions.



Sandhya *et al.,* (1997) have reported the Synthesis of 7-chloro-4-substituted aminoquinolines and their in vitro ability to produce methemoglobin in canine hemolysate, Synthesis of aminoquinoline derivatives (2–15) and their in vitro effects on methemoglobin formation and methemoglobin reductase activity are delineated. Some of the screened compounds have shown considerable methemoglobin toxicity.

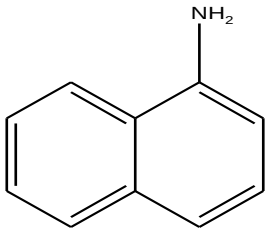


Francisco *et al.,* (1997) have reported the An efficient and general method for the synthesis of 3-phosphorylated 4-aminoquinolines from β-phosphine oxide and phosphonate enamines, 4-aminoquinolines substituted with a phosphine oxide Full-size image (<1 K), phosphine sulphide Full-size image (<1 K) and phosphonate Full-size image (<1 K) group in the 3-position is described. The key step is a regioselective addition of lithiated β-enamino phosphine oxides Full-size image (<1 K) and phosphonate Full-size image (<1 K) to isocyanate and isothiocyanates to give functionalized amides Full-size image (<1 K) and thioamide Full-size image (<1 K). Subsequent cyclization of these compounds with phosphorus oxychloride in the presence of triethylamine afforded the substituted 4-aminoquinolines Full-size image (<1 K) and 13.

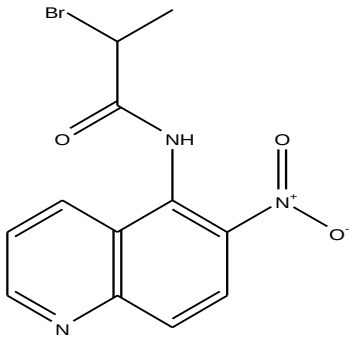


Kazuhiko *et al.,* (1987) have reported the Structure-mutagenicity relationship among aminoquinolines, aza-analogues of naphthylamine, and their N-acetyl derivatives, the mutagenicity of 7 positional isomers of aminoquinolines (AQ) and their N-acetyl derivatives (AcAQ) was tested in *Salmonella typhimurium* TA100 and TA98 in the presence and absence of S9 mix. In a series of aminoquinolines, the order of mutagenic potency in the presence of S9 mix is: 5-AQ > 8-AQ > 7-AQ > 3-AQ > 2-AQ ⩾ 4-AQ, 6-AQ. The α-positional isomers, 5-AQ and 8-AQ, are more mutagenic than the β-isomer, 2-, 3-, 6-, 7-AQ's. These results are in contrast

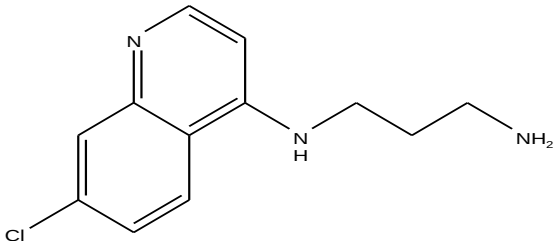
to the finding that β-naphthylamine is more mutagenic than α-naphthylamine. In a series of N-acetylaminoquinolines, the order of mutagenic potency in the presence of S9 mix is: 7-AcAQ > 6-AcAQ > 8-AcAQ ⩾ all the others. It is suggested that the AQ and AcAQ series might exert their mutagenicity through different molecular mechanisms (i.e., metabolic activation) from each other.



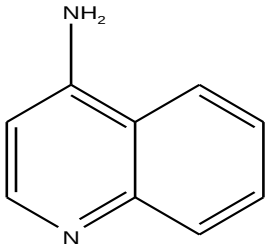
Goda *et al.,* (2005) have reported Synthesis and biological evaluation of novel 6-nitro-5-substituted aminoquinolines as local anesthetic and anti-arrhythmic agents: molecular modeling study, series of 6-nitro-5-[1-oxo-2-(substituted amino) ethylamino and 2-(substituted amino)propylamino] quinoline (4a–i and 5a–i) was synthesized and evaluated for their local anesthetic and anti-arrhythmic activity.



Frans *et al.,* (2014) have reported the Synthesis, in vitro antimalarial activity and cytotoxicity of novel 4-aminoquinolinyl-chalcone amides,4-aminoquinolinyl-chalcone amides 11–19 were synthesized through condensation of carboxylic acid-functionalized chalcone with aminoquinolines, using 1,1′-carbonyldiimidazole as coupling agent. These compounds were screened against the chloroquine sensitive (3D7) and chloroquine resistant (W2) strains of Plasmodium falciparum. Their cytotoxicity towards the WI-38 cell line of normal human fetal lung fibroblast was determined. All compounds were found active, with IC50 values ranging between 0.04–0.5 μM and 0.07–1.8 μM against 3D7 and W2, respectively. They demonstrated moderate to high selective activity towards the parasitic cells in the presence of mammalian cells. However, amide 15, featuring the 1,6-diaminohexane linker, despite possessing predicted unfavourable aqueous solubility and absorption properties, was the most active of all the amides tested. It was found to be as potent as CQ against 3D7, while it displayed a two-fold higher activity than CQ against the W2 strain, with good selective antimalarial activity (SI = 435) towards the parasitic cells. During this study, amide 15 was thus identified as the best drug-*Candida*te to for further investigation as a potential drug in search for new, safe and effective antimalarial drugs.



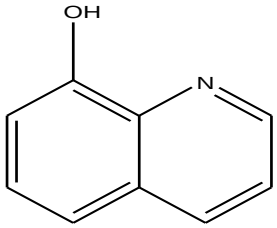
Leona *et al.,* (1972) have reported the inhibition in vitro of bacterial DNA polymerases and RNA polymerase by antimalarial 8-aminoquinolines and by chloroquine. The effects of various 8-aminoquinolines, two of their hydroxylated potential metabolites, and chloroquine on the in vitro activities of DNA polymerase of *Micrococcus luteus* (*Micrococcus lysodeikticus*) and of *Escherichia* coli and RNA polymerase of *E. coli* were determined. The antimalarial 8-aminoquinolines (including primaquine, and two hydroxylated potential metabolites) inhibited the activity of each bacterial DNA polymerase, and the levels of inhibition were not decreased appreciably by increasing the DNA concentration.



4-aminoquinoline

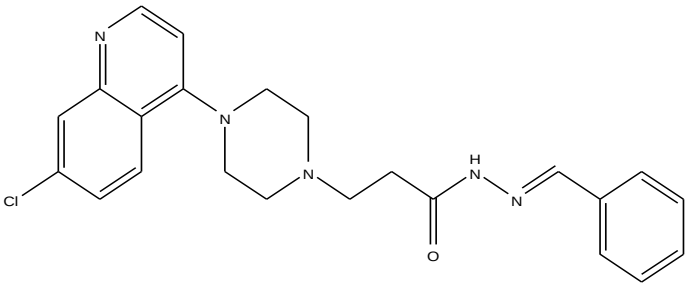
Freier *et al.,* (1986) have reported the Monoclonal antibodies to lipophilic and short-sized haptens: Application to the 4-amino-quinoline antimalarial drugs, Monoclonal antibodies recognizing the 4-amino-7-chloro-quinoline (ACQ) structure, which represents the backbone of the 4-amino-quinoline antimalarial drugs, were obtained in mice, after injection of ACQ coupled to hemocyanin via the glutaraldehyde method. The resulting antibodies show a definite specificity to this

hapten, but react better with compounds substituted on the exocyclic amino group in 4. It is postulated that the quinoline ring is not sufficient for the reaction with the antibodies, and that an enlarged structure, which is given by the bridge used to link hapten and carrier, entails an important increase (1000-fold) in the apparent affinity. The striking similarities between this bridge and the lateral chains of the antimalarial drugs are accountable for this enhanced recognition. This result allows us to indicate that in some instances, the bridge-structure of the immunogen should be positively involved in the epitope. This observation may become useful in the conception of immunogens, aiming to obtain antibodies directed against some lipophilic and small-sized haptens.



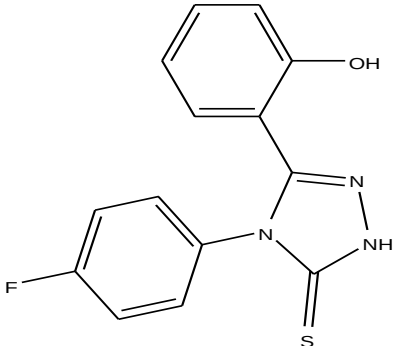
8-hydroxy-quinoline

Afreen *et al.,* (2014) have reported the Design, synthesis and biological evaluation of 3-[4-(7-chloro-quinolin-4-yl)-piperazin-1-yl]-propionic acid hydrazones as anti protozoal agents, N-Acylhydrazones derived from 7-chloro-4-piperazin-1-yl-quinoline were synthesized and biologically evaluated for blood-stage of *Plasmodium falciparum* and *Entamoeba histolytica* trophozoites. N-Acylhydrazone F12 was found to inhibit the P. falciparum growth as well as its life cycle with good selectivity, which was achieved by inhibiting hematin formation. Compound F24 showed better IC50 value than the amoebicidal drug metronidazole.

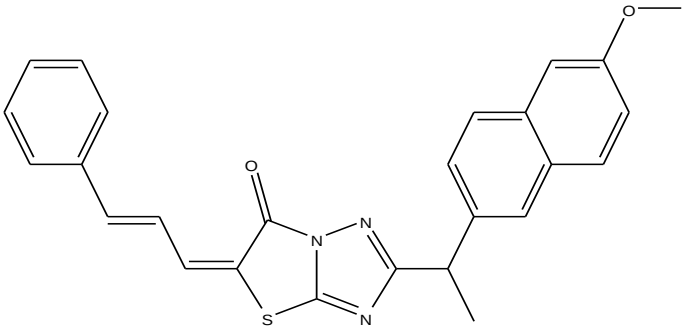


Triazole

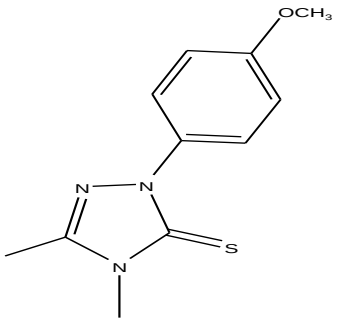
Plech *et al.,* (2015) have reported the factors affecting antibacterial activity and toxicity of 1,2,4-triazole-ciprofloxacin hybrids, The target compounds (23–44) were synthesized by Mannich reaction of 1,2,4-triazole-3-thione derivatives with ciprofloxacin (CPX) and formaldehyde. Their potent antibacterial effect on Gram-positive bacteria was accompanied by similarly strong activity against Gram-negative strains. The toxicity of the CPX-triazole hybrids for bacterial cells was even up to 18930 times higher than the toxicity for human cells. The results of enzymatic studies showed that the antibacterial activity of the CPX-triazole hybrids is not dependent solely on the degree of their affinity to DNA gyrase and topoisomerase IV.



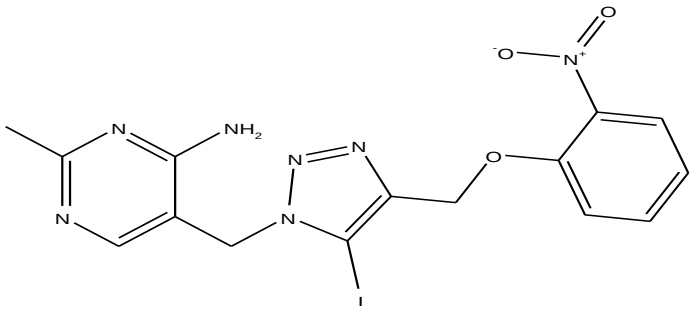
Sarigol *et al.,* (2015) have reported the Novel thiazolo [3,2-b]-1,2,4-triazoles derived from naproxen with analgesic/anti-inflammatory properties: Synthesis, biological evaluation and molecular modelling studies,3-Substituted-1,2,4-triazole-5-thiones are versatile synthetic intermediates for the preparation of several biologically active N-bridged heterocyclic compounds, given that they have two reactive sites, thiocarbonyl and an amine nitrogen (N1/N4). For several years, our interest has focused on the synthesis of novel heterocyclic systems derived from 3-substituted-1,2,4-triazole-5-thiones having analgesic/anti-inflammatory activity. In this study, a series of novel thiazolo[3,2-b]-1,2,4-triazole-6(5H)-one derivatives bearing naproxen was synthesized and evaluated for their in vivo analgesic and anti-inflammatory properties in acute experimental pain and inflammation models. The compounds were also tested for their ulcerogenic potential. Our findings showed that all the newly synthesized derivatives attenuate nociception and inflammation compared with a control. All the synthesized compounds exhibited much lower ulcerogenic risk than the standard drugs indomethacin and naproxen. Some compounds with significant analgesic and/or anti-inflammatory activities as well as low ulcer scores were further evaluated for in vitro COX-1 and COX-2 inhibitory potential in a COX-catalyzed prostaglandin biosynthesis assay. Among the tested compounds, compound 1q showed the highest selectivity index (SI) of 4.87. The binding mode for some of the tested compounds to the cyclooxygenase (COX) enzymes was predicted using docking studies.



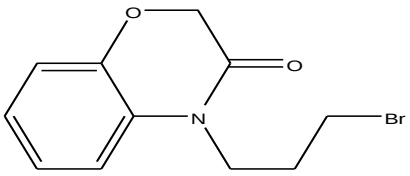
Fliegera *et al.,* (2015) have reported the RP-HPLC analysis and in vitro identification of antimycobacterial activity of novel thiosemicarbazides and 1,2,4-triazole derivatives,1,2,4-triazole derivatives. Chromatographically determined lipophilicity descriptors log kw, S and φ0 and computer generated molecular descriptors were obtained for 32 compounds and Rifampicin as a representative anti-tuberculosis drug. As experimental parameters were not significantly related to the calculated values, the data were analyzed by the principal component analysis PCA allowing for the extraction of "dipole moment" and "energy due to solvation" as the most powerful parameters from large set of diverse data. The approach ranked the examined analytes as active and inactive against Mycobacterium strains. More significant clustering of examined compounds was achieved by construction of 3D graph relating computational (dipole moment, energy due to solvation) and experimental log kw (MeOH) descriptors. It was proved that lack of substituent in the C5 position in the triazole ring appears to be characteristic for active derivatives.



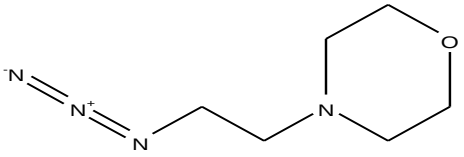
JunBo *et al.,* (2015) have reported the Synthesis and antifungal activity of 5-iodo-1,4-disubstituted-1,2,3-triazole derivatives as pyruvate dehydrogenase complex E1 inhibitors, antifungal lead compound based on inhibitors of pyruvate dehydrogenase complex E1, a series of 5-iodo-1,4-disubstituted-1,2,3-triazole derivatives 3 were prepared and evaluated for their *Escherichia* coli PDHc-E1 inhibitory activity and antifungal activity. The in vitro bioassay for the PDHc-E1 inhibition indicated all the compounds exhibited significant inhibition against *E. coli* PDHc-E1 (IC50 <21 μM), special compound 3g showed the most potent inhibitory activity (IC50 = 4.21 ± 0.11 μM) and was demonstrated to act as a competitive inhibitor of PDHc-E1. Meanwhile, inhibitor 3g exhibited very good enzyme-selective inhibition of PDHc-E1 between pig heart and *E. coli*. The assay of antifungal activity showed compounds 3e, 3g, and 3n exhibited fair to good activity against *Rhizoctonia solani* and *Botrytis cinerea* even at 12.5 μg/mL. Especially compound 3n (EC50 = 5.4 μg/mL; EC90 = 21.1 μg/mL) exhibited almost 5.50 times inhibitory potency against *B. cinerea* than that of pyrimethanil (EC50 = 29.6 μg/mL; EC90 = 113.4 μg/mL). Therefore, in this study, compound 3n was found to be a novel lead compound for further optimization to find more potent antifungal compounds as microbial PDHc-E1 inhibitors.



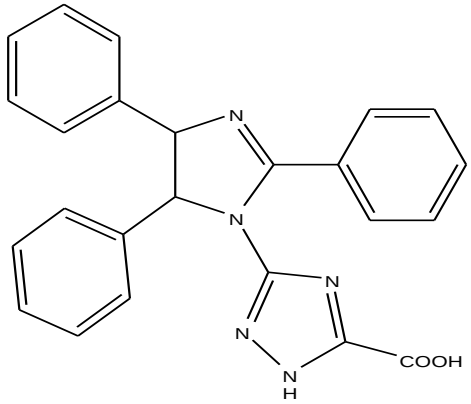
Bollu *et al.,* (2015) have reported the Rational design, synthesis and anti-proliferative evaluation of novel 1,4-benzoxazine-[1,2,3]triazole hybrids, the 1,2,3-triazole-1,4-benzoxazine hybrids 5a–n were efficiently synthesized employing click chemistry approach and evaluated for anti-proliferative activity against four cancer cell lines such as HeLa (cervical), MIAPACA (pancreatic), MDA-MB-231 (breast) and IMR32 (neuroblastoma). Compounds 5n and 5g exhibited promising anti-proliferative activity with GI50 values ranging from 1.2 to 2.5 μM and 0.1–1.1 μM respectively against all cell lines, like HeLa, MDA-MB-231, MIAPACA and IMR32, while compound 5l showed significant activity against MDA-MB-231 and IMR32 with GI50 values ranging from 1.1 and 1.4 μM. This is the first report on the synthesis and in vitro anti-proliferative evaluation of 1,2,3-triazole-1,4-benzoxazine hybrids.



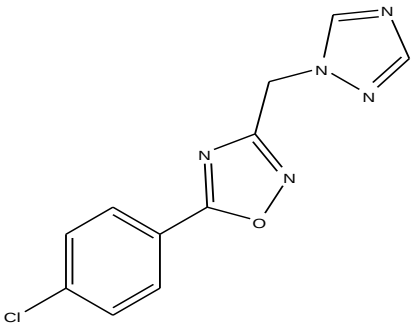
Taleli *et al.,* (2015) have reported the In vitro antiplasmodial activity of triazole-linked chloroquinoline derivatives synthesized from 7-chloro-N-(prop-2-yn-1-yl)quinolin-4-amine,The 15 synthesized target compounds were obtained by means of a copper(I)-mediated click reaction between a variety of 1,2- and 1,3-azidoamines and 7-chloro-N-(prop-2-yn-1-yl)quinolin-4-amine in moderate to good yields (53–85%). The compounds were screened for antiplasmodial activity against NF54 chloroquine-sensitive and Dd2 chloroquine-resistant strains, alongside chloroquine and artesunate as reference compounds. Six of the test compounds revealed a 3–5 fold increase in antiplasmodial activity against chloroquine-resistant strain Dd2 compared to chloroquine. Among the six compounds with good antiplasmodial activity, a reduced cross-resistance relative to artesunate (>3 fold in comparison to chloroquine) was observed, mainly in derivatives that incorporated chloroquine-resistance reversing pharmacophores. A general trend for reduced chloroquine cross-resistance was also detected among 12 out of the 15 compounds tested.



Nikalje *et al.,* (2015) have reported the CAN catalyzed one-pot synthesis and docking study of some novel substituted imidazole coupled 1,2,4-triazole-5-carboxylic acids as antifungal agents, The present work describes a facile, one-pot three component synthesis of a series of 3-[(4,5-diphenyl-2-substituted aryl/heteryl)-1H-imidazol-1-yl]-1H-1,2,4-triazole-5-carboxylic acid derivatives M(1–15). Benzil, aromatic aldehydes and 3-amino-1,2,4-triazole-5-carboxylic acid was refluxed in ethanol using cerric ammonium nitrate (CAN) as a catalyst to give the title compounds in good yields. The compounds were evaluated for their in vitro antifungal and antibacterial activity. Compounds M1, M9, and M15 were found to be equipotent against *Candida albicans* when compared with fluconazole. Compounds M2, M5, and M14 showed higher activity against *Streptococcus pneumoniae, Escherichia coli* and *Streptococcus pyogenes,* respectively, compared with ampicillin. Docking study of the newly synthesized compounds was performed, and the results showed good binding mode in the active sites of *C. albicans* enzyme cytochrome P450 lanosterol 14α-demethylase. The results of in vitro antifungal activity and docking study showed that synthesized compounds had potential antifungal activity and can be further optimized and developed as a lead compound.

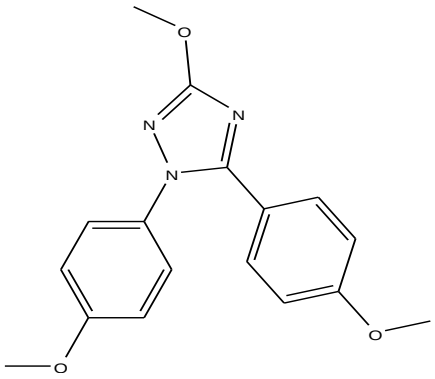


Ayati *et al.,* (2016) have reported the importance of triazole scaffold in the development of anticonvulsant agents, many antiepileptic drugs have shown unwanted side effects and drug interactions. Therefore there are continuing interests to find new anticonvulsant drugs. Triazole ring has been found in the structure of many compounds with diverse biological effects. Due to the success of several triazole-containing drugs that entered the pharmaceutical market as CNS-active drugs, this class of heterocyclic compounds has great importance for discovery and development of new anticonvulsant drugs.

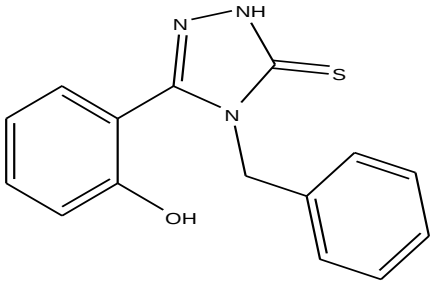


Perrone *et al.,* (2015) have reported the General role of the amino and methyl sulfamoyl groups in selective cyclooxygenase(COX)-1 inhibition by 1,4-diaryl-1,2,3-triazoles and validation of a predictive pharmacometric PLS model, 1,4-diaryl-1,2,3-triazoles were projected as a tool to study the effect of both the heteroaromatic triazole as a core ring and a variety of chemical groups with different electronic features, size and shape on the catalytic activity of the two COX isoenzymes. The new triazoles were synthesized in fair to good yields and then evaluated for their inhibitory activity towards COXs arachidonic acid conversion catalysis. Their COXs selectivity was also measured. A predictive pharmacometric Volsurf plus model, experimentally

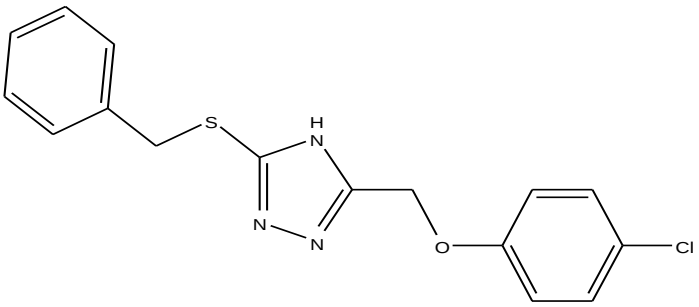
confirmed by the percentage (%) of COXs inhibition at the concentration of 50 μM and IC50 values of the tested compounds, was built by using a number of isoxazoles of known COXs inhibitory activity as a training set. It was found that two compounds {4-(5-methyl-4-phenyl-1H-1,2,3-triazol-1-yl) benzenamine (18) and 4-[1-(4-methoxy phenyl)-5-methyl-1H-1,2,3-triazole-4-yl]benzenamine (19)} bearing an amino group (NH2) are potent and selective COX-1 inhibitors (IC50 = 15 and 3 μM, respectively) and that the presence of a methylsulfamyl group (SO2CH3) is not a rule to have a Coxib. In fact, 4-(4-methoxyphenyl)-5-methyl-1-[4-(methylsulfonyl) phenyl]-1H-1,2,3-triazole (23) has COX-1 IC50 = 23 μM and was found inactive towards COX-2.



Plech *et al.*, (2014) have reported the Studies on the anticonvulsant activity of 4-alkyl-1,2,4-triazole-3-thiones and their effect on GABAergic system, 4-alkyl-5-(3-chlorobenzyl/2,3-dichlorophenyl)-2,4-dihydro-3H-1,2,4-triazole-3-thiones (1a–14a) were designed, synthesized and screened for their anticonvulsant properties. Moreover, the acute adverse-effect profile of the active compounds (1a–7a, 12a) with respect to impairment of motor performance was evaluated in the chimney test. Among 4-alkyl-5-(3-chlorobenzyl)-2,4-dihydro-3H-1,2,4-triazole-3-thiones, ethyl, butyl, pentyl, hexyl, and heptyl derivatives administered intraperitoneally in a dose of 300 mg/kg protected 100% of the tested animals at four pre-treatment times (i.e., 15, 30, 60, 120 min). Taking into account the median effective and toxic doses as well as the time-course profile of anticonvulsant activity, 5-(3-chlorobenzyl)-4-hexyl-2,4-dihydro-3H-1,2,4-triazole-3-thione (4a) was proposed as the best tolerated and the most promising potential drug *Candida*te. Finally, a radio ligand binding assay was used to check whether the anticonvulsant activity of 4-alkyl-1,2,4-triazole-3-thiones was a result of their interactions (direct or allosteric) with GABAA receptor complex and/or their affinity to benzodiazepine (BDZ) binding sites.

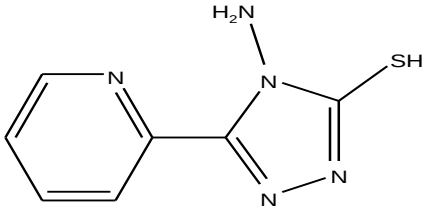


Rao *et al.*, (2014) have reported the Synthesis, characterization and pharmacological studies of sulphur containing 1,2,4-triazole derivatives, a five step procedure for the synthesis of seven novel sulphur containing 1,2,4-triazole derivatives namely 4-[(3-(4-Chloro-phenoxymethyl)-5-(4-substituted-benzylsulfonyl)-1,2,4-triazol-4-yl)methyl] Morpholine from 4-Chloro-phenol and Ethylbromo acetate as starting compounds and to screen for their pharmacological activity,All compounds were evaluated for antimicrobial activity against selected bacteria and fungi by the methods reported in the literature. The drug-like characteristics were assessed by *in silico* studies.

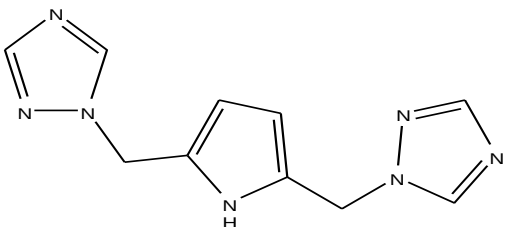


Yong *et al.*, (2014) have reported the Synthesis, crystal structures, molecular docking and urease inhibitory activity of nickel(II) complexes with 3-pyridinyl-4-amino-5-mercapto-1,2,4-triazole,Three novel complexes, [NiII(dpp)2(L)2] (1), [NiII(eda)2(L)2] (2) and [NiII(deda)2(L)2] (3) (L = 3-pyridinyl-4-amino-5-mercapto-1,2,4-triazole, dpp = 1,3-diaminopropane, eda = ethanediamine, deda = N,N-dimethyl ethylenediamine), were synthesized by reacting 3-pyridinyl-4-amino-5-mercapto-1,2,4-triazole with diamines and nickel(II) salt. The complexes were structurally determined by single-crystal X-ray diffraction. The inhibitory activity was tested in vitro against jack bean urease. Molecular docking was investigated to insert complexes into the crystal structure of jack bean urease at the active site to determine the probable binding mode. The experimental values and

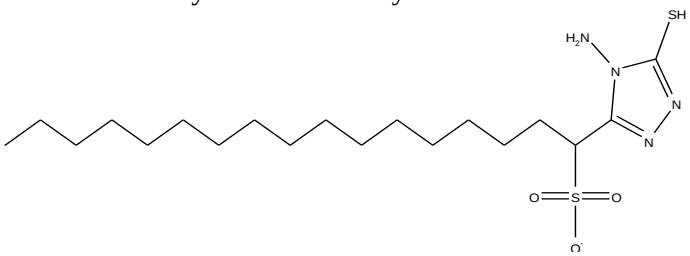
docking simulation exhibited that complexes 1, 2, 3 had better inhibitory activity than the positive reference aceto hydroxamic acid, showing IC50 values of 48.16, 32.35 and 15.22 μM, respectively. These complexes exhibited inhibitory activities as potent urease inhibitor.



Katie *et al.,* (2014) have reported the Pyrrole pincers containing imidazole, pyrazole and 1,2,4-triazole groups, the compounds containing a central pyrrole linked through methylene groups in the 2,5-positions to two N-imidazole, N-pyrazole and N-1,2,4-triazole heterocyles have been prepared via a common quaternary amine precursor. Alkylation of the imidazole groups using methyl iodide or benzyl bromide gave imidazolium compounds. The alkylated cations which were investigated as precursors to pyrrole-carbene pincer ligands, but all attempts to either coordinate palladium or deprotonate using silver oxide led to cleavage of the heterocycles from the central pyrrole. The result was the formation of palladium and silver complexes containing 3-N-methylimidazole (3-N-MeIm) or 3-N-benzylimidazole (3-N-BzIm) ligands: (3-N-MeIm) PdI2, (3-N-MeIm)PdCl2 and [(3-N-MeIm)2Ag]I, with the (3-N-MeIm)PdI2 complex characterised by crystallography. Pyrazole, 3,5-dimethylpyrazole and 1,2,4-triazole pincer compounds were prepared, the latter characterised by a molecular structure determination.



Adil *et al.,* (2014) have reported the 1,3,4-Oxadiazole, 1,3,4-thiadiazole and 1,2,4-triazole derivatives as potential antibacterial agents,1,3,4-Oxadiazole; 1,3,4-thiadiazole; 1,2,4-triazole and some of their derivatives are involved in modifications at the following axes: First, attaching a thio-group into heterocyclic rings. Second, introducing different substitutions at position 5 which often are the residuals of the synthetic starting materials such as simple aliphatic, substituted aliphatic chains, aromatic carbocyclic and heterocyclic residues.



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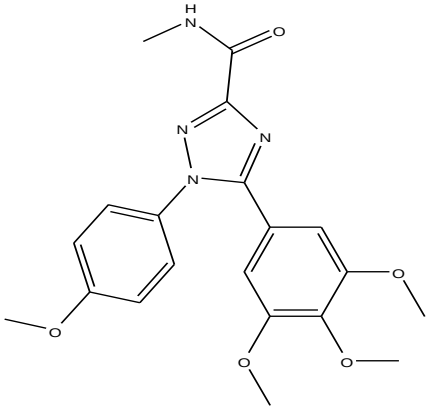
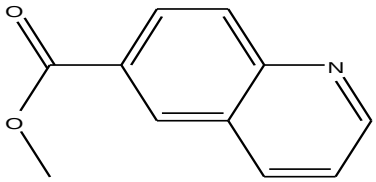
Abdel *et al.,* (2014) have reported the 1-(4-Methoxyphenyl)-5-(3,4,5-trimethoxy phenyl)-1H-1,2,4-triazole-3-carboxamides: Synthesis, molecular modelling, evaluation of their anti-inflammatory activity and ulcerogenicity, A series of novel 1-(4-methoxyphenyl)-5-(3,4,5-trimethoxyphenyl)-1H-1,2,4-triazole-3-carboxamides were synthesized and confirmed with different spectroscopic techniques. The prepared compounds exhibited remarkable anti-inflammatory activity that represents 38%–100% of indomethacin activity and 44%–115% of celecoxib activity after 3 h. The anilides 5a–l and hydrazide 6 exhibit low incidence of gastric ulceration compared to indomethacin which was confirmed with histopathological investigation. In vitro COX-1/COX-2 inhibition studies showed compounds 4b (COX-1 IC50 = 45.9 μM; COX-2 IC50 = 68.2 μM) and 6 (COX-1 IC50 = 39.8 μM; COX-2 IC50 = 46.3 μM) are the most potent COX inhibitors in the tested compounds. The binding mode for some of the tested compounds to the enzymes was predicted using docking studies.

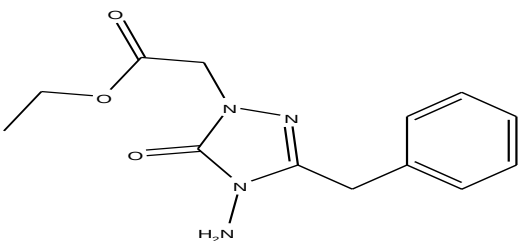


Patel *et al.,* (2014) have reported the Access to a new class of biologically active quinoline based 1,2,4-triazoles, a series of 1,2,4-triazol-3-ylthio-acetamides was constructed and in vitro analyzed for their antimicrobial activity against several bacteria and fungi. Aiming to establish an increased potency, the bioassay results were matched to those of 1,3,4-oxadiazoles, utilized previously. Remarkably, 1,2,4-triazoles were

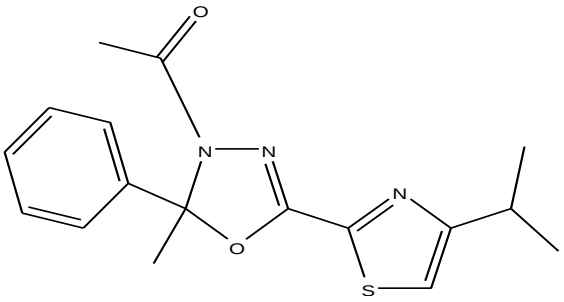
found to possess a good spectrum of antifungal potency, which eventually suggested the azole template as an essential pharmacophore to diversify the biological occupations of the attendant molecules. However, it was noticed that the potency of final analogs against each strain placed reliance on the type of substituent present on benzothiazole ring.



Demirbas *et al.*, (2004) have reported Synthesis and antimicrobial activities of some new 1-(5-phenylamino-[1,3,4]thiadiazol-2-yl)methyl-5-oxo-[1,2,4]triazole and 1-(4-phenyl-5-thioxo-[1,2,4]triazol-3-yl)methyl-5-oxo-[1,2,4]triazole derivatives, Acetic acid ethyl esters containing 5-oxo-[1,2,4]triazole ring (2) were synthesized by the condensation of compounds 1a–f with ethyl bromoacetate in basic media. The reaction of compounds 2a–f with hydrazine hydrate led to the formation of acid hydrazides (3a–f). The treatment of compounds 3 with two divers aromatic aldehydes resulted in the formation of arylidene hydrazides as *cis–trans* conformers (4a,c,e,f, 5a,e,f). The thio semicarbazide derivatives (6a,c,d,f) were afforded by the reaction of corresponding compounds 3 with phenylisothiocyanate. The treatment of compounds 6a,c,d,f with sulfuric acidic caused the conversion of side-chain of compounds 6a,c,d,f into 1,3,4-thiadiazol ring; thus, compounds 7a,c,d,f were obtained. On the other hand, the cyclization of compounds 6a,c,d,f in the presence of 2 N NaOH resulted in the formation of compounds 8a,c,d,f containing two [1,2,4]triazole rings which are linked to each other via a methylene bridge. Compounds 4a, f, 5a, 7a, d, f, 8a and d have shown antimicrobial activity against one or more microorganism, but no antifungal activity has been observed against yeast like fungi. Also inhibitory effect on mycelial growth by compounds 4e, 7d and 8f has been observed. Compounds 4c and 5f were found to possess antitumor active towards breast cancer.

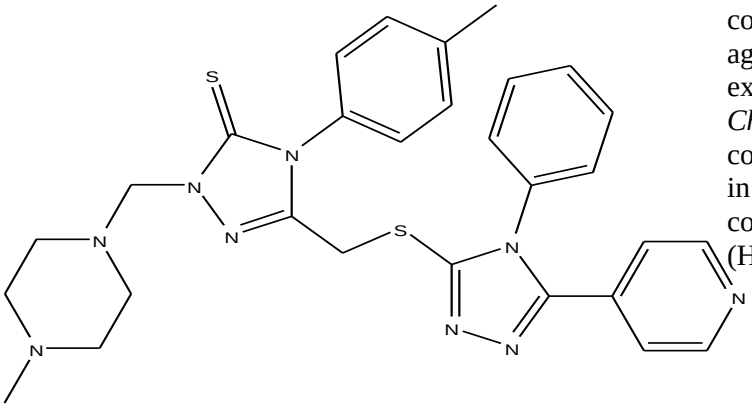


Kumar *et al.*, (2010) have reported Synthesis of some novel 2-substituted-5 [isopropyl thiazole] clubbed1,2,4-triazole and 1,3,4-oxadiazoles as potential antimicrobial and antitubercular agents, series of 2-substituted-5-[isopropylthiazole] clubbed 1,2,4-triazole and 1,3,4-oxadiazole derivatives have been synthesized and characterized by IR, 1H NMR, 13C NMR and mass spectral analysis. Synthesized compounds were evaluated for their preliminary cytotoxicity, antimicrobial and antitubercular activity against Mycobacterium tuberculosis H37Rv strain by broth dilution assay method. Antimycobacterial activity tested against M. tuberculosis indicated that compounds 4b and 6g exhibited twofold enhanced potency than parent compound 1 and the results indicate that some of them exhibited promising activities and they deserve more consideration as potential antitubercular agents. Compound 3c, 4b and 6c exhibited good or moderate antibacterial inhibition and compounds 3h and7c showed excellent antifungal activity.

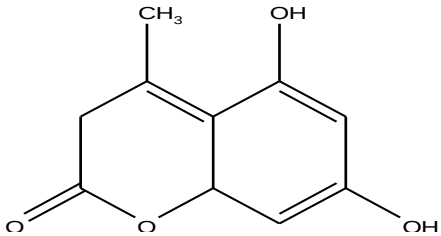


Bayrak *et al.*, (2009) have reported the Synthesis of some new 1,2,4-triazoles, their Mannich and Schiff bases and evaluation of their antimicrobial activities, 4-Phenyl-5-pyridin-4-yl-4H-1,2,4-triazole-3-thiol (3) was obtained in basic media via the formation of 2-isonicotinoyl-N-phenylhydrazinecarbothioamide (2), and converted to some alkylated derivatives (4a,b) and Mannich base derivatives (5aec). 2-[(4-Phenyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-yl)thio]acetohydrazide (7) that was obtained by using compound 3 as precursor in two steps was converted to thiosemicarbazide derivative (8), Schiff base derivatives (9) and 5-{[(4-phenyl-5-pyridin-4-yl-4H-1,2,4-triazol-3 yl)thio] methyl}-1,3,4-oxadiazole-2-thiol(10). Moreover, 5-{[(4-phenyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-yl)thio]methyl}-3-{[(2-morpholine-4-ylethyl) amino] methyl}-1,3,4 oxadiazole-2(3H)-thione (11) was synthesized via reaction of compound 10 with 2-(4-morpholino)ethylamine. The treatment of compound 8 with NaOH gave 4-(4-methylphenyl) -5-{[(4-phenyl-5-pyridine-4-yl-4H-1,2,4-triazol-3-yl)thio]methyl}-4H 1,2,4-triazole-3-thiol (12), while the acidic treatment of compound 8 afforded 5-{[(4-phenyl-5-

pyridin-4-yl-4H-1,2,4-triazol-3-yl) thio] methyl}-2(4-methyl phenyl)-amino-1,3,4-thiadiazole (14). N-Methyl derivative of compound 14 and a Mannich base derivative of compound 12 were synthesized from the reactions of these precursors with methyl iodide and methyl piperazine, respectively. All newly synthesized compounds were screened for their antimicrobial activities. The antimicrobial activity study revealed that all the compounds screened showed good or moderate activity except compounds 3, 5c, 7, 9c, 9e, 9g, 9h, 11, and 13.

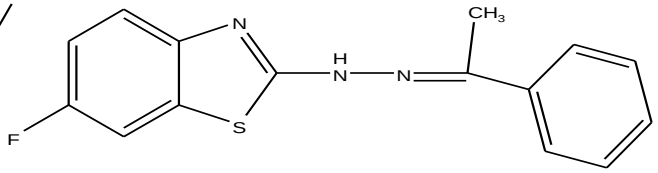


Shi *et al.,* (2011) have reported Synthesis and evaluation of a class of new coumarin triazole derivatives as potential antimicrobial agents, coumarin-based 1,2,4-triazole derivatives were designed, synthesized and evaluated for their antimicrobial activities in vitro against four Gram-positive bacteria (*Staphylococcus aureus*, *MRSA*, *Bacillus subtilis* and *Micrococcus luteus*), four Gram-negative bacteria (*Escherichia coli*, *Proteus vulgaris*, *Salmonella typhi* and *Shigella dysenteriae*) as well as three fungi (*Candida albicans*, *Saccharomyces cerevisiae* and *Aspergillus fumigatus*) by two-fold serial dilution technique. The bioactive assay showed that some synthesized coumarin triazoles displayed comparable or even better antibacterial and antifungal efficacy in comparison with reference drugs Enoxacin, Chloromycin and Fluconazole. Coumarin bis-triazole compounds exhibited stronger antibacterial and antifungal efficiency than their corresponding mono-triazole derivatives.

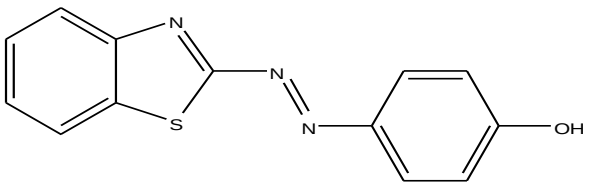


Benzothiazole

Gabr. *et al.,* (2015) have reported the Synthesis, antimicrobial, antiquorum-sensing and cytotoxic activities of new series of benzothiazole derivatives, The newly synthesized compounds were screened for their antibacterial activity against *Escherichia coli*, *Staphylococcus aureus* and *Bacillus cereus*. Compounds 6j and 6o showed the highest activity against *E. coli* and *S. aureus*. The antifungal activity of these compounds was also tested against *Candida albicans* and *Aspergillus fumigatus* 293. Compounds 4c, 4g and 6j exhibited the highest activity against *C. albicans*. In addition, compounds 4a and 6j displayed promising activity against *A. fumigatus* 293. The same compounds were examined for their antiquorum-sensing activity against *Chromobacterium violaceum* ATCC 12472, whereas compounds 4a, 6j and 6p showed moderate activity. The in vitro cytotoxicity testing of the synthesized compounds was performed against cervical cancer (HeLa) and kidney fibroblast cancer (COS-7) cell lines.

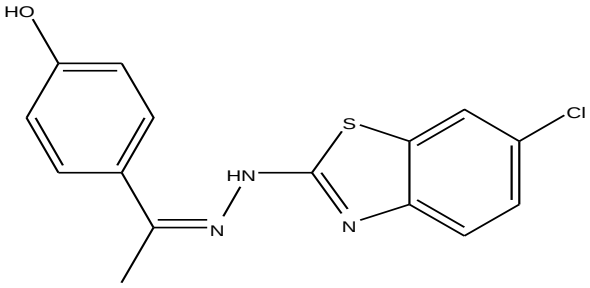


Ivan *et al.,* (2010) have reported the Synthesis, characterization and comparative study the microbial activity of some heterocyclic compounds containing oxazole and benzothiazole moieties. The compounds were screened for antibacterial activity against *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aerugenosa* in nutrient agar medium, and for antifungal activity against *Aspergillus niger* and *Candida albicans* in Sabourauds dextrose agar medium. The results show that the derivatives containing benzothiazole moiety are more active than the derivatives containing oxazole moiety.

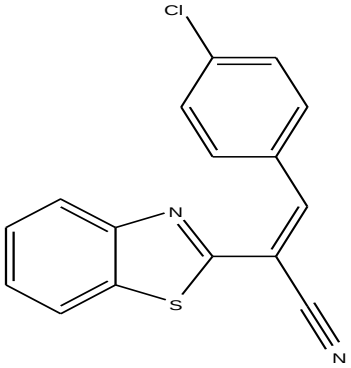


Asati *et al.,* (2015) have reported the Synthesis, characterization and antimicrobial evaluation of some 1,3-benzothiazole-2-yl-hydrazone derivatives,*in-vitro* antimicrobial activity was evaluated against the four pathogenic bacterial strains, *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas alkaligenes* and three fungal strains

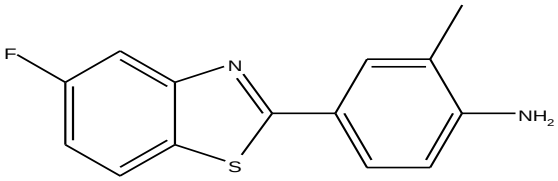
Aspergillus niger, *Rhizopus oryzae* and *Candida albicans*. The compounds have shown moderate activity.



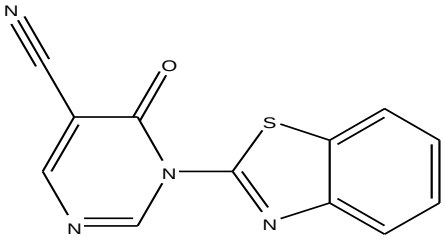
Maddila *et al.*, (2016) have reported the Synthesis, antibacterial and antifungal activity of novel benzothiazole pyrimidine derivatives, a series of 5-amino-6-(benzo[d]thiazol-2-yl) -2 -(2- (substituted benzylidene) hydrazinyl)-7-(4 chlorophenyl) pyrido [2,3d] pyrimidin-4(3H)-one derivatives (7a–k) were synthesized. All the newly synthesized compounds were screened for their in vitro antibacterial activity, against *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Streptococcus pyogenes* and for antifungal activity against *Aspergillus flavus*, *Aspergillus fumigatus*, *Candida albicans*, *Penicillium marneffei and Mucor*. Compounds 7b, 7e, 7f, 7g, 7h and 7j showed excellent in vitro antibacterial activity and antifungal activity than the standard drugs.



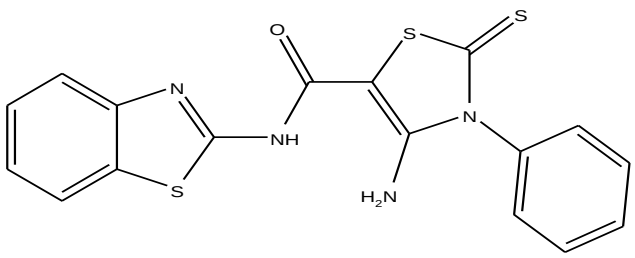
Talib *et al.*, (2011) have reported the Synthesis and biological evaluation of new benzothiazoles as antimicrobial agents, new series of hydrazide derivatives were synthesized, characterized, and biologically evaluated. The reaction of 2-chloro benzo[d]thiazole 1, with ethyl 2-(piperazin-1-yl) acetate 2, led to the formation of ethyl 2-(4-(benzo[d]thiazol-2-yl)piperazin-1-yl)acetate 3. The reaction of compound 3 with excess amount of hydrazine hydrate gave 2-(4-(benzo[d]thiazol-2-yl) piperazin-1-yl) acetohydrazide 4. Hydrazide derivatives 5(a–j) were prepared by the reaction of compound 4 with the appropriate acid chloride. The in vitro antibacterial activity of compounds 3, 4, 5a, and 5b were screened against *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* bacteria.



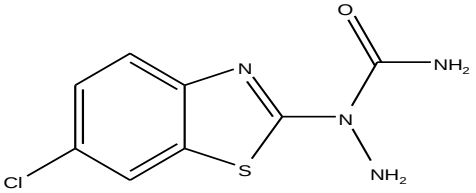
Bondock *et al.*, (2009) have reported the Enaminonitrile in heterocyclic synthesis: Synthesis and antimicrobial evaluation of some new pyrazole, isoxazole and pyrimidine derivatives incorporating a benzothiazole moiety.



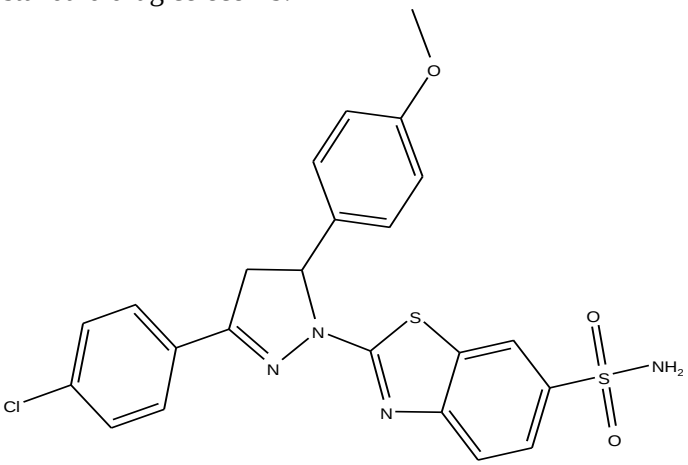
Bondock *et al.*, (2010) have reported the Synthesis and antimicrobial activity of some new thiazole, thiophene and pyrazole derivatives containing benzothiazole moiety, a new class of antimicrobial agents, a series of thiazole, thiophene, pyrazole and other related products containing benzothiazole moiety were prepared via the reaction of N-(benzothiazol-2-yl)-2-cyanoacetamide (1) with appropriate chemical reagents. These compounds were screened for their antibacterial activity against Gram-positive bacteria (*Staphylococcus aureus* and *Streptococcus pyogenes*), Gram-negative bacteria (*Pseudomonas phaseolicola* and *Pseudomonas fluorescens*) and antifungal activity against Fusarium *oxysporum* and *Aspergillus fumigatus*. Among the synthesized compounds, thiophene 13 showed equal activity with chloroamphenicol against S. *aureus* (MIC 3.125 mg/ mL), while its activity was 50% lower than of chloroamphenicol against *S. pyogenes*. Thiazole 3 and pyrazolo [1,5-a] pyrimidine 21b were found to exhibit the most potent in vitro antifungal activity with MICs (6.25 mg/mL) against *A. fumigatus* and *F. oxysporum*.



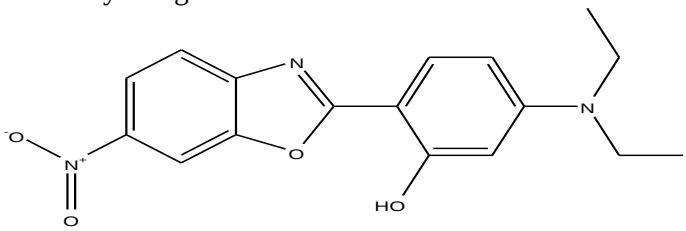
Gilani *et al.,* (2012) have reported the Benzothiazole incorporated thiazolidin-4-ones and azetidin-2-ones derivatives: Synthesis and in vitro antimicrobial evaluation, a series of novel thiazolidin-4-ones (5a–g) and azetidin-2-ones (6a–g) were synthesized from N-(6-chlorobenzo[d]thiazol-2-yl)hydrazine carboxamide derivatives of the benzothiazole class. Antimicrobial properties of the title compound derivatives were investigated against one Gram (+) bacteria (*Staphylococcus aureus*), three Gram (-) bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*) and five fungi (*Candida albicans*, *Aspergillus niger*, *Aspergillus flavus*, *Monascus purpureus* and *Penicillium citrinum*) using serial plate dilution method.



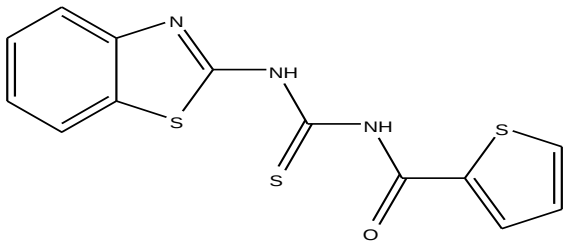
Kharbanda *et al.,* (2014) have reported the Synthesis and evaluation of pyrazolines bearing benzothiazole as anti-inflammatory agents. The synthesized compounds were evaluated for their anti-inflammatory potential using carrageenan induced paw edema model. Two compounds 5a and 5d alleviated inflammation more than the standard drug celecoxib.



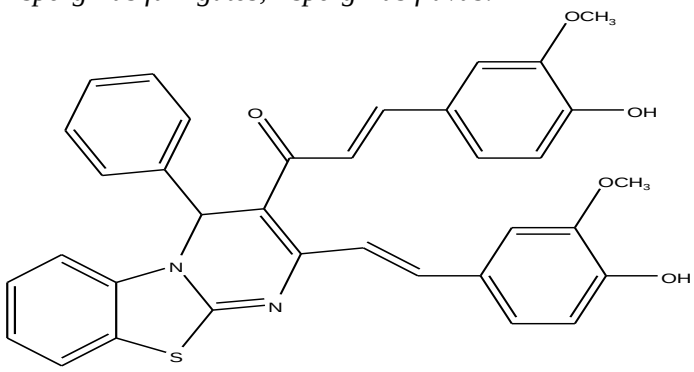
Padalkar *et al.,* (2016) have reported Synthesis and antimicrobial activity of novel 2-substituted benzimidazole, benzoxazole and benzothiazole derivatives,a series of 2 (1H-benzimidazol-2-yl)-5-(diethylamino) phenol, 2-(1,3-benzoxazol-2-yl)-5 (diethyl amino) phenol, 2-(1,3-benzothiazol-2-yl)-5-(diethylamino) phenol and their derivatives were synthesized starting from p-N,N-diethyl amino salicylaldehyde with different substituted o-phenylenediamine or o-aminophenol or o-aminothiophenol. All compounds were evaluated for in vitro antibacterial activities against *Escherichia coli* and *Staphylococcus aureus* strains and in vitro antifungal activity against *Candida albicans* and *Aspergillus niger* strains by using serial dilution method.



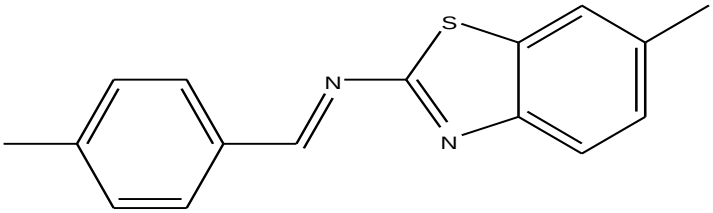
Saeed *et al.,* (2010) have reported the Synthesis, characterization and biological evaluation of some thiourea derivatives bearing benzothiazole moiety as potential antimicrobial and anticancer agents, five series of thiourea derivatives bearing benzothiazole moiety (20 compounds) were efficiently synthesized and evaluated for antimicrobial and anticancer activities. The results indicated that the compounds possessed a broad spectrum of activity against the tested microorganisms and showed higher activity against fungi than bacteria. Compounds 1b, 2b, 3b, 4b and 5b exhibited the greatest antimicrobial activity.



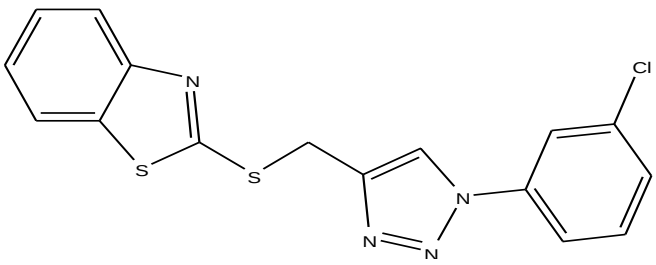
Sahu *et al.,* (2012) have reported the Synthesis and evaluation of antimicrobial activity of 4H-pyrimido [2,1-b] benzothiazole, pyrazole and benzylidene derivatives of curcumin,The synthesized compounds were evaluated for their antibacterial activity against gram-positive and gram-negative bacteria viz. *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella typhi*, *Escherichia coli*, *Bacillus cereus* and *Providencia rettgeri* and antifungal activity against fungi viz., *Aspergillus niger*, *Aspergillus fumigates*, *Aspergillus flavus*.



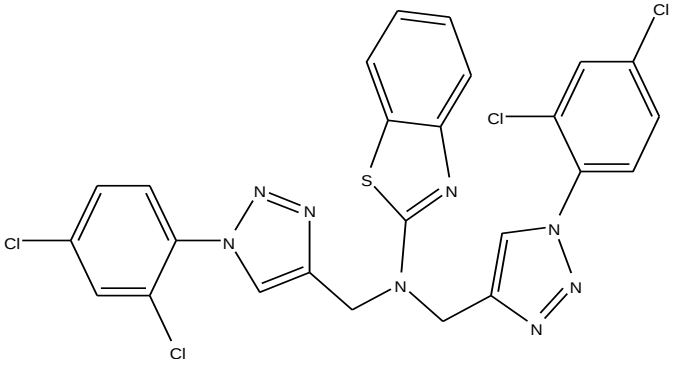
Sakarya *et al.,* (2016) have reported Synthesis and characterization of novel substituted N-benzothiazole-2-yl-acetamides,Schiff base derivatives of benzothiazole 2a–e have been synthesized by reacting with substituted 2-aminobenzothiazole 1a–e and different substituted benzaldehydes 5a–e. The obtained Schiff bases reaction with NaBH4 has afforded the corresponding some novel amines 3a–e. The condensation of amines with chloroacetylchloride leads to novel amide derivatives 4a–e.



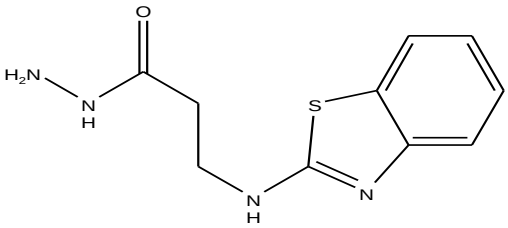
Shafi *et al.,* (2012) have reported the Synthesis of novel 2-mercapto benzothiazole and 1,2,3-triazole based bis-heterocycles: Their anti-inflammatory and anti-nociceptive activities. The synthesized compounds have been tested for their anti-inflammatory activity by using biochemical cyclooxygenase (COX) activity assays and carrageenan-induced hind paw edema. Among the tested compounds, compound 4d demonstrated a potent selective COX-2 inhibition with COX-2/COX-1 ratio of 0.44. Results from carrageenan-induced hind paw edema showed that compounds 4a,4d,4e and 4f possess significant anti-inflammatory activity as compared to the standard drug Ibuprofen.



Singh *et al.,* (2013) have reported the Design, synthesis and antimicrobial activity of novel benzothiazole analogs, a new class of antimicrobials, dialkyne substituted 2-aminobenzothiazole was reacted with various substituted aryl azides to generate a small library of 20 compounds (3a-t) by click chemistry. Structures of the newly synthesized compounds were established on the basis of spectral data. These compounds were screened for their antibacterial activity against Gram + ve bacteria (*Staphylococcus aureus* and *Enterococcus faecalis*), Gram -ve bacteria (*Salmonella typhi*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and antifungal activity against *Candida tropicalis*, *Candida albicans*, *Candida krusei*, Cryptococcus *neoformans*) as well as molds (*Aspergillus niger*, *Aspergillus fumigatus*).

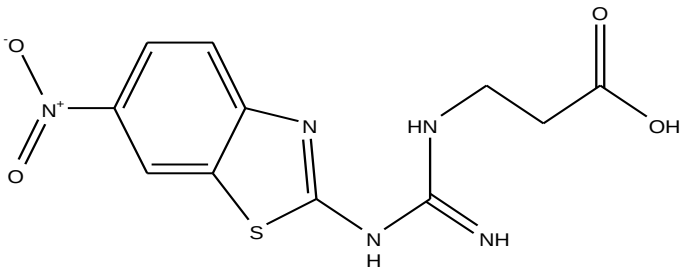


Soni *et al.,* (2010) have reported the Synthesis and evaluation of some new benzothiazole derivatives as potential antimicrobial agents, benzothiazole has proven to be good antimicrobial agent, a novel series of Schiff bases of benzothiazole derivatives were synthesized. Thus condensation of 5-[2-(1,3-benzothiazol-2-yl-amino)ethyl]-4-amino-3-mercapto-(4H)-1,2,4-triazole 5 with appropriate aromatic aldehydes afforded 5-[2-(1,3-benzothiazol-2-yl-amino)ethyl]-4-(arylideneamino)-3-mercapto-(4H)-1,2,4 triazoles 6a-g.

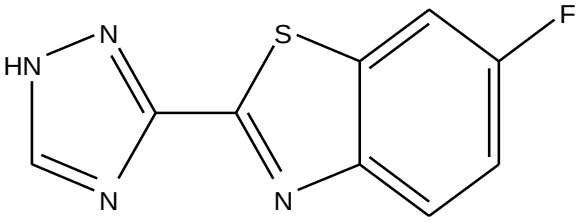


Venkatesh *et al.,* (2016) have reported the Design and synthesis of Quinazolinone, Benzothiazole derivatives bearing guanidinopropanoic acid moiety and their Schiff bases as cytotoxic and antimicrobial agents, Two series of Benzothiazole, Quinazolinone derivatives bearing guanidinopropanoic acid (38 compounds including 27 intermediates) and one series of Schiff base derivatives (14 compounds) were synthesized, characterized then evaluated for their cytotoxicity against human cervix cell line (HeLa) by MTT assay; antimicrobial activity against 11 pathogenic bacteria, 10 pathogenic fungus using standard of ciprofloxacin and Clotrimazole respectively. Compounds 13–18 showed significant activity against HeLa with IC50 range of 2–550 lM. Compound 3-(3-(6-hydroxybenzo[d]thiazol-2-yl)guanidino) propanoic acid (18) showed potent activity against human HeLa cell line with the half maximal inhibitory concentration (IC50) values of 1.8 l M which was close to the value of the positive control, doxorubicin. Antimicrobial result

indicated that, compounds showed differential activity against the tested fungus and bacteria. Compounds 11, 14, 38 and 49 exhibited potent antibacterial and antifungal activity.



Sidhu *et al.*, (2015) have reported the Synthesis of novel fluorinated benzothiazol-2-yl-1,2,4-triazoles: Molecular docking, antifungal evaluation and in silico evaluation for SAR,6-flouro-1,3-benzothiazol-2-amine and 1,2,4-triazoles in a single molecule, with the aim of discovery of high potential novel fungicides. Antifungal evaluation of synthesized 6-flourobenzothiazol-2-yl-1,2,4-triazoles against various phytopathogenic fungi revealed synergistic effect of combination of leads with one another in all the test compounds. Some of the synthesized compounds showed excellent fungi toxicity comparable with the standard fungicides used. *In silico* toxicity of all the compounds was equivalent to the standard fungicides used. Docking studies and Lipinski filtration were performed in order to present the rationale of structure activity relation.



Conclusion

The extensive pharmacological investigation of newly synthesized compounds have been carried out.These compounds showed experimental evidence indicating the significant contribution in biological activities, hence we can say that these derivatives are potent antimicrobials, anti-inflammatory and analgesics, anti-inflammatory, anti-HIV. Overall the research findings reveal that aminoquinoline and triazole and Benzothiazole derivatives were found active towards all the screened activities hence these active moieties have wide scope in innumerable ailment management.

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