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1,3-Oxazole Derivatives: A Review of Biological Activities as Antipathogenic

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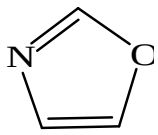
ABSTRACT

Oxazole is heterocyclic five membered rings that have been investigated in the development of novel compounds with promising therapeutic activities. Therefore, these compounds have been synthesized as target structures by many researchers and were evaluated for their biological activities. In this review, we report the structures of 1,3-oxazole with their corresponding biological activities as antipathogenic agent.

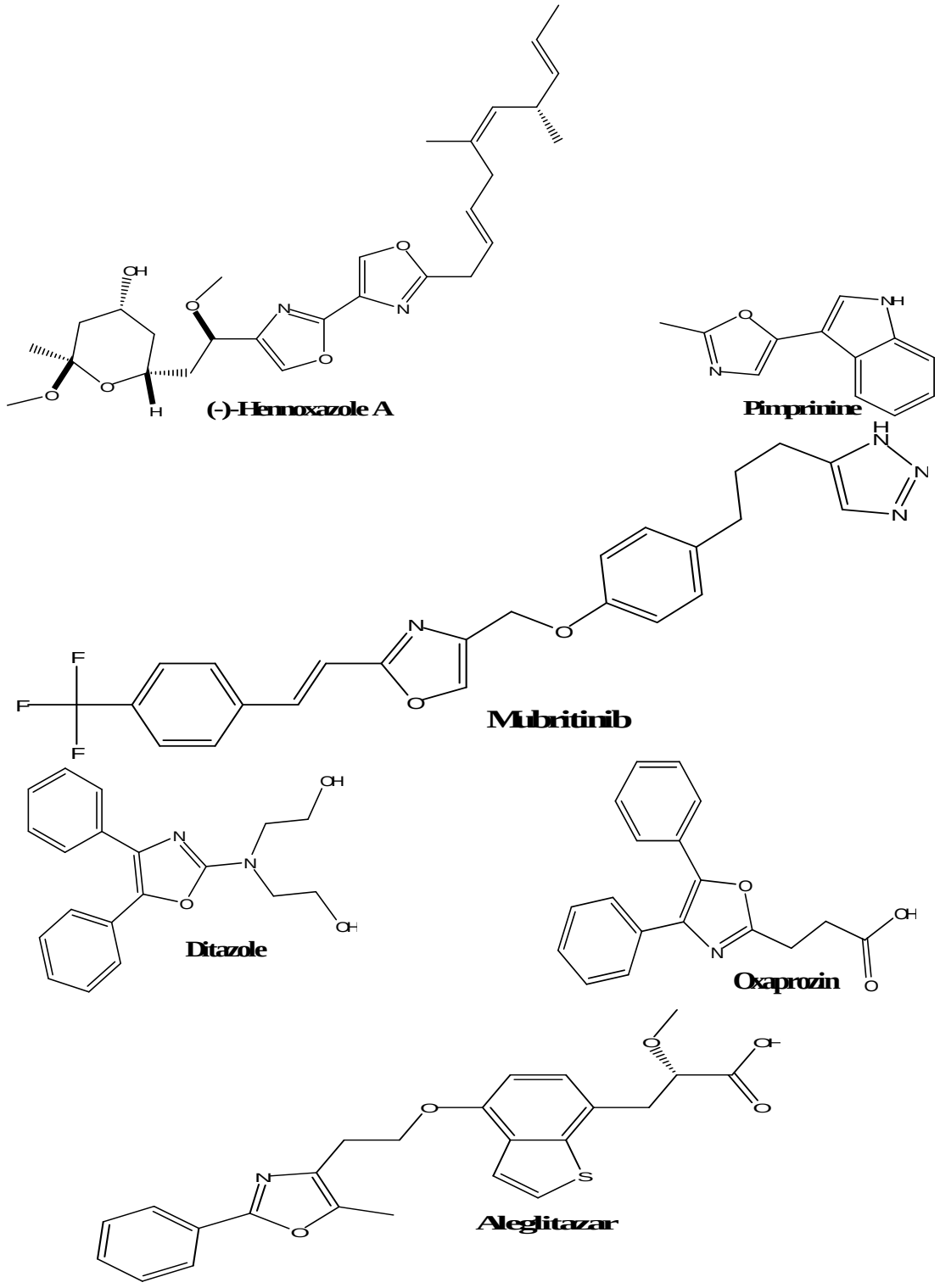
Key words: Oxazole, biological activity, Medicinal chemistry.

INTRODUCTION

Amongst the class of planar heterocycles, the oxazole parental skeleton is found (scheme 1). Oxazole is unique in its structure and the scaffold is a constituent of several natural products with a good biological activity such as (-)-hennoxazole A (antiviral) [1] and pimperinine (alkaloide) [2] (scheme 2). Also oxazole and its derivatives have been incorporated into a number of medicinally relevant compounds, both as exploratory and advanced drug candidates. Oxazole-containing compounds have been used as diabetes II treatment e.g. aleglitazar [3], platelets aggregation inhibitor e.g. ditazole [4], as part of tyrosine kinase inhibitor such as mubritinib [5], and as COX-2 inhibitors such as oxaprozin [6] (scheme 2).



Scheme.1. Oxazole Structure



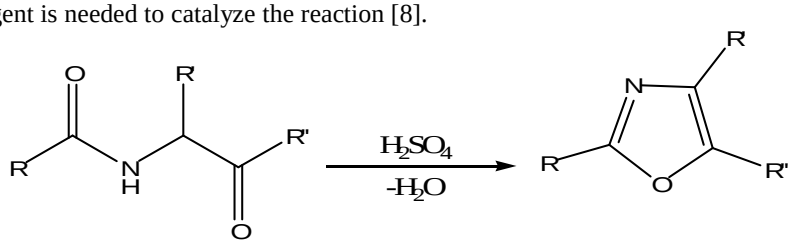
Scheme.2. Some of the oxazole derivatives found in nature and in some drugs

This review critically evaluates the pharmacological activity of the oxazole derivatives as antipathogenic agent that were reported recently in medicinal chemistry studies.

1. Preparation of oxazole derivatives

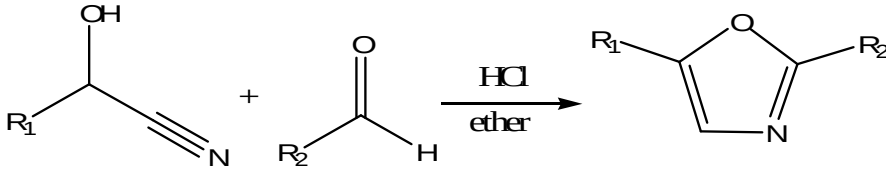
Oxazoles consist of a doubly unsaturated 5-membered ring containing one oxygen atom (position 1) separated by one carbon from a nitrogen at (position 3) of the ring (Scheme 1). The first recorded oxazole was synthesized in the 1800s and the chemistry of this heterocycle was expanded during World War II as part of the penicillin effort, which was thought to contain an oxazole core. The parent compound is a stable liquid at room temperature, with a boiling point of 69 ^{O}C, and was first prepared in 1947 [7].

There are many reported procedures for the synthesis of oxazole, among them, The Robinson–Gabriel synthesis in which a 2-acylamino-ketone reacts intramolecularly followed by a dehydration to give an oxazole. A cyclodehydrating agent is needed to catalyze the reaction [8].



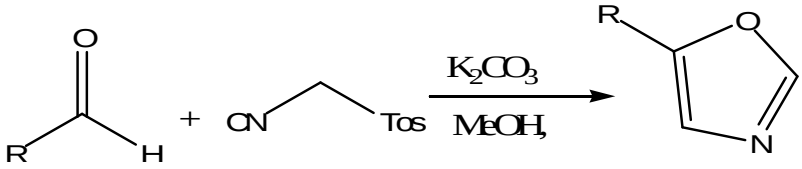
Scheme.3. The Robinson–Gabriel synthesis for oxazole

Fischer and coworker described an elegant synthesis of oxazole derivatives which was introduced in 1896 by reacting a cynohydrin and an aldehyde in the presence of anhydrous hydrochloric acid to give oxazole. [9]



Scheme.4. The Fischer and coworker synthesis for oxazole

Finally, there was the Van Leusen reaction which was first described in 1977 by Van Leusen and co-workers [10]. Ketones reacted with TosMIC (Toluenesulfonylmethyl isocyanide) leading to the formation of a nitrile. When aldehydes are employed, the Van Leusen reaction is particularly useful to form oxazoles .



Scheme.5. The Van Leusen synthesis for oxazole

3. Biological activity of Oxazoles

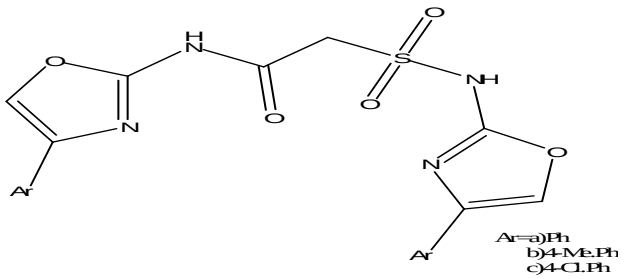
Oxazole derivatives are among the most useful heterocyclic compounds from both synthetic and medicinal chemistry aspects and we have highlighted here the most recent developments in synthesis of oxazole and their activity profile as antipathogenic

3.1. Antibacterial Activity

The dramatically rising prevalence of multi-drug resistant microbial infections in the past few decades remains an important and challenging task for medicinal chemists to develop new antimicrobial agents with novel chemical structures and oxazoles are important component in antibacterial drug discovery.

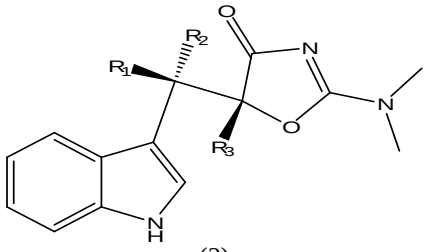
Chokkappagari et al. synthesized a new class of amido sulfonamido methane linked bisoxazoles, bisthiazoles, and bisimidazoles in simple and versatile synthetic methodologies. The lead compounds were assayed for antimicrobial activity [11].

It is noteworthy that the tested compounds containing oxazole in their structure displayed comparable antibacterial activity towards gram-negative bacteria and gram-positive bacteria when compared to references (1). Oxazole containing compound may become a promising class of antibacterial agents.



(1)

Analogues of the aminoacyl tRNA synthetase inhibitor, indolmycin, have been synthesized by Witty et al.. It has been found that antibacterial and enzyme inhibitory potency is related to steric properties and conformational preferences for these derivatives. It was observed from the inhibitory results that the better inhibitors were chromatographically the less polar isomers, and possessed the relative stereochemistry of indolmycin [12].

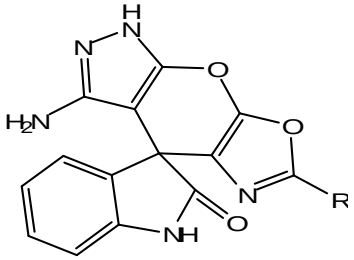


(2)

Abdel-Rahman et al. synthesized several new spiro indoline-based heterocycles by prior preparation of the 4-(20-oxo-indol-30-ylidene)-oxazol-5-one derivatives and subsequent reaction of the produced indol-3-ylidene based heterocycles with activated nitrile reagents [13].

The obtained products were allowed to react with hydrazine hydrate in alcoholic basic to give the target compounds. The antibacterial as well as antifungal activities of a solution of the synthesized compounds in dimethyl formamide (DMF) were tested and evaluated against some gram positive (*Bacillus subtilis* and *Bacillus megatherium*), gram negative (*Escherichia coli*) and fungi (*Aspergillus niger* and *Aspergillus oryzae*) and compared with respect to some reference antibiotics.

The biological results revealed that while most of the prepared spiro 3H-indole-3,40-pyrano(30,20-d) oxazole derivatives showed comparable activity, the spiro 3H-indole-3,40-pyrazolo(30,40-b)pyrano(30,20-d)oxazole derivatives (3, 4, and 5) revealed very high activity with respect to the used references . On the other hand, nearly all of the prepared compounds exhibited an interesting high antifungal activity reaching to 90 mm zone of inhibition against the reference chemotherapeutics 22 mm.



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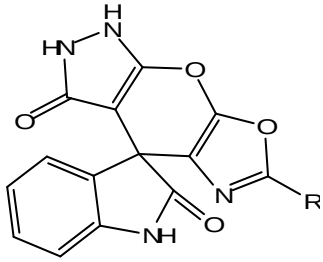

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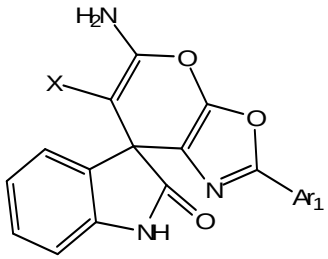
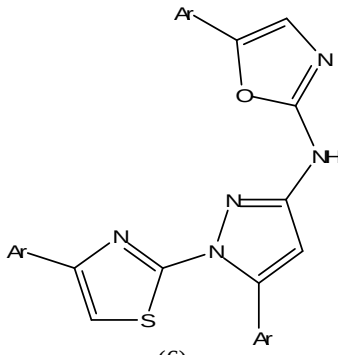


(5)

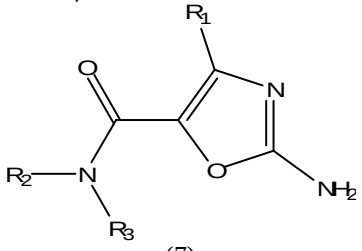
A series of amine linked bis- and tris-heterocycles were prepared from heteroaryl cinnamamides and tested for antimicrobial activity by Prakash et al. [14]. Among the screened derivatives the compounds that contained oxazole (6) exhibited excellent antibacterial activity showing zone of inhibition of that 21 mm at 100mg/well against *staphylococcus aureas* (reference -chloramphenicol- 31 mm) and 22 mm at 100mg/well against *klebsiella pneumoniae* (reference- chloramphenicol- 42 mm) and as expected the oxazole derivatives displayed good activity as antifungal.



(6)

By combining classical screening and ligand-based pharmacophore modeling approaches in two drug-design stages, Skedelj et al. have successfully identified and experimentally characterized the first inhibitors of the bacterial enzyme D-aspartate ligase from *Enterococcus faecium* [15].

A series of aminooxazoles and thio-oxazoles were assayed for *in-vitro* inhibitory activity toward recombinant Aslfm using a pyruvate kinase lactate dehydrogenase enzymatic assay. It has been found that inhibitors showed low micromolar activity, and set of inhibitors derived from structure (7) discovered will provide novel lead compounds in antibacterial drug design efforts to combat *E. faecium* infections.

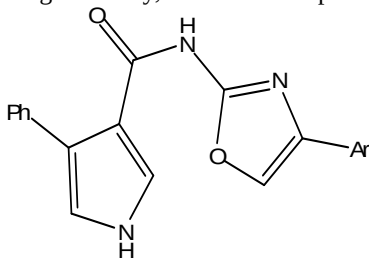


(7)

A new class of amido linked bis heterocycles, pyrrolyl/pyrazolyl-oxazoles, thiazoles and imidazoles were prepared by cycloaddition to yield different derivatives and screened for antimicrobial activity by Padmavathi et al. [16].

From the obtained results, it has been revealed that of that Gram-negative bacteria were more susceptible towards the tested compounds containing oxazole (8, and 9) more than Gram positive ones.

Regarding antifungal activity, the tested compounds inhibited the spore germination against tested fungi.



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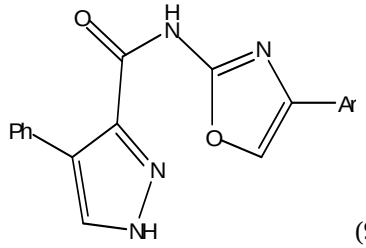
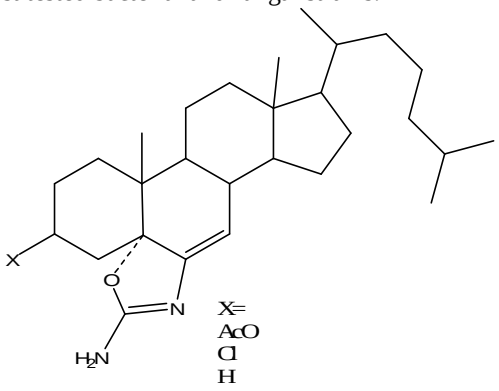


(9)

Shamsuzzaman et al. report a convenient one-pot synthesis of 20-amino-5a-cholest-6-eno [6, 5-d] oxazole derivatives [17]. The synthesis involves the reaction of cholestan-6-ones (1–3) with urea and iodine. All the

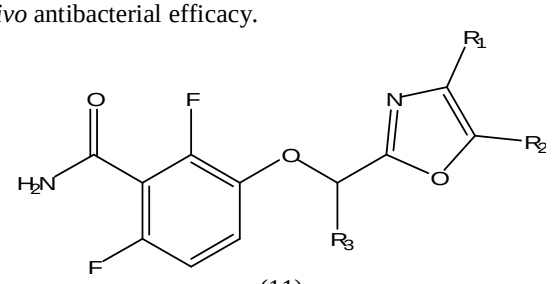
synthesized compounds (10) were tested for their inhibitory action against both types of the bacteria (Gram-positive and Gram-negative) and five strains of fungus and then the minimum inhibitory concentration (MIC) of all the synthesized compounds were determined. The biological result showed that all of tested compound had antibacterial as well as antifungal activity against tested bacterial and fungal strains.



(10)

Stokes et al. designed, synthesized and made structure–activity relationships of a series of oxazole–benzamide inhibitors (11) of the essential bacterial cell division protein FtsZ ((Filamenting temperature sensitive mutant Z) [18].

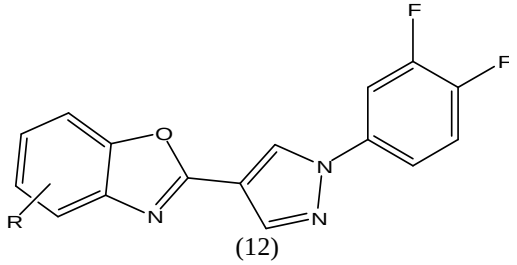
The synthesized Compounds had potent anti-staphylococcal activity and inhibited the cytokinesis of the clinically-significant bacterial pathogen *Staphylococcus aureus*. This study has provided small-molecule inhibitors of FtsZ with enhanced *in vitro* and *in vivo* antibacterial efficacy.



(11)

A series of fluorine containing 4-(substituted-2-hydroxybenzoyl) pyrazoles and pyrazolyl benzo[d]oxazoles were synthesized and evaluated for their antibacterial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Bacillus subtilis* and antifungal activity against *Candida albicans* by Gadakh et al.[19].

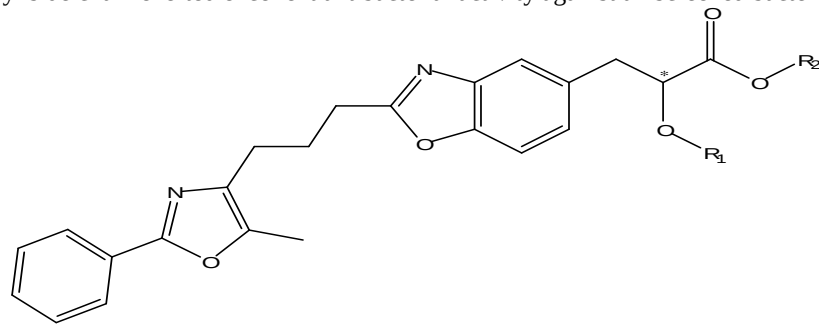
Among the screened compounds, The 4-substituted-2- [1-(3,4-difluorophenyl) -1H-pyrazo-4-yl]-benzoxazole derivatives (12) exhibited promising activities against tested bacterial strains especially against *Pseudomonas aeruginosa* reaching to (100 μg/ml) for some derivatives comparable to ampicillin, but weaker than chloramphenicol (50μgml). None of the compounds showed promising antifungal activity.



(12)

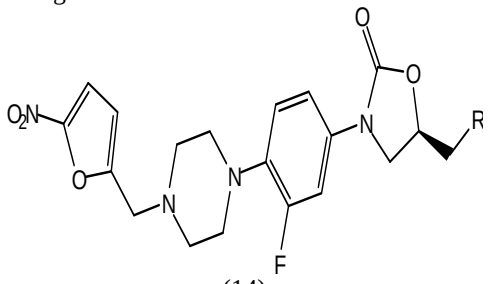
Zhang et al. prepared different Chiral 2-(substituted-hydroxyl)-3-(benzo[d]oxazol-5-yl) propanoic acid derivatives (13) and their antibacterial activities were evaluated against Gram-negative and Gram-positive bacteria. Antifungal activity was tested also [20].

In general, the derivatives showed *in vitro* activities against all screened Gram-negative and Gram positive bacteria, but poor MIC values for fungus *Candida albicans*. Interestingly the results showed that the (S)-configuration substituted phenoxyl side chain exerted excellent antibacterial activity against all screened bacteria.



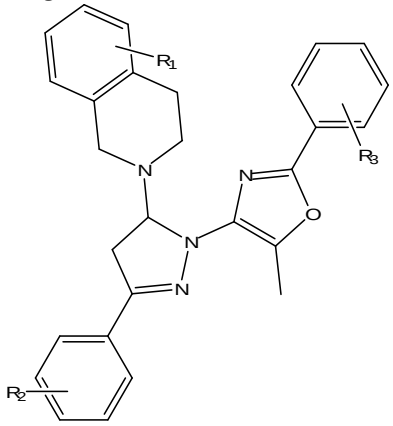
(13)

Das et al. synthesized 5 derivatives of Ranbezolid, a novel oxazolidinone, with different substitutions (14) and tested them against a number of sensitive and resistant bacteria [21]. The synthesized compound showed promising results as antibacterial agent and further investigation is needed.



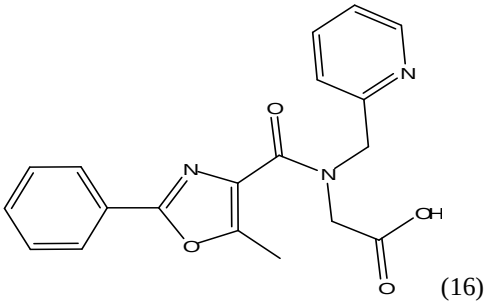
(14)

A series of new 2-(1-(2-(substituted-phenyl)-5-methyloxazol-4-yl)-3-(2-substitued-phenyl)-4,5-dihydro-1H-pyrazol-5-yl)-7-substitued-1,2,3,4-tetrahydroisoquinoline derivatives (15) were synthesized by Lu et al. [22]. It has been found that some of the screened derivatives can strongly inhibit *Staphylococcus aureus* DNA gyrase and *Bacillus subtilis* DNA gyrase at very low concentration. On the basis of the biological results, structure–activity relationships were discussed to provide the best knowledge for these derivatives.



(15)

High-throughput screening on HldE-kinase (an enzyme involved in the biosynthesis of heptose) activity of *E. coli* led to the discovery of inhibitors (16) and (17) with excellent IC_{50}. On this basis, Desroy et al. synthesized a series related to (16) and (17) and they found that these derivatives had the potential for being selective of HldE [23]. Furthermore, a study of the structure–activity relationship of this series were conducted and resulted in a considerable improvement of potency for the derivatives.



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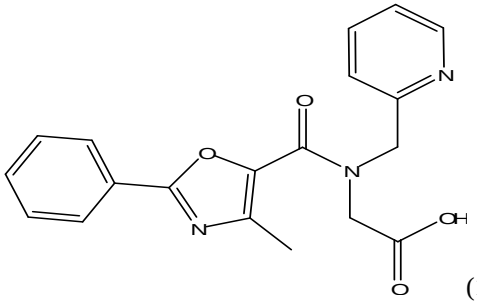
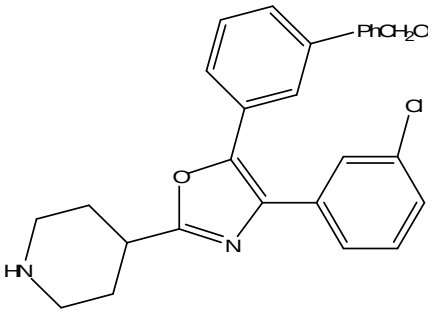


(17)

Tanitame et al. have described the synthesis and SARs of new pyrazole, oxazole and imidazole derivatives that have been derived from 1-(3-chlorophenyl)-5-(4-phenoxyphenyl)-3-(4-piperidyl)pyrazole, that has previously shown improved DNA gyrase inhibition and target-related antibacterial activity [24]. Among all the oxazole analogues, compound (18) showed comparatively strong antibacterial activity. It possessed potent antibacterial activity against not only susceptible strains, but also against multidrug resistant strains and against clinically isolated quinolone-resistant Gram-positive bacteria than sparfloxacin.

Though the inhibitory activity of sparfloxacin against DNA gyrase was more than 20- fold that against topoisomerase IV, the pyrazole, oxazole and imidazole derivatives synthesized in this study showed almost the same inhibitory activity against both enzymes.

These results suggest that the pyrazole, oxazole and imidazole derivatives would not be easily resisted by bacteria and they may become promising class as antibacterial.

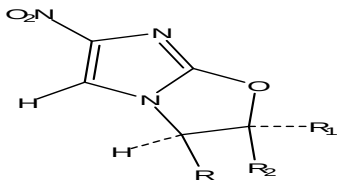


(18)

3.2. Anti tuberculosis Activity

Tuberculosis is chronic communicable infectious disease caused by *Mycobacterium tuberculosis*, spread from one person to another through air. Tuberculosis most commonly affecting lungs and it is curable and preventable.

Nagarajan et al. reported the synthesis of 2,3-dihydro-6-nitroimidazo [2,1-b] oxazoles derivatives [25], among the synthesized derivatives, two compounds (19,20) exhibited excellent antimycobacterial activity *in vivo* and *in vitro* that are comparable for some standard antituber cular drugs such as isoniazid and ethambutol.



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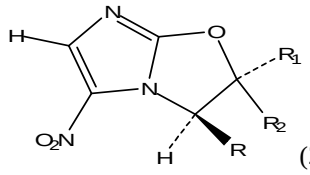
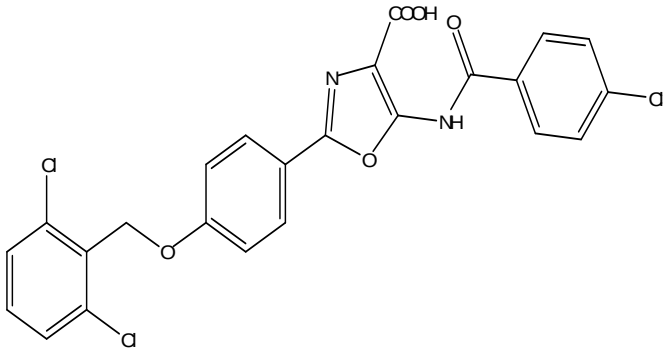


(20)

Lu et al. synthesized a series of 4-(2, 6-dichlorobenzyloxy)phenyl thiazole, oxazole and imidazole derivatives (21, and 22) and the derivatives were evaluated for their anti-tubercular activity [26]. The derivatives were screened for *in vitro* anti-tubercular activities and promising results were obtained.



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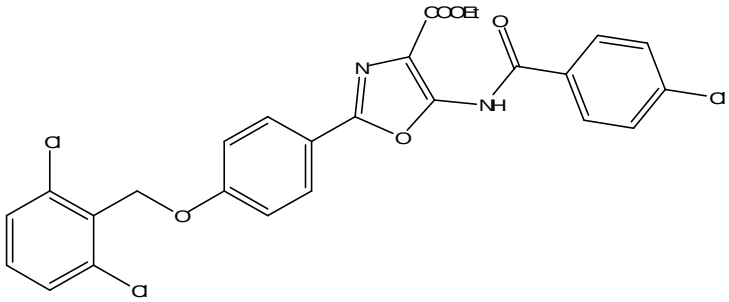
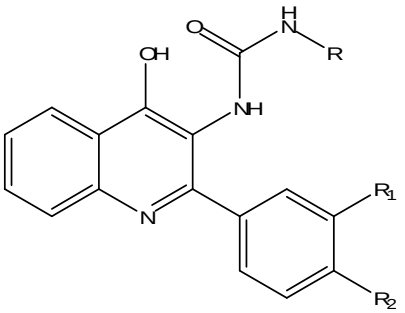


(22)

A class of fused oxazoloquinoline derivatives was synthesized by Eswaran et al. and were evaluated for their *in vitro* antibacterial against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and antituberculosis activity against *Mycobacterium tuberculosis* H37Rv (*ATCC 27294*) [27]. Preliminary results indicated that most of the derivatives such as (23, and 24) demonstrated very good antibacterial and antituberculosis activities which are comparable with the first line drugs.

The structure–activity relationship (SAR) study reveals that with the introduction of 1,3-oxazole ring has tremendously increased the activity of the derived molecules.



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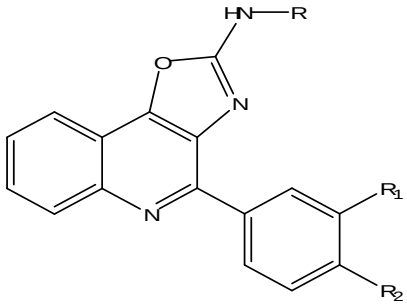
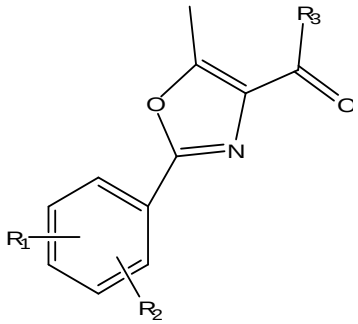


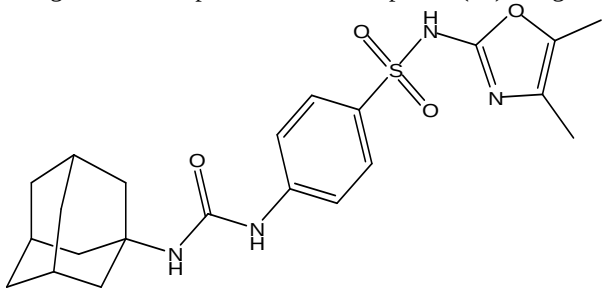
(24)

Moraski et al. reported elaboration of SAR as well as the syntheses and evaluation of a hundred oxazoline- and oxazole-containing compounds derived from an efficient three step process: 1) formation of β-hydroxy amides with serine or threonine; 2) cyclization to afford oxazolines; and 3) dehydration to give the corresponding oxazoles [28]. An impressive activity against *Mycobacterium tuberculosis*, with extremely low toxicity had been shown from synthesized compounds (25) and therefore high therapeutic indexes.



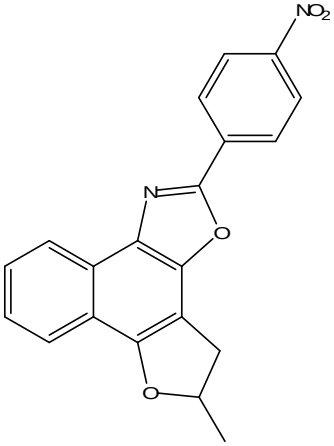
(25)

Recently, a new series of 1-adamantyl-3-heteroaryl ureas was designed and synthesized by North et al. [29], replacing the phenyl substituent of the original series with pyridines, pyrimidines, triazines, oxazoles, isoxazoles, oxadiazoles and pyrazoles. This study produced substituted adamantyl ureas with improved *in vitro* pharmacokinetic profiles, increased selectivity and good anti-TB potencies and compound (26) is a good example in this study.



(26)

Twenty-three naphthoimidazoles and six naphthoxazoles were synthesised and evaluated against susceptible and rifampicin- and isoniazid-resistant strains of *Mycobacterium tuberculosis* by Moura et al. [30]. Among all the compounds evaluated, fourteen presented MIC values in the range of 0.78 to 6.25 lg/mL against susceptible and resistant strains of *M. tuberculosis*. These substances (27, 28, and 29) are promising antimycobacterial prototypes.



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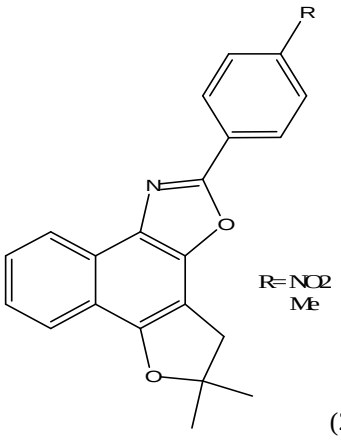

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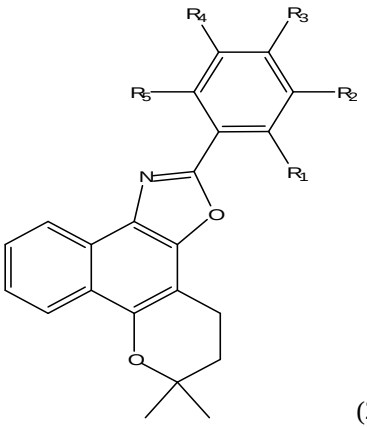


(29)

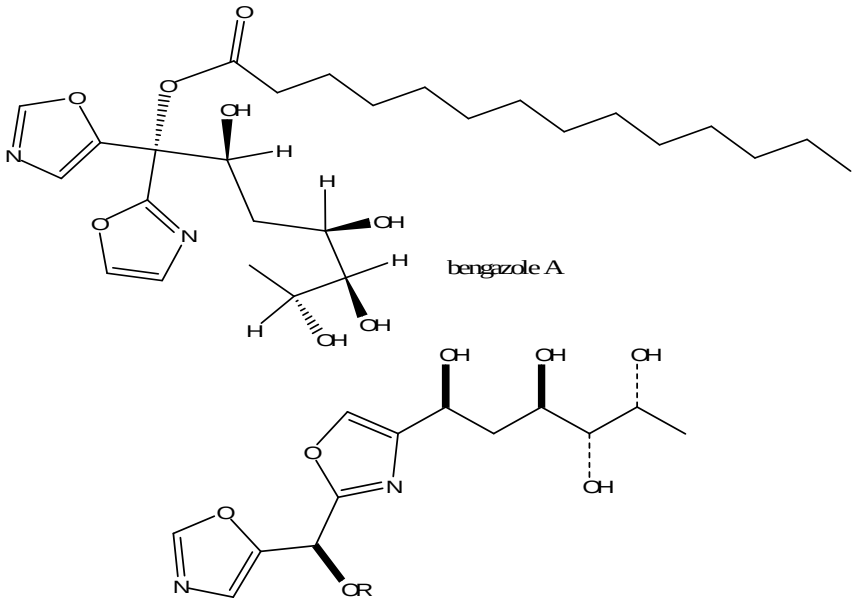
3.3. Antifungal Activity

Fungus are eukaryotic microorganisms which are more closely related to humans than bacteria at cellular level and can cause important number of human diseases.

Despite the recent introduction of new antifungal agents with promising activity, the incidence of invasive fungal infections has been increasing dramatically during the past two decades.

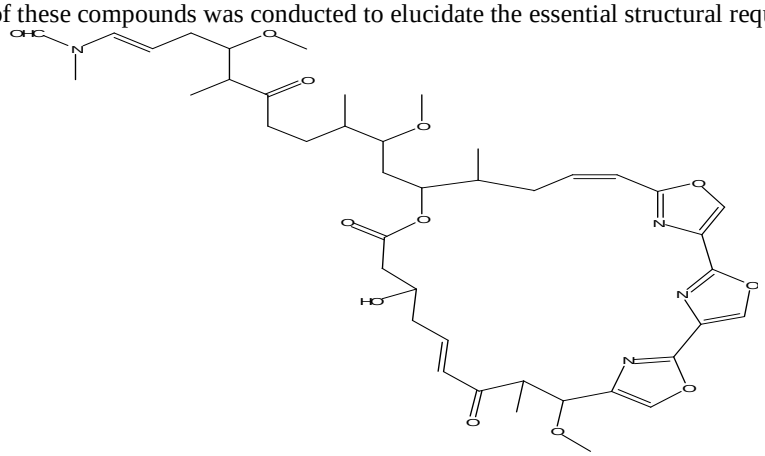
There is an emergent need to develop new antifungal drugs with novel chemical structures and novel mechanism of action.

Mulder et al. prepared Analogs of the potent antifungal agent, bengazole A, and evaluated them against *Candida spp*. using both microbroth dilution and disk diffusion assays [31]. Good activity was observed in some compounds analogs of bengazole A such as compound (30) that contained one or two 1,3-oxazole rings but none were more potent than bengazole A.



(30)

In 2011, Chung et al. reported a series of novel Oxazole-containing macrolides isolated from the marine sponge *Chondrosia corticata* and evaluated them for their actin depolymerizing activities by monitoring fluorescent intensity of pyrene F-actin [32]. These studies led to the identification of (19 Z)-halichondramide (31) as a new actin depolymerizing agent. The actin depolymerizing activity by (19Z)-halichondramide (31) was four times more potent than that of halichondramide (32). Both compounds also have potent antifungal activity and preliminary structure–activity relationship of these compounds was conducted to elucidate the essential structural requirements.



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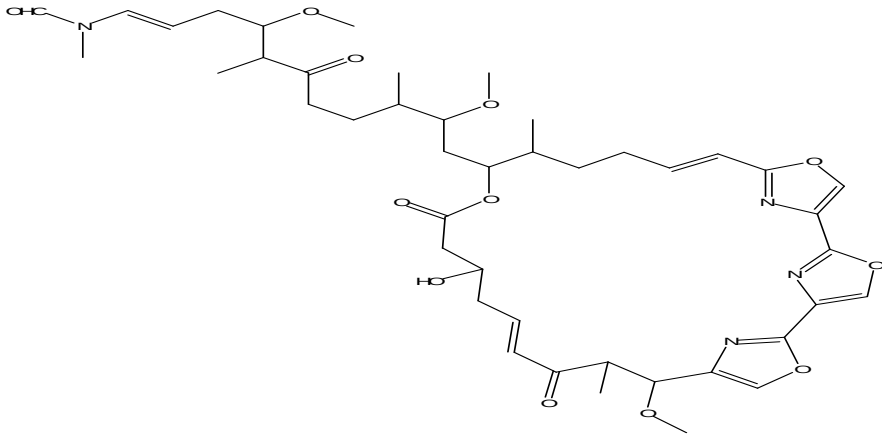
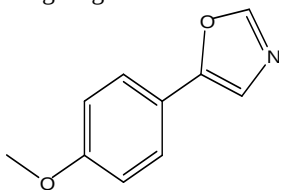


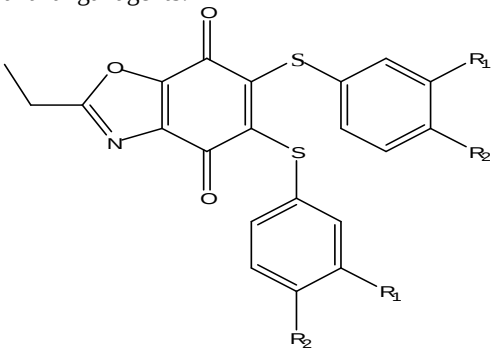
(32)

Yamamuro et al. reported the synthesis of nineteen 5-(4-Methoxyphenyl)-oxazole (MPO) derivatives and tested them as an inhibitor of hatch and growth of *Caenorhabditis elegans* [33]. The structure activity releationship study of the derivatives suggested that the whole structure of MPO (33) is essential for anti-*C. elegans* activity that has to be taken in consideration in the design of antifungal agent.



(33)

Benzo[d]oxazole-4,7-diones derivatives (34, 35, and 36) were synthesized by Ryu et al. and tested for *in vitro* antifungal activity [34]. Remarkable antifungal inhibition of some compounds (MIC 0.8 µg/ml) against *C.albicans* and *A. niger* had been obtained. The obtained biological results suggested that benzo[d]oxazole-4,7-diones would be potent antifungal agents.



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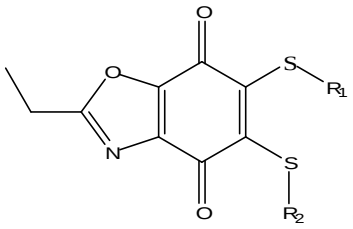

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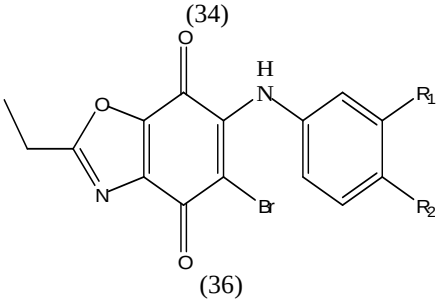
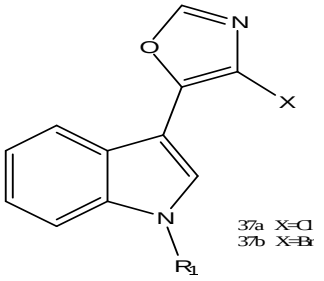


(36)

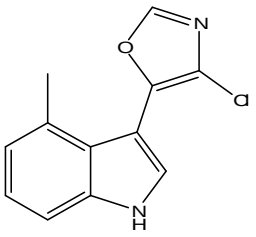
Zhang et al. synthesized a series of novel analogues of natural product pimprinine [35]. Bioassay conducted showed that several of the synthesized compounds exhibited fungicidal activity. Compounds (37a, b) in particular showed

activity against the four pathogens screened in artificial media; *Pythium dissimile*, *Alternaria solani*, *Botryotinia fuckeliana* and *Gibberella zeae.*



(35)

In 2015, Zhang et al. also synthesized a series of indole modified streptochlorin analogues [36]. They measured their activities against seven phytopathogenic fungi. Among the screened compound there were seven compounds (38, 39, 40, 41, 42, 43 and 44) were identified as the most promising candidates for further study.



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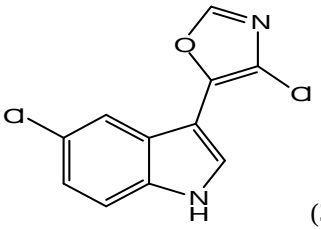

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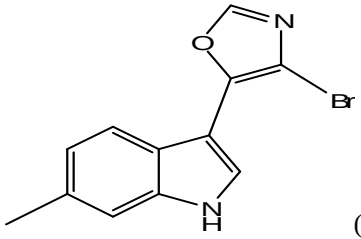

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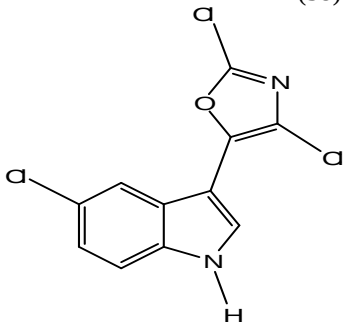

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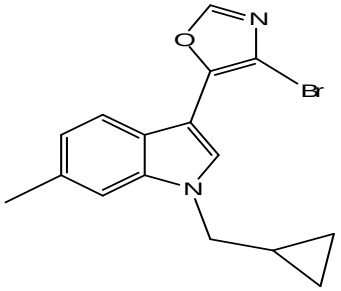

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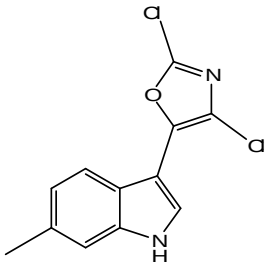

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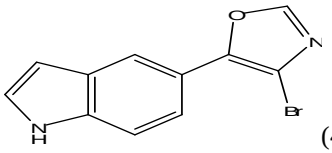

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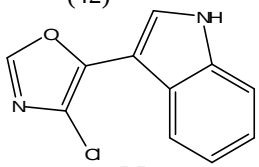


Streptochlorine

3.4. Antimalarial Activity

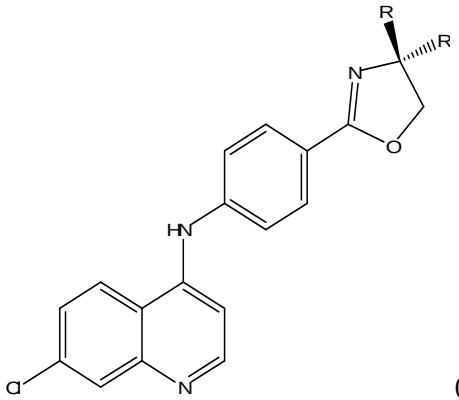
Today there are huge effort to find effective treatment for malaria which is one of the most serious, complex and refractory health problem facing humanity this century.

Human malaria caused by four species of protozoan parasites of the *plasmodium* genus and is transmitted from person to another by an insect vector, the female anopheline mosquito.

There are optimistic perspectives on the continuing investigation for the treatment of malaria, and they will certainly lead the scientific community to find solution to this disease along with improvements in the existing synthetic and semi synthetic drugs.

In 2011, Gordey et al. carried out the synthesis (Palladium -mediated coupling strategy) of a short series of quinoline–oxazole hybrid compounds (45, 46) and found that these compounds were moderately active against *Plasmodium falciparum in vitro*, with activities in the sub-micromolar range, and display acceptable cytotoxicity to

mononuclear leukocytes. Chemical modification strategies, with the intention to increase the biological potency of this new class of anti-malarial agents, had been discussed in this search [37].



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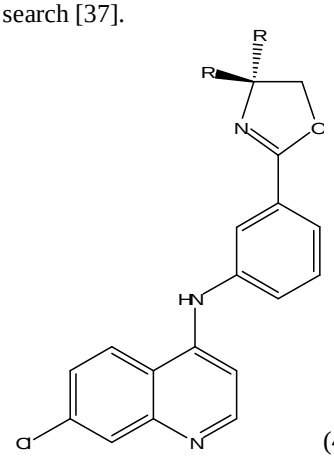
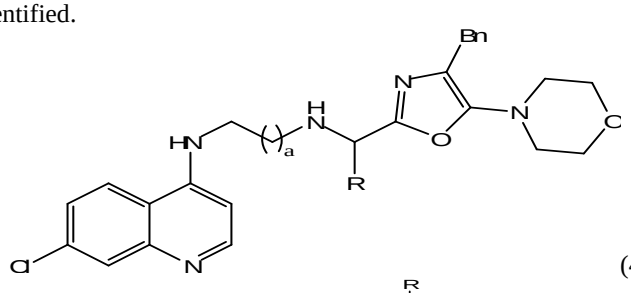


(46)

The synthesis and antimalarial activity of a novel series of first generation 4-aminoquinoline-containing 2,4,5-trisubstituted aminoxazoles against two strains of the *Plasmodium falciparum* parasite *in vitro* is described by Musonda et al. [38]. A number of compounds (derivatives of 47, and 48) significantly more potent than the standard drug chloroquine were identified.



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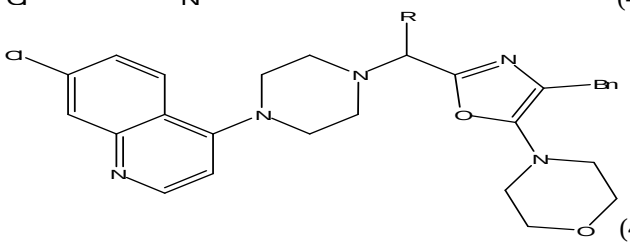
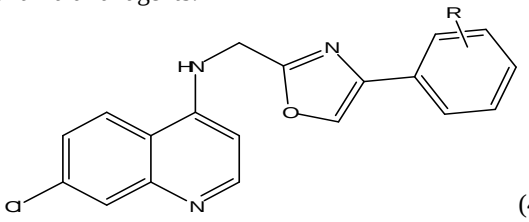


(48)

A set of 7-chloro-N-(heteroaryl)-methyl-4-aminoquinoline and 7-chloro-N-(heteroaryl)-4-aminoquinoline was synthesized and tested *in vitro* against 2 strains of *Plasmodium falciparum* by Casagrande et al. [39]. All compounds exhibited from moderate to high antiplasmodial activities. The activity was strongly influenced both by the presence of a methylenic group, as a spacer between the 4-aminoquinoline and the heterocyclic ring, and by the presence of a basic head. The molecules that contained oxazole as heteroatom inhibited the growth of both strains of *P. falciparum* in good micromolar concentration and were not toxic against human endothelial cells (49). These results confirm that the presence of a heteroaryl moiety in the side chain of 7-chloro-4-aminoquinoline is useful for the design and development of new powerful antimalarial agents.



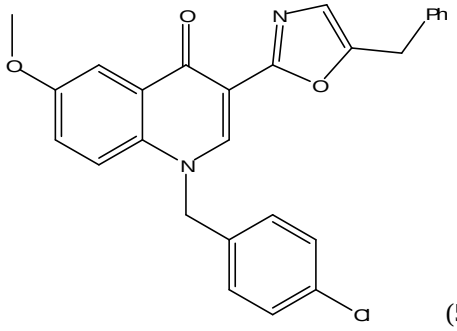
(49)

3.5. Antiviral Activity

Viruses are parasites that can cause serious infections for human such as HIV disease. The number of existing drug as antiviral is not enough and development of antiviral drugs is still in requirement, because of the viral resistance.

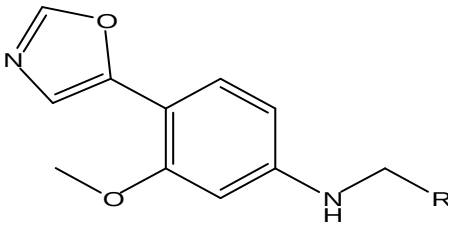
The discovery and optimization of a novel class of quinolone small-molecules that inhibit NS5B polymerase, nonstructural protein 5B, a key enzyme of the hepatitis C virus viral life-cycle, is described by Kumar et al. [40].

The research led to the replacement of a hydrolytically labile ester functionality with bio-isosteric heterocycles such as oxazole and oxazdiazoles. Compound (50) was potent with IC_{50} (1.8 µM).



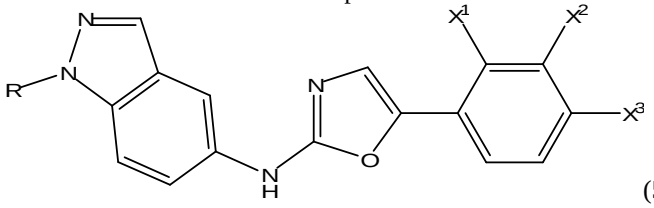
(50)

A series of novel (5-oxazolyl)phenyl amine derivatives were synthesized and their antiviral activities against the hepatitis C virus (HCV) and the coxsackie virus B3 (CVB3) and B6 (CVB6) were evaluated *in vitro* by Zhong et al. [41]. Bioassays showed that the synthesized compounds exhibited potent antiviral activity against HCV and most synthesized compounds had low cytotoxicity, compared to telaprevir. The derivatives of compound (51) showed strong activity against the hepatitis C virus at low concentrations (IC_{50} < 2.0 µM).



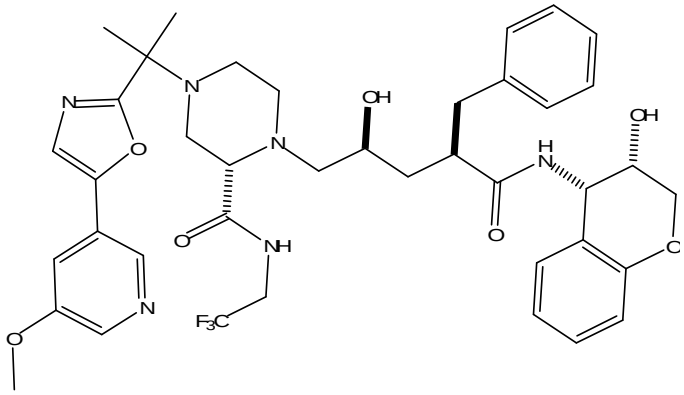
(51)

New oxazole containing inhibitors of HIV-1 (52) have been discovered through cell-based screening of an in-house library and subsequent scaffold modification by Kim et al. [42]. The SAR study focusing on substituent on the 5-aryl moiety of the oxazole core led to the identification of potent inhibitors.



(52)

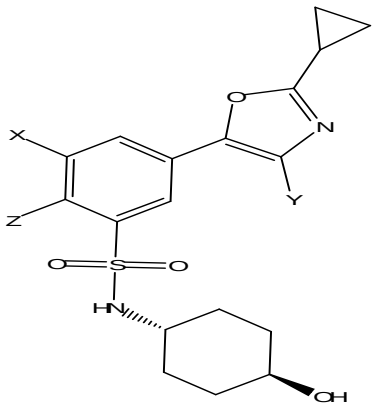
Replacement of the pyridylmethyl moiety in indinavir with a pyridyl oxazole yielded HIV-1 protease inhibitors (PI) with greatly improved potency against PI-resistant HIV-1 strains had been tested by Zhang et al. [43]. A meta-methoxy group on the pyridyl ring and a gem-dimethyl methyl linkage afforded compound (53) with notable *in vitro* antiviral activity against HIV-1 viral strains with reduced susceptibility to the clinically available PIs. Compound (53) also demonstrated favorable *in vivo* pharmacokinetics in animal models.



(53)

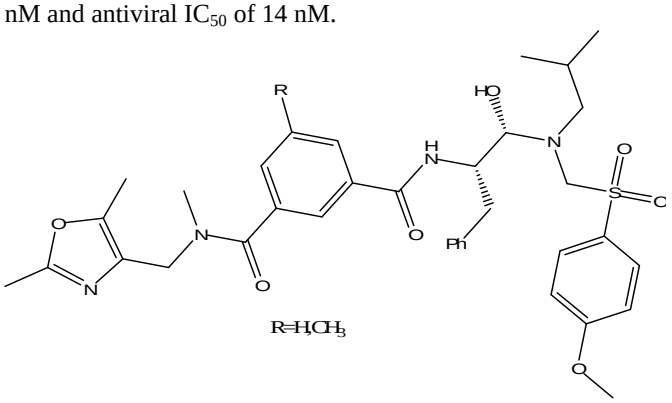
Synthesis and SAR of 2-alkyloxazoles (54) as class III phosphatidylinositol-4-kinase beta (PI4KIIIb) inhibitors is described by Keaney et al. [44]. These compounds demonstrate that inhibition of PI4KIIIb leads to potent inhibition of HCV replication.

The 2-alkyloxazole series represents a new class of compounds that are highly potent and selective inhibitors of PI4KIIIb that targets cellular proteins as a potential route toward novel HCV therapies.



(54)

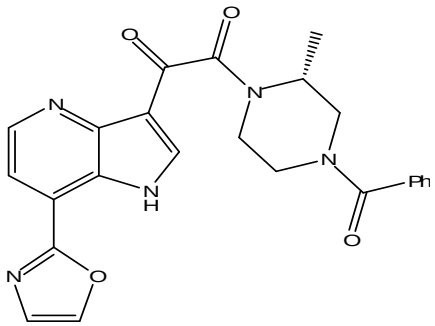
Ghosh et al. described the design, synthesis and biological evaluation of a series of novel HIV-1 protease inhibitors bearing isophthalamide derivatives [45]. Their work was based on investigation a range of acyclic and heterocyclic amides. In particular, they examined substituted prolines and oxazoles which contain hydrogen bond donor and acceptor groups for specific interactions. These inhibitors displayed good to excellent HIV-1 protease inhibitory activity. Compound (55) containing isophthalamide dimethyloxazolylmethyl amide has shown an enzyme Ki (The inhibitor constant) of 0.17 nM and antiviral IC_{50} of 14 nM.



(55)

A series of novel and potent 4-azaindole core containing compounds was prepared and evaluated for potential utility as inhibitors of HIV-1 attachment and infection *in vitro* by Wang et al. [46].

Synthetic chemical approaches were successfully developed that allowed for the investigation of SAR around the key 7-position of 4-azaindole. Modifications at the 7-position of the 4-azaindole core modulated potency significantly and SAR showed that certain compounds with a 5-membered ring heteroaryl group at that position were the most potent (56, and 57).



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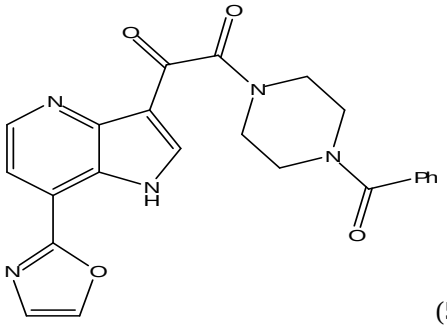

(57)

CONCLUSION

The oxazole heterocycle is often incorporated in medicinal chemistry studies, and this review reported the structures of oxazole derivatives with their corresponding biological activities as antipathogenic agents.

Acknowledgements
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