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MOST COMMON BENZOXAZOLE DERIVATIVES AS ANTIMICROBIAL AGENT (1990-2018)

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Abstract:

In this review, it was aimed to identify antimicrobial activity of newly synthesized benzoxazole derivatives which were synthesized and assayed for antibacterial and antifungal activity in previous study and showed a better antimicrobial effect that could be more effective against resistant pathogens. Benzoxazole derivatives have been extensively studied in the past few decades. The benzoxazole have shown significant antimicrobial activity against a wide variety of microorganisms like fungi, Gram +ve and Gram –ve bacteria. The review focuses out various important synthetic derivatives of benzoxazole which may in turn helpful to the information seekers to develop some novel derivatives of medicinal interest possessing benzoxazole moiety that could be better agents in term of efficacy and safety.

Key word: benzoxazole , benzoxazole derivatives , Antimicrobial Agent

Introduction

Bacterial infection is a major category of human disease, for which many antibacterial compounds were developed. The dramatically rising prevalence of multidrug-resistant microbial infection in the past few decades has become a serious health care problem. Under these circumstances, the development of novel class of antimicrobial agent is going on. Benzoxazole plays an important role in medicinal chemistry and exhibit wide range of biological activities. The main objective of the medicinal chemistry is to synthesize the compounds that show promising activity as therapeutic agents with lower toxicity.

Benzoxazole

Benzoxazole is an aromatic organic compound having benzene fused oxazole ring structure as shown in **Fig.1**(1).

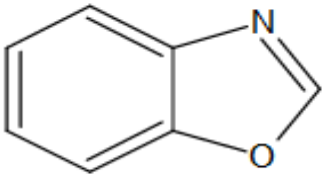
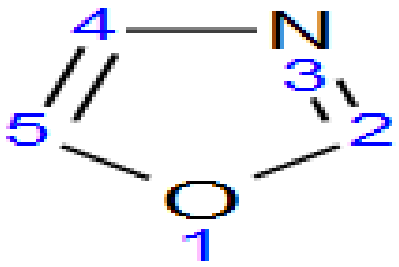


Fig.1: General Structure of Benzoxazole.

Benzoxazole finds use in research as a starting material for the synthesis of larger bioactive structures. Biologically active benzoxazole derivatives have been known for long time, they are the isosteres of cyclic nucleotides and easily interact with the biopolymers of the organisms(2) .

History

Oxazole is considered to be derived from furan by the replacement of –CH= (methane group) from the position -3 by the azomethine nitrogen (-N=). Oxazole ring system is numbered as follows.



The chemistry of oxazoles began in 1876 with the synthesis of 2-methyloxazole, although parent oxazole 5 was synthesized in 1947and 1962. The interest in the chemistry of oxazole was developed during the world war when the penicillin was consider to contains the oxazole ring system. But discovery of oxazoles as dienes in Diels-Alder reaction and in 1,3-dipolarcycloaddition reaction of mesotonic heterocycles gave impetus to the development of oxazoles chemistry. The fusion of benzene ring to the 4,5-positions of the oxazole ring results in benzoxazole and numbering as shown in **Fig.1** (3).

The heterocyclic ring comprises of very core of the active moiety or the pharmacophore. Several Benz-fused hetero, bicyclic ring systems as indole, benzoxazole, have been studied and found to be possessing interesting pharmacological activities (4).

A number of methods have been reported for the preparation of these heterocycles including the condensation of carboxylic acids, orthoesters, acid chlorides, nitriles amides, aldehydes and esters with o-substituted amino aromatics derivatives from orthoesters (3).

Reactions of benzoxazole

1. Nitration

The nitration of benzoxazole proceeds readily. In most cases nitration appears to take place preferentially in the 5 or 6 places. However the nitro group may also enter 4 or 7-position, especially if 5 or 6 positions are blocked as shown in **Fig.2** (3).

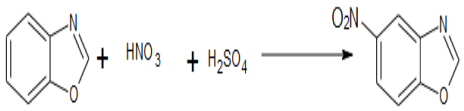


Fig.2: Nitration Reaction of benzoxazole.

2. Chloroacetylation

2-mercapto benzoxazole on chloroacetylation gave 2-chloroacetyl mercaptobenzoxazole **Fig.3.** (3).

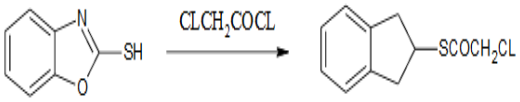


Fig.3: Chloroacetylation Reaction of Benzoxazole.

3-Alkylation

The reaction of sub. benzoxazole with butylcyclohexanol gave (2-butylcyclohexyloxy) benzoxazole **fig 4.**(3).

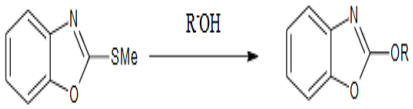


Fig.4: Alkylation Reaction of Benzoxazole.

Use of Benzoxazole

Recent observations suggest that substituted benzoxazoles and related heterocycles, possess potential activity with lower toxicities in the chemotherapeutic approach in man. Benzoxazole is used primarily in industry and research, and has no household use. Benzoxazole finds use in research as a starting material for the synthesis of larger, usually bioactive structures. Benzoxazoles can be considered as structural isosteres of

the naturally occurring nucleic bases adenine and guanine, which allow them to interact easily with polymers of living systems (5).

Benzoxazoles have been reported to show a broad spectrum of biological activities such as, antihistaminic (6), antifungal (7), Cyclooygenase inhibiting (8), antitumor (9), antiulcer (10), anti-convulsant (11), hypoglycemic (12), anti-inflammatory(13), cytotoxic activity(14), antimicrobial (15), DNA Topoisomerase Inhibitor (16), antibacterial (17), Herbicidal Activity (18), antiviral, analgesic (19), antitubercular (20), antioxidant (21) and anthelmintic activities (22), antiparasitics ,elastase inhibitors, protein kinase inhibitors, steroid sulfatase inhibitors.

Chemistry of Benzoxazole

Benzoxazole is an aromatic organic compound with a molecular formula C7H5NO, a benzene -fused oxazole ring structure, and an odor similar to pyridine (1).

General Properties

Table1: chemical characteristics of Benzoxazole

IUPAC name	1-Oxa-3-aza-1H-indene
Molecular formula	C_7H_5NO
Molar mass	119.12 g/mol
Solubility in water	Insoluble
Physical state	white to light yellow solid
Melting Point	27-30^{o} C

Structure Activity Relationship (SAR)

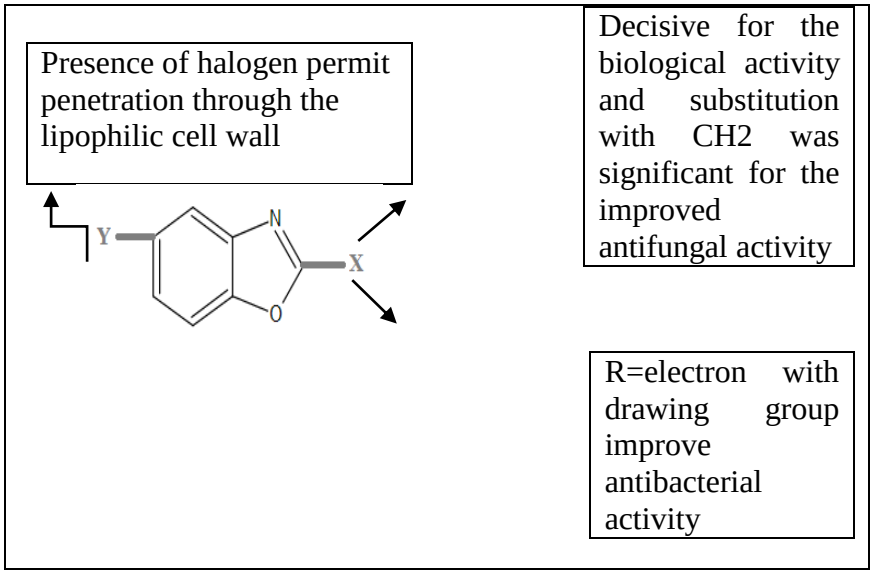


Fig.5: Structure Activity Relationship of Benzoxazole.

SAR of benzoxazole been studied and found that **position 2(X)** decisive for the biological activity and **position 5 (Y)** prevailing the intensity of activity.

The substitution at **position X** with the **CH2** group was significant for the improved antifungal activity and hydrophobic properties of the substituents at **position X** are indicative for the antifungal activity (4).Presence of **halogen at position 5 (Y)** of benzoxazole ring will permit these compounds penetrate through the lipophilic cell wall (23).

The Substitution of **R at position 2** at benzoxazole ring with electron withdrawing group favourable for the antibacterial activity (24). **Hydrophobicity** which is important for the penetration and distribution of benzoxazole derivatives (25).

2,5-disubstituted benzoxazoles have potent antimicrobial activities against some Gram-positive, Gram-negative bacteria and the yeast. Candida albicans, providing a wide variety of in-vitro antimicrobial effects, especially indicating significant activity against the enterobacter Pseudomonas aeruginosa.

These examples highlight the level of interest in new synthetic approaches to benzoxazole derivatives and have prompted researches around the globe to synthesize and explore the wide applicability of this important pharmacophoric scaffold (26).

Benzoxazole Derivatives

The design of new compounds to deal with resistant bacteria and fungi has become one of the most important areas of antibacterial and antifungal research today. The benzoxazoles are a large chemical family used as antimicrobial agents against a wide spectrum of microorganisms. The high therapeutic activity of the related drugs have encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents. The incorporation of the benzoxazole nucleus is an important synthetic strategy in drug discovery. This class of molecules have broaden the scope in remedying various dispositions in clinical medicine. This heterocyclic system has different activities as it can act as bacteriostatic or bactericid, as well as fungicide (27).

In the pharmaceutical field, new drugs are continuously discovered by molecular modification of compound. Molecular modification can possibly result in augmenting the activity. Molecular modification involves combination of separate group having similar activity in one compound by eliminating, substituting or adding new moiety to compound. Molecular modification is a productive source of new drug; therefore

the need to synthesize new molecules as potential medicinal agents is more relevant today. Among medicinal agents, there is growing interest in the development of newer, effective antifungal and antimicrobial agents. Among the variety of compounds studied, benzoxazole derivatives form an important class (3).

Turker L.et al,1990;(28) have been studied structure activity relationship of 5-substituted-phenyl-benzoxazole derivatives **Fig.6** exhibited that benzoxazole ring moiety is the most important part in the molecule for the interaction with the receptor site.

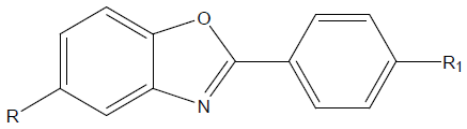


Fig.6: 5-substituted-phenyl-benzoxazole derivatives.

Esin Sener et al., 1994; (29)have been synthesized5-substituted-2-(3 pyridyl)benzoxazoles**Fig.7**, Antimicrobial activities of derivatives for some Gram-positive bacteria and Gram-negative bacteria and the yeast *Candida albicans* was performed and the compounds indicated significant activity against the screened microorganisms.

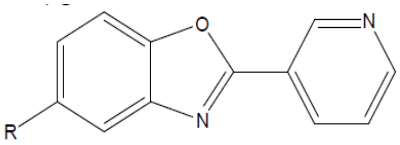


Fig.7:5-substituted-2-(3 pyridyl)benzoxazoles.

Ilkay Oren et al.,1997;(30) have been synthesized 5(or 6- methyl-2-substituted) benzoxazoles **Fig. 8,** the synthesized compounds has been tested for antimicrobial activity and indicated that the compounds are able to inhibit growth of a number of microorganisms. The synthesized compounds had a wide range of antibacterial activity against the tested microorganisms.

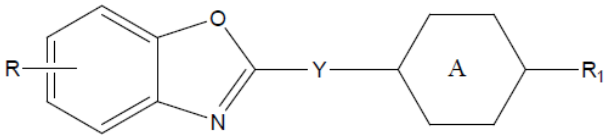


Fig.8:5(or 6-methyl-2-substituted)benzoxazoles.

Ismail Yalcin et al., 1998;(31) have been synthesized 5- or 6-methyl-2-(2,4-disubstituted phenyl) benzoxazoles **Fig.9** , and tested for their antimicrobial activities. The results indicated that the synthesized compounds possess a broad spectrum of antibacterial activity against the tested microorganisms.

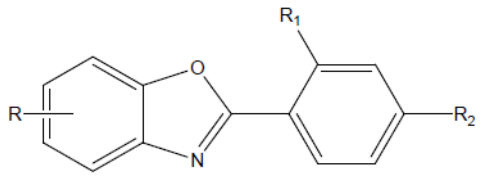


Fig.9:5- or 6-methyl-2-(2,4-disubstituted phenyl) benzoxazoles.

Esin Aki Sener et al., 2000; (32)have been synthesized 5-phenylacetamidosubstituted-2-phenylbenzoxazole derivatives **Fig.10** antimicrobial activities of these derivatives exhibited that the synthesized compounds possessed a broad spectrum of activity against the tested microorganisms.

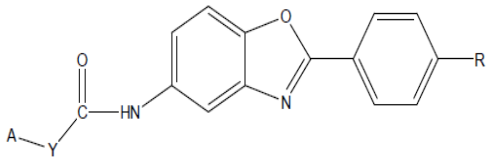


Fig.10:-5-phenylacetamidosubstituted-2- phenylbenzoxazole derivatives.

Arpaci O.T., 2001;(33) has been synthesized of some 5- or 6- methyl-2-substituted benzoxazoles/ benzimida zoles **Fig.11** and have been screened for the antifungal activity. The resulting QSAR exhibited that substitution at position Y with the CH2 group was significant for the improved antifungal activity and hydrophobic properties of the substituents at position R2 are indicative for the antifungal activity against *C. Albicans.*

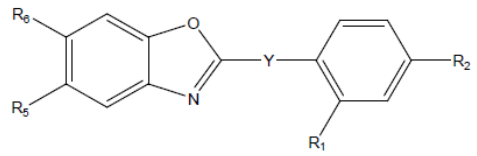


Fig.11: 5- or 6- methyl-2-substituted benzoxazoles/ benzimidazoles.

OzlemTemiz-Arpaci et al., 2002;(34) have been synthesized2-[*p*-substituted phenyl]benzoxazol-5-yl-arylcarboxy amides derivatives **Fig.12** Antimicrobial activities of the compounds have been investigated against different Gram positive and Gram-negative bacteria and the yeast *C. Albicans* in comparison with standard drugs. The results exhibited that the synthesized compounds possess a broad spectrum of activity against the tested microorganisms.

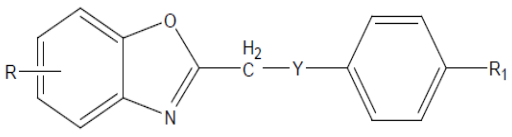


Fig.12:2-[p-substituted phenyl] benzoxazol-5ylarylcarboxyamides derivatives.

Oren I.Y.,et al, 2004;(35) have been synthesized new antimicrobial active N-(2-hydroxy-4-nitrophenyl)-p-substituted benzamides**Fig.13** and phenylacetamide analogues and Their antimicrobial activities have been tested against various Gram-positive and Gram-negative bacterias & the fungus *Candida albicans*, Most of the compounds exhibited antifungal activity against *C. albicans*. On the other hand, the antimicrobial activity of these derivatives have been investigated. The compounds significantly possessed better antimicrobial activity than its heterocyclic derivative, 2-(p-*t*-butylphenyl)-5- nitrobenzoxazole derivatives, against *Staphylococcus aureus*, *Streptococcus faecalis, Klebsiella pneumonia*, and *Escherichia coli*.

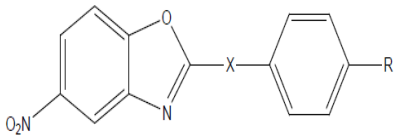


Fig.13: N-(2-hydroxy-4-nitrophenyl)-p-substituted benzamides.

P. Kohli et al.,2007;(36) have been synthesized [(5-Benzylidene)-2-aryl-4-oxo-1,3-thiazolidinhydra zinoacetyl]-mercaptobenzoxazole **Fig.14,** It shows good antimicrobial activity against bacterial strains.

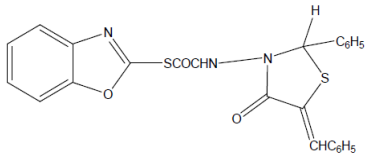


Fig.14:[(5-Benzylidene)-2-aryl-4-oxo-1,3- thiazolidin hydrazinoacetyl] mercapto benzoxazole.

Nagranjan A.S., et al, 2009;(37) has been synthesized novel benzoxazole substituted thiazolidinone derivatives **Fig.15**. The synthesized compounds have been tested for antibacterial activity. The synthetic compounds efficiently inhibited the growth of certain bacterial strains.

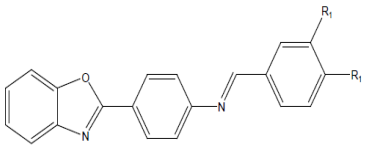


Fig.15: benzoxazole substituted thiazolidinone derivatives.

Ilkay Yildiz et al.,2009;(38) have been synthesized 5(or 6)-nitro/amino-2-(substituted phenyl/ benzyl)benzoxazole derivatives **Fig.16,** antibacterial and antifungal activities have been tested against *Staphylococcus aureus, Bacillus subtilis, Klebsiella pneumoniae, Pseudomonas aeruginosa, Escherichia coli, Candida albicans* ,the results indicated that the synthesized compounds possessed a broad spectrum of activity against the tested microorganisms .

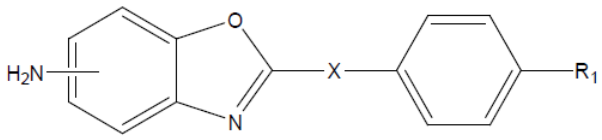


Fig.16: 5 or 6-nitro/amino-2-(substituted phenyl/benzyl) benzoxazole derivatives.

Shailendra K. Saraf et al.,(2010);(39) have been synthesized some 2-Phenyl-benzoxazole Derivative **Fig.17 ,** a new series of Schiff's bases derived from (4-Benzoxazol-2-yl-phenyl)isopropylidine-amine.

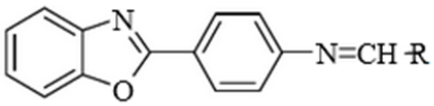


Fig.17: 2-Phenyl - benzoxazole Derivative.

The synthesized compounds have been investigated for their antimicrobial activity against different strains of bacteria and fungi. The results have been exhibited that 2-phenyl benzoxazole derivatives appeared potent activity against both, bacteria and fungi. The presence of halogen atom increases the activity. This could be due to the better penetration of the microbial cell-wall or selective uptake of the compound by the micro-organisms.

Mustafa Arisoy et al.; (2010); (40) have been synthesized 2-(p-substituted-benzyl)-5-[[4-(p-chloro/fluoro phenyl)piperazin-1-yl]acetamido]-benzoxazoles **Fig.18**, The results have been indicated that the activity of standard drugs against tested microorganisms were higher than benzoxazole derivatives tested in this study.

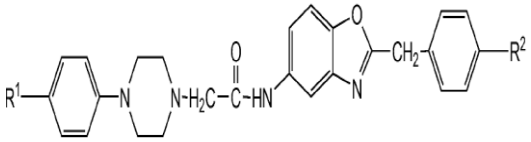


Fig.18: 2-(p-substituted-benzyl)-5-[[4-(p-chloro/fluorophenyl)piperazin1yl]acetamido]-benzoxazoles.

Raviraj R. Jadhav et al.;(2011);(41) have been synthesized some novel mercapto Benzoxazole derivatives **Fig.19** .

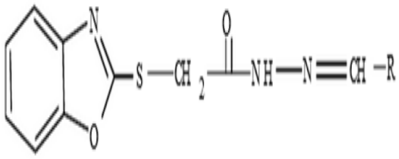


Fig.19: Substituted2mercaptobenzoxazole Derivatives.

The synthesized compounds have been tested for antibacterial activity against the organisms, *S.aureus* and *E.coli.* And Antifungal activity using *Candida albicans*. The standard drug used was Amoxicillin for antibacterial and Ketoconazole as standard for antifungal activity. The compounds B, C, D, E have shown the very good activity against *S.aureus* when compared withthe standard drug Amoxicillin. The compounds A, B, D, E, F have shown good anti-bacterial activity due to the presence of electron donating group OCH3, N(CH3)2 , CH3 group which is attached at 4 fourth position of the phenyl ring system and the compounds B and E may be due to the presence of electron withdrawing group like NO2, Br are attached at the second and fourth position of the phenyl ring system .The same Compounds also screened for the anti-fungal activity against *Candida albicans* the compounds A, B, D, E Showed highest degree of inhibition against C.albicans when compared with the standard drug Ketoconazole. However the activities shown by all the compounds tested were less than that of the standard.

Vikas S. Padalkar et al.; (2011);(42) have been synthesized 2-(1,3benzoxazol2yl)5(diethylamino)phenol derivatives **fig.20** , the compounds had been 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. The results indicate that, synthesized compounds displayed variable inhibitory effects on the growth of *Escherichia coli* and *Staphylococcus aureus* (bacterial strain), *Candida albicans* and *Aspergillus niger* (fungal strain). In general, most of the tested compounds exhibited better activity against the antibacterial strains (*E. coli, S. aureus*) and antifungal strains (*C. albicans, A. niger*).

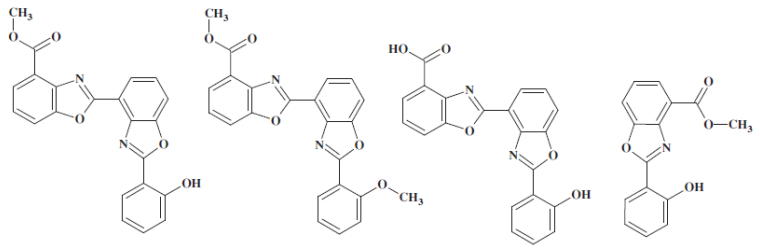


Fig.20:2-(1,3-benzoxazol-2-yl)-5-(diethylamino)phenol derivatives.

G. Balaswamy et al; (2012);(43) have been synthesized benzoxazole derivative containing heterocyclic ring .In this type of derivative three different heterocycles were incorporated to benzoxazole moiety to obtain the 1-[2-substituted (1,3-benzoxazol-5-yl) carbonyl] tetrahydropyridazine-3,6-dione,1-[2-

substituted(1,3-benzoxazol-5-yl)carbonyl]- 1,2-dihydropyridazine-3,6-dione and 2-[2-substituted (1,3-benzoxazol-5-yl)carbonyl]-2,3- dihydrophthalazine-1,4-dione as shown in **Fig.21.**

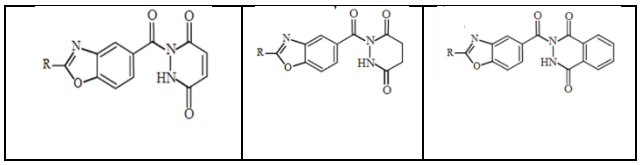


Fig.21: Benzoxazole Derivative ontaining heterocyclic ring.

The synthesized compounds had been screened for antimicrobial activity using four strains of Gram (+ ve) and Gram (-ve) bacteria. The strains used were *Staphylococcus Aureus, Bacillus pumilis, Proteus mirabilis (+ve)* and *Escherchia Coli (-ve*). Compounds 1c and 3c were found to be more active against *Escherchia Coli* (-ve) organism and 1b is more active against *Bacillus pumilis* used. The remaining compounds showed moderate and low activity against organisms.

P.Christina Ruby Stella et al.; (2012)(44) have been synthesized thioaniline benzoxazole Derivatives **Fig.22**

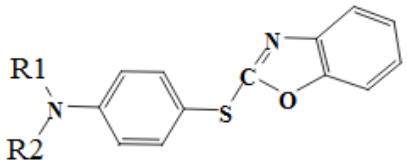


Fig.22:ThioanilinebenzoxazoleDerivative.

Antimicrobial activity against bacteria and fungi had been screened for the synthesized compounds. the test microorganisms(*Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Candida albicans, Aspergillus niger*). The results indicated that compounds B1 and B3 showed marginal activity, while compound B5 was the most active among the tested compounds.

Mustafa Arisoy et al.;(2013);(45) have been synthesized a new series of 5-(*p*-substitutedbenzamido/phenylacetamido)-2-(*p-tert*-butylphenyl)benzoxazole derivatives **fig.23** and have been evaluated for their antibacterial and antifungal activities The compounds possessed broad-spectrum activity against all of the tested Gram-positive and Gram-negative bacteria and yeasts. One compound had significant antibacterial activity against an antibioticresistant *Enterococcus faecalis* isolate, having twice the potency of the compared standard drugs vancomycin and gentamycin sulfate.

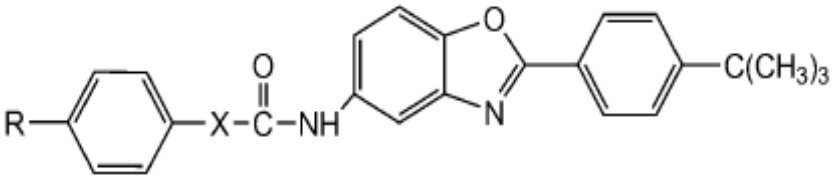


Fig.23:5(psubstitutedbenzamido/phenylacetamido)-2-(p-tertbutylphenyl) benzoxazoles.

Anupama Parate et al.;(2013);(46)have been synthesized 5-Ethylsulphonyl/methyl-2-(Substituted-phenyl/benzyl and/or phenyl ethyl) benzoxazoles **fig.24** and the compounds have been revealed the significant antibacterial activities when compared with reference drug(ampicillin). Substituted phenyl group reveals better activity against than substituted benzyl group. 5-ethylsulphonyl substituted benzoxazole is slightly more active than methyl substituted benzoxazole against *S. aureus.* All the compounds have exhibited a significant activity towards *Staphylococcus aureus*.

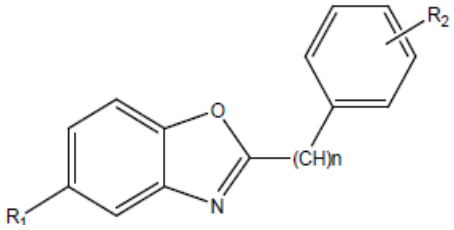


Fig.24:5-Ethylsulphonyl/methyl-2-(Substitutedphenyl/benzyland/orphenylethyl)benzoxazoles.

P. Anusha & J .Venkateshwar Rao; (2014); (47) had been synthesized 2-Mercapto-N-(substituted benzyldiene)-5-Carbohydrazid benzoxazole derivatives **Fig.25.**

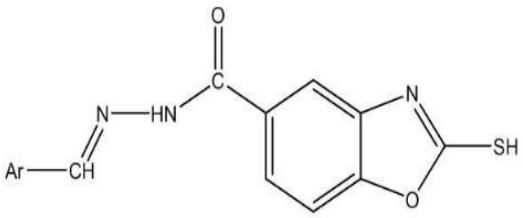


Fig.25: 2MercaptoN(substitutedbenzyldiene)-5-Carbohydrazid-benzoxazole Derivative.

The antibacterial activity of these compoundshad have been screened against four different strains of bacteria. Benzoxazole derivatives revealed good antimicrobial activity. The most potent compound was (4-methoxy phenyl) and the other compounds moderately exhibited antimicrobial activity. Only one compound revealed very poor antimicrobial activity .

Abu Mohsen (2014);(48) have been synthesized a series of seven novel compounds of 2-methyl-5-[4-(substitutedpiperazin/piperidin)acetamido]benzoxazole derivatives **fig.26**. Antimicrobial activity results indicated that synthesized compounds not showed remarkable activity.

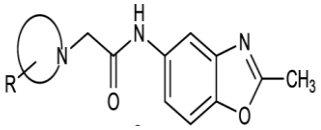


Fig.26:2-methyl-5-[4-(substituted piperazin/piperidin) acetamido] benzoxazole derivatives.

Naga Raju et al.; (2015) ;(49) have been synthesized a novel series of 2-(Cyclic amine)-1,3-benzoxazole derivatives **Fig.27,** The synthesis of 2-cyclic amine benzoxazole derivatives have achieved under solvent free microwave irradiation.

The advantage of the present method over the conventional methods is the use of zinc dust as a recyclable catalyst. This is remarkable and makes the method environmentally friendly and economically valuable as shown in**.**

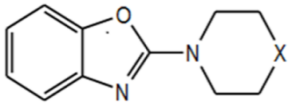


Fig.27: Synthesis of 2-Cyclic amine Benzoxazole Derivative.

the 2(3H)-Benzoxazolone derivatives have screened their antimicrobial activities to investigate the effect of the alkyl group when placed in 2nd position of the Benzoxazole nucleus.Test have carried out on four bacterial strains, namely *Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli* and two fungal strains, namely *Candida albicans* and *Aspergilla niger*. only **H**, **J** and **L** exhibited moderate antibacterial activity **H** contains N-(2-hydroxyethyl) group while **J** and **L** contains NH and O respectively at the 4th position of cyclic amine. These compounds are compared with the standard reference (Streptomycin) for their antibacterial activities. Only **B** with N-ethyl group and **C** with N-benzyl group at the 4th position of cyclic amine and **K** with piperidine as cyclic amine exhibited moderate antifungal activity while other compounds were inactive. These compounds are compared with the standard reference (Amphotericin-B) for their antifungal activities.

The results revealed that larger groups at 4th position of cyclic amine have no significant contribution to the antifungal activity of these compounds. The result revealed that the compound **H**, **J**, and **L** exhibited moderate antibacterial activity while compound **B**, **C**, and **K** exhibited good antifungal activity .

RajeshH.Tale (2015);(50) have been synthesized a new series of 2-(3-Arylureido)benzoxazole derivatives **Fig.28** the synthesized compounds have been screened for their in-vitro antimicrobial activity (antibacterial and antifungal). The antimicrobial results exhibited most of compounds were more potent that the standard control drug.

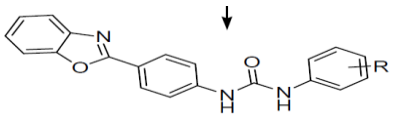
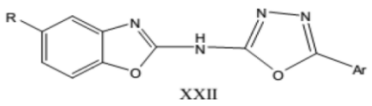


Fig.28: 2-(3-Arylureido)benzoxazole derivatives.

Chilumula Nageshwar Rao et al.;(2015);(51)have been synthesized the novel 5-substituted-n-(5-aryl-1, 3,4-oxadiazol-2-yl)benzoxazol-2amines **Fig.29** and the compounds have been evaluated for their *in-vitro* antibacterial activity against four pathogenic bacteria and the compounds had been evaluated for their *in vitro* antifungal activity against *C.albicans*and.



XXII

Fig.29:5-substituted-n-(5-aryl-1,3,4-oxadiazol-2-yl) benzoxazol-2amines

Ozlem Temiz-Arpaci et al.;(2016);(52) have been synthesized a series of 2-(*p*-substituted phenyl)-5-[(4-substituted phenyl) sulfonylamido]-benzoxazoles **Fig.30.**

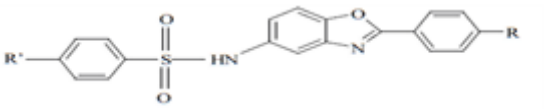


Fig.30:2-(*p*-substituted phenyl)-5-[(4-substituted phenyl) sulfonylamido]-benzoxazole.

The newly synthesized benzoxazoles have been tested for their *in vitro* antimicrobial activity against some Gram-negative, Gram-positive bacteria, and its isolate and *C. albicans* and its isolate.A*para*-substituted-phenyl sulfonylamido moiety on fifth position and different *p*-substituted phenyl groups on second position of benzoxazole ring for increasing the antimicrobial activity, the benzoxazole derivatives have found to show a broad spectrum of antimicrobial activity and the standard drugs were more active against the tested pathogens.

Tugba Ertan-Bolelli at al.; (2016) ;(53)have been synthesized the novel 2-substituted-5-(4-nitro/aminophenylsulfonamido)benzoxazole derivatives **Fig.31** Antimicrobial evalution results appeared that the compounds showed a broad spectrum of activity against the strains.

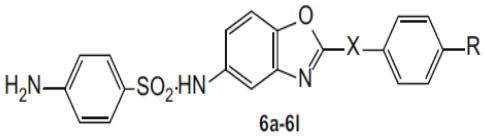


Fig.31:2-substituted 5(4nitro/amino phenyl sulfonamido)benzoxazole derivatives.

Shana Parveen S et al.; (2016);(54) had been synthesized 5-ethylsulphonyl- 2-(p-amino phenyl) benzoxazole **Fig. 32 .**

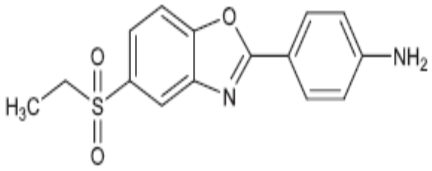


Fig.32:5-ethylsulphonyl-2-(p-aminophenyl) benzoxazole.

Jabbar et al., 2018;(55) have been synthesized a series of new isatin derivatives(3a-d) **Fig.33**, have been synthesized by condensation isatin(2,3-indolinendione) with piperidine(hexahydropyridine), hydrazine hydrate and Boc-amino acids respectively. the in vitro antibacterial properties have been tested against *E. coli, P. aeruginosa,* and *Bacillus cereus, S. aureus* by employing the well diffusion technique. A majority of the synthesized compounds were showing good antibacterial activity and from comparisons of the compounds, compound 3d has been determined to be the most active compound.

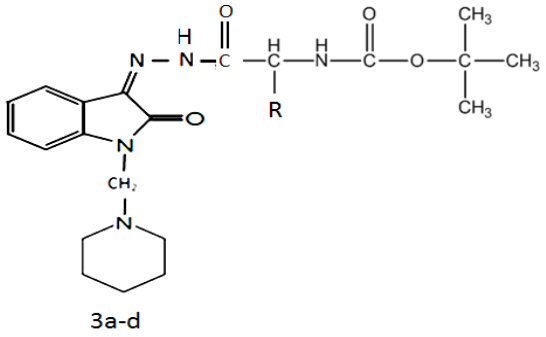


Fig.33: Carbamate Derivatives of Isatin.

Conclusion

This review has highlighted the use of benzoxazole derivatives having antimicrobial activity and reveals that most of the modified drugs show high to moderate antimicrobial activity,therefore,it is necessary to continue with research projects that help to synthesize new compounds with benzoxazole with better inhibiting characteristic against resistant pathogens. These classes of compounds are considered as scaffolds in

medicinal chemistry to drug development with different antimicrobial activites. Modification of benzoxazole drugs using different principles of chemical reaction. The biological profiles of these new generations of benzoxazole represent much progress with regards to older compounds. Therefore, recent approach is to study the QSAR of the benzoxazole derivatives, optimize the structure, synthesize certain newer derivatives of benzoxazole according to the reaction schemes producing higher yield and screen them for their antimicrobial activities which results in a lead compound for future development of new drug to be used against variety of pathogen.

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