INTERNATIONAL JOURNAL OF ADVANCES IN PHARMACY, BIOLOGY AND CHEMISTRY

Review Article

# Vistas of Novel Oxazole Derivatives as Potent Antimicrobial Agents

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**ABSTRACT**

Due to the problem of microbial resistance towards antimicrobial agents, there is an urgent requirement to design and synthesize novel antimicrobial agents. A series of heterocyclic derivatives bearing nitrogen and oxygen atoms constitutes the core structure of several biologically active compounds. Oxazole nucleus is one of the most important and well known heterocycle which is a vital chemical feature of a variety medicinal agents having broad spectrum of activities like antibacterial, anti fungal, anti-inflammatory, analgesic, antiviral, antineoplastic, antimalarial and antitubercular activities etc. Oxazole scaffold has been consistently rewarded as a promising versatile lead molecule with a special position in modern medicinal chemistry. The present communication is a logical attempt to review novel oxazole derivatives as potent antimicrobial agents reported in recent most literature. The vital information given in this manuscript may facilitate the development of more potent and effective antimicrobial agents for future.

**Keywords:** Oxazole, antibacterial, antifungal activity.

## INTRODUCTION

The term infection is used to refer to the presence and multiplication of microorganisms in the body. Infectious diseases are common diseases all over the world. Microbial infections caused by various types of bacteria and fungi are one of the leading infections which are responsible for the deaths of the millions of patients globally[1]. Microbial resistance is mainly related to bacteria and fungi that are not inhibited by usually achievable systemic concentration of an agent with normal dosage schedule and/or fall in the minimum inhibitory concentration ranges. Likewise the multiple drug resistance is defined as the resistance to two or more drugs or drug classes[2]. Acquisition of resistance to one antibiotic conferring resistance to another antibiotic, to which the organism has not been exposed is called cross resistance[3]. The past three decades have witnessed a dramatic change in the epidemiology of resistant gram-positive infections all over the world. Moreover the spread and dissemination of multidrug-resistant bacteria is a major limitation to the treatment of infectious diseases with known antibiotics[4].

During recent years, increase of invasive fungal infections have been observed which are cause of morbidity and mortality[5] particularly in immunosuppressed, haematological and as well as patients undergoing general surgeries and transplantations patients. Despite introduction of new antifungal drugs into medical practice, antifungal therapy still remains unsuccessful. Because of Failures in antifungal treatment arising from resistant stains affect economical aspects of pharmaceutical industry developments[6].

Tuberculosis (TB), one of the earliest recorded human diseases, a highly contagious and air-borne disease caused by *Mycobacterium tuberculosis*, is the greatest single infectious cause of mortality worldwide. It typically affects the lungs (pulmonary TB) but can affect other sites as well (extra pulmonary TB). The World Health Organization (WHO) Global Tuberculosis Report 2012 provides the latest information and analysis about the tuberculosis (TB) epidemic and progress in TB care and control at global, regional and country levels. In 2011, there were an estimated 8.7 million new cases of TB (13% co-infected with HIV) and 1.4 million people died from TB, including almost one million deaths among HIV-negative individuals and 430000 among people who were HIV-positive. TB is one of the top killers of women, with 300000 deaths among HIV-negative women and 200000 deaths among HIV-positive women in 2011. Moreover, the emergence of multi-drug resistant TB (MDR-TB) and extensive drug resistant TB (XDR-TB) become one of the biggest challenges in the treatment of this disease, creating an urgent need to develop new therapeutics[7].

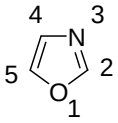
The drug design and development of recently used clinically available antimicrobial drugs have been compiled in the **Table 1** as given below:

**Table 1: Development of Clinically Used Antimicrobial Agents**[8-12]

| S. No. | Conventional Drugs | Mode of Action | Resistant Stains | Recent Drugs |
|---|---|---|---|---|
| 1. | ß-lactams, Cephalosporins Cefradine, Cefaclor, Cefixime, Carbapenems, Imipenem, Meropenem | Inhibits bacterial cell wall synthesis | *S.aureus* *E. faecalis* *E. faecium* *E. coli* *K. pneumoniae* | Cefditoren Pivoxil Ceftaroline Ertapenem Doripenem Biopenem |
| 2. | Fluoroquinolones Ciprofloxacin Ofloxacin Levofloxacin | Prevent bacterial DNA from unwinding and duplicating | *S. aureus, S. pneumoniae, E. coli* | Gemifloxacin Besifloxacin Sitafloxacin Moxifloxacin |
| 3. | Tetracyclines Chlortetracycline Oxytetracycline | Protein synthesis inhibitors | *S. aureus* *P. aeroginosa* *S. pneumonia* | Tigecycline |
| 4. | Aminoglycosides Streptomycin Gentamicin | Protein synthesis inhibitors | *E. faecalis* *E. faecium* | Tobramycin Sisomycin |
| 5. | Glycopeptides Vancomycin | Inhibit synthesis of bacterial cell wall | *E. Faecalis* *E. faecium* | Vancomycin Teicoplanin |
| 6. | Streptogramins Streptogramin A Streptogramin B | Inhibit protein synthesis | *Staphylococci, E. faecium, E. faecalis* | Dalfopristin Quinopristin |
| 7. | Macrolides and ketolides Erythromycin, Clarithromycin | Protein synthesis inhibitors | *S. pneumococci* *S. pyrogens* | Fidaxomicin, Telithromycin |
| 8. | Azoles Fluconazole | Inhibit ergosterol synthesis | *C. krusei* *C. glabrata* | Voriconazole Itraconazole |

Chemistry of heterocyclic compounds is one of the most important lines of investigations in the organic chemistry. Heterocyclic compounds are widely distributed in nature and are essential for life[13] and have played valuable role in pharmaceutical and drug discovery process. Nitrogen, sulphur and oxygen containing five member heterocyclic compounds have occupied enormous significance in the field of drug discovery process[14]. In recent years, a substantial number of substituted oxazoles have been reported to possess various pharmacological activities such as antibacterial, antifungal, anti-inflammatory, antidepressant, analgesics, antihyperglycemic, antirheumatic, anticancer and antiviral activities etc[15].

Oxazole **(1)** is the parent compound for a vast class of heterocyclic aromatic organic compounds with molecular formula $C_3H_3NO$. These are azoles with oxygen and nitrogen atoms separated by one carbon atom[16].

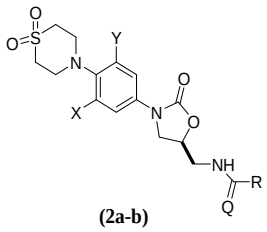



**(1)**

## ANTIMICROBIAL ACTIVITIES

Oxazole derivatives are known to have a broad spectrum of antibacterial and antifungal activities against variety of bacterial and fungal stains as per the recent most literature which has been presented as given below:

A new series of antimicrobial oxazolidinones bearing dihydrothiopyran or dihydrothiazine derivatives **(2a-2b)** were prepared by Renslo *et al*. The new oxazolidinone analogs were tested against a panel of gram-positive (*S. aureus, S. pneumoniae, E. faecium*) and fastidious gram-negative bacteria (*H. influenza, M. catarrhalis*) at concentration of l µg/mL. One compound provided the best activity against gram-negative while other compound was 4 to 8-fold more potent and conferred excellent activity against gram-positive bacteria as compared to standard thiomorpholine oxazolidinone PNU-288034[17].

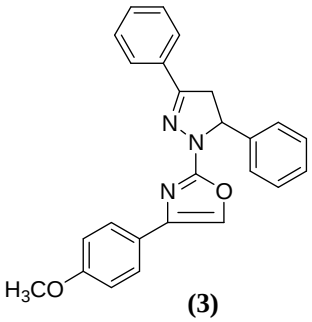



| | X | Y | Q | R |
|---|---|---|---|---|
| **2a** = | H | H | O | $CHCl_2$ |
| **2b** = | F | F | S | $CHCF_2$ |

**(2a-b)**

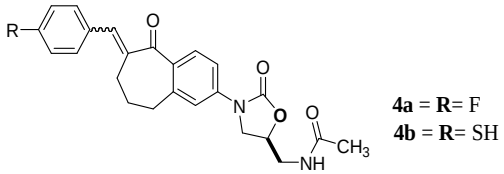
1-(4-aryl-2-oxazolyl)-3,5-diaryl-2-pyrazolin derivatives **(3)** were introduced by Dawood *et al.* These analogues were screened for their antimicrobial activity against Gram-positive (*Staphylococcus aureus* and *Pseudomonas acruginosa)*, Gram-negative (*Bacillis subtillis* and *Escherichia coli)* and pathogenic fungi (*Syncephalastrum racemosum, Aspergillus fumigatus, Candida albicans* and *Geotrichum candidum).* One Compound showed significant antifungal activity against *Aspergillus fumigates, Candida albicans, Geotrichum eandidum* with MIC

values of 31.25, 62.5 and 62.5mg/mL respectively when compared to Fluconazole as standard drug[18].



**(3)**

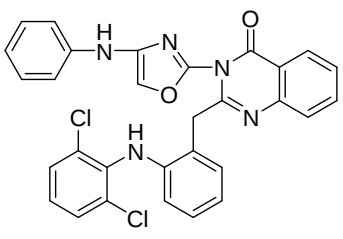
Prasad *et al* reported the synthesis of novel oxazolidinones possessing various benzocycloalkyl ring derivatives **(4a-4b)** and evaluated for antimicrobial activity against Gram-negative and Gram-positive organisms. More significantly, two compounds showed surprisingly potent activity against the fastidious Gram-negative organisms (*Haemophilus influenza, Moraxella catarrhalis*) an d Gram-positive organisms (*Staphylococ us aureus, Streptococcus pneumoniae, Enterococcus faecalis*) at MIC value of 2µg/mL and 0.5 µg/mL respectively when compared to standard drug linezolid[19].



**4a** = **R**= F
**4b** = **R**= SH

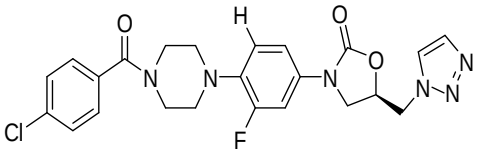
**(4a-b)**

2-[2-(2,6-dichloro-phenylamino)-phenylmethyl]-3-{4-[(substituted phenyl)amino]-1,3-oxazol-2-yl-}quinazolin-4(*3H*)ones derivatives **(5)** were introduced and evaluated for antibacterial activity against Gram-positive (*S. aureus, S. pyogenes)* and Gram-negative (*E. Coli, P. aeruginosa)* microorganisms and also evaluated for their antifungal activity against *C. albicans, A. niger, A. clavatus* by Patel *et al*. One compound showed good antifungal activity (MIC=100µg/mL) comparable to standard drug nystatin (MIC=100µg/mL)[20].



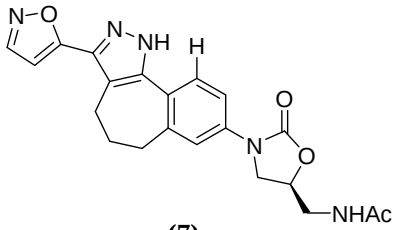
**(5)**

The synthesis of series of novel arylcarbonyl-piperazinyl-5-triazolylmethyl oxazolidinones **(6)** were reported and investigated against a panel of Gram-positive (methicillin resistant *S. aureus* (MRSA), methicillin-resistant coagulasenegative *staphylococci* (MR-CNS), penicillin-resistant *Streptococcus pneumoniea* (PRSP) and vancomycin-resistant enterococcus (VRE) and Gram-negative (*H. influenzae, M. catarrhalis and E. coli*) bacteria by Phillips *et al.* All compound showed significant activity against Gram-positive bacteria but one compound showed superior activity than PH-027, linezolid and vancomycin as standard drugs[21].



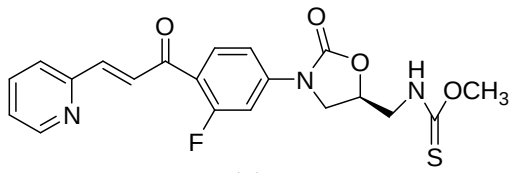
**(6)**

Boyer *et al* synthesized a novel series of conformationally-restricted oxazolidinones **(7)** which possessed a fused pyrazole ring substituted with various alkyl, aryl and heteroaryl substituents. All the compounds were screened for their antimicrobial activity against Gram-positive (*Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus pyogenes, Enterococcus faecalis*) and Gram-negative (*Haemophilus influenzae, Moraxella catarrhalis*) microorganisms. One compound was found to be the most potent compound which possessed broad-spectrum activity against Gram-positive and Gram-negative organisms when compared to standard drug linezolid[22].



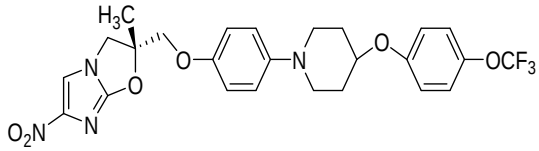
**(7)**

Selvakumar *et al* synthesized several hybrid compounds possessing both chalcone and oxazolidinone moieties **(8)** and tested for antibacterial activity against *Staphylococcus aureus* (methicillin-resistant), *Staphylococcus aureus, Enterococcus faecalis* (vancomycin sensitive); *Enterococcus faecium* (vancomycin resistant). The result of activity revealed that one compound exhibited potent *in-vitro* activity when compared to linezolid and vancomycin as standard drugs[23].



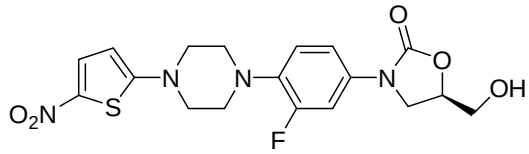
**(8)**

Novel series of optically active 6-nitro-2,3-dihydroimidazo[2,1-*b*]oxazoles derivatives **(9)** were designed and synthesized by Sasaki *et al*. Antituberculer activity of analogues were screened both *in-vitro* and *in-vivo* against both drug-susceptible and drug-resistant stains of *Mycobacterium tuberculosis*. One compound in particular displayed excellent *in-vitro* activity against both drug-susceptible and drug-resistant strains of *M. tuberculosis* having MIC value of 0.006 µg/mL) comparable to that of standard drug rifampicin[24].



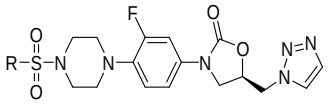
**(9)**

Rudra *et al* introduced novel oxazolidinone derivatives **(10)** containing methylene oxygen and methylene sulphur linked substituents at the C-5 position. Antibacterial screening of these compounds against a panel of resistant and susceptible Gram-positive (*Staphylococcus aureus, methicillin-resistant Staphylococcus aureus, Enterococcus faecalis, vancomycin-resistant Enterococcus faecium* (VRE), *Streptococcus pyogenes, Streptococcus pneumonia*) and fastidious Gram-negative bacteria (*Moraxella catarrhalis, Haemophilus influenza*) gave one potent compound as new antibacterial agent having MIC value at 0.5µg/mL as compared to standard drug[25].



**(10)**

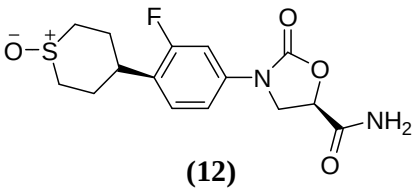
Fan *et al* synthesized derivatives of oxazolidinones containing triazolyl group **(11a-11b)** and evaluated for *in-vitro* antibacterial activity by MIC determination against a panel of resistant and susceptible Gram-positive organisms ( Methicillin-susceptible *S. aureus*, Methicillin-resistant *S. aureus*, Methicillin-susceptible *Streptococcus epidermidis*, Methicillin-resistant *S. epidermidis*, *Enterococcus faecalis*, Penicillin-resistant *S. pneumonia*). Most of the analogues in this series displayed good activity whereas two compounds showed more potent antibacterial activity at the MIC value of 0.125-.05µg/mL in comparison to linezolid and vancomycin as standard drugs[26].



**11a** = **R** = 4-ClPh
**11b** = **R** = 3-$NH_2$Ph

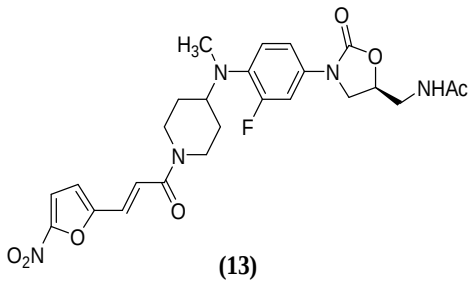
**(11a-b)**

A new series of oxazolidinones possessing a C-5 carboxamide functionality compounds **(12)** were introduced by Poel *et al*. The synthesized compounds were screened for the antibacterial activity. Results of *in-vitro* studies revealed that like linezolid, one compound exhibited anti bacterial activity at the MIC value of 4µg/mL against *S. aureus*[27].



**(12)**

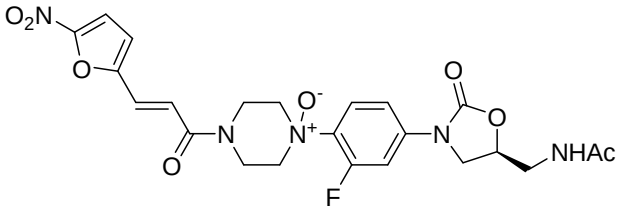
Srivastava *et al* reported the synthesis of a few novel methylamino piperidinyl substituted oxazolidinones **(13)** and their *in-vitro* antibacterial activities were screened against broader panel of both susceptible and resistant gram-positive stains. Some compounds showed appreciable antibacterial activity as compared to standard drugs linezolid and eperezolid; additionally one compound showed potent and better antibacterial activity with an *in-vitro* MIC value of 4 µg/mL against resistant *Staphylococcus aureus* when compared with standard drug linezolid having MIC value of 16 µg/ml[28].



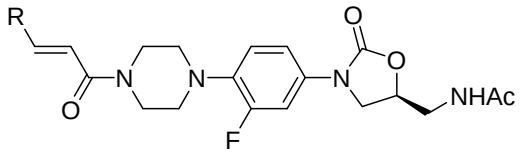
**(13)**

Srivastava *et al* reported the synthesis of novel piperazinylaryloxazolidinones possessing heteroaryl groups **(14, 15a-15b)** and their *in-vitro* antibacterial activities were evaluated against

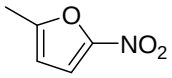
*Bacillus pumilus, B. cereus, S. aureus, Staphylococcus epidermidis, S. pyogenes, Streptococcus pneumoniae* and *E. faecalis*. Result of activity revealed that some compounds showed superior antibacterial activities than standard drug linezolid and were also active against the linezolid resistant *Staphylococcus aureus* stains[29].



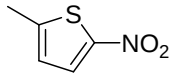
**(14)**



**15a = R =**

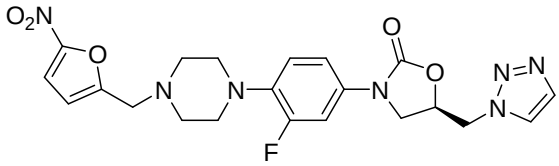


**15a =R =**



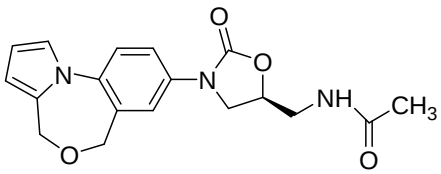
**(15a-b)**

Fan *et al* synthesized a new series of derivatives of oxazolidinones bearing N-linked 5-triazolylmethyl group **(16)** and investigated for their *in-vitro* antibacterial activities against a spectrum of resistant and susceptible gram-positive organisms like *Staphylococcus aureus*, Methicillin-susceptible *Staphylococcus aureus (MSSA), Streptococcus pneumonia* and *Enterococcus faecalis*. Some of the analogues in this series displayed good antibacterial activity whereas one compound was found to be the most potent one which exhibited more potent antibacterial activity with MIC value of 0.06 µg/mL than standard drugs like linezolid and vancomycin[30].



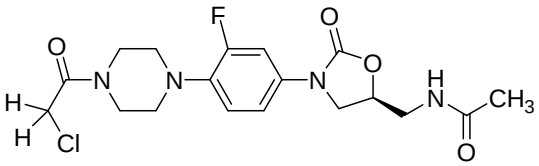
**(16)**

A series of novel azolo benzoxazepinyl oxazolidinones **(17)** mimicking the conformationally constrained structure of standard drug linezolid were reported by Das *et al* and evaluated for their antibacterial activity. Some molecules showed promising antibacterial activity against the panel of organisms gram-positive bacteria including both sensitive and resistant strains: *S. aureus* (MSSA), *S. aureus* (MRSA), *Enterococcus faecalis*, vancomycin-resistant *Enterococcus faecalis* (VRE) and vancomycin-resistant *Enterococcus faecium* (VREF)[31].



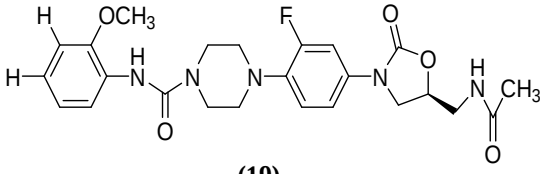
**(17)**

Wang *et al* synthesized oxazolidinone derivatives with substituted acetyl piperazinyl groups **(18)**. All the compounds were evaluated for *in-vitro* antibacterial activities against gram-positive pathogens including methicillin-resistant *Staphylococcus aureus, Staphylococcus aureus, Staphylococcus epidermidis* and *Enterococcus faecalis*. Some compounds with chloroacetyl-piperazinyl group were found to have superior antibacterial activities when compared to linezolid as standard drug against most of tested gram-positive pathogens[32].



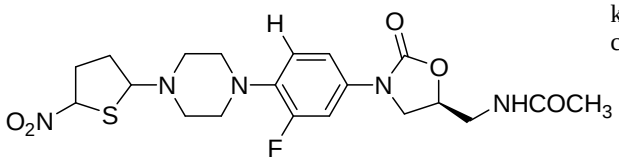
**(18)**

Synthesis of novel oxazolidinone derivatives possessing urea functionality **(19)** were reported by Selvakumar *et al* and screened for their antibacterial activity. Some compounds showed significant antibacterial activity in comparison to standard drug linezolid[33].



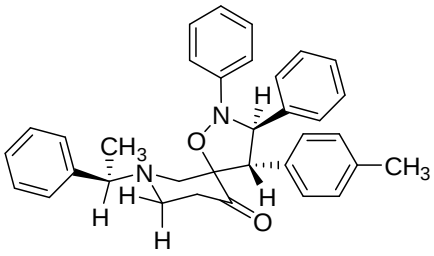
**(19)**

A novel series of oxazolidinones **(20)** were prepared by Rudra *et al*. All the synthesized compounds were screened for their antimicrobial activity against a series of Gram-positive and Gram-negative organisms like methicillin-resistant *Staphylococcus aureus* (MRSA), methicillin-resistant *Staphylococcus epidermidis* (MRSE), vancomycin-resistant *Enterococcus faecium* (VRE), *Streptococcus pyogenes* and *Streptococcus pneumoniae*. One compound found to be the most potent compound with MIC value of 1µg/ml when compared to standard drugs Linezolid and Vancomycin[34].



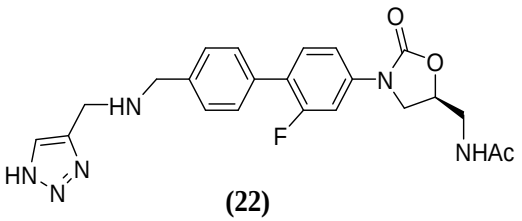
**(20)**

A series of novel spiroisoxazolidines **(21)** were reported by Kumar *et al*. The synthesized compounds were evaluated for their *in-vitro* activity against *Mycobacterium tuberculosis*. One compound was found to possess maximum anti-tubercular activity with MIC value of 3.02 mM, being 2.5 times more potent than the first-line anti-TB drug ethambutol[35].



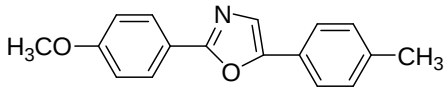
**(21)**

Some novel biaryloxazolidinones derivatives **(22)** were designed by Zhou *et al*. These analogues were tested for their antibacterial activity against both linezolid-susceptible and resistant Gram-positive bacteria *Enterococcus faecalis, Staphylococcus aureus, Streptococcus pyogenes, Streptococcus pneumonia* as well as the fastidious Gram-negative bacteria such as *Haemophilus influenzae* and *Moraxella catarrahalis*. One compound displayed potent antibacterial activity at MIC value of 0.5µg/ml against *E. Faecium* when compared to linezolid as standard drug[36].



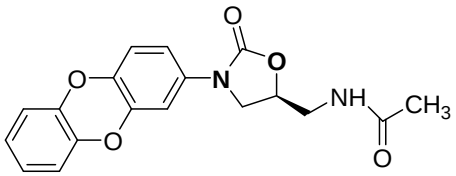
**(22)**

Tomi *et al* synthesised new derivatives of five member heterocyclic compounds containing oxazole ring **(23)** and evaluated for the antibacterial activity against *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aerugenosa* and for antifungal activity against *Aspergillus niger* and *Candida albicans*. One compound showed moderate activity when compared to standard drugs ofloxacin for antibacterial activity and ketoconazole for antifungal activity at concentration of 50µg/mL[14].



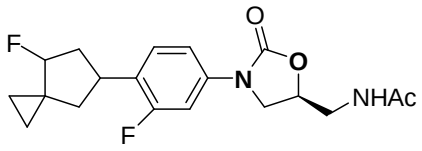
**(23)**

The novel oxazolidinone derivatives containing a benzodioxin ring system **(24)** were synthesized by Ebner *et al*. The antimicrobial activities of the new oxazolidinones against resistant Gram-positive bacterial infections were measured and the MIC against *Staphylococcus aureus* for one of the antimicrobials was determined to be 3 µg/mL which was comparable to well-known oxazolidinone based standard drug linezolid[37].



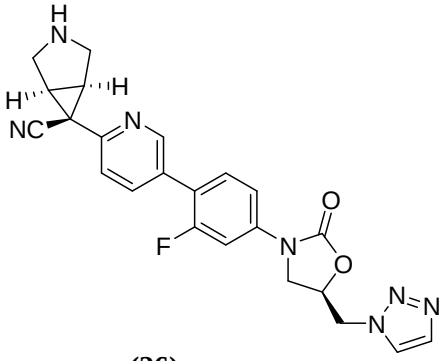
**(24)**

Synthesis of a new series of oxazolidinones having spiro[2,4]heptane moieties **(25)** were reported by Kim *et al* and their *in-vitro* antibacterial activities against both Gram-positive and Gram-negative bacteria were evaluated and the effect of substituents on the oxazolidinone ring was investigated. Result revealed that one compound having fluoro group showed the most potent antibacterial activity at the MIC value of 1.56µg/mL as compared to standard drug[38].



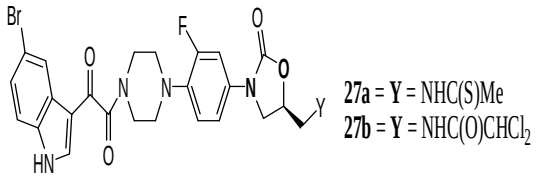
**(25)**

Novel antibacterial biaryl oxazolidinones **(26)** were introduced and their *in-vitro* antibacterial activity and structure-activity relationships (SAR) were reported by Komine *et al*. Most of the synthesized compounds showed good antibacterial activity but one molecule containing a cyano group at C-6 position was highly potent antibacterial agent with MIC value of 0.06 µg/mL when compared with standard drug[39].



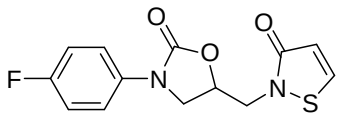
**(26)**

Takhi *et al* introduced novel oxazolidinone derivatives bearing a variety of 3-indolylglyoxamide substituents **(27a-27b)**. These derivatives were screened against a panel of clinically relevant Gram-positive organisms such as *E. Faecalis* and *E. faecium* pathogens and fastidious Gram-negative organisms such as *Moraxella catarrhalis, Haemophilus influenzae*. Several analogues displayed good antibacterial activity against linezolid resistant Gram-positive organisms by having MIC value in range of 2-4 µg/mL as compared to standard drug[40].



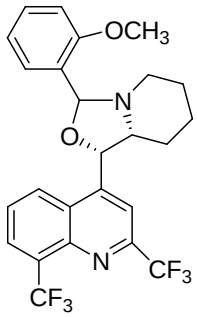

**(27a-b)**

Synthesis and antibacterial activity against *Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli, Salmonella typhimurium* and *Pseudomonas aeruginosa* of isothiazolyl oxazolidinones derivatives **(28)** were reported by Adibpour *et al*. One compound was found to be the most active compound with MIC value of 0.75 µg/ml superior to standard drug linezolid[41].



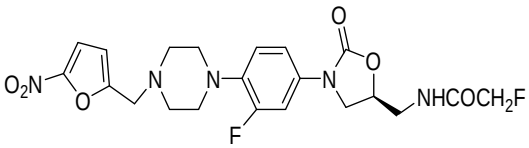
**(28)**

New mefloquine-oxazolidine derivatives **(29)** were prepared and their antitubercular activity was screened against *Mycobacterium tuberculosis* as the minimum inhibitory concentration (MIC) in mM by Goncalves *et al*. One compound displayed the greatest activity with a MIC value comparable with the first line tuberculostatic agent ethambutol[42].



**(29)**

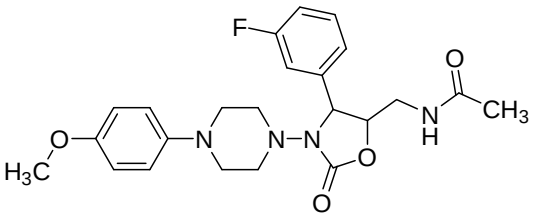
Das *et al* explored and synthesized novel oxazolidinone derivatives **(30)**. These derivatives were screened for antibacterial activity against a number of sensitive and resistant bacteria such *as Staphylococcus aureus,* methicillin-resistant *Staphylococcus aureus (MRSA), Enterococcus faecalis,* vancomycin-resistant *Enterococcus faecium (VRE), Streptococcus pyogenes* and *Streptococcus pneumoniae.* One compound in which the methyl group was replaced by fluoromethyl showed MIC value of 2µg/mL against gram-positive stains compared to standard drug Ranbezolid[43].



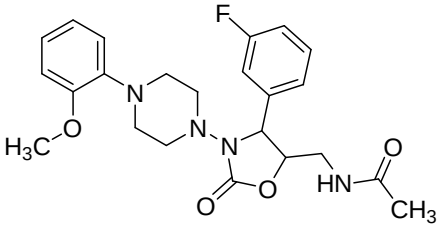
**(30)**

Analogues of 3-(methoxyl-phenyl)-piperazinyl-phenyl oxazolidinone **(31, 32)** were prepared by Liu *et al*. All the synthesized compounds were evaluated *in-vitro* against six Gram-positive

organisms (*S. aureus, S. epidermidis, S. pneumoniae, S. albus, Streptococcus enteridis and S. nonhemolyticus*). One compound was found active against five Gram-positive organisms except *S. nonhemolyticus*, whereas other compound was found active only against two gram-positive organisms, *S. albus, S. enteridis* with MIC value in range of 3.13-6.25 µg/mL when compared with standard drug[44].

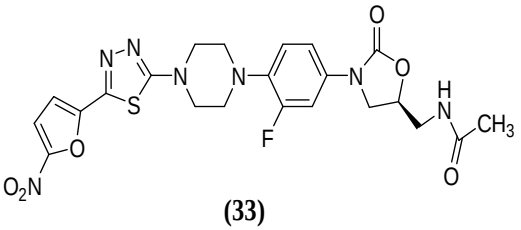


**(31)**



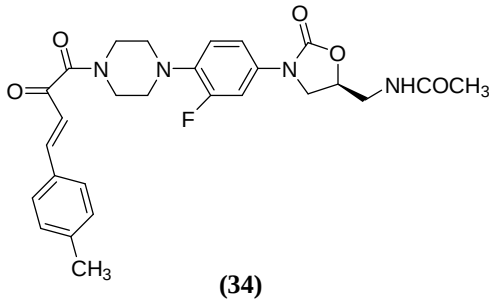
**(32)**

Khalaj *et al* synthesized some novel nitroimidazolyl-oxazolidinone derivatives **(33)** and evaluated them as antibacterial agents against a panel of Gram-positive (*Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus warneri, Staphylococcus lentus, Staphylococcus xylosus, Staphylococcus saprophyticus, Micrococcus luteus, Corynebacterium glutamicum, Bacillus subtilis*) and Gram-negative (*Escherichia coli, Klebsiella pneumonia* and *Pseudomonas aeruginosa*) bacterial stains. Amongst synthesized compounds, one compound exhibited more potent inhibitory activity at MICs value of 0.391 µg/mL with respect to other synthesized compounds and reference drug linezolid[45].



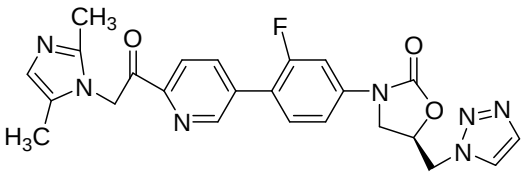
**(33)**

Novel (5S)-N-[3-(3-fluoro-4-{4-[2-oxo-4-(substituted aryl)-but-3-enoyl]-piperazin-1-yl}-phenyl)-2-oxooxazolidin-5-ylmethyl]-acetamide analogues **(34)** were explored and their *in- vitro* antibacterial activity against Gram-positive: *Staphylococcus aureus* (methicillin resistant), *Staphylococcus aureus* (vancomycin resistant), *Bac illus cereus, Enterococcus faecalis, Streptococcus pyogens* and Gram-negative such as *Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas aeruginosa* bacteria was evaluated by Varshney *et al*. Some compounds showed significant antibacterial activity with MIC values in range of 0.04–0.39 µg/mL when compared with standard drug[46].



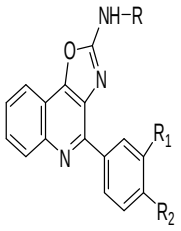
**(34)**

Novel substituted (pyridin-3-yl)phenyloxazolidinones **(35)** were introduced by Reck *et al*. Their antibacterial activity was tested against Gram-positive bacteria including linezolid-resistant *Streptococcus pneumonia.* One Compound showed excellent activity against linezolid-resistant *Streptococcus pneumonia* when compared to standard drug linezolid[47].



**(35)**

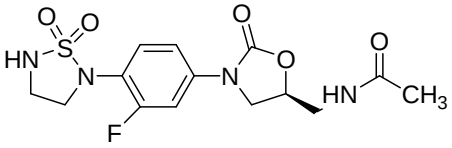
A new class of fused oxazoloquinoline derivatives **(36a, 36b)** were prepared by Eswaran *et al*. The newly synthesized compounds were screened for their *in-vitro* antibacterial activity against *Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa* and *Klebsiella pneumoniae* and anti-tubercular activity against *Mycobacterium tuberculosis*. Results of activity revealed that two compounds emerged as the lead antitubercular agents and one compound was found to be the most potent compound with MIC value of 1 µg/mL than standard drug isoniazid having MIC value of 1.5 µg/mL[48].




| | | |
|---|---|---|
| **36** = **R** | $R_1$ | $R_2$ |
| **36a** =2-O-$CH_3$ | F | H |
| **36b** = 3-Cl Ph | H | F |

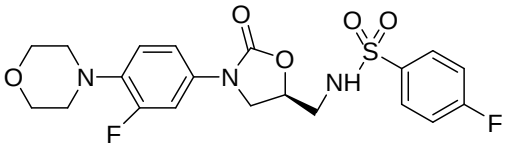
**(36a-b)**

Kim *et al* synthesized a new series of oxazolidinones having cyclic sulfonamide moieties **(37)**. The synthesized derivatives were screened for their *in-vitro* antibacterial activities against both Gram-positive and Gram-negative bacteria. A particular compound having [1,2,5]thiadiazolidin-1,1-dioxide moiety exhibited the most potent antibacterial activity at MIC value of 3.12µg/mL when compared to reference drug linezolid with MIC value of 1.56 µg/mL[49].

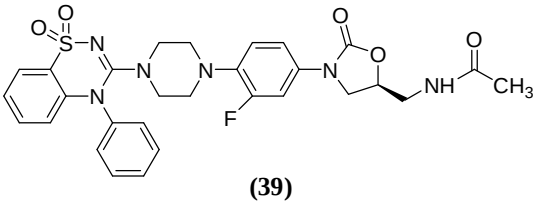



**(37)**

The synthesis and *in-vitro* antitubercular activity of a new class of arylsulfonamido conjugated oxazolidinones derivatives **(38, 39)** were reported by Kamal *et al*. One compounds having MIC value of 1µg/mL was found to be the most active molecule against *Mycobacterium tuberculosis* by using rifampicin and linezolide as standard drugs[50].

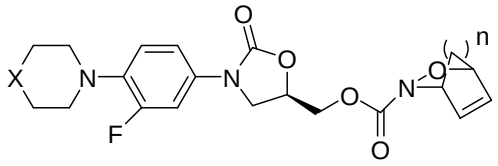



**(38)**




**(39)**

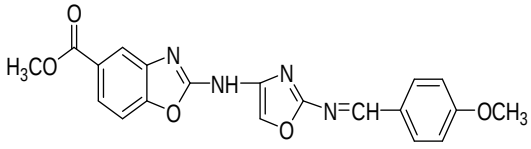
Yana *et al* introduced some novel oxazolidinone antibiotics **(40)** and their *in-vitro* antibacterial activities were evaluated against Gram-positive organisms including *Bacillus subtilis, S. aureus, E. faecalis, M. Luteus* and Gram-negative organisms such as *Escherichia coli, Pseudomonas aeruginosa, Mycobacterium vaccae.* Results revealed that some of the synthesized compounds had comparable activity as compared to linezolid as standard drug[51].




**X** = NBoc, n = 1

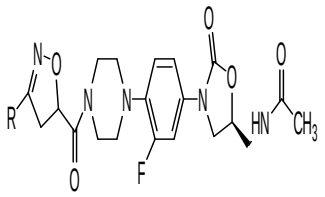
**(40)**

Chilumula *et al* reported a series of methyl-2-(arylideneamino)oxazol-4-ylamino) benzoxazole-5-carboxylate derivatives **(41)** and their antimicrobial activities were investigated *in-vitro* against Gram-positive (*Staphylococcus aureus* and *Bacillus subtilis)* and Gram-negative (*S.typhi* and *Escherichia coli )* bacteria and the yeast (*Candida albicans* and *A. niger*). One compound bearing a methoxy moiety at position C-4 of phenyl ring at the C-2 position of benzoxazole ring was the most active derivative against *S. aureus, Bacillus subtilis, S. typhi, Escherichia coli* with a zone of inhibition of 23mm, 21mm, 20mm, 18mm, and *Candida albicans* and *A.niger* with a zone of inhibition of 28mm, 20mm when compared to Ampicillin sodium (10 µg/disc) in case of bacteria and clotrimazole (10 µg/disc) in case of fungi as their respective standard drugs[52].




**(41)**

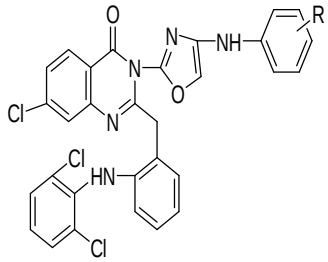
Varshney *et al* synthesized (5S) N-(3-{3-fluoro-4-[4-(3-aryl-4,5-dihydro-isoxazole-5-carbonyl)-piperazin-1-yl]-phenyl}-2-oxo-oxazolidin-5-ylmethyl)-acetamide derivatives **(42a-42b)** and their *in-vitro* antibacterial activity against various resistant Gram-positive and Gram-negative bacteria were investigated. The result of activities revealed that two compounds showed excellent activity against Gram-negative bacteria with MIC values 0.1657µM and 0.1627µM respectively when compared to linezolid as standard drug[53].



**42a** = 4-Cl Ph
**42b** = 3,4-methylene dioxyphenyl

**(42a-b)**

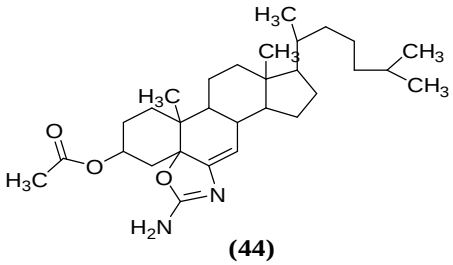
2-[2-(2,6-Dichlorophenyl)amino]phenylmethyl-3-{4-[(substituted phenyl)amino]-1,3-oxazol-2-yl}-7-chloroquinazolin-4(3*H*)ones derivatives **(43a-c)** were prepared by Patel *et al*. All the derivatives were screened for their antibacterial and antifungal activity against *E. Coli, P. Aeruginosa, S. aureus, S. pyogenes* and *C. Albicans, A. Niger, A. Clavatus* respectively. Some compounds revealed good antimicrobial activity when compared with their respective standard drugs like gentamycin, ampicillin, chloramphenicol, ciprofloxacin, norfloxacin, nystatin and griseofulvin[54].



**43a**= **R** = H
**43b**= **R** = 2,5-$(Cl)_2$
**43c**= **R** = 2-Cl, 4-$NO_2$

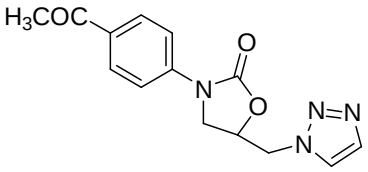
**(43a-c)**

Shamsuzzaman *et al* synthesized 20-amino-5a-chol est-6-eno [6,5-d] oxazole derivatives **(44)** and evaluated for the antibacterial activity *in-vitro* by the disk diffusion assay against three Gram-positive (*B. subtilis S. pyogenes, S. aureus*) and three Gram-negative (*P. aeruginosa, S. typhimurium, E. Coli*) stains of bacteria. All the synthesized compounds were also evaluated for their inhibitory action against five stains of fungus (*Candida albicans, Candida glabrata, Penicillium spp., Fusarium oxyporium, Aspergillus niger)* and then the minimum inhibitory concentration (MIC) of all the synthesized compounds were determined. One compound showed MIC value of 32µg/mL against *B. subtilis* by using Chloramphenicol as standard drug in case of bacteria and 10 mm zone of inhibition against *Candida glabrata* when compared to nystatin as a standard drug in case of fungi[55].



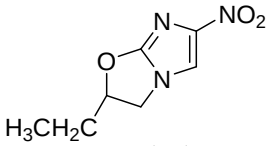
**(44)**

A novel series of C-5-substituted triazole-oxazolidinones derivatives **(45)** were synthesized and evaluated for their antibacterial activity against *Mycobacterium smegmatis, Bacillus subtilis* and *Enterococcus faecalis* by Demaray *et al*. One compound showed an MIC of 1µg/mL against *M. smegmatis* which was four fold lower than the MIC measured for isoniazid as standard drug[56].



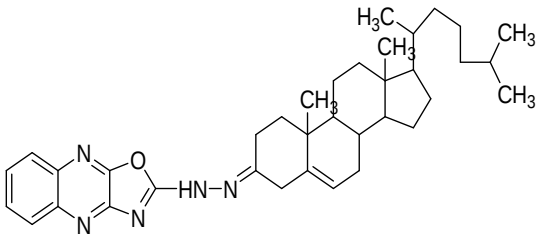
**(45)**

A series of 2,3-dihydro-7-nitroimidazo[5,1-b]oxazole analogues **(46)** were reported by Zwawiak *et al*. All the synthesized compounds were screened *in-vitro* for antimycobacterial activity against *Mycobacterium tuberculosis, Mycobacterium avium* and other resistant stains. One compound confirmed antitubercular activity at the MIC value of 0.15µg/mL against *Mycobacterium tuberculosis* when compared to isoniazid as reference drug[57].



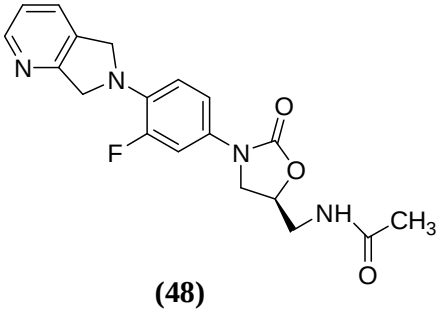
**(46)**

Khan *et al* synthesized steriodal heterocyclic systems namely cholest-5-en-3-oxazolo, thiazoloquinoxaline derivatives **(47)** and evaluated them for antibacterial activity by the microdilution method against two Gram-positive (*S. aureus, S. pyogenes*) and two Gram-negative bacteria (*S. typhimurium, E. coli*). Result of activity revealed that one compound showed significant activity (MIC=0.78µg/mL) against Gram-positive and (MIC=0.39 µg/mL) against Gram-negative organisms when compared to standard drug Amoxicillin[58].



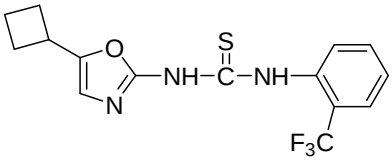
**(47)**

Paget *et al* prepared a novel series of oxazolidinones containing a pyrroloaryl substituent **(48)**. All the synthesized compounds were evaluated for their *in-vitro* antibacterial activity against susceptible and resistant Gram-positive bacteria. One compound exhibited the best *in-vitro* profile with MIC value of 0.5 µg/mL against *staphylococci* species when compared to linezolid as standard drug[59].



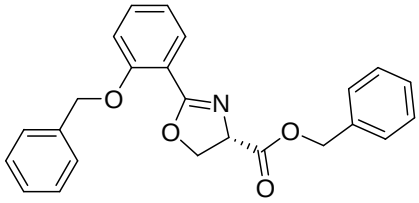
**(48)**

Sriram *et al* reported a series of new 1-(5-cyclobutyl-1,3-oxazol-2-yl)-3-(sub)-phenyl/pyridylthiourea compounds **(49)** and evaluated their *in-vitro* and *in-vivo* antimycobacterial activities. One compound was found to be the most active with an *in-vitro* MIC of 0.14 mM and was 2.5 and 80 times more active when compared to standard drug isoniazid against MTB and MDR-TB respectively[60].



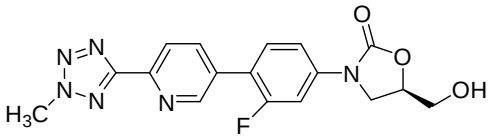
**(49)**

Moraski *et al* serendipitously discovered oxazoline containing intermediate **(50)** and evaluat-ed it for anti-tubercular avtivity against *Mycobacterium tuberculosis*. Outcome of activity revealed that intermediate compound displayed surprising anti-tuberculosis activity (MIC=7.7 mM) when compared to Rifampin as positive control[61].



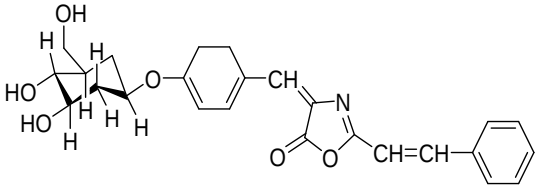
**(50)**

Im *et al* prepared a series of novel substituted pyridyl phenyl oxazolidinone analogues **(51)**. All the synthesized compounds were investigated for their *in-vitro* and *in-vivo* antibacterial activities against Gram-positive (methicillin resistant *Staphylococcus aureus* and vancomycin-resistant *enterococci*), and Gram-negative (*Haemophilus influenzae*). One compound showed higher *in-vitro* antibacterial activity with MIC values of 0.5mg/mL against methicillin resistant *Staphylococcus aureus* when compared to positive control linezolid[62].



**(51)**

4-(4-*o*-*β*-d-glucoxybenzylidene)-2-(substituted styryl) oxazol-5-ones derivatives **(52)** were prepared and evaluated for antibacterial activity against Gram-positive (*Staphylococcus aureus, Bacillus subtilis)* and Gram-negative (*Escherichia coli, Klebsiella aerogenes)* organisms and also evaluated for anti fungal activity against fungus (*Aspergillus niger, Candida albicans)* by Taile *et al*. One compound showed significant activity when compared to Ciprofloxacin and Clotrimazole as standard drugs in case of bacteria and fungi respectively at a concentration of 100$\mu$g/mL by using the cup plate diffusion method[63].



**(52)**

**CONCLUSION**

Oxazole is a versatile heterocyclic nucleus having a great demand in medicinal chemistry and drug design because of having variety of considerable biological activities like antimicrobial, anticancer,

anti-inflammatory and antiviral activities etc. Due to microbial resistance to conventional antimicrobial agents by various mechanisms, millions of patients die every year which describe the severity of microbial infections. So to save the valuable human lives there must be an effective antimicrobial therapy. Looking into the medicinal importance of oxazole scaffold, it was considered worthwhile to review novel oxazole derivatives for their antimicrobial activities to provide better treatment for microbial infections.

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