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Review on antimicrobial activity of 1,5-benzodiazepines

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Abstract
1, 5- benzodiazepines has been extended to various biological activities such as cancer, viral infection and cardiovascular disorders. 1,5-benzodiazepines showed antidepressive, analgesic, antianxiety, antifungal, antibacterial, anthelmintic, anti-inflammatory and anticancer activities, as dyes for acrylic fibre in photography, also valuable synthons used for the preparation of other fused ring compounds such as triazolo, oxadiazolo, oxazino, or furano benzodiazepines. Due to their wide range of biological, industrial and synthetic applications in synthetic organic chemistry. In this review, we have collected information about the 1, 5-benzodiazepines derivatives and its antimicrobial activity for further research and development.

Keywords: 1, 5-benzodiazepines, antibacterial, antifungal, and antianxiety activity

Introduction
Benzodiazepine structure an important class of heterocyclic compounds containing two nitrogen atoms, especially the seven-membered ring systems play an important in the biological activity of these molecules. The 1,5–benzodiazepines moiety is a privileged class of pharamacophore, as compounds bearing this structural unit possess a broad spectrum of biological activities.

Pharmacological Activities
K Mogilaiah *et al*., (2003) synthesized pyrazoline, pyrimidine and 1, 5-benzodiazepine derivatives of 1, 8-naphthyridine to screen them for antibacterial activity by filter paper disc technique against bacteria like *Escherichia coli* and *Bacillus subtilis*. All the compounds exhibited better antibacterial activity in comparison with standard drug streptomycin [1].

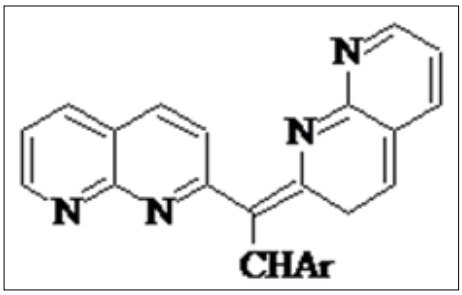

Fig 1

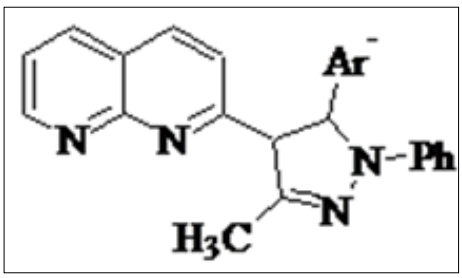

Fig 2

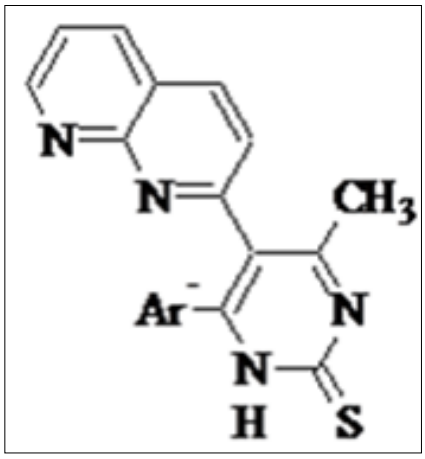

Fig 3

Raviraj A Kusanur *et al*., (2004) synthesized a series of spiro [indolo-1,5-benzodiazepines] derivatives from 3-acetylcoumarins and assessed for their antimicrobial activity by cup plate method against bacteria like *Escherichia coli* and *Bacillus subtilis*, fungi like *Aspergillus niger*. Ciprofloxacin and Griseofulvin were used as standard drug. Compounds showed moderate activity [2].

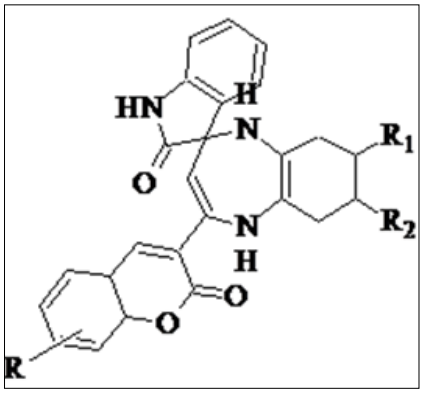

Fig 4

Rajesh Kumar *et al*., (2007) synthesized derivatives of 3H-1,5-benzodiazepine derivatives to evaluate their antimicrobial activity by cup plate method using standard drugs like Crofloxin, Ciclopiroxolamine, against bacteria like *Staphylococcus aureus* and *Klebsiella pneumoniae*,fungi like *Aspergillus niger* and *Candida albicans*. Compounds exhibited significant antibacterial and antifungal activity. [3]

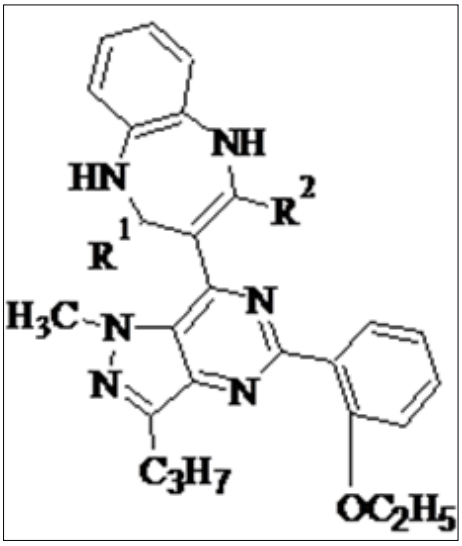

Fig 5

Vijai N Pathak *et al*., (2007) synthesized a series of 7-chloro-2-alkyl/aryl-4-alkyl/aryl-3-arylidene-3*H*-1,5-benzodiazepines derivatives to evaluate their antimicrobial activity by inhibition zone technique against bacteria like *Escherichia coli* and *Staphylococcus aureus*, fungi like *Aspergillus niger* and *Candida albicans.* Standard drugs used were Streptomycin and Ketaconazole. Compounds showed greater antimicrobial activity in the *o*-methoxy and *m*-fluoro substituents of 6c and 6e, *p*-chloro and *p*-fluoro substituents with 4-chlorophenyl ring 2-position of 6f and 6g, *p*-fluoro and 3,4-difluoro substituents with phenyl ring at 2-position of 6i and 6j [4].

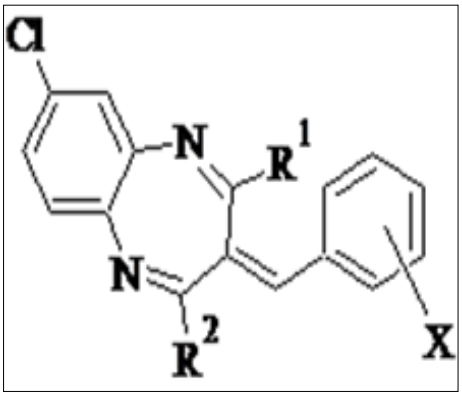

Fig 6

Varala Ravi *et al*., (2007) synthesized a series of 1,5-benzodiazepine derivatives to assess their antibacterial and antifungal activity by paper disc diffusion method against bacteria like *B.subtilis, P.vulgaris, K.pneumoniae, P.aeruginosa* and fungi like *Candida albicans, Aspergillus* niger, while using agar streak dilution method determined minimum inhibitory concentration [5].

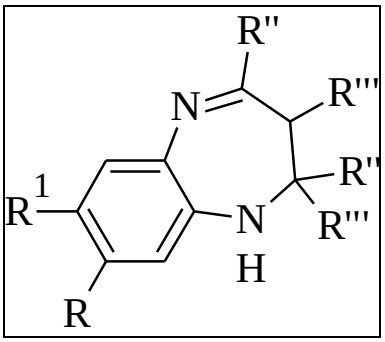

Fig 7

Rajesh Kumar *et al*., (2008) synthesized some derivatives of 3*H*-1,5-benzodiazepines to screen them for antimicrobial activity by the cup-plate method against bacteria like *Staphylococcus aureus* and *Klebsiella pneumoniae*, fungi like *Aspergillus niger* and *Candida albicans*, where Crofloxin and Ciclopiroxolamine were used as standard drugs. 8c showed greater antibacterial and antifungal activities in comparison with standard drugs [6].

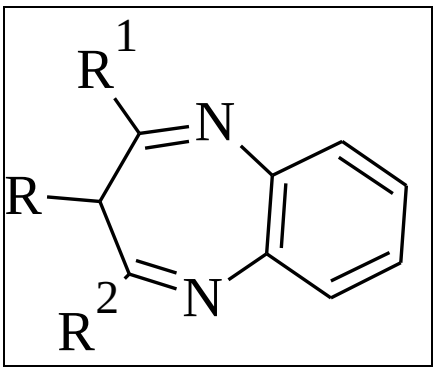

Fig 8

Bhawani singh *et al*., (2010) synthesized a series of 1,5-benzodiazepine and their oxygen substituted hydroxylamine derivatives to evaluate their antimicrobial activity by well diffusion method against bacteria like *Bacillus subtilis, Escherichia coli, Proteus mirabilis* and *Salmonella* typhi, fungi like *Aspergillus fumigatus* and *Candida albicans* using sabouraud agar medium. Compounds exhibited greater antibacterial and antifungal activity in comparison with standard drug like Streptomycin [7].

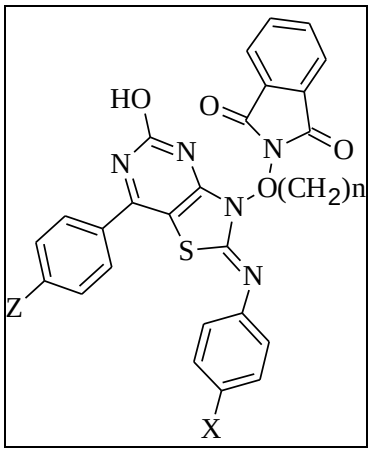

Fig 9

Rajeev K Singla *et al*., (2011) synthesized 3-(4-1H-Indol-3yl)-(2,3-dihydro-1H-benzo[b]diazepin-2-yl)-2H-Chromen-2-one to screen them for antimicrobial activity by Kirby baur agar diffusion method against bacteria like *Bacillus subtilis, Micrococcus luteus, Escherichia coli, Pseudomonas aeruginosa* and *Staphylococcus aureus* on the muller hinton agar medium. Ciprofloxacin was used as standard drug [8].

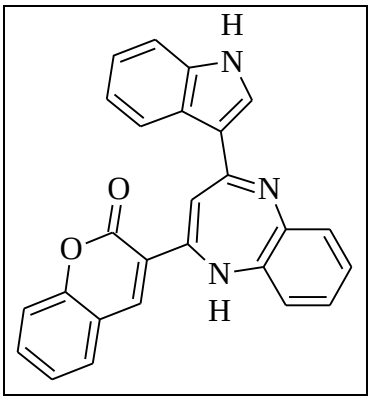

Fig 10

Janardan Singh Yadav *et al*.,(2011) synthesized series of 1,5-benzodiazepines and 1,5-benzothiazepines by microwave irradiation techniques to evaluate their antibacterial and antifungal activity by disc diffusion method against bacteria like *Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa* using Cifuroxacin as standard drug, fungi like *Candida albicans* and *Aspergillus niger* using Fluconazole as standard drug. Compounds showed moderate antibacterial and significant antifungal activity [9].

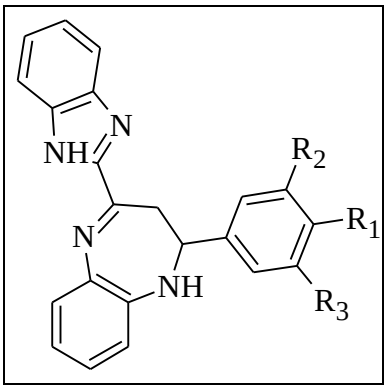

Fig 11

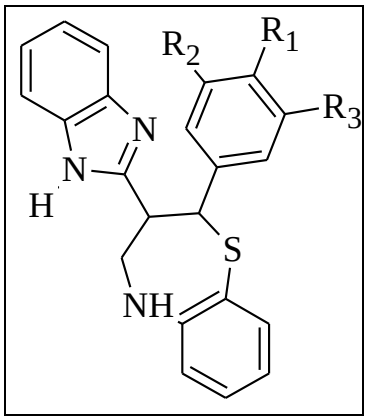

Fig 12

Archana Y Vibhute *et al*., (2011) synthesized derivatives of 2-methyl-4-(substituted phenyl)-1,5-benzodiazepines to screen them for antimicrobial activity by disc diffusion method against *Escherichia coli, Bacillus subtilis, Xanthomonas citri* and *Ervinia carotovara*. Compounds exhibited better antibacterial activity [10].

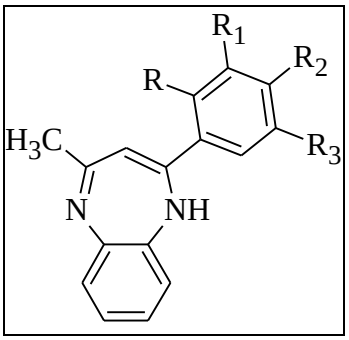

Fig 13

Kamal M El-Gaml *et al*., (2012) synthesized a series of [1,5]-benzodiazepine derivatives to assess their antimicrobial activity by serial plate dilution method against *Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli* and *Candida albicans*, where Ampicillin and Nystatin were used as standard drugs. Compounds showed moderate antibacterial and antifungal activity [11].

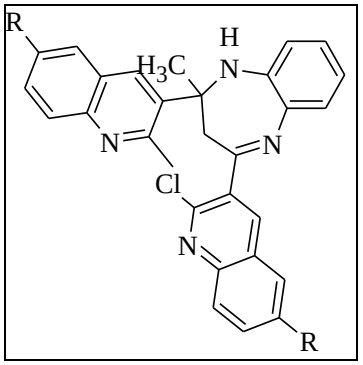

Fig 14

Shahid Shaikh *et al*., (2013) synthesized a series of 2,3-dihydro-1,5-benzodiazepine derivatives to screen them for antimicrobial activity by cup-plate agar diffusion method against bacteria like *Bacillus subtilis, Staphylococcus aureus, Escherichia coli* and *Salmonella typhi*, fungi like *Aspergillus niger, Aspergillus oryzae, Aspergillus fumigatus* and *Candida parapsilosis*.Compounds showed significant moderate activity. Standard drug used was Ampicillin [12].

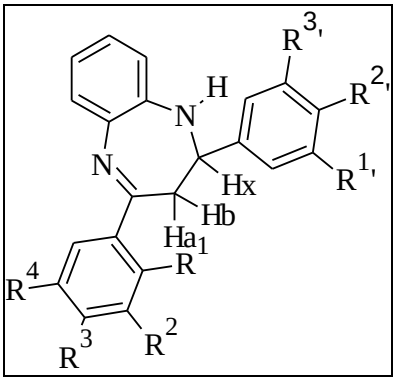

Fig 15

S S Ilango *et al*., (2013) synthesized series of some novel 1,5-benzodiazepine derivatives to screen them for antimicrobial activity by disc diffusion technique, where sterile muller hinton agar plates were prepared for bacteria against *Escherichia coli* and *Staphylococcus aureus*, fungi like *Candida albicans.* Standard drugs used were Amikacin, Ciprofloxacin, Norfloxacin, Clotrimazole, Nystatin. Compound 16f showed an excellent antibacterial activity against *Staphylococcus aureus* and 16g showed better antifungal activity against *Candida albicans* [13].

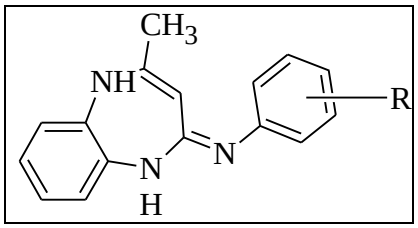

Fig 16

Reena Singh *et al*., (2013) synthesized series of 2,4-disubstituted-1,5-benzodiazepine derivatives to screen them for antimicrobial activity by Kirby-bauer disc diffusion method against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa.* Compounds exhibited significant antimicrobial activity [14].

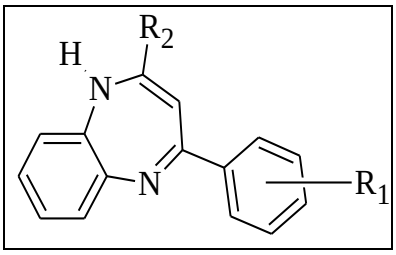

Fig 17

S Ponnuswamy *et al*., (2015) synthesized N-acetyltetrahydro-1,5-benzodiazepines to evaluate their antimicrobial activity by disc diffusion technique using muller hint agar medium against bacteria like *Proteus mirabilis, Staphylococcus, Escherichia coli, Enterococcus faecalis* and *Klebsiella*, fungi like *Aspergillus niger, Aspergillus flavus, Aspergillus oryzae, Aspergillus fumigates, Tricoderma viride,* where Chloramphenicol was used as standard drug. Compounds showed highly significant antimicrobial activity [15].

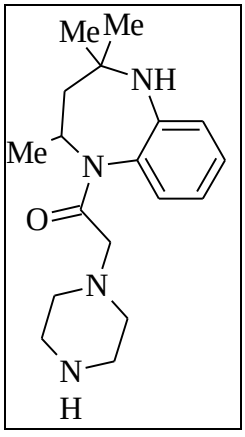

Fig 18

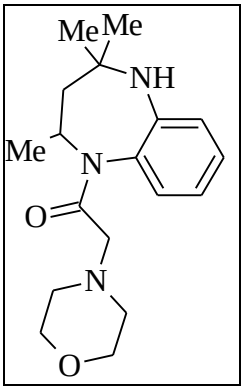

Fig 19

Dr Shrikrishna D *et al*., (2017) synthesized series of 1,5-benzodiazepines derivatives by microwave irradiation techniques to screen them for antibacterial activity by paper disc diffusion plate method. Compounds exhibited highly significant antibacterial activity. Standard drug used was Penicillin [16].

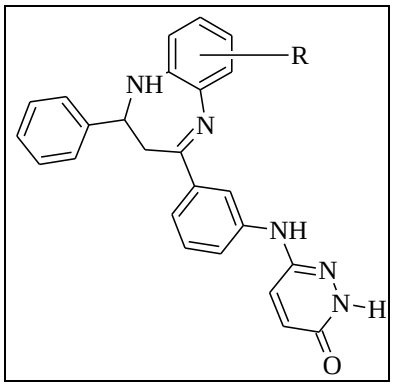

Fig 20

Apoorva misra *et al*., (2018) synthesized bioactive pyrimidine derivatives of 1,5-benzodiazepine. Compounds which are synthesized exhibits strong antibacterial activity against bacteria like S.aureus and E.coli, while mode of action was confirmed through FE-SEM imaging and through molecular docking studies showed that compounds act through bacterial DHFR inhibition [17].

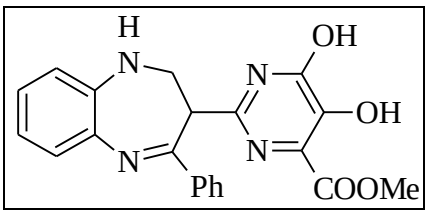

Fig 21

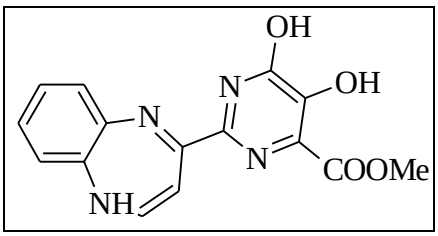

Fig 22

Nisheeth C Desai *et al*., (2020) synthesized a series of pyrazole bearing benzodiazepine derivatives to screen them

for antimicrobial activity by serial dilution method against bacteria like *E.coli, P.aeruginosa, S.aureus* and *S.pyogenes*, fungi like *C.albicans, A.niger, A. clavatus.* Compounds exhibited greater antibacterial and antifungal activity [18].

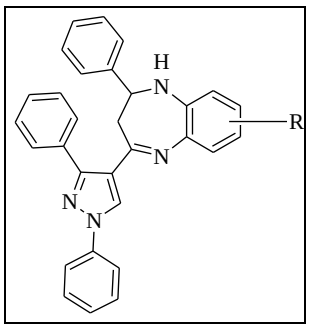

Fig 23

Chhaya S Karle *et al*., (2020) synthesized a series of 2,3-dihydro-1H-1,5-benzodiazepine derivatives to evaluate their antimicrobial activity by well diffusion method against bacteria like *Staphylococcus aureus* and *Escherichia coli*, fungi like *Aspergillus*. Compounds exhibited good antibacterial and antifungal activity [19].

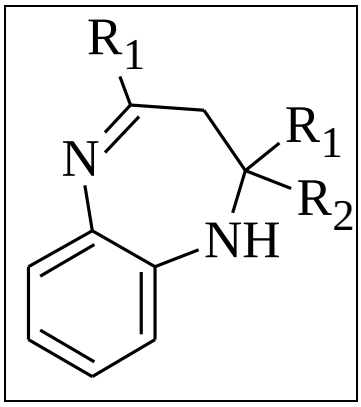

Fig 24

Malath Khalaf Rasheed *et al*., (2021) synthesized series of 1,5-benzodiazepines derivatives containing cyclic imides and mannich bases to screen them for antibacterial activity by disc and well diffusion method against bacteria like *Escherichia coli* and *Bacillus pumilus*, antifungal activity by cup-plate method against fungi like *C.albicans*. Standard drug used were diazepam for antibacterial and Nystatin for antifungal activity. Compounds showed better antimicrobial activity [20].

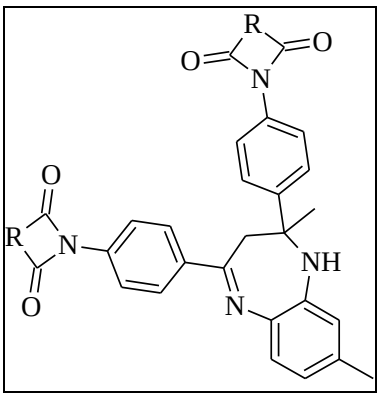

Fig 25

Acknowledgement
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