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A Study on Biologically Active Chalcone Based Benzodiazepines

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ABSTRACT – Heterocycles that include nitrogen are now indispensable to humanity. The majority of the major pharmaceuticals on the market are composed of heterocycles that include nitrogen. One such substance is benzodiazepine, which was shown to have potential as an anti-anxiety medication in 1955. A novel class of chalcone-based benzodiazepines continues to receive the most attention because of their enhanced pharmacological, medicinal, and biological actions. The present study covers the chemistry of some important biologically active chalcone-based benzodiazepines.

Keywords: *Benzodiazepines, Chalcones, Heterocycles and Pharmaceuticals.*

I. Introduction

Benzodiazepines are essential class of heterocycles having nitrogen atoms in the bicyclic ring [1]. The first benzodiazepine Chlordiazepoxide developed in 1955 by Leo H. Sternbach showed excellent sedative, anticonvulsant and muscle relaxing effects [2]. Later, Scientists developed many Benzodiazepine based drugs like diazepam, oxazepam and clonazepam etc.[3] Further studies on benzodiazepines led to the conclusion that they exhibited good anti-cancer[4,5], antibacterial[6], antifungal[7], anti-inflammatory[8,9], antitubercular[10], and anticonvulsant properties[11,12]

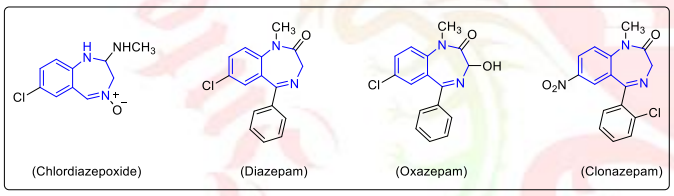

Figure 1 Benzodiazepine based Drugs.

Chalcone, a biologically active compound was extracted naturally from plants and was used for the formation of many flavonoids and isoflavonoids heterocycles.[13-16] Chalcone being a biologically active compound itself reported many properties like antibacterial[17], antioxidant[18], antimycobacterial[19], antitumor[20], antituberculosis[14], and cytotoxicity[21]. Apart from this, they are also used to synthesise many heterocycles such as benzodiazepines [22], pyrazolines [23, 24], isoxazoles[25] etc. The chapter discusses the biological activities of benzodiazepines which are synthesised using chalcones as starting materials.

II. Biological properties of chalcone based Benzodiazepines

Dulawat et al. synthesised and screened aryl substituted 1,5-benzodiazepines for their antibacterial studies and with 200 µg/ml concentration in N,N-dimethyl formamdie solvent against various gram negative and gram positive bacteria. The final molecules with -OCH_3 and -OH substitution showed maximum antibacterial property and the rest of molecules exhibited the inhibition activity appears in between 21-26mm.[26]

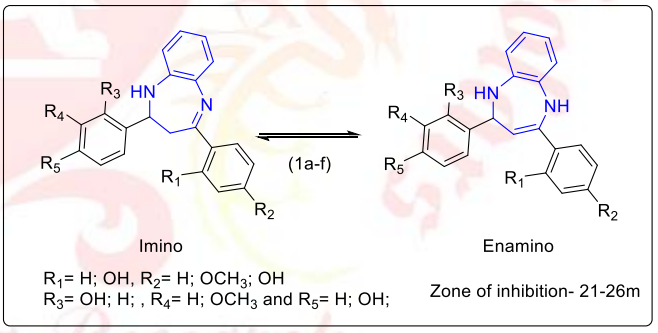

Figure 2 Antibacterial activity of aryl substituted 1,5-benzodiazepine derivatives

Bhatia et al. tested newly developed 2,4-disubstituted 1,5-benzodiazepines for their antibacterial activities against S. aureus and P. aeruginosa. The result showed that the compounds exhibited good antibacterial property and, particularly those having substituents 4-Cl (2d) and 4-NO2 (2e), showed maximum property..[27]

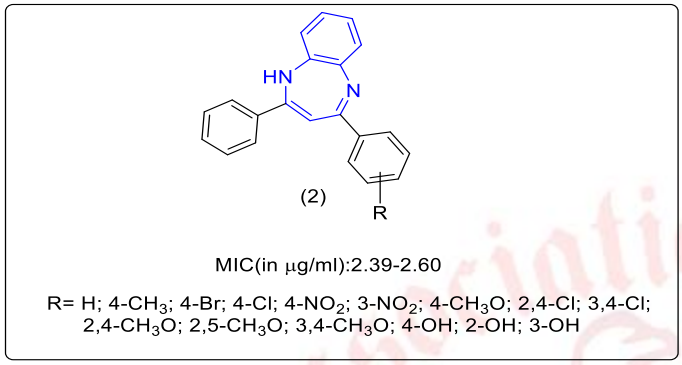

Figure 3 Antibacterial activity of 2,4-disubstituted 1,5-benzodiazepines

Kamal et al. described the anti-cancer property of various cinnamido-pyrrolo [2,1-c][1,4]-benzodiazepines against 60 human cancer cell lines. The **compound 3a** was found to be most potent especially against leukaemia, CNS, prostrate and melanoma cancerous cell lines with GI_{50} values in range of 68-732 µM.[28]

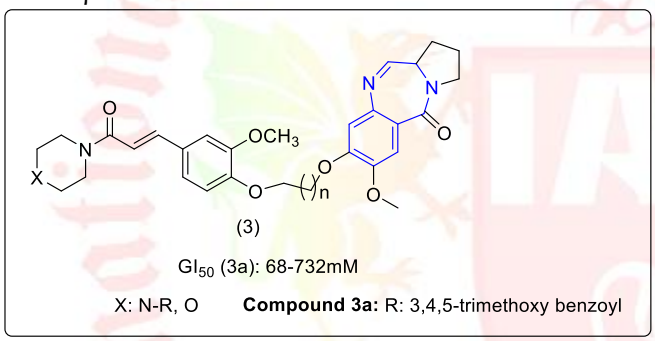

Figure 4 Anti-cancer property of various cinnamido-pyrrolo [2,1-c][1,4]-benzodiazepines

Hussain et al. recorded the antibacterial as well as antifungal properties of derivatives of chalcone based benzodiazepines. The result showed that the compounds were not much effective and showed only moderate inhibition activity appears in between 14-21mm.[29]

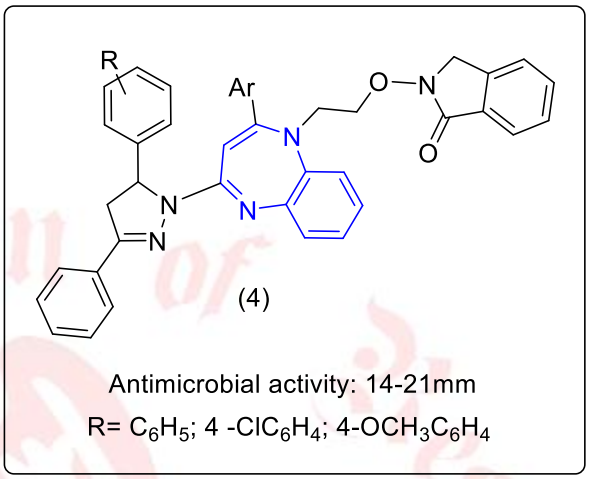

Figure 5 Antimicrobial property of chalcone based benzodiazepines

Srivastava and Yadav evaluated antimicrobial activities of chalcone based benzodiazepines against gram negative and gram positive bacteria along with some fungal agents. The result showed that the compound proved to be a better antifungal agents with zone of inhibition values of 12-16mm while the antibacterial property showed by them was of moderate nature with values of 20-34 mm.[30]

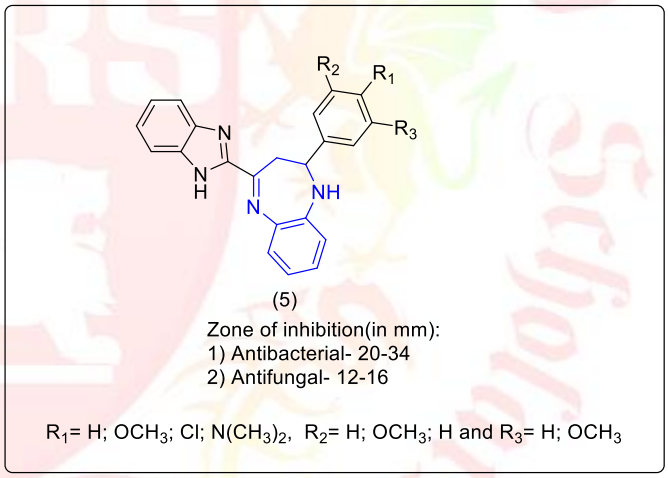

Figure 6 Antimicrobial activity of compound reported by Srivastava and Yadav

Suryawanshi Venkat S in his experimental result showed the contribution of electron withdrawing groups in enhancing the antimicrobial activities of chalcone based benzodiazepines. The antimicrobial activity was evaluated against gram positive, gram negative and a fungal strain. The results showed promising activity against all the bacterial and fungal strains used in the experiment with MIC value in the range or 2-25 µg/ml.[31]

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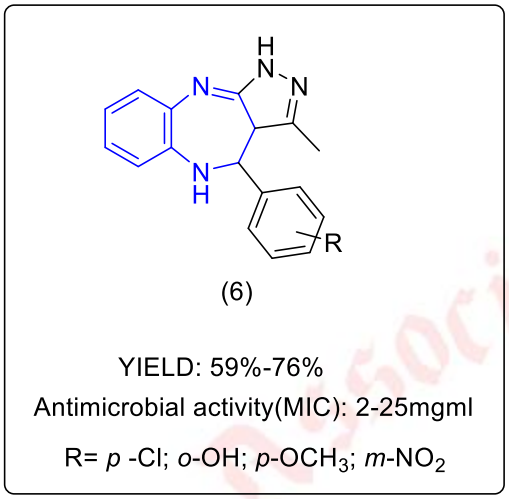

Figure 7 Role of electron withdrawing group in antimicrobial activity.

Salve and Mali showed the antimicrobial activity of various chalcone based benzodiazepines. The compounds were tested against different bacterial species and the experimental outcome showed that the compounds with substituents Cl, Br, OCH_3, CH_3 had maximum antibacterial activity. Furthermore, the compounds were synthesised for their antifungal activities and the result showed that compounds with substituents Cl, Br, NO_2, CH_3, OCH_3 had maximum antifungal property.[32,33]

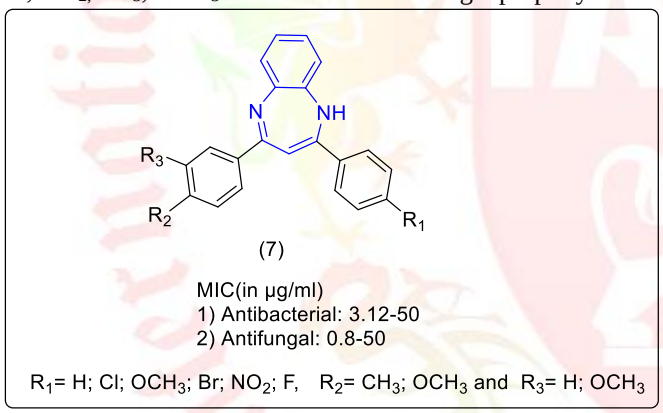

Figure 8 Antimicrobial activity of benzodiazepines reported by Salve and Mali

Saikh and Baseer checked the antibacterial activity of various chalcone based benzodiazepines against various gram negative and gram positives bacterial strains. The test solution of compounds were taken at concentration of 200 ppm put in 5% of DMSO. The compounds **8b (-OH, Br,-CH_3), 8h (-OH, -I) and 8j (-OH, -Cl,-Br)** were identified as potential antibacterial agents (Inhibition range: 10-20nm). These compounds were also tested for their antifungal activity and observed that the inhibition zone in the range of 0-20nm.[34]

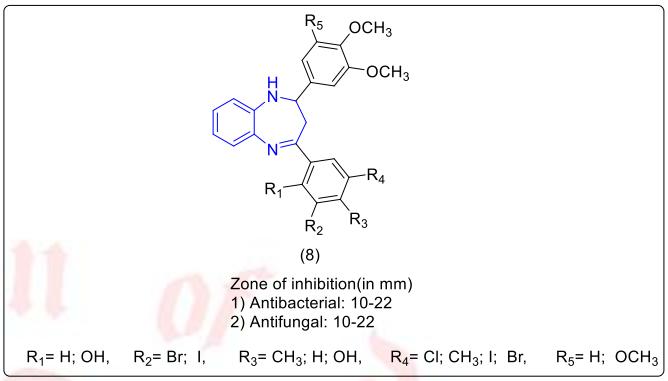

Figure 9 Antimicrobial activity of chalcone based Benzodiazepines.

Sharma et al. synthesised novel chalcone based benzodiazepines and tested the spermicidal and antibacterial activities. Among the synthesized compounds, 9b (-OCH3,-H), 9h(-Br) and 9j (-Cl) were shown the 50% reduction in sperm motility and the fluoro substituted compound 9f and 10f shown 25% sperm motility. The antibacterial inhibition activity was observed in the range of 8-10mm.[35]

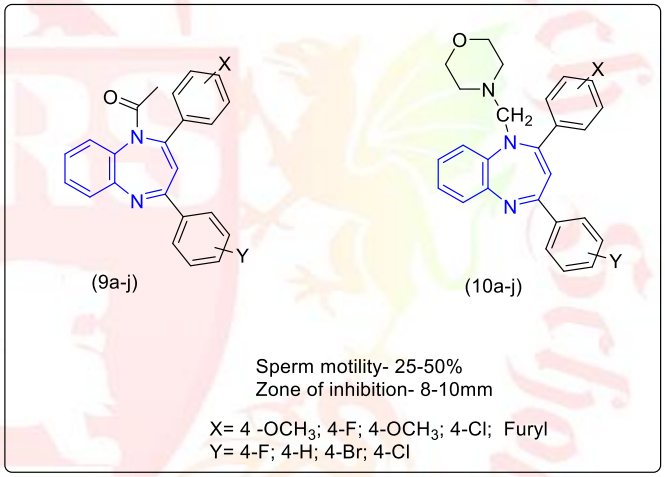

Figure 10 Antibacterial and spermicidal activity of chalcone based Benzodiazepines.

Sharma and Kumar developed chromone substituted 1,5 benzodiazepine and evaluated the product for its antibacterial property against Bacillus bacteria. The result came out to be very promising as the compound showed 100% inhibition against this strain of bacteria.[36]

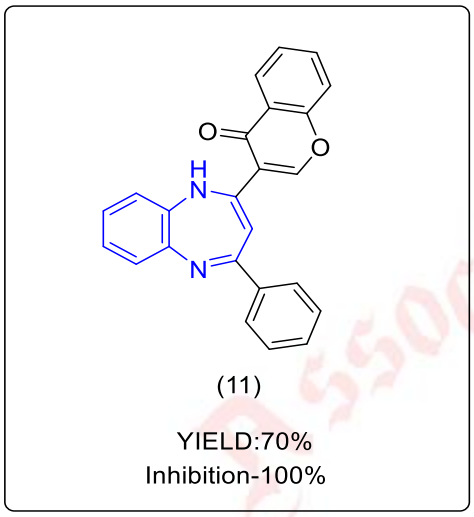

Figure 11 Complete inhibition of bacillus bacteria by chalcone based benzodiazepine

Subbagh et al. confirmed exceptional DHFR inhibition of chalcone based benzodiazepines with mono methoxy and di-methoxy substituents with the half maximal concentrations of 0.004-0.6μM and also observed that the presence of halo substituents were ineffective toward the DHFR inhibition.[37]

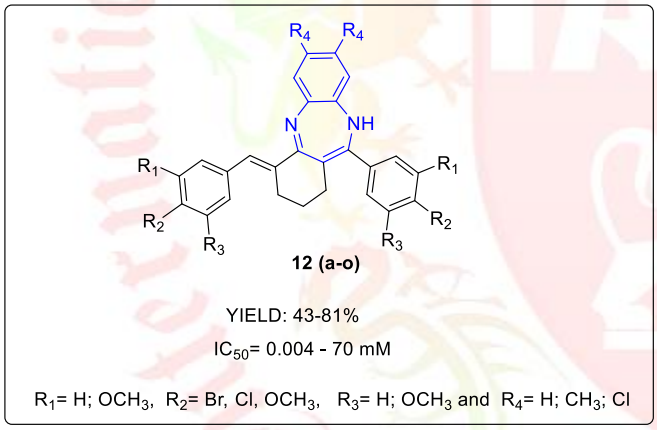

Figure 12 DHFR inhibition of chalcone based benzodiazepines

III. Conclusion

Chalcone-derived benzodiazepines have procured a predominant place in bioorganic and medical chemistry due to their notable pharmacological and biological applications. The present study summarizes an overview of the different biological activities of various benzodiazepines derivatives with the available data.

IV. Acknowledgement

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