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ASSESSMENT OF 1, 5-BENZOTHIAZEPINES AND ITSPOSSIBLE HEALTH BENEFITS

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Abstract

This thesis describes the synthesis of a library of chalcones and several flavanones and 1, 5-benzothiazepines derived from chalcones and some biological studies of these compounds against neuraminidase (NA). The environmentally benign one-pot method using PMA/SiO_2 in ethanol has successfully been applied toward the preparation of flavanone analogues from 2'-hydroxychalcones, 2'-aminochalcones and 2'-mercaptochalcones in reasonable yields. Reactions were screened in a variety of parameters, including solvents, temperatures, reaction time and amount of catalyst used. The nature of the solvent played a key role in the reaction where the reaction performed well in a polar protic solvent such as ethanol and only moderately in a polar aprotic solvent like acetonitrile.

INTRODUCTION

Thiazepines and diazepines are seven-membered heterocyclic rings with two hetero iotas. Benzothiazepine and benzodiazepine moieties are two subgroups of this group of heterocycles in which the thiazepine or diazepine rings are intertwined to a benzene ring.1, 5-Benzodiazepines are an imperative class of organic mixes. They are powerful pain relieving, against convulsant and narcotic prescriptions in light of the fact that they are totally consumed as well as they are lipophilic, they can enter the mind effortlessly. Consequently, this class of heterocyclic mixes keeps on drawing in numerous scientists and pharmacologists since 1955 when the primary benzodiazepine "Chlordiazepoxide" (Librium) was found by Leo Sternbach and thusly incorporated by Hoffmann_ Laroche in 1960. Business "diazepam" was marketed in 1963 out of the blue. In light of molecular structures, benzothiazepines can be separated to some different subclasses, i.e. 1,4-

benzothiazepines, 4,1-benzothiazepines and 1,5-benzothiazepines. 1,5-Benzothiazepines extensively utilized as against feedant, sedative, energizer, CNS stimulant, calcium channel blocker hostile to microbial specialist. Additionally, 1, 5-benzothiazepines have been joined with other understood pharmaceutically dynamic mixes, for example, benzofuran subordinates to shape a solitary atom with enhanced pharmaceutical properties. The general structure of 1,5-benzodiazepine and 1,5-benzothiazepine is appeared in Figure 5.1 [1].

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Figure 5.1 General structure of 1, 5-benzodiazepines and 1, 5- benzothiazepines

1, 5-benzodiazepines are well established in pharmacological and medicinal chemistry. However, limited number of studies had been carried out on the synthesis and SAR for 1,5-benzothiazepines, especially in terms of anti-viral activities [2].

ANTI-VIRAL EFFECT:

The counter popular impacts of benzodiazepines and benzothiazepines have for the most part been centered around HIV and hepatitis infections. Nicol and colleagues demonstrated that dibenzothiazepinethione subordinates to have hostile to viral exercises against Varicella-Zoster infection, hepatitis B and HIV-1.

In another investigation, Delpa and colleagues indicated 1, 4-benzothizapines and 1,4-benzodiazepines with a peptide side-tie to have inhibitory impact on hepatitis B, and D infections by influencing the authoritative of the hepatitis infection to annexin V. A gathering of thiazolothiazepines have additionally been accounted for to guarantee candidates for the HIV treatment by focusing on the integrase catalyst. Tetrahydro-imidazo [4, 5, 1-jk][1,4]-benzodiazepin-2(1H)- one and - thione (TIBO), are likewise known for their movement on HIV-1 infection. A number of tricyclic subsidiaries of 1,4-benzothiazine and 1,5-benzothiazepine were additionally answered to have against HIV properties in vitro. Furthermore, 2H-pyrrolo [3, 4-b] [1,5] benzothiazepine subordinates were likewise answered to be intense candidates for HIV-1. Our current interest in 1,5-benzothiazepines has been motivated by the counter popular properties of this class of mixes. Consequently, in this examination we investigated on neuraminidase inhibitory movement of this class of heterocycles [3].

PLATELET AGGREGATION INHIBITORY EFFECT:

Platelet aggregation is a process in which platelets in the blood will clump together. This process can eventually lead to the formation of clot in the blood vessels and cause cerebral vascular complications. Few 1,5-benzothiazepine derivatives bearing N-amino groups (Figure 5.2) have been reported to have potent platelet aggregation caused by platelet activating effectors, collagen, epinephrine and arachidonic acid.

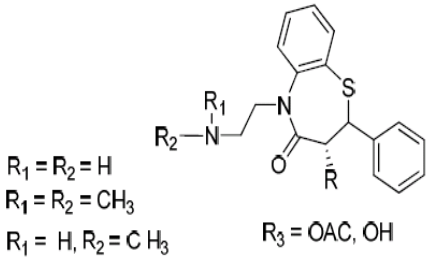

Figure 5.2 Structure of 1,5- bezothiazepines with potential anti-platelet aggregationproperties

ANTI-CANCER EFFECT:

The anti-cancer properties of benzothiazepine derivatives have been shown in number of studies. For example, 1,4- benzothizepine and its analogues synthesized by Garofalol and co-workers were shown to have potent anti-tumors activities against murine L1210 and human lymphoblastic CCRF_CEM leukemia cell growth. Evaluation of some synthesized pyrrolo [1, 5] benzoxa (thia) zepine analogues against tumor cell showed these compounds to be promising potent apoptotic agents. 1, 4-Benzodiazepine-2, 5-diones was also reported to exhibit anti-tumor activity by disrupting Hdm2:p53 interaction [4].

ANTI-BACTERIAL AND ANTI-FUNGAL EFFECT:

A number of benzothiazepines have been investigated for their anti-bacterial and anti-fungal activities. A group of synthesized methylene-bis-benzofuranyl-[1, 5]-benzothiazepines were found to have *in vitro* anti-bacterial activities, nearly as active as those well known anti-bacterial medicines such as streptomycin and penicillin. Substitution at the 4^{th} position of this class of benzothiazepines was observed to play a key rule in enhancing the potent bioactivity. Moreover, these compounds exhibited moderate to good anti-fungal activities. 2, 4-Diaryl-2,3-dihydro-1,5-benzothiazepines and their 1, 1- dioxide derivatives were also found to have anti-bacterial and anti-fungal properties [5].

CNS ACTIVITY EFFECT:

1, 5- Benzothiazepine derivatives such as thiazesim and quentiapine have been clinically approved to be effective candidates for CNS (Central Nervous System) disorders. Pyrrolo-derivatives of benzothiazepines have been shown to have excellent sedative action comparable with diazepam. Imidazolo-derivatives were also reported to be fairly active on CNS inhibition with notable anti-inflammatory activities. Furthermore, oxadiazolo-derivatives have been tested against seizures and have exhibited comparable activity to clobazam [6].

CONCLUSION

The data presented in this review clearly demonstrate the high synthetic potential of o-aminothiophenol (1) and its derivatives. Many biologically active 1,5-benzothiazepine derivatives have been obtained on the basis of reactions of these reagents and carbonyl compounds and other functional groups.

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