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VARIOUS ACTIVITIES OF AZETIDINE-2-ONE DERIVATIVES - A REVIEW

DHEEPIKA.S, DEEPAK.M, CHANDRU.B .S, DURAISEELAN, M.VIJEY AANANDHI AND S.RAMACHANDRAN*

Department of Pharmaceutical Chemistry and Analysis, Vels Institute of Science Technology and Advanced Studies (VISTAS), Chennai-600 117, Tamilnadu, India

***Corresponding Author: Dr. S.Ramachandran: E Mail: ramachandrans.sps@velsuniv.ac.in**

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ABSTRACT

Many biological components required for life are heterocyclic molecules. Many antibiotics found in nature are heterocyclic compounds. For us as drugs, modern society is reliant on synthetic heterocycles. Antibacterial, antifungal, anticonvulsant, anti-inflammatory, cardiovascular, and antidepressant properties have been described for azetidine-2-one derivatives. Antimicrobial properties have been reported for pyridine derivatives. In organic chemistry, four-membered nitrogen heterocycles like -lactam and azetidines are excellent substrates for designing and manufacturing biologically active molecules. The many activities of azetidine are depicted in this article.

Keywords: Azetidine-2-One Derivatives, Antibacterial, antifungal, anticonvulsant, anti-inflammatory, cardiovascular, and antidepressant properties

INTRODUCTION

Antibacterial **[1, 2]** and antifungal **[3]** properties have been observed for azetidinone derivatives. Antimicrobial properties have been reported for pyridine derivatives. nitrogen-containing heterocyclic with four members. In organic chemistry, substrates like 2-azetidine are useful. Azetidinones are a type of antibiotic that has a number of biologically interesting properties. Antibacterial, antifungal, anti-inflammatory, herbicidal, hypocholesterolemic, anticonvulsant, anti-

tubercular, anticancer, and antibiotic activity can be found in a vast variety of 3-chloromonocyclic ß-lactam rings with substitution at positions 1 and 4. They also work as enzyme inhibitors and are effective against the central nervous system. These are azetidine carbonyl compounds with a carbonyl group at position -2. They are also referred to as 2-azetidine or -lactams.

ACTIVITIES

ANTIMICROBIAL ACTIVITY

The most important nitrogen containing heterocycles of pyridine containing substituted phenyl azetidine-2-ones have found pharmacological application such as antibiotics and these compounds also have practical importance. The structure of the new derivatives was confirmed by the spectral data and elemental analyses. Out of five new derivatives, three were revealed mild to moderate activity compared with Streptomycin & Fluconazole as a reference standard. Among this new series, 3-chloro-1-(4-fluoro phenyl)/(4-chloro phe-nyl)-4-(pyridine-3-yl) azetidine-2-one (**4a & b**) were found most activity **[4]**.

ANTITUBERCULAR ACTIVITY & ANTI-INFLAMMATORY ACTIVITY

The compounds were produced and evaluated for structure activity relationship for Phospholipase A2 (PLA2) [E.C. 3.1.1.4] enzyme inhibition, according to Mayur etal [5]. The anti-tubercular, PLA(2) enzyme inhibitory, and in vivo anti-inflammatory actions of azetidin-2-one derivatives in mice are highlighted. Based on the first action against Mycobacterium tuberculosis, analogues of azetidin-2-one were created (Mtb).

The anti-tubercular activity of certain azetidin-2-one compounds disclosed here was moderate to good. Two compounds (4f) and (4g) in particular had MIC values of 1.56 and 0.78 microg/mL against the Mtb H(37)Rv strain, respectively. In the azetidin-2-one series shown here, chloro substitution on aryloxy acid appeared to improve antimycobacterial action as well as PLA2 inhibition. The anti-inflammatory properties of azetidin-2-one analogues have also been determined. The findings reveal a link between anti-inflammatory and anti-tubercular action and PLA2 enzyme expression.

ANTICONVULSANT ACTIVITY

Rahul Mishra **[6]** had synthesised a novel series of ten N-(aryl)-2-(2-methyl-1H-imidazol-1-yl)acetamides (5a-j) by reacting 2- methylimidazole (4) with the corresponding ω- chloroacetanilides (3a-j) in Dimethly Formamide and potassium carbonate. The compounds have been characterized on the basis of elemental analysis and spectral data. All the synthesized compounds were screened for their anticonvulsant activity. Among the

compounds subjected to anticonvulsant activity, compounds 5a, 5b, 5d, 5f, 5g, 5h, 5i and 5j, at a dose of 100mg/kg body weight i.p. showed significant anticonvulsant activity ($p<0.01$) as they delayed the onset of convulsions. The compounds 5a, 5d, 5h, 5i and 5j also decreased the duration of seizures significantly ($p<0.01$ and $P<0.05$) and the results were comparable to the diazepam treated group. Compound 5g is the most active molecule as; it increased the onset of convulsion time to nearly two fold and comparable duration of action to that of diazepam.

CARDIOVASCULAR ACTIVITY

Several steroid derivatives have prepared as inotropic drugs; however, there are few reports on azetidine-steroid derivatives with inotropic activity. The aim of this study was to synthesize four azetidine-steroid derivatives (compounds 3 to 6) to evaluate their biological activity on left ventricular pressure. The first stage was achieved by preparation of azetidine-derivatives using reactions of etherification and addition. The second stage involves the evaluation of biological activity from azetidine derivatives on left ventricular pressure in a heart failure model using estrone as control. The results showed that only compound 3 increases left ventricular pressure compared with estrone, compounds 2 and 4 to 6. In conclusion, the positive inotropic effect exerted by compound 3 depends on the functional groups involved in their chemical structure **[7]**.

ANTIOXIDANT ACTIVITY

The Schiff bases and azetidines are important intermediates used in synthesis of several therapeutics and medicinally contributing molecules. This research was focused on synthesis of Schiff bases and azetidines, characterization and subsequent evaluation of their in-vitro antioxidant potentials. Methods: In this work, the Schiff bases and azetidines were derived from phenyl urea derivatives. They were tested qualitatively for melting point and characterized by TLC, FTIR, 1H-NMR, 13C-NMR and GCMS for their chemical structures. The Schiff bases and azetidines were screened for in-vitro antioxidant activity by employing hydrogen peroxide free-radical inhibition method. The compounds 1-[(1E)-2-(3-fluorophenyl) ethylidene]-3-(4- ethoxyphenyl) urea and 3-chloro-2-(3-fluorophenyl)-N-(4-methoxyphenyl)-4-oxoazetidine-1-carboxamide were derived by nucleophilic addition and cycloaddition reactions and had displayed moderate to significant antioxidant effects compared to ascorbic acid. Thus, medicinally and chemically important Schiff bases and azetidines were synthesized successfully. Conclusion: The

present research can be a base to explore further simple and easy means of other synthetic schemes in processing of complex and potent bulk chemicals as well as medicinal agents **[8]**.

Alegaon S G *et al*., **[9]** described the synthesis of new (Z)-2-(5-arylidene-2, 4-dioxothiazolidin-3-yl) acetic acid derivatives. The compounds were also evaluated for their anti-microbial and anti-cancer activities.

Babaoglu K *et al*., **[10]** synthesized substituted thiazolidinediones for the inhibition of enzymes-dTDP-rhamnose synthesis which is essential in the biosynthetic pathway of Mycobacterium tuberculosis.

Malipeddi H *et al*., **[11]** synthesized a series of twelve novel thiazolidinediones by cyclo condensation of various Schiff base of amino thiadiazole with thioglycolic acid and the compounds were evaluated for in vitro antitubercular activity by Microplatealamar assay method showed that two compounds showed higher antitubercular activity than standard drugs.

Cheptea C *et al*., **[12]** reported the synthesis and evaluation of acute toxicity and anti-tumor activity of thiazolidine-2, 3-disubstituted derivatives of 1'-acetamidyl-5'-nitro indazole.

Bhaumik A *et al*., **[13]** reported the synthesis, characterization, and evaluation of the anticonvulsant activity of some novel 4-thiazolidinone derivatives using MES induced convulsions in mice.

SUMMARY AND CONCLUSION:

The literature survey shows that azetidin-2-ones has diverse biological potential. Azetdine-2-one derivatives has a broad spectrum of pharmacological properties i.e. Antifungal, Anti-tubercular, Antimicrobial, Antioxidant, Cytotoxic, Anti-inflammatory, Analgesic activities. Antimicrobial activity is the most potent activity of the thiazolidine-4-ones. Anticonvulsant and cardiovascular activities are the most encouraging activities of azetidine-2-ones for the researchers which are the requirement of today's medicinal field.

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