Activities of Thiazolidine-4-one and Azetidine-2-one Derivatives- A Review

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ABSTRACT:
Thiazolidine-4-ones containing thiazole moiety have been synthesized by condensing 6-amino Coumarin, Isatin and Primary amines, and aromatic aldehydes. Azetidine derivates were synthesized followed by cyclizations by C-N bond formation and by the C-C bond formation, the amine-catalyzed cycloaddition of allenoates and imines, photocycloadditions of imines and alkenes, ring contraction and expansion rearrangements, and reduction of azetidine-2-ones (β-lactams). Thiazolidine-4-ones has been considered as a magic moiety because it posses almost all types of biological activities such as Antifungal, Antitubercular, Antimicrobial, Antioxidant, Antibacterial, Cytotoxic, Anti-inflammatory, Analgesic, Anti YFV (yellow fever virus) activities. Azetidine-2-one derivatives were reported to possess antibacterial, antifungal and antidepressant activity, anticonvulsant activity, anti-inflammatory activity and cardiovascular activities, antimycobacterial activity, antihypertensive activity. This article is a review of various biological activities of thiazolidine-4-ones and Azetidine-2-ones derivatives

KEYWORDS: Thiazolidine-4-one, Azetidine-2-one, Biological activity.

INTRODUCTION:

The chemistry of heterocyclic compounds is as logical as that of aliphatic or aromatic compounds. Their study is of great interest both from the theoretical as well as practical importance. Various compounds such as alkaloids, essential amino acids, vitamins, hemoglobin, hormones, a large number of synthetic drugs and dyes contain heterocyclic ring systems. There Heterocycles containing sulphur and nitrogen atoms in the core structure, it shows several pharmacologically and biologically active compounds.

Thiazolidine-4-ones[1] are usually solids, often melting with decomposition but the attachment of an alkyl group to the nitrogen lowers the melting point. Thiazolidine-4-ones are derivatives of thiazolidine with a carbonyl group at the fourth position. The carbonyl group of thiazolidine-4-ones is highly un-reactive.

The nucleus is also known as a wonder nucleus because it shows different types of biological activities. Thiazolidine-4-ones are important compounds due to their broad range of biological activities and pharmacological properties i.e. Antifungal[2], Antioxidant,[3] Cytotoxic[3], Anti-inflammatory[3], Analgesics, Anti YFV (yellow fever virus) activity, Antitubercular[4] Antimicrobial[5-8], Antibacterial[9], Thiazolidinediones[10] are the derivatives of thiazolidine which belong to an important group of heterocyclic compounds.

Azetidinone is a ß-lactam cyclic amide with four atoms in a ring. Traditionally ß-lactam is a part of structure of broad spectrum antibiotic class of drugs- penicillins and cephalosporins.

The β-Lactam nucleus is the key to the biological activity of a large class of compounds characterized by the presence of this four-membered ring and differentiated by side chains, unsaturations, hetero atoms, and, in many cases, by the presence of five- or six-membered rings

Azetidinones are a part of the antibiotic structure, which possesses interesting biological activities. A large number of 3-chloromonocyclic ß-lactam rings having substitution at positions 1 and 4 exhibits powerful antibacterial, antifungal, pharmaceutical, anti-inflammatory, herbicidal, hypocholesterolemic, anticonvulsant, anti-tubercular,

anticancer and antibiotic activities. They also function as enzyme inhibitors and are effective against the CNS. These are carbonyl derivatives of azetidine containing carbonyl group at position -2. They are also known as 2-azetidine or more commonly β-lactams

SAR of Thiazolidine-4-ones:

- The thiazolidine-4-ones bearing 2,4-dichlorophenyl group hydroxyl methoxy phenyl 4-chlorophenyl group and dimethylamino group in the second position have shown good antitubercular activity.
- Thiazolidine-4-ones having 2,4-dimethyl amino phenyl at second position shows good antitubercular activity in all the species.[11]
- The unsubstituted phenyl group at the fourth position of thiazolidine-4-one increases antioxidant activity.
- The unsubstituted phenyl ring at the third position shows less activity against gram-negative strains and moderately effective against gram-positive strains.[12]
- The nitro group at meta and para position of the aryl ring respectively, possess stronger antibacterial activity electron-withdrawing moiety shows less activity compared to electron-donating groups eg OCH3. NMe[13]

Activity:

S. Ramachandran, R. Sundararajan *et al*[14] A new series of N-(2-(2-hydroxyphenyl)-4-oxothiazolidin-3-yl) isonicotinamide derivatives were synthesized and it showed good antibacterial activity against *Staphylococcus aureus* and *Escherichia coli.*

K H Patel and A G Mehta[15] had synthesized 2-azetidinones and 4-thiazolidinediones derivatives respectively. The prepared compounds are screened on some strains of bacteria for antimicrobial activity.

KG and Desai KR[16] had synthesized five-membered sulphur-containing heterocyclic derivatives 2-(aryl)-3-[2-(benzothiazolylthio)-acetamidyl]-4-oxo-thiazolidines. All the compounds have been screened for their antibacterial activity against *Escherichia coli* (Gram−ve), *Staphylococcus aureus* and *Bacillus subsitilis* (Gram+ve).

Bhoot *et al*[17] had synthesized 2-(p- tolyl imino)-3-(4-tolyl)-5-[5-(3,4-dichlorophenyl)-2-furylidene]-4-thiazolidinone and derivatives as an antimicrobial agent. Compounds were screened *in vitro* for their antimicrobial activity toward a variety of bacterial strains such as *B. mega, S. aureus, E.coli, P. vulgaris* and fungi such as *Aspergillus niger.*

H. Bhaskar[18], M. Kumar, B. Sangameswaran and B. R. Balakrishnan had synthesized 2-(substituted phenyl)-3-(4,5-diphenyl-1Himidazol-2-yl)-1,3 thiazolidin 4-one (IIIa-e). The compounds were characterized by elemental analysis, 1H NMR, Mass, and IR spectral studies. All compounds were screened for antibacterial and antifungal activity.

P. Shanmugapandiyan, A. Ramesh[19] *et* al had synthesized a new series of 1-(benzothiazol-2'-yl)-3-chloro-azetidine-2-ones and 3-(benzothiazol-2'-yl)-thiazolidin-4-ones. The synthesized compounds were screened for antibacterial (*Staphylococcus aureus, Bacillus cereus, Escherichia coli,* and *Pseudomonas aeruginosa*), antifungal (*Aspergillus niger* and *Candida albicans*) and analgesic activity by writhing reflex method.

P. Shanmugapandiyan *et al*[20] A new series of 2-[4-(azetidine-2-one)-3-Chloro-4-phenyl]-1H-Phenylbenzimidazoles and 2-(thiazolidin-4-one)-Phenyl]-1H-Phenylbenzimidazoles were synthesized. The synthesized compounds were screened for antibacterial (*Bacillus cereus, Escherichia coli, Micrococcus luteus, Klebsiella pneumoniae, Staphylococcus aureus,* and *Salmonella epidermidis*), antifungal (*Aspergillus niger* and *Candida albicans*), analgesic activity by writhing reflex method and anti-inflammatory activity by Carrageenan induced paw edema method.

Alegaon SG *et al.*,[21] reported synthesis, pharmacophore modeling, and *in vitro* anticancer activity of a series of 2-thioxothiazolidin-4-one derivatives.

Eleftheriou P *et al.*,[22] reported fragment-based design, docking, synthesis, biological evaluation, and structure-activity relationships of 2- benzo/ benzisothiazole imino-5-aryliden-4-thiazolidinones as cyclooxygenase/lipoxygenase inhibitors.

Nasr T *et al.*[23] reported the design, synthesis and *in vitro* antimicrobial evaluation of new functionalized 2, 3-dihydrothiazoles and 4-thiazolidinones tagged with sulfisoxazole moiety.

Unsal-Tan O *et al.*,[24] designed and synthesized a series of novel 2-aryl- 3-(4-sulfamoyl/ methylsulfonylphenylamino)-4-thiazolidinones were designed, synthesized and evaluated for their *In vitro* COX-1/COX-2 inhibitory activities.
Havrylyuk D *et al.*[25] synthesized and evaluated anticancer activity of novel 4-thiazolidinone based conjugates with pyrazoline moiety. The screening of antitrypanosomal and antiviral activities of 5-(3-naphthalene-2-yl-5-aryl-4,5-dihydropyrazol-1-yl)-thiazolidine-2,4-diones was also carried out.

Küçükgüzel I *et al.*,[26] reported the design, synthesis, and evaluation of some novel allosteric inhibitors bearing the 4-thiazolidinone scaffold as inhibitors of HCV NS5B polymerase.

Alegaon S G *et al.*,[27] 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.

Vicini P *et al.*,[28] synthesized 2-heteroarylimino-5-benzylidene-4- thiazolidinediones and assayed *in vitro* for their antimicrobial activity against Gram-positive and Gram-negative bacteria, yeasts, and mold.

Aneja D K *et al.*,[29] synthesized a new pyrazolyl-2,4-thiazolidinediones by Knoevenagel condensation and the synthesized compounds were tested for *in-vitro* their antibacterial and antifungal activities.

Babaoglu K *et al.*,[30] 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.*,[31] 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.*,[32] 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.*,[33] reported the synthesis, characterization, and evaluation of the anticonvulsant activity of some novel 4-thiazolidinone derivatives using MES induced convulsions in mice.

Ravindra Kumar *et al*[34] stated that Azetidinones have been synthesized by the cyclo condensation of chloroacetylchloride with Schiff base. The compounds have been characterized based on analytical and spectral data. They have been screened of antibacterial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *E.coli*, and *Salmonella typhi*

Havaldar *et al.*[35] synthesized azetidine analogs by treating 2-oxo-2*H*-chrome-4-yl 2-(benzylidene) hydrazine carboxylates with chloroacetyl chloride in the presence of triethylamine and reported their antibacterial activity.

SUMMARY AND CONCLUSION:

The literature survey shows that thiazolidine-4-ones has diverse biological potential. Thiazolidin-4-one and Azetdine-2-one derivatives has a broad spectrum of pharmacological properties i.e. Antifungal, Anti-tubercular, Antimicrobial, Antioxidant, Cytotoxic, Anti-inflammatory, Analgesic, Anti YFV (yellow fever virus) activities. Antimicrobial activity is the most potent activity of the thiazolidine-4-ones. Anticancer and anti-HIV are the most encouraging activities of thiazolidine-4-ones for the researchers which are the requirement of today's medicinal field.

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