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Short Communication

ANTIMICROBIAL ACTIVITY OF NEW SERIES OF BENZOTHIOPHENE CONTAINING THAIZOLIDINONE DERIVATIVES

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ABSTRACT

Thiazolidinones have become an important class of heterocyclic compounds since their introduction in the form of glitazones into the clinical use for the treatment of diabetes. In addition, this class of heterocyclic compounds possesses various other biological activities such as antihyperglycemic, antimicrobial, anti-inflammatory, anticonvulsant, insecticidal, etc. In the present study thaizolidinone derivatives containing benzothiophene moiety synthesized in our previous study have been evaluated for their antibacterial and antifungal activity against three bacterial *Escherichia coli*, *Pseudomonas aeruginosa, Staphylococcus aureus* and three fungal strains *Candida albicus, Aspergillus niger, Aspergillus fumigatues* using cup or well method. These compounds have exhibited very encouraging results showing inhibition zone from 10 mm to 16 mm against three bacterial strain and from 14 mm to 23 mm against fungal strain which is much closer to zone of inhibition of standard Ciprofloxacin and Griseofulvin respectively.

Keywords: Antibacterial, Antifungal, Thaizolidinone, Benzothiophene

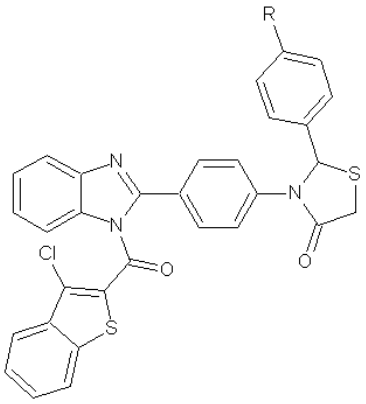
1. INTRODUCTION

Thiazolidinone, a saturated form of thiazole with carbonyl group on fourth carbon has been considered as a moiety of choice as it possesses a broad spectrum of pharmacological activities against several targets. Thiazolidinones belong to an important group of heterocyclic compounds have been extensively explored for their application in the field of medicinal chemistry. The chemistry of heterocycles lies at the heart of drug discovery [1, 2]. Thiazolidinone is one of the most intensively investigated class of five member heterocycles [3, 4]. Thiazolidinone are the heterocyclic compounds having nitrogen and sulfur atoms and are known for a long time for their wide range of interesting biological activities namely anticonvulsant activity, anti-inflammatory activity, anti-tubercular activity, anthelmintic activity, antiviral activity, antifungal activity, antibacterial activity, anticancer activity and anti-HIV activity [5-13] etc. Due to its wide range of biological activity thaiazolidinone ring constitutes a relevant synthetic route in pharmaceutical industry. In fact, such a heterocyclic moiety represents the core structure for number of drugs.

Thiophene ring clubbed with benzene nucleus is known as benzothiophene. In recent year an interest in the chemistry of benzothiophene derivatives increases because of their biological and pharmacological importance. Beside the currently established drugs Raloxifene, Zileuten and Sertaconazole, benzothiophene derivatives are associated with diverse class of biological activities viz. antitubercular [14], antiallergic [15], antibacterial [16], anticonvulsant [17], antifungal [18], antiviral [19] antihistaminic [20], anti-inflammatory [21], analgesic [22] antitumor [23], anticancer [24], neuroleptic [25]. In present study benzothiophene based thiazolidinone derivatives evaluated for their inhibitory action against bacterial and fungal strain.

2. MATERIAL AND METHODS

All the synthesized compounds were used for antibacterial and antifungal tests. The pure culture of pathogenic bacteria and fungus used for activity were sub cultured and characterized by standard method of identification. For evaluation of antimicrobial activity cup or well method was used.



Compound - 5a, 5b, 5c, 5d

R- -H, -Cl, $-OCH_3$, $-N(CH_3)_2$

Fig. 1: Structure of Synthesized Compounds

2.1. Cup or Well method

Nutrient agar medium was sterilized by autoclaved at 15 psi and 121°C for twenty minutes. Sterilized Petri dishes were placed in laminar flow bench. One end of the lid of each Petri dish was lifted and approximately 15- 20 ml. of molten agar medium was poured into it and left for solidification. These were then inoculated with 0.2 mL suspension of organism by spread plate method [26]. Three or four wells of 12 mm diameter were made in the medium with the help of a sterile borer and filled with 50 ppm solution of testing compound in DMF. Similarly other wells were made for standard drug and filled with standard concentration [27]. These Petri dishes were sealed with parafilm and incubated at 37°C in an incubator. The Petri dishes were examined for zone of inhibition after 48 hr.

2.2. Antibacterial Activity

Studies of antibacterial activity of synthesized compounds have been carried out against three bacterial strains i.e. *Escherichia coli, Pseudomonas aeruginosa* and *Staphylococcus aureus*.

Growth medium preparation for bacteria- Growth culture for all bacterial strain nutrient agar medium was used. The composition of nutrient agar culture was Pepton-10 gm, Yeast extract-10 gm, Beef extract-6 gm, Agar-30 gm, and Distilled water-2000 mL.

Above mentioned quantities of peptone, beef extract and agar were mixed with two liters of double distilled water. The pH of this medium was adjusted at 6.8 with the help of 0.1 N hydrochloric acid and 0.1N sodium hydroxide. This medium was then transferred into conical flask, plugged and autoclaved at 121°C for 15 minutes. For further experimentations they were cooled and placed under aseptic conditions.

2.3. Antifungal Activity

In present investigation synthesized compounds have been screened for their antifungal activities against three pathogens. *Candida albicus*, *Aspergillus niger* and *Aspergillus fumigatues*.

Preparation of a growth medium for fungi- Potato dextrose agar (PDA) medium was used as a growth medium. The medium consist of Peeled potato-400 gm, Dextrose-40 gm, Agar-30 gm and Distilled water-2000 mL.

Potato (400gm) was cut into small pieces and boiled in 2000 mL distilled water till they can easily be penetrated by glass rod. After sieving, through two fold muslin cloths, the volume of extract was again made up to 2000 mL. It was boiled further after mixing 30 g of agar and 40 g of dextrose and was again filtered.

3. RESULTS AND DISCUSSION-

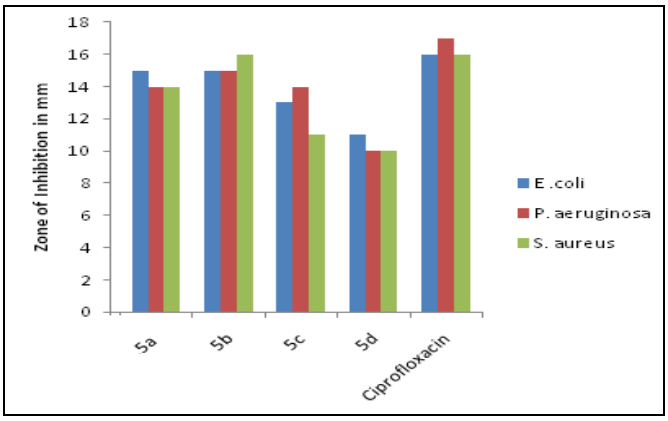
Results of antibacterial and antifungal activity are given in table 2 and table 3 respectively. Activities also represent graphically in graph I and II.

Table 1: Study of antibacterial activities of synthesized compounds at 50 ppm.

Code of compound	Zone of inhibition in mm.(Activity index)		
	E .coli	***P. aeruginosa***	***S. aureus***
5a	15(0.93)	14(0.82)	14(0.87)
5b	15(0.93)	15(0.88)	16(1.00)
5c	13(0.81)	14(0.82)	11(0.68)
5d	11(0.68)	10(0.58)	10(0.62)
Ciprofloxacin	16	17	16

*(Zone of Inhibition in mm) (Activity index)**

**Activity index = Inhibition area of the sample/inhibition area of the standard.(Standard = Ciprofloxacin)*



Graph I - Zone of inhibition for Antibacterial Activity

3.1. Inhibition of Bacterial Strains

Results of antibacterial activity are summarized in Table 1. Zone of inhibition is measured in mm. Activity index of all the synthesized compounds is also calculated for all bacterial strains against ciprofloxacin.

The data in the table reveal that all the compounds show significant antibacterial activity against all the selected strains. The activity (Zone of Inhibition) ranges generally between 11-15 for *E. coli*, 10-15 for *P. aeruginosa* and 10-16 for *S. aureus*. Majority of the compounds exhibited strong activity against *S. areus* as compared to standard drug ciprofloxacin. All the tested compounds have been found to exhibit moderate to strong inhibition against *P. aurginosa* and *S. areus*. Compound **5b** displayed promising antibacterial activity against *S. areus*. Similarly **5b** exhibited strong inhibition against *P. aeruginosa*. Similarly compound **5a** and **5b** give strong inhibition toward *E. coli*. Overall activities of synthesized compounds against bacteria are moderate to strong as compared to standard ciprofloxacin.

3.2. Inhibition of Fungal strains

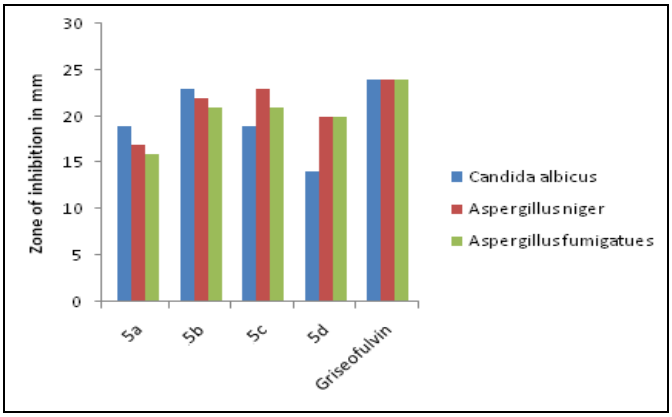
Antifungal screening results of compound are summarized in Table 2 in the form of zone of inhibition. By observation of this table it can be concluded that all compounds shown moderate to strong activity against all the three fungal strain.

Table 2: Study of antifungal activity of synthesized compounds at 50 ppm.

Name of compound	Zone of inhibition in mm.(Activity index)		
	Candida albicus	*Aspergillus niger*	*Aspergillus fumigatues*
5a	19(0.79)	16(0.66)	19(0.79)
5b	14(0.58)	20(0.83)	22(0.91)
5c	18(0.75)	19(0.79)	12(0.50)
5d	20(0.83)	18(0.75)	18(0.75)
Griseofulvin	24	24	24

(Zone of inhibition in mm) (Activity index)

**Activity index =Inhibition area of the sample/inhibition area of the standard. (Standard = Griseofulvin)*



Graph II - Zone of inhibition for Antifungal Activity

Among the tested compounds highest antifungal activity 23 mm was exhibited by compound **5b** against *C. albicus and* compound **5c** against *A. niger*. Compound **5b** also show zone of inhibition 22 mm against *A. niger*. Compound **5d** exhibited excellent prevention toward *A. niger* and *A. fumigatues*.

Finally it can be concluded that all the synthesized compounds tested for antifungal activity, possess moderate to good activity against the pathogenic fungi.

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