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ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF PYRAZOLE CLUBBED BENZOTHIOPHENE DERIVATIVES

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Abstract- *In the present study pyrazole containing benzothiophene derivatives synthesized in our previous study[1]have been evaluated for their antibacterial and antifungal activity against three bacterial Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureusand three fungal strain Candida albicus,Aspergillusniger,Aspergillusfumigatuesusing cup or well method.These compounds have shown very encouraging results showing inhibitionzone from 9 mm to 17 mm against three bacterial strain and inhibition zone from 12 mm to 22 mm against three fungal strain which is much closed to zone of inhibition of standard Ciprofloxacin and Griseofulvin respectively.*

Keywords: *- Antibacterial, Antifungal, Pyrazole, Benzothiophene.*

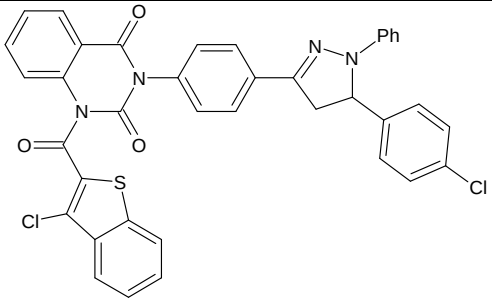
Introduction

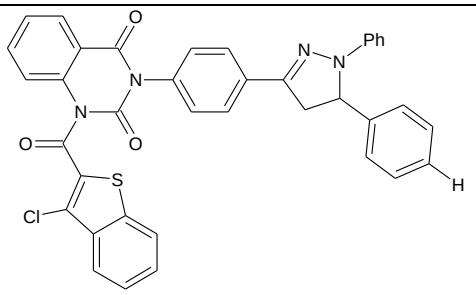
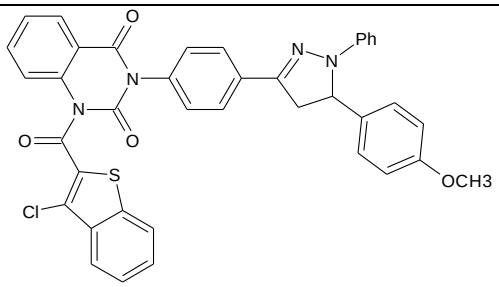
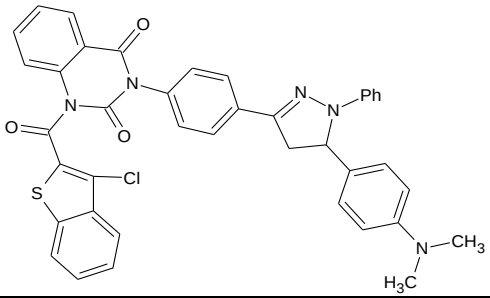
The chemistry of pyrazoles has been extensively investigated in the past. Pyrazoles are five member ring heterocyclic compounds, have some structural features with two nitrogen atoms in adjacent position and are also called as azoles. Pyrazole derivatives have a long history of application in agrochemicals and pharmaceutical industry as herbicides and active pharmaceuticals. A systematic investigation of this class of heterocyclic lead revealed that pyrazole containing pharmacophore active agents play important role in medicinal chemistry. Now a day's vast number of compounds with pyrazole nucleus have been reported to show a broad spectrum of biological activity including. Antimicrobial[2], antiviral[3], antitumor[4,5], anti-histaminic[6], anti-depressant[7], insecticides[8] and fungicides[9]. Due to its wide range of biological activity, pyrazoles 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 fused with benzene nucleus is known as benzothiophene. In recent years there has been an increasing interest in the chemistry of benzothiophene derivatives because of their biological significance. Beside the currently estabilished drugs Raloxifene, Zileuten and Sertaconazole. Benzothiophene derivatives are associated with diverse biological activities viz. antitubercular[10], antiallergic[11], antibacterial[12], anticonvulsant[13], antifungal[14], antiviral[15] antihistaminic[16], antiinflammatory[17], analgesic[18] antitumor[19], anticancer[20], antidiuretic[21], hypoglycemic[22], insecticidal[23], neumatocide[24], neuroleptic[25].

Experimental

Table 1:- Structure and name of synthesized compounds

Serial No.	Compounds Name	Structure	IUPAC Name
1	5a		{3-[1-(3-chlorobenzo[b]thiophene-2-carbonyl)-1*H*-indole-3-yl]-4-chlorophenyl)-4,5-dihydro-1H-pyrazol-3-yl]phenyl}-quinazoline-2,4-dione

2	5b		{3-[1-(3-chlorobenzo[b]thiophene-2-carbonyl)-1*H*-indole-3-yl]phenyl)-4,5-dihydro-1H-pyrazol-3-yl]phenyl}-quinazoline-2,4-dione
3	5c		{3-[1-(3-chlorobenzo[b]thiophene-2-carbonyl)-1*H*-indole-3-yl]-4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]phenyl}-quinazoline-2,4-dione (2.5c):
4	5d		{3-[1-(3-chlorobenzo[b]thiophene-2-carbonyl)-1*H*-indole-3-yl]-4-N,N dimethylaminophenyl)-4,5-dihydro-1H-pyrazol-3-yl]phenyl}-quinazoline-2,4-dione

Materials and method

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 activitycup or well method was used.

***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.

ANTIBACTERIAL ACTIVITY

Studies of antibacterial activity of synthesized compounds have been carried out against following bacterial strain.

1. *Escherichia coli*
2. *Pseudomonas aeruginosa*
3. *Staphylococcus aureus*

Growth medium preparation for bacteria

To culture all the bacteria nutrient agar medium was used. The composition of nutrient agar was-

Peptone = 10 g
Yeast extract = 10g
Beef extract = 6 g
Agar = 30 g
Distilled water = 2000 mL

The 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.

ANTIFUNGAL ACTIVITY

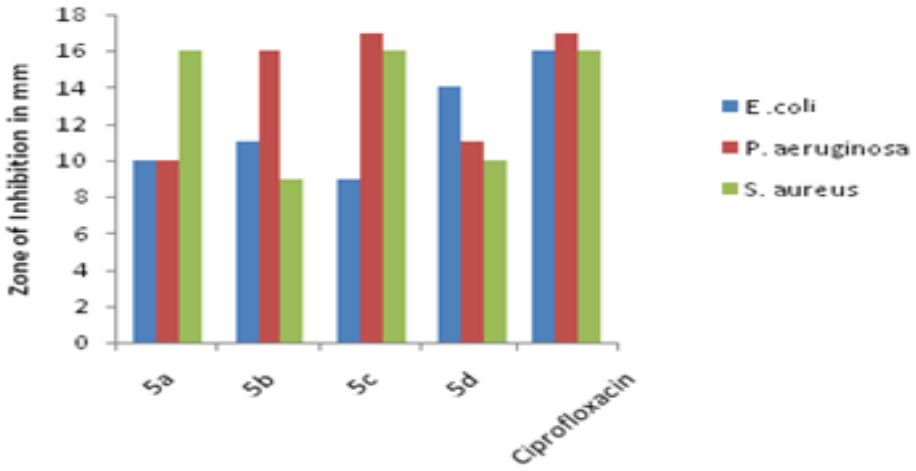
In present investigation synthesized compounds have been screened for theirantifungal activities against three pathogens.
(a)*Candida albicus*
(b) Aspergillusniger
(c) *Aspergillusfumigatues*

Preparation of a growth medium for fungi
Potato dextrose agar (PDA) medium was used as a growth medium. The medium consist of following ingredients and preparative method has been described in preceding paragraph
Peeled potato = 400 g
Dextrose = 40 g
Agar = 30 g
Distilled water = 2000 mL
Potato (400gm) was cut into small pieces and boiled in 2000mL distilled water till they can easily be penetrated by glass rod. After sieving through two fold muslin cloth the volume of extract was again made to 2000 mL. It was boiled further after mixing 30 g of agar and 40 g of dextrose and was again filtered.

Table2:-Study of antibacterial activities of synthesized compounds at 50 ppm. (Zone of Inhibition in mm.) (Activity index)*

S. No.	Name of compound	Zone of inhibition in mm.(Activity index)		
		E .coli	***P. aeruginosa***	***S. aureus***
1	5a	10(0.62)	10(0.58)	16(1.00)
2	5b	11(0.68)	16(0.94)	9(0.56)
3	5c	9(0.56)	17(1.00)	16(1.00)
4	5d	14(0.87)	11(0.64)	10(0.62)
5	Ciprofloxacin	16	17	16

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

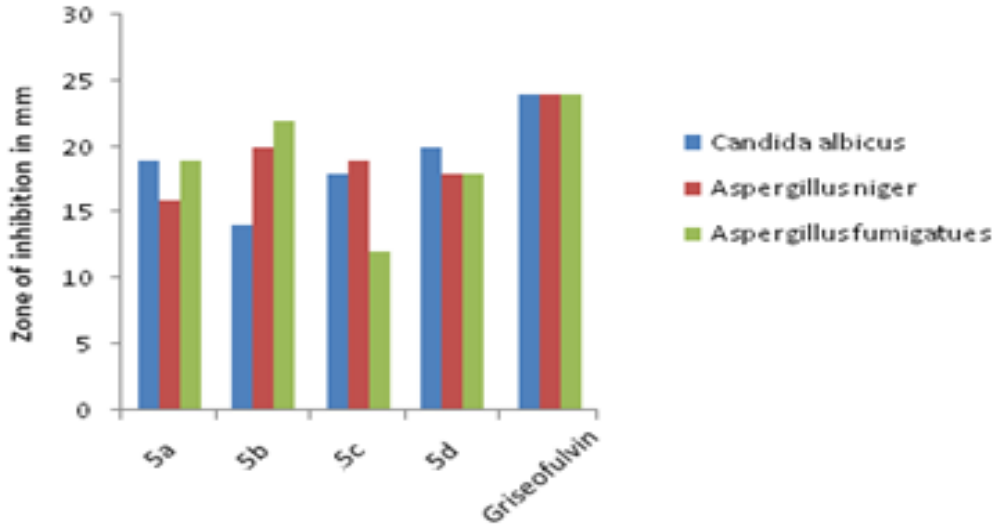


Graph I: - Zone of inhibition for Antibacterial Activity

Table 3:-Study of antifungal activity of synthesized compounds at 50 ppm. (Zone of inhibition in mm.) (Activity index)*

S. No.	Name of compound	Zone of inhibition in mm.(Activity index)		
		Candida albicus	***Aspergillusniger***	***Aspergillusfumigatues***
1	5a	19(0.79)	16(0.66)	19(0.79)
2	5b	14(0.58)	20(0.83)	22(0.91)
3	5c	18(0.75)	19(0.79)	12(0.50)
4	5d	20(0.83)	18(0.75)	18(0.75)
5	Griseofulvin	24	24	24

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



Graph II: - Zone of inhibition for Antifungal Activity

Result and Discussion

Inhibition of Bacterial activity

Results of antibacterial activity are summarized in Table 2. 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 the all the selected strains.The activity (Zone of Inhibition) ranges generally between 9-14 for *E. coli*, 10-17 for *P. aeruginosa* and 9-16 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 show moderate to strong inhibition against *P. aurginosa* and *S. areus*. Compound 5a, and 5c displayed promising antibacterial activity against *S. areus*. Similarly 5c exhibited strong inhibition against *P. aeruginosa* and Compound 5dshowstrong inhibition toward *E. coli*. Overall antibacterial activity of synthesized compounds is moderate to strong as compared to ciprofloxacin.

Inhibition of Fungal Activity

Antifungal screening results of compounds are summarized in Table 3 (in the form of zone of inhibition). By observation of this table it can be concluded that all the compounds show moderate to strong activity against all the three fungal strain.

Among all the tested compounds highest antifungal activity 22 mm was exhibited by compound 5b against *A. fumigatues* And 20 mm against *A. niger*. Compound 5d exhibited excellent prevention toward *C. albicus.*

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

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