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Antimicrobial and Antifungal Activity of Chromene and Pyrimidine derivatives

Mahesh Walle
Sundarrao More Arts, Commerce and Science College Poladpur-Raigad
mahesh.walle@gmail.com

Abstract: *Chromene analogues are widely recognized for their diverse biological activities, including antimicrobial properties. In this study, we evaluated the antifungal and antibacterial potential of four chromene derivatives: 2-Amino-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile (4-nitro derivative), Dioxooctahydroxanthene (4-hydroxyl derivative), Tetrahydro[b]pyran (4-chloro derivative), Pyrano[2,3-d]pyrimidine diones (4-methoxy derivative). The bioactivity of these compounds was assessed against selected bacterial and fungal strains using standard antimicrobial assays. The results demonstrated significant antibacterial and antifungal activity, with variation in potency depending on the substituent groups present on the chromene core. Among the tested compounds, some showed moderate to good antimicrobial efficacy against selected strains, while the some comound showed notable antifungal activity. The findings suggest that structural modifications in chromene scaffolds influence their antimicrobial properties, highlighting their potential as lead compounds for novel antimicrobial drug development.*

Keywords: Chromene, antifungul, antimicrobial, Bacillus subtilis, Pseudomonasaerugianosa, E Coli, Staphylococcus aureus, Aspergillusnigar

I. INTRODUCTION

Bacterial infections are regarded as a major global health threat [1]. In recent days, the main global threat to human public health has become antimicrobial resistance (AMR) [2]. The deaths may increase from seven hundred thousand to 10,000,000 yearly by 2050 due to antimicrobial resistance [3]. Candida sp. is considered to be answerable for most of the yeast-like foundational mycosis. Over the most recent couple of years, the augmentation of contagious diseases [4,5], especially nosocomial, ensuring protection from antifungal specialists has animated the quest for new antifungal specialists [6,7]. This search can be carried out by adopting any of these two approaches: (a) the quest for molecules that can work on the action of an all-around perceived antifungal specialist or/and (b) the quest for particles with antifungal action related to the obstruction in a particular objective on the fungal cells [8]. An alarming fact is that most antimicrobial drugs are associated with several clinical limitations, such as side effects, for example, hypersensitivity [9], hepatotoxicity [10], nephrotoxicity [11], serum levels [12], and multiple interactions [13,14]. The high mortality rate in our world is caused by antimicrobial clinical limitations and infectious diseases, so we need to develop novel therapeutic agents [15,16]. DNA gyrase is a decisive target for antimicrobial drugs [17,18] as it plays an essential role in bacterial DNA duplication by presenting negative supercoils in DNA topology [19]. It aided in the expansion of drugs and the existing resistance mechanisms in the patient's body [20]. The use of antibiotics resulted in increased bacterial resistance to present drugs [21,22]. Therefore, the search for novel antibacterial substances is urgently required, possibly acting through a different mechanism than the existing drugs [23]. Nitrogen and Oxygen heterocycles are becoming more popular because of their wide range of pharmacological and biological properties [24].

The chemistry of heterocycles has garnered a lot of studies since they are useful reagents due to their use as precursors for synthesizing polyfunctional substituted heterocycles (e.g., pyran, chromene, xanthene, pyrimidine, etc.) which are otherwise not so readily obtainable heteroaromatics. In continuation of our previous work this work of bioactivity has been extended after synthesis of some heterocyclic derivatives.[25-27]

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Experimental

Well plate diffusion method-The inoculums microorganism was prepared from the bacterial cultures. 15 ml of nutrient agar (Hi media) medium was poured in clean sterilized Petri plates and allowed to cool and solidify. 100 µl of broth of bacterial strain was pipette out and spread over the medium evenly with a spreading rod till it dried properly. Wells of 6µl in diameter were bored using a sterile cork borer. Solutions of all the compounds (5000 µg/ml) in DMSO were prepared. 100 µl of plant extracts solutions was added to the wells. The Petri plates were incubated at 37°C for 24 h. streptomycin (1mg/ml) was prepared as positive control DMSO was taken as a negative control. Antibacterial activity was evaluated by measuring the diameter of the zone inhibitions (ZI) all the determinations were performed in triplicates.

II. RESULT AND DISCUSSION

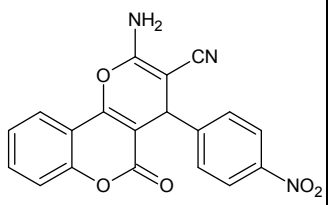
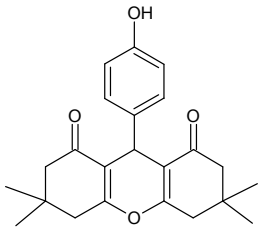
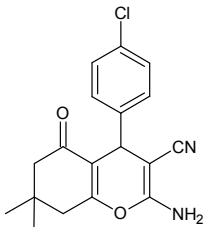
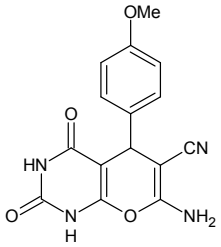
Antifungal activity against *Aspergillusnigar* by Agar Well plate diffusion method

Stock solution for antifungal activity: For the antifungal study, each compound was dissolved in DMSO at a concentration of 5 mg/ml and stored in a refrigerator till further used.

Antifungal activities of the compounds were evaluated usingan agar well diffusion assay. The assay was carried out according to the method of Sabouraud dextrose agar (Hi media) was used for the growth of fungus[28]. Media with acidic pH (pH 5.5 to 5.6) containing a relatively high concentration of glucose (40%) is prepared by mixing (SDA) Sabouraud dextrose and distilled water and autoclaved at 121°C for 15 minutes. 25 ml of molten (45°C) SDA medium was aseptically transferred into each 100mm x15mm sterile Petri dish.For counting of spore (fungi) were suspended in normal saline to make volume up to 1ml and then counted with help of hemocytometer (Neubauer chamber). Once the agar was hardened, 8mm wells were bored using a sterile cork borer. Then 0.1 ml (100 µl) from each well and plate were incubated for 24 hours at 29°C.Two wells in each Petri dish were supplemented with DMSO and reference antifungal drug streptomycin (1 mg/ml) dissolved in DMSO serve as negative and positive control respectively. The antifungal activity was measured as the diameter (mm) of the clear zone of growth inhibition[29].

The B1 to B4 compounds were selected for the antimicrobial and antifungal activity against different types of strains shown in Table 1.

Table 1- Selected compounds for bioactivity

B1-2-amino-5-oxo-4,5-dihydropyrano[3,2-c]chromene-3-carbonitrile 4-nitro derivative	B2-1,8-Dioxooctahydroxanthene 4-hydroxyl derivative	B3-Tetrahydro[b]pyran 4-chloro derivative	B4- pyrano[2,3-d]pyrimidine diones 4-methoxy derivative
			

The antimicrobial activity was evaluated against gram positive and gram negative type of bacteria. The Bacillus subtilis and Pseudomonas aerugianosaare gram positive whileBacillus subtilis and Pseudomonas aerugianosa are gram negative bacteria the details are shown in Table 2 and Table 3.

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Table 2- Antimicrobial activity of B1 to B4 compounds against *Bacillus subtilis and Pseudomonas aerugianosa*

Entry	Samples	Conc. (mg/ml)	Zone in diameter (mm) against *Bacillus subtilis*	Zone in diameter (mm) against *Peudomonasaeruginosa*
	Control	-	00	00
	Standard (*Streptomycin*)	1	16	17
1	B1	1	01	05
2	B2	1	03	11
3	B3	1	05	01
4	B4	1	09	01

Table 3 - Antimicrobial activity of B1 to B4 compounds against *Bacillus subtilis and Pseudomonas aerugianosa*

Entry	Samples	Conc. (mg/ml)	Zone in diameter (mm) against *E Coli*	Zone in diameter (mm) against *Staphylococcus aureus*
	Control	-	00	00
	Standard (Streptomycin)	01	16	17
1	B1	01	09	03
2	B2	01	12	07
3	B3	01	01	01
4	B4	01	01	02

The antifungal activity was evaluated for the fungi *Aspergillusnigar*for all for compounds by taking streptomycin as a standard shown in table 4.

Table 4- Antifungal activity of synthetic compounds against *Aspergillusnigar*

Entry	Samples	Conc.(mg/ml)	Zone in diameter (mm) against *Aspergillusnigar*
	Control	-	00
	Standard (Streptomycin)	01	16
1	B1	01	10
2	B2	01	01
3	B3	01	02
4	B4	01	03

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The images of bioactivity shown by the evaluated compounds B1 to B4 for the antimicrobial and antifungal nature using appropriate standard and control. (Figure 1 to Figure 8)

Images of bioactivity of B1, B2, B3, and B4 against different bacteria and fungi			
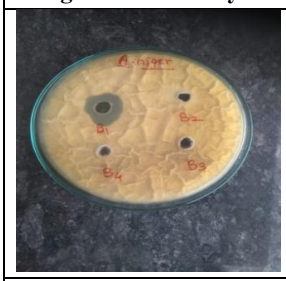		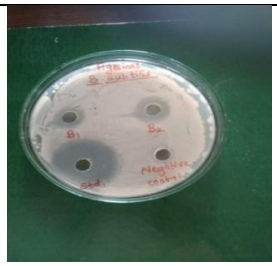	
Figure 1- B1 and B2 *A.niger*	**Figure 2- B3 and B4 *A.niger***	**Figure 3- B1 and B2 *B.Subtilis***	**Figure 4- B3 and B4 *B.Subtilis***
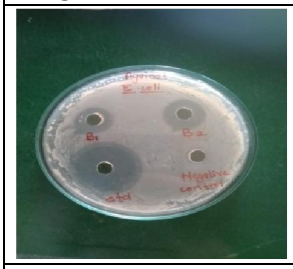	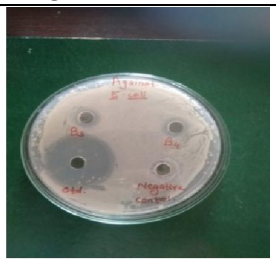		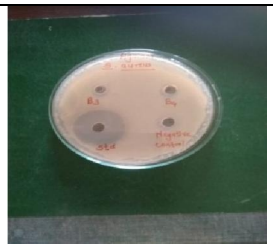
Figure 5- B1 and B2 against *E.coli*	**Figure 6- B3 and B4 against *E.coli***	**Figure 7- B1 and B2 against *S.aureus***	**Figure 8- B3 and B4 against *S.aureus***

III. CONCLUSION

The antibacterial activity of the compounds studied on gram +ve and gram –ve bacteria, in which compound B2 against *P aerurogenosa,* B4 against *Bacillus subtilis*, B1 and B2 against *E.coli*, B2 against *Staphylococcus aureus* showed moderate activity.

The antifungal activity of the synthetic compounds studied on *Aspergillusnigar*, in which compounds B1 showed moderate to good activity.

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