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Investigation of antimicrobial potential of some thiazolyl chalcone derivatives

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Summary

Due to the ever increasing resistance to antibiotics by the microbes, new molecules need to be evaluated for antimicrobial efficacy. Twenty new chalcone derivatives were tested for their ability as antimicrobial compounds. The minimum inhibition concentration of the compounds was evaluated against *E. coli*, *P. aeruginosa*, *B. subtilis* and *S. aureus* by serial dilution technique. All the tested compounds were found to be to possess MIC values between 50-6.25 µg/mL and the most potent compounds were found to contain a substitution at the para position of ring B. The study led to the conclusion that chalcones with heterocyclic ring A posses the potential to be a promising lead molecule for newer antimicrobial agents.

Keywords: Chalcone, antimicrobial, MIC, serial dilution technique

Introduction

The introduction of antibiotics in 1940 was thought to eliminate most of the deadliest and widespread epidemics in human civilization. The ever growing use and misuse of these drugs have led to development of resistance by bacteria against the currently available antibiotics [1, 2]. This indicates the need for development of new antimicrobial drugs.

Chalcone (1,3-diphenylpropen-1-one) represent a class of compounds possessing several biological properties [3-7]. Several reports have also been made for the antimicrobial potential of chalcones obtained either from plant source or from chemical synthesis [8-11].

As a part of our ongoing research, herein, we describe investigation of the ability of a series of previously synthesized chalcones to inhibit the growth of microorganisms *in vitro.*

Experimental

Twenty thiazolyl chalcones used in this study were synthesized using method described in our other report. Origins of the bacterial strains used in this study are *E. coli* MTCC 3261, *P. aeruginosa* MTCC 647 as Gram negative bacteria and *B. subtilis* MTCC 1134, *S. aureus* MTCC 3382 as the Gram positive strains. The MTCC strains of microorganisms used in this study was obtained from Institute of microbial technology, Chandigarh, India.

Preparation of test solutions

The synthesized chalcones were dissolved in dimethyl sulfoxide (DMSO) and the further dilutions of the test compounds were prepared at the required quantities of 100, 50, 25, 12.5 and 6.25 µg/mL concentrations with Mueller-Hinton broth medium.

Antimicrobial Assay

All the synthesized compounds were evaluated for minimum inhibitory concentration (MIC). The cultures for all the bacterial strains were obtained from Mueller-Hinton broth after 24 h of incubation at 37 ± 1°C. Antimicrobial evaluation of the compounds was carried out in Mueller-Hinton broth at pH 7.4 and the two-fold serial dilution technique was applied [12]. The final inoculum size was maintained to 10^5 CFU/mL. A set of tubes containing only the inoculated broth was used as the negative control, and one containing only the broth was used to ensure the sterility of the medium. Ampicillin (128µg/mL) was used as the positive control. Different concentrations of each compound were incubated with 1 mL broth and 1 mL of the bacterial culture for 24 h at 37 ± 1°C. The last tube with no growth of microorganism was recorded to represent the MIC expressed as µg/mL. Every experiment was performed in triplicate to ensure the accuracy of the tests.

Results

The chemical structures and MIC values of the synthesized compounds are presented in table 1. The combined data reveals that all the synthesized compounds show MIC values between 50 and 6.25µg/mL against all the screened microorganisms.

see Table 1.

While the compounds **3d**, **3i** and **3n** exhibited the best results against all the four tested bacterial strains, all the other compounds except **3k**, **3s and 3t** exhibited MIC value of less than or equal to 12.5 µg/mL. The compounds **3k** and **3s** were considered to be poorly active as they had a MIC value of more than 25µg/mL in the tested pathogen.

Discussion

The antimicrobial potential of the synthesized compounds has been evaluated by determining the minimum inhibition concentration values by broth dilution method using Mueller-Hinton broth for culturing the pathogen. MIC is the minimum concentration of the test compound that exhibits no

growth of microorganism. Both gram negative and gram positive bacteria were used in the study, as much of the resistance has been acquired by the gram positive bacteria against the currently available antibiotics. Though the resistant strains were not used in the study, the preliminary investigations reveal high potential of the synthesized compounds against all the four tested microorganisms. The results obtained indicate the role of substitution at R_3 in the antibacterial potential of the compounds. Compounds having substitution at R_3 were found to be active particularly against the gram negative bacteria at lower concentrations. Also they exhibited significant potency against the gram negative bacteria. The higher MIC values (≥ 25 µg/mL) indicate that presence of substitution at R_1 is detrimental of the antimicrobial action of the synthesized compounds.

Conclusion

The study led to the conclusion that chalcones with heterocyclic ring A posses the potential to be a promising lead molecule for newer antimicrobial agents. The significant results obtained from the study also help to investigate the role of different substitutions on the ring B of chalcone in the antimicrobial potential of the compounds. The preliminary structure activity relationship could be concluded which needs to be investigated further to establish the molecule as lead compound for antimicrobial activity.

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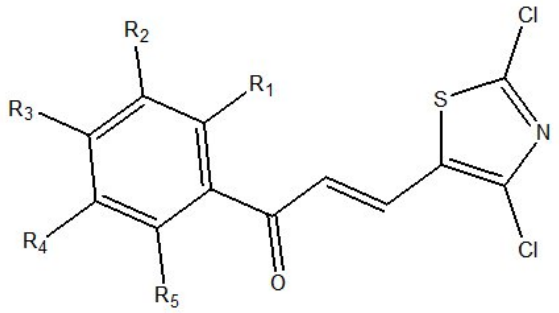

Compd. No.	R_1	R_2	R_3	R_4	R_5	MIC (µg/mL)			
						E.coli	*B. subtilis*	*P. aeuriginosa*	*S. aureus*
3a	H	H	H	H	H	25	12.5	12.5	12.5
3b	H	H	OH	H	H	12.5	12.5	6.25	6.25
3c	H	H	NH_2	H	H	6.25	6.25	12.5	6.25
3d	H	H	NO_2	H	H	6.25	6.25	6.25	6.25
3e	H	H	Br	H	H	25	12.5	6.25	12.5
3f	H	H	CH_3	H	H	25	25	6.25	6.25
3g	H	H	OCH_3	H	H	12.5	25	6.25	6.25
3h	H	H	Cl	H	H	6.25	6.25	12.5	6.25
3i	H	H	F	H	H	6.25	6.25	6.25	6.25
3j	H	H	H	NO_2	H	25	25	12.5	6.25
3k	NH_2	H	H	H	H	50	6.25	25	25
3l	H	NH_2	H	H	H	6.25	6.25	12.5	12.5
3m	H	Br	H	H	H	12.5	12.5	25	25
3n	Cl	H	Cl	H	H	6.25	6.25	6.25	6.25
3o	Cl	H	H	H	H	6.25	12.5	12.5	12.5
3p	H	OH	H	H	H	12.5	6.25	25	25
3q	CH_3	H	H	H	H	50	25	25	25
3r	H	Cl	H	H	H	12.5	12.5	12.5	12.5
3s	OH	H	H	H	OH	25	25	25	25
3t	OH	H	H	H	H	12.5	12.5	25	25
Ampicillin						2.56	1.28	1.28	1.28

Table 1: MIC of the synthesized compounds against gram positive and gram negative bacterial