Research Journal of Biological Sciences 6 (12): 632-634, 2011
ISSN: 1815-8846

Evaluation of Anti-Fungal Activity of Synthesized Chalcone Semicarbazone Derivatives

[1]Manmohan Singhal and [2]Arindam Paul
[1]School of Pharmaceutical Sciences, Jaipur National University, 302025 Rajasthan, Jaipur, India
[2]GD Memorial College of Pharmacy, 342005 Rajasthan, Jodhpur, India

Abstract: In the present study, researchers designed a Pharmacophore Model chalconesemicarbazone which is having hydrogen acceptor site, hydrogen donor site, lipophilic site, etc., using Ligandscout-2.02 software. A series of chalcone semicarbazones was synthesized and evaluated for their anti-fungal activity by Paper Disk Diffusion Method. Based on the results of an anti-fungal study, compound CS-10 was the most active compound. It was observed that methoxy substitution in aldehydic moiety and hydroxyl substitution in the acetophenic moiety significantly increased anti-microbial spectrum against fungi.

Key words: Anti-fungal, semicarbazones, chalcone, disk diffusion, lipophilic site, India

INTRODUCTION

The semicarbazides which are the raw material of semicarbazones have been known to have biological activity against many of the most common species of bacteria (Dogan *et al*., 1999). Semicarbazone, themselves are of much interest due to a wide spectrum of anti-fungal and anti-bacterial activities (Singhal and Paul, 2011a). Recently, some researchers had reviewed the bioactivity of semicarbazones and they have exhibited anti-convulsant (Pandeya *et al*., 2000), anti-tubercular (Sriram *et al*., 2004), anti-oxidant (Singhal and Paul, 2011b), anti-microbial, analgesic, anti-pyretic (Singhal and Paul, 2011c), anti-inflammatory (Singh *et al*., 2010).

Microbial resistance, a world health hazard is dramatically increasing. Microbial resistance towards the drug creates a very serious problem since last 3 decades because of this development of resistance many drugs are now useless which were very effective before (Cohen, 1992; Cunha, 1998). Moreover, the toxic effects produced by these anti-biotics are also reducing their significance. So, the need for new anti-microbial is always be there. Anti-fungal screening of synthesized chalcone semicarbazone derivatives was conducted using a filter paper disc method.

MATERIALS AND METHODS

Chemistry: Chalcone semicarbazones (Singhal and Paul, 2011d) were synthesized according to synthetic scheme as shown in Fig. 1. The structure (Fig. 2) and physicochemical properties of the synthesized title compounds are shown in Table 1.

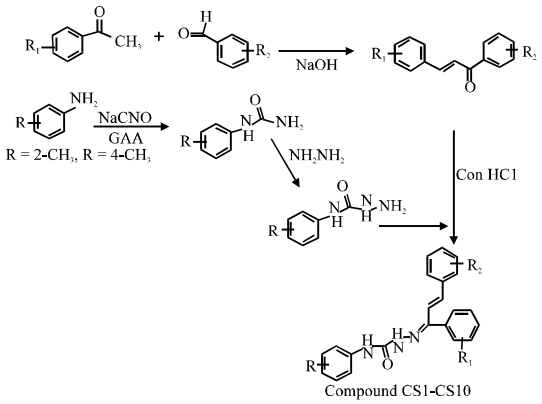

Fig. 1: Synthetic scheme for synthesizing the chalconesemicarbazone derivatives

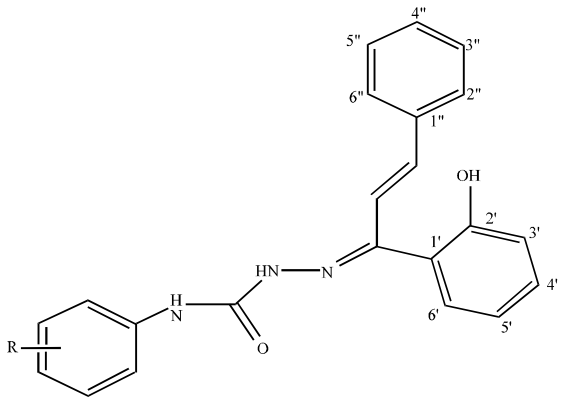

Fig. 2: Structure of synthesized chalconesemicarbazones

Anti-fungal activity: All the synthesized compounds were screened for their anti-fungal activity against four fungi

Corresponding Author: Manmohan Singhal, School of Pharmaceutical Sciences, Jaipur National University, 302025 Rajasthan, Jaipur, India

Table 1: Physicochemical data of chalconesemicarbazones

Comp No.	R	R_1	R_2	Yield (%)	Mol wt.	Mol formula	mp (°C)	Rf value
CS1	2-CH_3	H	H	57	371	$C_{23}H_{21}N_3O_2$	150	0.78
CS2	2-CH_3	H	4''-OH	66	387	$C_{23}H_{21}N_3O_3$	145	0.71
CS3	2-CH_3	H	4''-OCH_3	65	401	$C_{24}H_{23}N_3O_3$	135	0.65
CS4	2-CH_3	H	4''-$N(CH_3)_2$	58	414	$C_{25}H_{26}N_4O_2$	148	0.57
CS5	2-CH_3	4-OH	6''-OH	57	403	$C_{23}H_{21}N_3O_4$	142	0.60
CS6	2-CH_3	4-OH	4''-$N(CH_3)_2$	50	430	$C_{25}H_{26}N_4O_3$	160	0.67
CS7	2-CH_3	H	6''-OH	63	387	$C_{23}H_{21}N_3O_3$	140	0.55
CS8	2-CH_3	5-OH	6''-OH	61	403	$C_{23}H_{21}N_3O_4$	135	0.63
CS9	2-CH_3	5-OH	4''-OH	56	403	$C_{23}H_{21}N_3O_4$	120	0.69
CS10	2-CH_3	5-OH	4''-OCH_3	57	417	$C_{24}H_{23}N_3O_4$	126	0.51

viz., *Candida albicans*, *Aspergillus niger*, *Asperillus orzane* and *Penicillium citrinum* at 100 μg mL^{-1} involving disc diffusion method with Saburoud's dextrose agar (Hi-Media).

Anti-fungal activity was determined by measuring the zone of inhibition in millimeters around each of the disk and compared with standard Fluconazole (Yamac and Bilgili, 2006). The anti-fungal activity was classified as standards (>27 mm) highly active (21-27 mm), moderately active (15-21 mm), least active (12-15 mm) and <12 mm was taken as inactive (Parmar *et al*., 1992).

RESULTS AND DISCUSSION

All the compounds were assessed for their *in vitro* anti-fungal activity against different strains of fungi such as *Candida albicans*, *Aspergillus niger*, *Asperillus orzane* and *Penicillium citrinum*. Solvent DMSO was used as solvent control and fluconazole was used as standard. The biological data of the compounds is shown in Table 2.

The substitution with different substituent on the phenyl of the aldehydic and acetophenic group of chalcone moiety (Mandge *et al*., 2007) plays an important role in the zone inhibition of fungi. As from Table 1 and 2, it could be seen that the compound CS10 exhibited highest anti-microbial activity against fungi. It is probably due to the presence of hydroxy group in the acetophenic moiety and methoxy group in aldehydic moiety of chalcone. The order of activity regarding substitution on chalconyl group for anti-fungal activity is OCH_3>OH> $(CH_3)_2$-N>H.

Among the synthesized compounds, compound CS10 showed the better or comparable anti-fungal activity in comparison to that of standard drug while the other compounds are moderate active (compound CS3), least active (compound CS8) or inactive (compound CS1, 2, 4, 5, 6, 7 and 9) against fungi.

Methoxy substitution in the aldehydic moiety of chalcone exhibited better anti-fungal activity. In case of the bulkier substitution (compound CS4, CS6), the substitution does not favor anti-microbial activity which may be due to improper binding with microorganism. The compounds with no substitution (compound CS1) showed very less anti-microbial effect in comparison to the substituted compounds.

Table 2: Anti-fungal activity of synthesized semicarbazone derivatives by Paper Disk Diffusion Method

	Diameter of zone of inhibition (mm) at 100 μg mL^{-1} concentration			
	Fungus strains			
Compounds	*C. albicans*	*A. niger*	*A. orzane*	*P. citrinum*
Control (DMSO)	-	-	-	-
CS1	5	6	4	5
CS2	9	11	10	12
CS3	19	18	20	18
CS4	6	7	4	7
CS5	9	11	9	10
CS6	9	10	8	10
CS7	9	12	12	11
CS8	11	12	11	13
CS9	10	12	10	12
CS10	27	25	28	25
Fluconazole	30	33	29	32

CONCLUSION

In this study, all the newly synthesized chalcone semicarbazone compounds were screened for their anti-fungal activity. DMSO is used as control and fluconazole was used as standard drug. Among the entire tested compound CS10 and CS3 displayed maximum activity. On critical overview of synthesized compounds, it has been found that methoxy (OCH_3) substitution in acetophenic moiety favors anti-fungal activity. Compounds with bulkier substitution or no substitution were inactive against fungi.

REFERENCES

Cohen, M.L., 1992. Epidemiology of drug resistance: Implications for a Post-anti-microbial Era. Science, 257: 1050-1055.

Cunha, B.A., 1998. Anti-biotic resistance. Drugs Today, 34: 691-698.

Dogan, H.N., A. Duran and E. Yemni, 1999. Synthesis and anti-bacterial activity of 1-(3-hydroxy-2-naphthoyl)-4-substituted thiosemicarbazides. Drug Metabol. Drug Interact., 15: 187-195.

Mandge, S., H.P. Singh, S.D. Gupta and N.S.H.N. Moorthy, 2007. Synthesis and characterization of some chalcone derivatives. Trends Applied Sci. Res., 2: 52-56.

Pandeya, S.N., P. Yogeeswari and J.P. Stables, 2000. Synthesis and anti-convulsant activity of 4-bromophenyl substituted aryl semicarbazones. Eur. J. Med. Chem., 35: 879-886.

Parmar, V.S., H.N. Jha, A.K. Gupta and A.K. Prasad, 1992. Agamanone, a flavanone from agave Americana. Phytochemistry, 31: 2567-2568.

Singh, H.P., C.S. Chauhan, S.N. Pandeya, C.S. Sharma and B. Srivastava *et al*., 2010. Synthesis, analgesic and anti-inflammatory activity of some novel chalconesemicarbazone derivatives. Der. Pharma. Lett., 2: 460-472.

Singhal, M. and A. Paul, 2011a. Anti-bacterial evaluation of synthesized methyl semicarbazone derivatives. Int. J. Pharm. Sci. Res., 2: 2602-2604.

Singhal, M. and A. Paul, 2011b. Anti-oxidant activity of synthesized methyl semicarbazone derivatives by DPPH scavenging assay. Global J. Pharmacol., 5: 60-66.

Singhal, M. and A. Paul, 2011c. Synthesis characterization and anti-pyretic evaluation of some novel chalcone semicarbazones derivatives. Res. J. Pharmacol., 5: 47-52.

Singhal, M., A. Paul, 2011d. 4-Methylphenylsemi-carbazone derivatives inhibits cow milk induced pyrexia in rabbits. Int. J. Mol. Med. Adv. Sci., 7: 16-18.

Sriram, D., P. Yogeeswari and R.S. Thirumurugan, 2004. Anti-tuberculous activity of some aryl semicarbazone derivatives. Bioorg. Med. Chem. Lett., 14: 3923-3924.

Yamac, M. and F. Bilgili, 2006. Anti-microbial activities of fruit bodies and/or mycelial cultures of some mushroom isolates. Pharm. Biol., 44: 660-667.