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Evaluation of Antifungal Activity of 4-Methylphenylsemicarbazone Derivatives

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Abstract: In present study, a series of 4-methylphenylsemicarbazones was synthesized and evaluated for their antifungal activity against four Fungi viz., *Candida albicans*, *Aspergillus niger*, *Asperillus orzane* and *Penicillium citrinum* by paper disk diffusion method. Based on the results of an antifungal study, compound MPS-10 was proved the most active compound. It was observed that methoxy substitution in aldehydic moiety and hydroxyl substitution in the acetophenic moiety significantly increased the antimicrobial spectrum against fungi. Compound with bulkier substitution or no substitution showed least antifungal activity.

Key words: Antifungal · Semicarbazide · Microbial resistance · Disk diffusion

INTRODUCTION

Microbial resistance towards the drug creates a very serious problem since last three decades, because of this development of resistance many drugs are now useless which were very effective in past [1, 2]. Moreover, the toxic effects produced by these antibiotics are also reducing their significance. So the need for new antimicrobial is always be there. 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 [3]. Semicarbazone, themselves are of much interest due to a wide spectrum of antibacterial and antifungal activities [4]. Recently some researchers had reviewed the bioactivity of semicarbazones and they have exhibited anticonvulsant [5], antitubercular [6], antioxidant [7], analgesic, antipyretic [8], anti-inflammatory [9] etc. Antifungal screening of synthesized chalconesemicarbazone derivatives was conducted using a filter paper disc method.

MATERIALS AND METHODS

Chemistry: Chalconesemicarbazones [7] were synthesized according to synthetic scheme as shown in Figure 1. The structure (Figure 2) and physicochemical properties of the synthesized title compounds are given in Table 1.

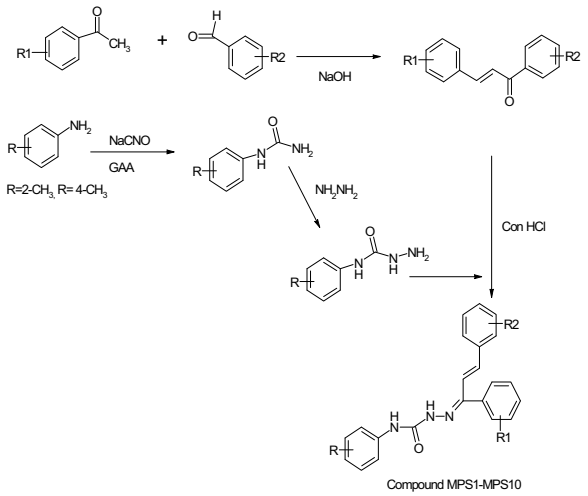

Fig. 1: Synthetic scheme for synthesizing the 4-methylphenylsemicarbazone derivatives

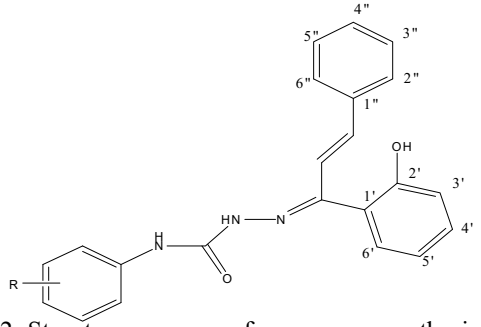

Fig. 2: Structure of synthesized 4-methylphenylsemicarbazones

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Table 1: Physicochemical data of 4-methylphenylsemicarbazones.

Comp no.	R	R_1	R_2	Yield (%)	Mol Wt.	Mol Formula	Mp (°C)	Rf Value
MPS1	4-CH_3	H	H	52	371	$C_{23}H_{21}N_3O_2$	206	0.53
MPS2	4-CH_3	H	4"-OH	65	387	$C_{23}H_{21}N_3O_3$	188	0.63
MPS3	4-CH_3	H	4"-OCH_3	63	401	$C_{24}H_{23}N_3O_3$	204	0.70
MPS4	4-CH_3	H	4"-$N(CH_3)_2$	64	414	$C_{25}H_{26}N_4O_2$	195	0.62
MPS5	4-CH_3	4-OH	6"-OH	55	403	$C_{23}H_{21}N_3O_4$	178	0.58
MPS6	4-CH_3	4-OH	4"-$N(CH_3)_2$	56	430	$C_{25}H_{26}N_4O_3$	185	0.66
MPS7	4-CH_3	H	6"-OH	54	387	$C_{23}H_{21}N_3O_3$	180	0.69
MPS8	4-CH_3	5-OH	6"-OH	67	403	$C_{23}H_{21}N_3O_4$	183	0.54
MPS9	4-CH_3	5-OH	4"-OH	50	403	$C_{23}H_{21}N_3O_4$	165	0.59
MPS10	4-CH_3	5-OH	4"-OCH_3	56	417	$C_{24}H_{23}N_3O_4$	172	0.77

Table 2: Antifungal activity of synthesized 4-methylphenylsemicarbazone derivatives by paper disk diffusion method.

	Diameter of zone of inhibition (mm) at 100µg/ml concentration		Fungus strains	
Compounds	*C. albicans*	*A. niger*	*A. orzane*	*P. citrinum*
Control (DMSO)	_	_	_	_
MPS1	09	10	10	09
MPS2	11	12	11	10
MPS3	23	21	24	20
MPS4	08	08	09	08
MPS5	09	12	10	10
MPS6	10	11	10	11
MPS7	10	12	13	12
MPS8	15	16	15	17
MPS9	13	15	15	16
MPS10	29	27	26	29
Fluconazole	30	33	29	32

Paper Disk Diffusion Technique: All the synthesized compounds were screened for their antifungal activity against four Fungi viz., *Candida albicans*, *Aspergillus niger*, *Asperillus orzane* and *Penicillium citrinum* at 100 µg/ml involving disc diffusion method with Saburoud's dextrose agar (Hi-Media). Antifungal activity was determined by measuring the zone of inhibition in millimeters around each of the disk and compared with standard Fluconazole [10]. The antifungal activity was classified as standards (>27 mm), highly active (21-27 mm), moderately active (15-21 mm), least active (12-15 mm) and less than 12 mm was taken as inactive [11].

RESULTS AND DISCUSSION

All the compounds were assessed for their *in vitro* antifungal 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 given in Table 2.

The substitution with different substituent on the phenyl of the aldehydic and acetophenic group of chalcone moiety plays an important role in the zone inhibition of fungi. As from the Tables it could be seen that the compound MPS10 exhibited highest antimicrobial 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 [12]. The order of activity regarding substitution on chalconyl group for antifungal activity is OCH_3>OH> $(CH_3)_2$-N> H.

Among the synthesized compounds, compound MPS10 showed the better or comparable antifungal activity in comparison to that of standard drug while the other compounds are highly active (compound MPS3), moderate active (compound MPS8, MPS9), least active (compound MPS7) or inactive (compound MPS1, MPS2, MPS4, MPS5, MPS6) against Fungi.

Methoxy substitution in the aldehydic moiety of chalcone exhibited better antifungal activity. In case of the bulkier substitution (compound MPS4, MPS6) the substitution does not favor antimicrobial activity which may be due to improper binding with

microorganism. The compounds with no substitution (compound MPS1) showed very less antimicrobial effect in comparison to the substituted compounds [13].

In summary, all the newly synthesized chalconesemicarbazone compounds were screened for their antifungal activity. DMSO is used as control and fluconazole was used as standard drug. Among the entire tested compound MPS10 and MPS3 displayed maximum activity. On critical overview of synthesized compounds, it has been found that methoxy ($-OCH_3$) substitution in acetophenic moiety favors antifungal activity. Compounds with bulkier substitution or no substitution were inactive against Fungi.

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