

## Evaluation of Anti-Fungal Activity of Synthesized Chalcone Semicarbazone Derivatives

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**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 acetophenone 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, 2011 b), anti-microbial, analgesic, anti-pyretic (Singhal and Paul, 2011 c), 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.

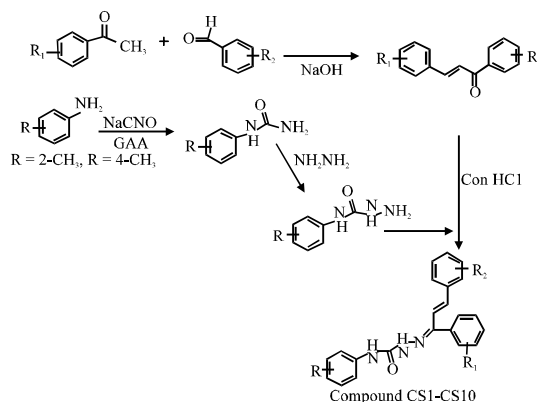


Fig. 1: Synthetic scheme for synthesizing the chalconesemicarbazone derivatives

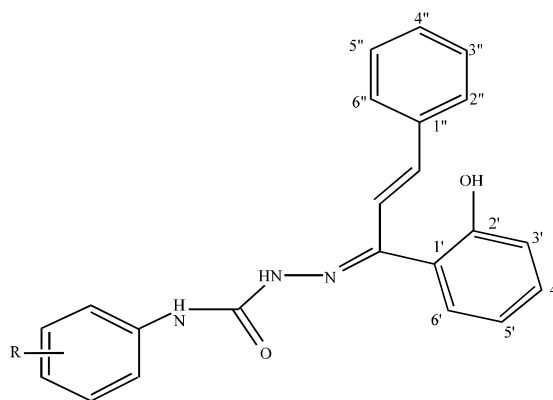


Fig. 2: Structure of synthesized chalconesemicarbazones

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

Table 1: Physicochemical data of chalconesemicarbazones

| Comp No. | R                 | R <sub>1</sub> | R <sub>2</sub>                       | Yield (%) | Mol wt. | Mol formula   | mp (°C) | Rf value |
|----------|-------------------|----------------|--------------------------------------|-----------|---------|---|---------|----------|
| CS1      | 2-CH <sub>3</sub> | H              | H                                    | 57        | 371     | C <sub>23</sub> H <sub>21</sub> N <sub>3</sub> O <sub>2</sub> | 150     | 0.78     |
| CS2      | 2-CH <sub>3</sub> | H              | 4''-OH                               | 66        | 387     | C <sub>23</sub> H <sub>21</sub> N <sub>3</sub> O <sub>3</sub> | 145     | 0.71     |
| CS3      | 2-CH <sub>3</sub> | H              | 4''-OCH <sub>3</sub>                 | 65        | 401     | C <sub>24</sub> H <sub>23</sub> N <sub>3</sub> O <sub>3</sub> | 135     | 0.65     |
| CS4      | 2-CH <sub>3</sub> | H              | 4''-N(CH <sub>3</sub> ) <sub>2</sub> | 58        | 414     | C <sub>25</sub> H <sub>26</sub> N <sub>4</sub> O <sub>2</sub> | 148     | 0.57     |
| CS5      | 2-CH <sub>3</sub> | 4-OH           | 6''-OH                               | 57        | 403     | C <sub>23</sub> H <sub>21</sub> N <sub>3</sub> O <sub>4</sub> | 142     | 0.60     |
| CS6      | 2-CH <sub>3</sub> | 4-OH           | 4''-N(CH <sub>3</sub> ) <sub>2</sub> | 50        | 430     | C <sub>25</sub> H <sub>26</sub> N <sub>4</sub> O <sub>3</sub> | 160     | 0.67     |
| CS7      | 2-CH <sub>3</sub> | H              | 6''-OH                               | 63        | 387     | C <sub>23</sub> H <sub>21</sub> N <sub>3</sub> O <sub>3</sub> | 140     | 0.55     |
| CS8      | 2-CH <sub>3</sub> | 5-OH           | 6''-OH                               | 61        | 403     | C <sub>23</sub> H <sub>21</sub> N <sub>3</sub> O <sub>4</sub> | 135     | 0.63     |
| CS9      | 2-CH <sub>3</sub> | 5-OH           | 4''-OH                               | 56        | 403     | C <sub>23</sub> H <sub>21</sub> N <sub>3</sub> O <sub>4</sub> | 120     | 0.69     |
| CS10     | 2-CH <sub>3</sub> | 5-OH           | 4''-OCH <sub>3</sub>                 | 57        | 417     | C <sub>24</sub> H <sub>23</sub> N <sub>3</sub> O <sub>4</sub> | 126     | 0.51     |

viz., *Candida albicans*, *Aspergillus niger*, *Asperillus orzane* and *Penicillium citrinum* at 100 µg mL<sup>-1</sup> involving disc diffusion method with Sabouroud'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<sub>3</sub>>OH>(CH<sub>3</sub>)<sub>2</sub>-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

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

| Compounds      | Diameter of zone of inhibition (mm) at 100 µg mL <sup>-1</sup> concentration |                 |                  |                    |
|----------------|--|-----------------|------------------|--------------------|
|                | <i>C. albicans</i>   | <i>A. niger</i> | <i>A. orzane</i> | <i>P. citrinum</i> |
| 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                 |

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.

## 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<sub>3</sub>) substitution in acetophenic moiety favors anti-fungal activity. Compounds with bulkier substitution or no substitution were inactive against fungi.

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