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Evaluation of DPPH free raical scavenging activity of chalconesemicarbazone derivatives

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ABSTRACT

In the present study a series of chalconesemicarbazones was synthesized and evaluated for antioxidant activity by DPPH free radical scavenging assay. Most of the compounds were found to be potent antioxidant. Free radicals play an important role in various pathological and xenotoxic effects so antioxidant may have protective role in these pathological conditions. Based on the results of an anti-oxidant study, Compound 23 was the most active compound. The highest scavenger activity observed in compound 23 is probably due to the presence of hydroxyl group in the acetophenic moiety and methoxy group in aldehydic moiety of the chalcone. It was found that methoxy and hydroyl substituted chalconesemicarbazones were potent free radical scavenger and unsubstituted compound showed very less activity.

KEYWORDS

Chalcones;
Antioxidant;
Semicarbazones;
DPPH scavenging;
Free radical.

INTRODUCTION

Reactive oxygen species (ROS) such as superoxide anions, hydrogen peroxide, hydroxyl and nitric oxide radicals, play an important role in oxidative stress related to the pathogenesis of various important diseases. Antioxidants act as a major defense against radical mediated toxicity by protecting the damages caused by free radicals. Antioxidant agents are effective in the prevention and treatment of complex diseases, like atherosclerosis, stroke, diabetes, Alzheimer's disease and cancer[1]. Semicarbazone, themselves are of much interest due to a wide spectrum of pharmacological activities like antibacterial, antifungal, anticonvulsant, antitubercular, analgesic and anti-inflammatory etc[2, 3]. The semicarbazone is an electron withdrawing group and exhibited antioxidant activity. Favorable substitution may increase their free radical scavenging effect[1].

MATERIALS AND METHODS

Chemistry

Chalconesemicarbazone derivatives were previously synthesized and characterized[1, 3]. The structure (Figure 1) and physicochemical properties of the synthesized title compounds are given in TABLE 1.

DPPH free radical scavenging assay

The antioxidant activity of the synthesized chalconesemicarbazone derivatives was evaluated using the DPPH free radical scavenging assay[4]. 200 µL of test sample solution (100µg/ml) was added to 4 mL of 100µM methanolic DPPH. After vortexing, the mixture was incubated for 20 minutes at room temperature and the absorbance at 517 nm was measured. Ascorbic acid (100µg/ml) was used as standard. A blank was prepared without adding standard or test compound. Lower the absorbance of the reaction mixture indicates higher free radical scavenging activity. The capability to scavenge the DPPH radical was calculated using the

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TABLE 1 : Physicochemical data of chalconesemicarbazones

Comp no.	R	R_1	R_2	Yield (%)	Mol Wt.	Mol Formula	mp (°C)	Rf Value
4	2-CH_3	H	H	57	371	$C_{23}H_{21}N_3O_2$	150	0.78
5	2-CH_3	H	4”-OH	66	387	$C_{23}H_{21}N_3O_3$	145	0.71
6	2-CH_3	H	4”-OCH_3	65	401	$C_{24}H_{23}N_3O_3$	135	0.65
7	2-CH_3	H	4”-$N(CH_3)_2$	58	414	$C_{25}H_{26}N_4O_2$	148	0.57
8	2-CH_3	4-OH	6”-OH	57	403	$C_{23}H_{21}N_3O_4$	142	0.60
9	2-CH_3	4-OH	4”-$N(CH_3)_2$	50	430	$C_{25}H_{26}N_4O_3$	160	0.67
10	2-CH_3	H	6”-OH	63	387	$C_{23}H_{21}N_3O_3$	140	0.55
11	2-CH_3	5-OH	6”-OH	61	403	$C_{23}H_{21}N_3O_4$	135	0.63
12	2-CH_3	5-OH	4”-OH	56	403	$C_{23}H_{21}N_3O_4$	120	0.69
13	2-CH_3	5-OH	4”-OCH_3	57	417	$C_{24}H_{23}N_3O_4$	126	0.51
14	4-CH_3	H	H	52	371	$C_{23}H_{21}N_3O_2$	206	0.53
15	4-CH_3	H	4”-OH	65	387	$C_{23}H_{21}N_3O_3$	188	0.63
16	4-CH_3	H	4”-OCH_3	63	401	$C_{24}H_{23}N_3O_3$	204	0.70
17	4-CH_3	H	4”-$N(CH_3)_2$	64	414	$C_{25}H_{26}N_4O_2$	195	0.62
18	4-CH_3	4-OH	6”-OH	55	403	$C_{23}H_{21}N_3O_4$	178	0.58
19	4-CH_3	4-OH	4”-$N(CH_3)_2$	56	430	$C_{25}H_{26}N_4O_3$	185	0.66
20	4-CH_3	H	6”-OH	54	387	$C_{23}H_{21}N_3O_3$	180	0.69
21	4-CH_3	5-OH	6”-OH	67	403	$C_{23}H_{21}N_3O_4$	183	0.54
22	4-CH_3	5-OH	4”-OH	50	403	$C_{23}H_{21}N_3O_4$	165	0.59
23	4-CH_3	5-OH	4”-OCH_3	56	417	$C_{24}H_{23}N_3O_4$	172	0.77

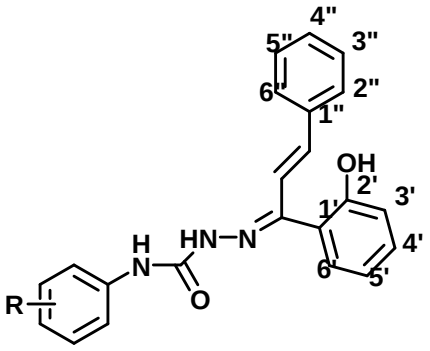

Figure 1 : Structure of synthesized chalconesemicarbazone derivatives

following equation.

$$\text{DPPH scavenged}(\%) = \frac{\text{A control} - \text{A test}}{\text{A control}} \times 100$$

Where, A control = Absorbance of the control reaction and A test = Absorbance in the presence of the samples of test compounds.

RESULTS AND DISCUSSION

The antioxidant activity of the synthesized chalconesemicarbazones was evaluated using DPPH free radical scavenging assay. The results of anti-oxidant screening were depicted in TABLE 2 and Figure 2. DPPH radical scavenging is considered a good *in vitro* model and is widely used to conveniently assess antioxidant efficacy. In its radical form, DPPH has an absorbance at 517 nm which disappears when DPPH is reduced by an antioxidant compound or a radical species to become a stable diamagnetic molecule. As a result, the color changes from purple to yellow. This color change is taken as an indication of the hydrogen donating ability of the tested compounds[5]. Antioxidants can react with DPPH and produce 1,1-diphenyl-2-picryl-hydrazine. The reducing abilities of the synthesized compounds were determined by their interaction with the free stable radical 1,-1-diphenyl-2-picryl-hydrazine (DPPH) at 20 µg concentrations for 20 min.

As from the TABLE it could be seen that most of the compounds showed significant antioxidant activity. The highest scavenger activity observed in compound 23 is probably due to the presence of hydroxyl group in the acetophenic moiety and methoxy group in aldehydic moiety of chalcone. The order of activity regarding substitution on chalconyl group is OH>OCH_3>$(CH_3)_2$-N> H[6, 7].

When the observed results compared, it observed that the 4-methyl substituted compounds showed more DPPH scavenging activity in comparison to the 2-methyl substituted compounds. The substitution with dif-

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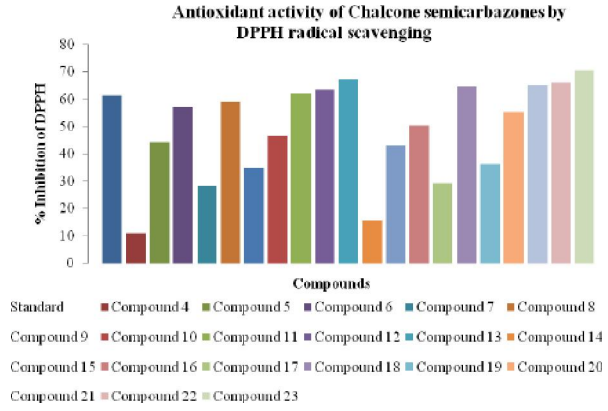

Figure 2 : Antioxidant activity of Chalcone semicarbazones by DPPH radical scavenging

ferent substituent on the phenyl of the aldehydic and acetophenic group of chalcone moiety played an important role in the scavenging of free radicals.

When the phenyl group of aldehydic and acetophenic moiety of chalcone is substituted with –OH group (Compound 8, 11, 12, 18, 21, 22) the compounds exhibited better activity in comparison to substitution with the other groups like p-dimethyl amino groups (compound 7, 17, 19) which may be due to more reducing potential.

Hydroxyl substitution on both moieties of chalcone has more scavenging effect than substitution on any one moiety[7, 8]. It was found that 5-hydroxyl substitution is more favorable than 4 or 6-hydroxyl substitution in the aldehydic moeity for antioxidant activity.

Methoxy substitution in the aldehydic moiety of chalcone also favors antioxidant activity. Highest DPPH free radical scavenging activity is shown when 5-hydroxyl substitution in acetophenic moiety and 4-methoxy substitution in aldehydic moiety is done.

Among the synthesized compounds, compound 6, 8, 11, 12, 13, 18, 20, 21, 22 and 23 showed the better or comparable activity in comparison to the standard drug. Bulkier substitution (compound 7, 9, 17, 19) is less favourable for antioxidant activity. The compounds with no substitution (compound 4, 14) or less substitution showed very less scavenging effect in comparison to the substituted compounds due to lesser electronegativity[6-8].

In summary, most of the synthesized compounds were potential lead for antioxidant activity. On the bases of observed results, it may be concluded that the substitution favors the activity, but the bulkier substitution disfavors the scavenging activity. The methoxy and hydroxyl substitution increases the DPPH free radical scavenging activity of the compounds.

TABLE 2 : Evaluation of antioxidant activity of chalconesemicarbazone derivatives using DPPH scavenging assay

Group	Absorbance (mean±S.D.; 517 nm)	% DPPH scavenging
Control	0.853±0.001	------
Standard	0.329±0.0015[a]	61.43
Compound 4	0.76±0.02 [a,b]	10.90
Compound 5	0.476±0.003 [a,b]	44.197
Compound 6	0.366±0.006 [a]	57.09
Compound 7	0.611±0.0085 [a,b]	28.37
Compound 8	0.349±0.0085 [a]	59.08
Compound 9	0.557±0.004 [a,b]	34.7
Compound 10	0.457±0.0075 [a,b]	46.42
Compound 11	0.326±0.0055 [a]	61.78
Compound 12	0.312±0.0025 [a]	63.42
Compound 13	0.281±0.003 [a]	67.06
Compound 14	0.72±0.005 [a,b]	15.59
Compound 15	0.486±0.004 [a,b]	43.02
Compound 16	0.424±0.003 [a,b]	50.29
Compound 17	0.603±0.003 [a,b]	29.31
Compound 18	0.304±0.003 [a]	64.36
Compound 19	0.542±0.002 [a,b]	36.46
Compound 20	0.383±0.004 [a]	55.09
Compound 21	0.298±0.002 [a]	65.06
Compound 22	0.29±0.0046 [a]	66.002
Compound 23	0.253±0.003 [a,b]	70.34

[a,b] P<0.001 compared to control and standard respectively. One way ANOVA followed by Tukey test

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