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Research Article

Anti-oxidant Activity of 2-hydroxyacetophenone Chalcone

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ABSTRACT

The novel series of chalcone was synthesized by 2-hydroxyacetophenone and substituted aldehyde. The structure of the synthesized compound was elucidated by melting point, retention factor, I.R. spectroscopic technique, ^{1}H NMR and elemental analysis. A series of various substituted chalcone were evaluated for *in- vitro* anti-oxidant activity by 2, 2-diphenyl-1-picrylhydrazyl method. Among the entire synthesized compound IIf showed the most potent anti-oxidant activity and the other derivatives like IId, IIe, IIg, IIk and IIm was showed mild anti-oxidant activity.

Keywords: Chalcone, 2-hydroxyacetophenone, substituted aldehyde, anti-oxidant activity, 2, 2-diphenyl-1-picrylhydrazyl.

1. INTRODUCTION

Chalcones are condensed products of substituted aromatic with simple or various substituted acetophenone in the presence of alkali [1]. It is the well known intermediates for synthesizing various derivatives of heterocyclic compounds. Chalcones are aromatic compound in which two aromatic rings are linked by a three carbon α, β-unsaturated carbonyl system. IUPAC name of chalcone is 1, 3-diphenyl-1, 2-propene-1-ene, in this, it possesses conjugate double bonds and a delocalized II electron on both benzene ring [2].

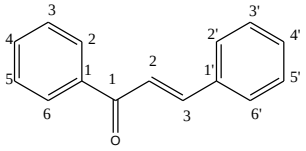


Figure 1: Structure of Chalcone

Compounds with the backbone of chalcone possesses various biological activities such as anti-microbial [3], anti-inflammatory [4], analgesic [5], anti-ulcerative [6], immune-modulatory [7], anti-malarial [8], anti-cancer [9], anti-viral [10], anti-leishmanial [11], anti-oxidant [12], anti-tubercular [13], anti-hyperglycemic [14] etc. A compound having anti-oxidant activity prevents and counteracts the damage of the human tissue by the normal effects of physiological oxidation [15]. Presence of the reactive keto group and the vinylenic group in the chalcone and their analogues possesses the antioxidant activity [16]. Compounds that associated with the antioxidant properties are hydroxyl and phenyl group. Oxidative stress which is caused by the free radical damage is help to deal with the antioxidants [17]. ROS (Reactive Oxygen Species) and RNS (reactive nitrogen species), contribute to tissue injury and also in the pathogenesis in asthma, burns and in rheumatisms [18]. DPPH is the most stable free radical with an unpaired of electron at nitrogen atom on a nitrogen-nitrogen bridge. DPPH assay were especially useful to assay concurrently antioxidant activity of each compound [19, 20]. Reaction of DPPH (2,2-diphenyl-1-picrylhydrazyl) free radical with the most reactive oxygen species which shows that in most of the reaction hydrazine is the major product in the DPPH, besides the nitro derivatives in the DPPH.

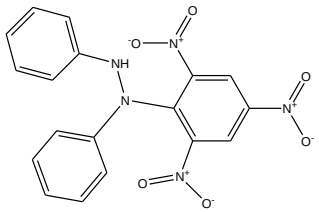


Figure 2: Chemical structure of DPPH radical

Mechanism of Chalcone:

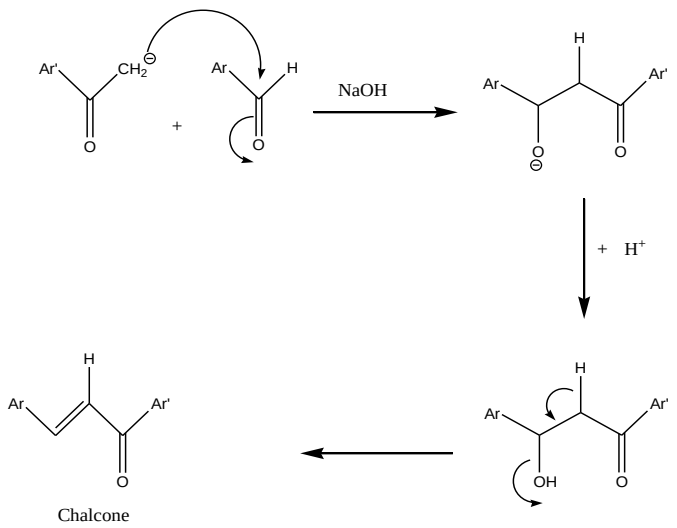


Figure 3: Mechanism of Chalcone

2. MATERIALS AND METHODS

All reagents and solvents were used as obtained from the supplier. Melting points were determined by using digital melting point apparatus in melting point capillaries and are uncorrected. The purity of the compounds were checked by TLC on silica gel G plates using ethyl acetate and n-hexane (4:6) solvent system, the spots were identified by iodine chamber and U.V lamp used as a visualizing agents. IR spectra were recorded by using KBr pellets on a FTIR Spectrophotometer (Shimadzu 8400S, 4000-400 cm^{-1}). Chemicals were purchased from the SIGMA and CDH and are supplied as "used without further purification".

3. GENERAL PROCEDURE FOR THE PREPARATION OF SUBSTITUTED CHALCONE DERIVATIVES

The substituted chalcone derivatives were prepared by stirring a mixture of substituted acetophenone (0.01 mol) and substituted aromatic benzaldehyde (0.01 mol) in adequate amount of ethanol for 3-4 hrs in presence of 40% NaOH. The reaction mixture was then allowed to stand for 1 hr. The precipitated product was filtered and purified by recrystallization from ethanol.

3.1 Synthesis of 3-(2-fluorophenyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (IIa): It was obtained from the reaction between 2- fluoro benzaldehyde and o-hydroxy acetophenone. **Mol. formula:** $C_{15}H_{11}FO_2$, **Colour:** Light green, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m p.:** 56-58°C, **Solvent system:** Ethyl acetate: n-Hexane (4:6), **R_f value:** 0.94, **Percentage yield:** 79.92%, **IR (KBr, cm^{-1}):** 3442.70 (OH str.), 1610.45 (Ar C=C), 1384.79 (Ar C-O), 754.12 (Ar C-H bend), 1265.22 (C-F), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.41-8.18 (d, 2H, CH), 6.88-7.34 (m, 8H, Ar-H), 4.9 (s, 1H, -OH), **Elemental analysis of $C_{15}H_{11}FO_2$ (242.25):** Calcd. C, 74.37; H, 4.58; F, 7.84; O, 13.21.

3.2 Synthesis of 3-(4-fluorophenyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (IIb): It was obtained from the reaction between 4-fluorobenzaldehyde and o-hydroxyacetophenone. **Molecular formula:** $C_{15}H_{11}FO_2$, **Colour:** light yellow, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m. p.:** 46-48°C, **Solvent system:** Ethyl acetate: n-Hexane (4:6), **R_f value:** 0.96, **Percentage yield:** 53.69%, **IR (KBr, cm^{-1}):** 3415.70 (OH str.), 1602.74 (Ar. C=C), 1348.15 (Ar. C-O), 752.19 (Ar. C-H bend), 1108.99 (C-F), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.52-7.82 (d, 2H, CH), 6.88-7.62 (m, 8H, Ar-H), 4.9 (s, 1H, -OH), **Elemental analysis of $C_{15}H_{11}FO_2$ (242.25):** Calcd. C, 74.37; H, 4.58; F, 7.84; O, 13.21.

3.3 Synthesis of 3-(2,4-difluorophenyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (IIc): It was obtained from the reaction between 2,4-dihydroxy benzaldehyde and o-hydroxy acetophenone. **Mol. formula:** $C_{15}H_{10}F_2O_2$, **Colour:** Light yellow, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m.p.:** 46-48°C, **Solvent system:** Ethyl acetate: n-Hexane (4:6), **R_f value:** 0.91, **Percentage yield:** 79.92%, **IR (KBr, cm^{-1}):** 3415.70 (OH str), 1602.74 (Ar C=C str), 1348.15 (Ar C-O), 1072.35 (C-F), 696.25 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.43-8.10 (d, 2H, CH), 6.89-7.35 (m, 8H, Ar-H), 4.9 (s, 1H, -OH). **Elemental Analysis of $C_{15}H_{10}F_2O_2$ (260.24):** Calcd. C, 69.23; H, 3.87; F, 14.60; O, 12.30.

3.4 Synthesis of 1-(2-hydroxyphenyl)-3-(2-methoxyphenyl) prop-2-en-1-one (IId): It was obtained from the reaction between 2-methoxybenzaldehyde and o-hydroxyacetophenone. **Mol. formula**: $C_{16}H_{14}O_3$, **Colour:** Yellowish, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m. p.:** 60-62°C, **Solvent system:** Ethyl acetate: n-Hexane (4:6), **R_f value:** 0.71, **Percentage yield:** 70%, **IR (KBr, cm^{-1}):** 3529.49 (OH str), 1612.38 (Ar C=C str), 1355.86 (Ar C-O), 684.68 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.33-8.02 (d, 2H, CH), 6.62-7.33 (m, 8H, Ar-H), 4.9 (s, 1H, -OH), 3.74 (t, 3H, $-OCH_3$). **Elemental Analysis of $C_{16}H_{14}O_3$ (254.28):** Calcd. C, 75.57; H, 5.55; O, 18.88.

3.5 Synthesis of 1-(2-hydroxyphenyl)-3-(4-methoxyphenyl) prop-2-en-1-one (IIe): It was obtained from the reaction between 4-methoxybenzaldehyde and o-hydroxyacetophenone. **Mol. formula:** $C_{16}H_{14}O_3$, **Colour:** Light yellow, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m. p.:** 68-70°C, **Solvent system:** Ethyl acetate: n-Hexane (4:6), **R_f value:** 0.83, **Percentage yield:** 34.60%, **IR (KBr, cm^{-1}):** 3446.56 (OH str.), 1608.52 (Ar. C=C), 1350.08 (Ar. C-O), 754.88 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.76-7.54 (d, 2H, CH), 6.67-7.53 (m, 8H, Ar-H), 4.9 (s, 1H, -OH), 3.72 (t, 3H, $-OCH_3$). **Elemental Analysis of $C_{16}H_{14}O_3$ (254.28):** Calcd. C, 75.57; H, 5.55; O, 18.88.

3.6 Synthesis of 1-(2-hydroxyphenyl)-3-(2, 4-dimethoxyphenyl) prop-2-en-1-one (IIf): It was obtained from the reaction between 2, 4-dimethoxybenzaldehyde and o-hydroxyacetophenone. **Mol. formula:** $C_{17}H_{16}O_4$, **Colour:** Yellowish, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m. p.:** 110-112°C, **Solvent system:** Ethyl acetate: n-Hexane (4:6), **R_f value:** 0.66**, Percentage yield:** 57.30%, **IR (KBr, cm^{-1}):** 3446.56 (OH str.), 1604.66 (Ar C=C), 1379.01 (Ar C-O), 756.64 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.56-8.23 (d, 2H, CH), 6.89-7.30 (m, 7H, Ar-H), 4.9 (s, 1H, -OH), 3.69 (m, 6H, $-OCH_3$). **Elemental Analysis of $C_{17}H_{16}O_4$ (284.31):** Calcd. C, 71.82; H, 5.67; O, 22.51.

3.7 Synthesis of 3-(2-chlorophenyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (IIg): It was obtained from the reaction between 2-chlorobenzaldehyde and o-hydroxyacetophenone. **Mol. formula:** $C_{15}H_{11}ClO_2$, **Colour:** Light yellow, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **Melting point:** 80-82°C, **Solvent system:** Ethyl acetate: n-Hexane (3:7),**R_f value:** 0.82, **Percentage yield:** 46.56%, **IR (KBr, cm^{-1}):** 3406.05 (OH str), 1604.66 (Ar C=C str), 1384.79 (Ar C-O), 765.69 (C-Cl), 717.47 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.30-8.10 (d, 2H, CH), 6.90-7.62 (m, 8H, Ar-H), 4.9 (s, 1H, -OH). **Elemental Analysis of $C_{15}H_{11}ClO_2$ (258.7):** Calcd. C, 69.64; H, 4.29; Cl, 13.70; O, 12.37.

3.8 Synthesis of 3-(3-chlorophenyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (IIh): It was obtained from the reaction between 3-chlorobenzaldehyde and o-hydroxyacetophenone. **Mol. formula:** $C_{15}H_{11}ClO_2$, **Colour:** Light yellow, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m. p.:** 80-82°C, **Solvent system:** Ethyl acetate: n-Hexane (4:6), **R_f value:** 0.82, Percentage yield: 65.65%, **IR (KBr, cm^{-1}):** 3529.49 (OH str), 1612.38 (Ar C=C str), 1355.86 (Ar C-O), 684.68 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.54-7.92 (d, 2H, CH),

6.82-7.61 (m, 8H, Ar-H), 4.9 (s, 1H, -OH). **Elemental Analysis of $C_{15}H_{11}ClO_2$ (258.7):** Calcd. C, 69.64; H, 4.29; Cl, 13.70; O, 12.37.

3.9 Synthesis of 3-(4-chlorophenyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (IIi): It was obtained from the reaction between 4-chlorobenzaldehyde and o-hydroxyacetophenone. **Mol. formula:** $C_{15}HS_{11}ClO_2$, **Colour:** Orange yellow, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **Melting point:** 94-96°C, **Solvent system:** Ethyl acetate: n-Hexane (3:7),**R_f value:** 0.82, **Percentage yield:** 60.29%, **IR (KBr, cm^{-1}):** 3425.34 (OH str), 1610.45 (Ar C=C str), 1352.01 (Ar C-O), 754.12 (C-Cl), 657.68 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.42-7.80 (d, 2H, CH), 6.72-7.62 (m, 8H, Ar-H), 4.9 (s,1H, -OH). **Elemental Analysis of $C_{15}H_{11}ClO_2$ (258.7):** Calcd. C, 69.64; H, 4.29; Cl, 13.70; O, 12.37.

3.10 Synthesis of 3-(2,4-dichlorophenyl)-1-(2-hydroxyphenyl) prop-2-en-1-one (IIj): It was obtained from the reaction between 2,4-dichlorobenzaldehyde and o-hydroxyacetophenone. **Mol. formula:** $C_{15}H_{10}Cl_2O_2$, **Colour:** Yellowish, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m. p.:** 58-60°C, **Solvent system:** Ethyl acetate: n-Hexane (3:7), **R_f value:** 0.92, **Percentage yield:** 30.87%, **IR (KBr, cm^{-1}):** 3425.34 (OH str), 1610.45 (Ar C=C str), 1352.01 (Ar C-O), 754.12 (C-Cl), 657.68 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.32-8.10 (d, 2H, CH), 6.89-7.36 (m, 7H, Ar-H), 4.9 (s, 1H, -OH). **Elemental Analysis of $C_{15}H_{10}Cl_2O_2$ (293.14):** Calcd. C, 61.46; H, 3.44; Cl, 24.19; O, 10.92.

3.11 Synthesis of 3-(2,6-dichlorophenyl)-1-(2-hydroxyphenyl)prop-2-en-1-one (IIk): It was obtained from the reaction between 2,6-dichlorobenzaldehyde and o-hydroxyacetophenone. **Mol. formula:** $C_{15}H_{10}Cl_2O_2$, **Colour:** Brown, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m. p.:** 78-80°C , **Solvent system:** Ethyl acetate: n-Hexane (3:7), **R_f value:** 0.89, **Percentage yield:** 71.46%, **IR (KBr, cm^{-1}):** 3456.07 (OH str), 1612.38 (Ar C=C str), 1346.22 (Ar C-O), 750.26 (C-Cl), 636.95 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.38-8.10 (d, 2H, CH), 6.89-7.62 (m, 7H, Ar-H), 4.9 (s, 1H, -OH). **Elementa Analysis of $C_{15}H_{10}Cl_2O_2$ (293.14):** Calcd. C, 61.46; H, 3.44; Cl, 24.19; O, 10.92.

3.12 Synthesis of 1-(2-hydroxyphenyl)-3-(2-nitrophenyl)prop-2-en-1-one (IIl): It was obtained from the reaction between 2-nitrobenzaldehyde and o-hydroxyacetophenone. **Molecular formula:** $C_{15}H_{11}NO_4$, **Colour:** Light brown, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m. p.:** 58-60°C, **Solvent system:** Ethyl acetate: n-Hexane (3:7), **R_f value:** 0.76, **Percentage yield:** 79.58%, **IR (KBr, cm^{-1}):** 3398.34 (OH str). 1685.67 (Ar C=C str), 1384.79 (Ar C-O), 1311.50 (C-N=O), 765.69 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.60-8.42 (d, 2H, CH), 6.88-8.11 (m, 8H, Ar-H), 4.9 (s, 1H, -OH). **Elemental Analysis of $C_{15}H_{11}NO_4$ (269.25):** Calcd. C, 66.91; H, 4.12; N, 5.20; O, 23.77.

3.13 Synthesis of 1-(2-hydroxyphenyl)-3-(4-nitrophenyl) prop-2-en-1-one (IIm): It was obtained from the reaction between 4-nitrobenzaldehyde and o-hydroxyacetophenone. **Molecular formula:** $C_{15}H_{11}NO_4$, **Colour:** Brown, **Solubility:** Ethyl alcohol, Methanol, Chloroform, DMSO, **m. p.:** 78-80°C , **Solvent system:** Ethyl acetate: n-Hexane (3:7), **R_f value:** 0.89, **Percentage yield:** 35.23%, **IR (KBr, cm^{-1}):** 3444.63 (OH str), 1600.81 (Ar C=C str), 1384.79 (Ar C-O), 1340.43 (Ar NO_2), 692.40 (Ar C-H bend), **^{1}HNMR ($CDCl_3$-d_6, δ, ppm):** 7.80-8.02 (d, 2H, CH), 6.90-8.12 (m, 8H, Ar-H), 4.9 (s, 1H, -OH). **Elemental Analysis of $C_{15}H_{11}NO_4$ (269.25):** Calcd. C, 66.91; H, 4.12; N, 5.20; O, 23.77.

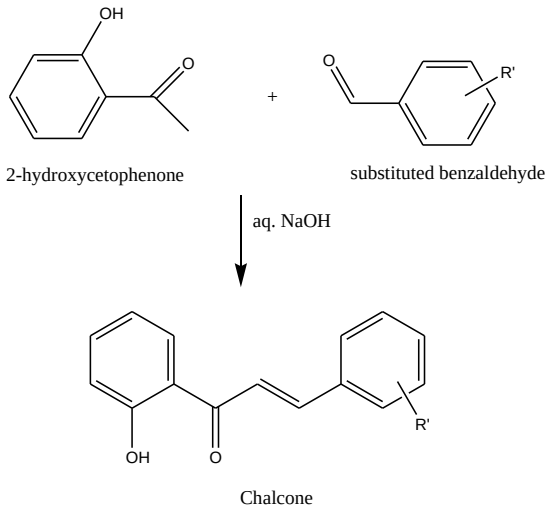
4. ANTIOXIDANT ACTIVITY

DPPH (2,2-Diphenyl-1-picryl hydrazyl) Scavenging Activity:

Antiradical activity of compounds was performed by DPPH model. Stock solution of DPPH (1.3 mg/ml) in methanol was prepared. Stock solution of DPPH solution 100 µl was added in 3ml of methanol and absorbance was recorded at 516nm. The various concentrations of compounds (100,200,400 and 600 µg/ml) were prepared. All sample solutions 1 ml each is diluted to 3 ml and 100 µl of stock solution of DPPH was added then absorbances were recorded at 516 nm.

Percentage inhibition = [Control – Test]/ Control × 100

5. REACTION SCHEME



R'= F, Cl, OCH_3, NO_2

Scheme 1: Reaction Scheme for synthesizing chalcone

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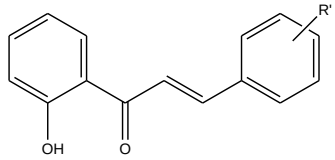
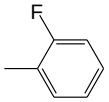
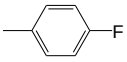
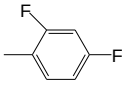
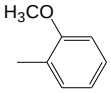
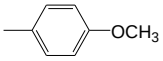
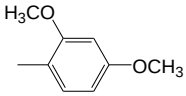
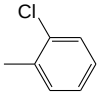
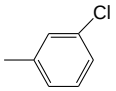
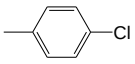
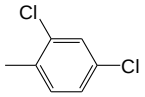
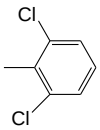
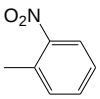
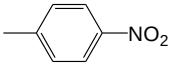


Table 1: Physical parameters of synthesized compounds (IIa-IIm)

S.No.	Compound[a]	R'	Molecular Formula	M. Wt.	R_f value[b]	% Yield[c]	m.p. (°C)
01.	IIa		$C_{15}H_{11}FO_2$	242.25	0.94	53.69%	56-58°C
02.	IIb		$C_{15}H_{11}FO_2$	242.25	0.96	79.92%	46-48°C
03.	IIc		$C_{15}H_{10}F_2O_2$	260.24	0.90	70%	60-62°C
04.	IId		$C_{16}H_{14}O_3$	254.28	0.71	75.07%	120-122°C
05.	IIe		$C_{16}H_{14}O_3$	254.28	0.83	34.60%	68-70°C
06.	IIf		$C_{17}H_{16}O_4$	284.31	0.66	57.30%	110-112°C
07.	IIg		$C_{15}H_{11}ClO_2$	258.7	0.82	46.56%	80-82°C
08.	IIh		$C_{15}H_{11}ClO_2$	258.7	0.78	65.65%	60-62°C
09.	Iii		$C_{15}H_{11}ClO_2$	258.7	0.95	60.29%	76-78°C
10.	IIj		$C_{15}H_{10}Cl_2O_2$	293.14	0.92	30.87%	58-60°C
11.	IIk		$C_{15}H_{10}Cl_2O_2$	293.14	0.89	71.46%	48-50°C
12.	IIl		$C_{15}H_{11}NO_4$	269.25	0.79	79.58%	78-80°C
13.	IIm		$C_{15}H_{11}NO_4$	269.25	0.76	35.23%	58-60°C

[a]Products were characterized by IR, [c]Synthesized yields.

6. RESULT AND DISCUSSION

From these data a preliminary result can be drawn for the synthesized compounds. A novel series of compounds (IIa-IIm) were synthesized and characterized. And all the above synthesized compounds were tested for anti-oxidant activity using DPPH method. Among the tested compounds IIf shows the most potent activity while the other like IId, IIe, IIg, IIk and IIm was found to be moderately mild active.

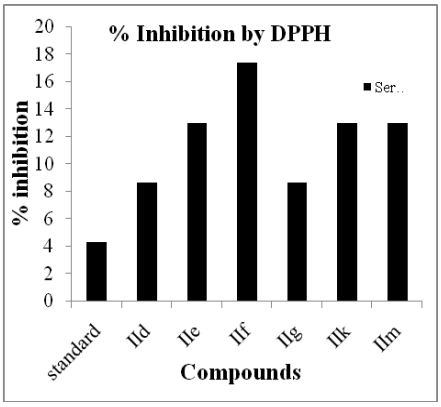


Table 2: Anti-oxidant Activity of synthesized compounds (IIa-IIm) by DPPH Method.

S.No.	Compound Name	% inhibition
01.	Standard	4.35
02.	IIa	0
03.	IIb	0
04.	IIc	0
05.	IId	8.7
06.	IIe	13.04
07.	IIf	17.39
08.	IIg	8.7
09.	IIh	0
10.	Iii	0
11.	IIj	0
12.	IIk	13.04
13.	IIl	0
14.	IIm	13.04

7. CONCLUSION

Chalcones possess various biological activities like anti-bacterial, anti-malarial, anti-fungal, anti-microbial etc. When these chalcone moieties screened for the anti-oxidant activity they showed good antioxidant property. Among these derivatives of chalcones 2-methoxy, 4-methoxy, 2, 4-dimethoxy, 2, 4-dichloro and 4-nitrobenzaldehyde substituted derivatives of chalcone showed the good anti-oxidant activity. From these derivatives 2, 4-dimethoxybenzaldehyde substituted derivative of chalcone showed the most potent anti-oxidant activity. And the other derivatives like 2-methoxy, 4-methoxy, 2, 4-dichloro and 4-nitro substituted chalcone shows moderately mild anti-oxidant activity.

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