Synthesis and antioxidant evaluation for monocarbonyl curcuminoids and their derivatives

Síntesis y evaluación antioxidante para monocarbonil curcuminoides y sus derivados

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ARTÍCULO DE INVESTIGACIÓN CIENTÍFICA Y TECNOLÓGICA

How to cite this paper:
Agel, K N, Abood, E, Alsalim, T., Synthesis and antioxidant evaluation for monocarbonyl curcuminoids and their derivatives, Basrah, Iraq. Innovaciencia Facultad de Ciencias Exactas, Naturales y Agropecuarias. 2018; 6(1) S1: 1-13.

Reception date:
Received: 15 August 2018
Accepted: 25 November 2018
Published Online: 28 December 2018

DOI:
http://dx.doi.org/10.15649/2346075X.481

Keywords:
Cucumine; Monocarbonylcurcuminoids; Antioxidant; DPPH; Pepronal; 4-thiomethoxy benzaldehyde

ABSTRACT

Introduction: Curcumin is a yellow pigment extracted from the Curcuma longa L, which have a several biological activities and pharmacological properties. Curcuminoids have a wide range as antioxidant not only in a food system, but also for biological systems. **Materials and Methods:** Acetone, 4-thiomethoxy benzaldehy, pepronal, thiosemicarbazide, 4-phenylthiosemicarbazide and chloroethylacetate. The two Analogous of monocarbonyl curcuminoids (MCCs) have been synthesized by claisen –Schmidt condensation from the reaction between one mole of acetone with two moles of appropriate aromatic aldehydes (4-thiomethoxy benzaldehyde and pepronal) then synthesized their hetero derivatives. The pyrazols derived from the reaction MCCs with hydrazine or one of their derivative (thiosemicarbazide, 4-phenylhydrazine).**Results and Discussion**:All synthesized compounds were characterized by various spectroscopic techniques such as FTIR, ^{1}HNMR, ^{13}CNMR, Mass spectroscopies and CHN analysis. The antioxidant activity of synthesized MCCs, 1, 2, 1a, 2a, 3, were determined by the ability to scavenge the stable 1,1-diphenyl-2-picryl hydrazyl (DPPH) free radical according to Blois method. The DPPH inhibition activity was measured by spectrophometric method. The polyhydroxy curcuminoid has showed a high activity for scavenging of DPPH radicals, the reason is the hydroxyl phenolic group OH give the compound high activity of scavenging the radical by donating hydrogen atom to the DPPH radicals and inhibition the radical activity by hydrogen atom transfer (HAT). Therefore the scavenge of radical activitywill be in the order: 3>2a>1a>2>1 andthe half maximal inhibitory concentration (IC_{50}) between (17.35-135.2) µmol/L.**Conclusions**: The proposed structure of the synthesized compounds were confirmed by used a spectroscopic technique such as, FTIR, Mass spectra (EI),^{1}H and ^{13}C NMR, The antioxidant activity of curcuminoids were studied by using DPPH as a source of radicals. The higher activity of compounds can be attributed to present the phenolic OH group.

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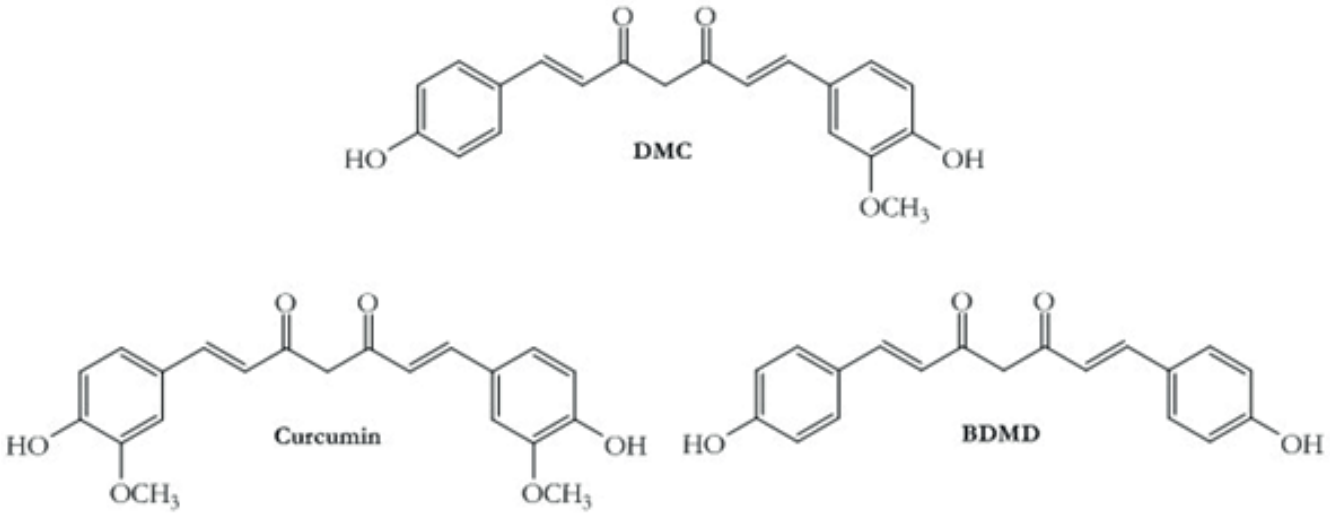
INTRODUCTION

Curcumine is a natural extract from rhizome of curcumine longa (Turmeric)[1] The pigment yellow color of extracted contained three isomers of curcuminoids (curcumine, demethoxy curcumine and bis demethoxy curcumine)[2]. This natural compound has been used as food pigment and in food industries[3].

Figure 1 Some examples of Curcumins



In the last decades the pharmacological activity of curcumine has many applications *in-vivo* and -*vitro* as antioxidant[4], anticancer[5], antifungalanti[6], inflammator[7], antibacterial[8], and antiviral[9]. Because of the curcumine poor solubility in aqueous media[10], which is the most cumin problems of this material leads to poor bioavailability and absorption then cause a rapid metabolism. Therefore, this material attracted a lot of attention in past decades, especially by modifying their structure and preparing new analogues to increase their bioactivity as anticancer and antioxidant[11]. In this study, two monocarbonyl curcumine analogous (MCCs) and their derivatives have been designed, and their activity as an antioxidant agents for scavenging of DPPH radicals have been nvestigated.

MATERIALS AND METHOD

Materials and Reagents

All the chemicals and solvents were used with analytical grade (AR) and highestpurity which included pepronal and thiomethoxybenzaldehyde (Aldrich), thiosemicarbazide, pyrogallol and chloroacetylchloride (Merck). All the solvents were used equipped by (BDH) company.

Instrumentation

FTIR spectra of all compounds were recordedon shimadzu FTIR model Affinity spectrophotometer using KBr pellets in the range (4000-400) cm^{-1}. The Mass spectra were scanned by the EI technique 70eV with an Agilent Technologies 5975 spectrometer. The experimental values of ^{1}H and $^{13}CNMR$ spectra for the studied compounds were scanned on a

Bruker 400MHz spectrometer with a field gradient to operateat 400 MHz for proton observation and 100 MHz for carbon observation using DMSO–$d_6$as solvent and TMS as internal standard. Elemental analysis (CHNS)weremeasured by using elementar Vario MICRO. UV-VISIBLEspectra were measured using a PG-instrument T80$^+$ spectrophotometer.

Synthesis

Preparation of monocarbonyl curcumicoids (MCCs) (1, and 2):

The monocarbonyl curcuminoids 1, and 2 were synthesized by Claisen–Schmidt condensation between acetone (16.65 mmol) with appropriate aromatic aldehydes (33.7 mmol) in (50 mL)etanol, and (34 mmol) of sodium hydroxide solution as a catalyst. The reaction mixture wasstirred for further 10hours at room temperature. The solid product was collected by filtration, and then waswashed by water several times, dried then recrystallized from the appropriate solvent (scheme 1).

(1E,4E)-1,5-bis(benzo[d][1,3]dioxol-5-yl) penta-1,4-dien-3-one (1):

Color: yellow powder, recrystallized from ethyl acetate, yield: 84%, M.P.: 186-188^{o}C, ^{1}HNMR (400 MHz, DMSO-d_6, δ ppm): 6.1(s,4H,-OCH_2O-),7.00 (d, 2H, *J*=5 Hz, CH=C), 7.19 (d, 2H,*J*=5Hz, aromatic),7.26 (d, 2H, *J*=10Hz, aromatic),7.45(s, 2H, aromatic),7.71(d, 2H,*J*= 5Hz, CH=C). ^{13}CNMR (100MHz, DMSO-d_6, δ ppm): 102.1, 107, 109, 124.3, 125.7, 129.7, 142.8, 148.2, 149.8, 189.1. MS (70 eV, m/z): 322[M], 279, 189, 175, 135. FTIR (KBr disk, υ, cm^{-1}): 3014, 2912, 1643, 1598, 1490, 1190, 1118. Anal. calc. for $C_{19}H_{14}O_5$: C, 70.80; H, 4.38; found: C, 69.47; H, 4.24.

(1E,4E)-1,5-bis(4-(methylthio) phenyl) penta-1,4-dien-3-one (2):

Color: yellow powder, recrystallized from ethanol, yield: 80%, M.P.: 158-159^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.52(s, 6H, -SCH_3), 7.33 (d, 2H, *J*=5 Hz, CH=C), 7.27 (d, 4H,*J*=10Hz, aromatic), 7.72 (d,4H, *J*=10Hz, aromatic), 7.75 (d, 2H,*J*= 5Hz, CH=C). ^{13}CNMR (100 MHz, DMSO-d_6, δ ppm):14.7, 125.3, 126.1, 129.4, 131.6, 142.2, 142.5, 186.6. MS (70 eV, m/z): 226.2[M], 311.2, 279.1, 204.2, 177.1, 134.1, 102.1, 89.1, 77.1, 48.1. FTIR (KBr disk, υ, cm^{-1}): 3016, 2919, 1643, 1589, 1489, 1337. Anal. calc. for $C_{19}H_{18}OS_2$: C, 69.90; H, 5.56; S, 19.64, found: C, 68.59; H, 5.48; S, 19.47.

General procedure for the synthesis pyrazols(1a-c) &(2a-b)

MACs (3.11 mmol) dissolved in (50mL) of etanol, and (3.13 mmol) of appropriate hydrazine was added or one of their derivatives (hydrazine monohydrate, thiosemicarbazide, and 4-phenyl hydrazine), then (0.6 g) sodium hydroxide was added to the mixture. The reaction mixture was heated under reflux for 16 hours, then cooled down and poured into iced water, then neutralized by the addition 0.1N HCl. The product was collectedby filtration, and then dried and recrystalized from a suitable solvent (scheme 2).

(E)-5-(benzo[d][1,3]dioxol-5-yl)-3-(2-(benzo[d][1,3]dioxol-5-yl) vinyl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (1a):

Color: yellow powder, recrystallized from benzene: petroleum ether,yield:55.9%, M.P: 208-210 ^{o}C, ^{1}HNMR (400 MHz, DMSO-d_6,δ ppm):2.97(dd, H, *J*=5Hz, CH_2-C pyrazole ring), 3.68(dd, H,*J*=10Hz, CH_2-C pyrazole ring), 5.81 (dd ,H, *J*=5Hz, CH-N pyrazole ring),5.97 (s, 2H, –OCH_2O-),6.05(s, 2H, -OCH_2O-), 6.58 (d,1H, *J*=10Hz, CH=C),6.62(s,1H, Ar) ,7.04(d,1H, *J*=5Hz, CH=H),6.83-7.28(d, 4H, *J*=10 Hz, aromatic),7.48(s, 1H, aromatic),8(s,2H, NH_2).^{13}CNMR (100MHz, DMSO-d_6, δ ppm) :41.9, 62.7, 101.3,101.8, 106.2, 108.7, 108.9, 116.4, 118.7, 123.7, 130.5, 137.8, 139.2,146.5,147.7,148.4,148.7,157,176,187.6.MS (70 eV, m/z): 395[M], 153, 125, 79, 51. FTIR (KBrdisk, υ, cm^{-1}), 3458, 3336, 3066, 2891,

1625, 1583, 1489, 1359, 1253, 1193,1039. Anal. calc. for $C_{20}H_{17}N_3O_4S$: C, 60.75; H, 4.33; N, 10.63; S, 8.11, found: C, 60.14; H, 4.08; N, 10.21; S, 7.88.

(E)-5-(benzo[d][1,3]dioxol-5-yl)-3-(2-(benzo[d][1,3]dioxol-5-yl) vinyl)-N-phenyl-4,5-dihydro-1H-pyrazole-1-carbothioamide (1b):

Color: yellow powder, recrystallized from benzene: petroleum ether, yield:49%, M.P.: 198-200°C, ^{1}HNMR (400 MHz, DMSO-d_6, δ ppm):3.00 (dd, H, *J*=15Hz, CH_2-Cpyrazole ring),3.68 (dd, H, *J*=10Hz, CH_2-C pyrazole ring), 5.43(dd, H, *J*=10 Hz, CH-N pyrazole ring),5.98 and 6.06 (s,4H, -OCH_2O-), 6.71 (d, 1H, *J*=10Hz, CH=C),6.74-7.36 (m, 11H,aromatic), 7.58(d, 1H, *J*=8Hz,CH=C),8.93 (s, 1H, N-H), ^{13}CNMR (100MHz, DMSO-d_6, δ ppm):41.7, 59.9,106.4, 108.7, 109, 110, 118.6, 119.1, 120.5, 128.7, 128.9, 130.8, 139.7, 146.7, 147.9, 148.4, 151.4, 153.8. FTIR (KBrdisk, υ, cm^{-1}) 3383, 3037, 2893, 1685, 1654, 1595, 1489, 1244, 1122,1039. Anal. calc. for $C_{26}H_{21}N_3O_4S$: C, 66.23; H, 4.49; N, 8.91; S, 6.80, found: C, 65.82; H, 4.31; N, 7.82; S, 6.44.

(E)-5-(benzo[d][1,3]dioxol-5-yl)-3-(2-(benzo[d][1,3]dioxol-5-yl) vinyl)-4,5-dihydro-1H-pyrazole (1c):

Color: yellow powder, recrystallized from methanol,yield: 50%, M.P.: 208-210°C, ^{1}HNMR (400 MHz, DMSO-d_6, δ ppm): 3.65 (dd, H, CH_2-C pyrazole ring), 4.1 (dd, H, CH_2-C pyrazole ring), 5.05 ppm (dd, H, CH-N pyrazole ring), 5.96(s, 2H,-OCH_2O-), 6.08 (s, 2H,-OCH_2O-), 6.7 (s, H,-NH), 6.81 (d, 1H, CH=C), 6.85-7.37 (m , 6H, aromatic), 7.43 (d, 1H, *J*=5 Hz, CH=C). MS (70 eV, m/z): 336.3[M], 309, 135, 123, 71. FTIR (KBr disk, υ, cm^{-1}), 3116, 2924, 1627, 1604, 1489, 1242, 1111, 1033. Anal. calc. for $C_{19}H_{14}N_2O_4$: C, 68.26; H, 4.22; N, 8.38, found: C, 67.85; H, 4.24; N, 8.09.

(E)-5-(4-(methylthio) phenyl)-3-(4-(methylthio) styryl)-4,5-dihydro-1H-pyrazole-1-carbothioamide (2a):

Color: yellow powder, recrystallized from ethanol, yield: 53.3%, M.P.: 138-140°C, ^{1}HNMR (400 MHz, DMSO-d_6, δ ppm):2.44 (s,3H, –SCH_3),2.49 (s,3H, –SCH_3),2.98 (dd, H,*J*=15 Hz , CH_2-C pyrazole ring), 3.7(dd, H, *J*=10 Hz, CH_2-C pyrazole ring),5.85 (dd, H, *J*=5 Hz, CH-Npyrazole ring), 7.04-8.08(m, 10H, aromatic & CH=C),8.4(s,2H,NH_2), MS (70 eV, m/z): 499.3[M], 339, 352, 276, 248, 191, 150, 60. FTIR(KBr disk , υ,cm^{-1}), 3417, 3248, 3039, 2916, 1620, 1589, 1489, 1342, 1265,1188,1087. Anal. calc. for $C_{19}H_{20}N_2S_2$: C, 67.02; H, 5.92; N, 8.23; S, 18.83, found: C, 66.83; H, 5.88; N, 8.01; S, 17.90.

(E)-5-(4-(methylthio) phenyl)-3-(4-(methylthio) styryl)-4,5-dihydro-1H-pyrazole (2b):

Color: yellow powder, recrystallized from ethanol: n-hexane, yield: 50.4%, M.P.: 169-171°C, ^{1}HNMR (400 MHz, DMSO-d_6, δ ppm): 2.44 (s,3H,-SCH_3), 2.49 (s,3H,-SCH_3), 2.9 (dd, H, *J*=5Hz, CH_2-C pyrazole ring), 3.8 (dd, H, CH_2-C pyrazole ring), 5.2 (dd, H, CH-N pyrazole ring), 6.47 (s,H ,NH), 7.17-7.56 (m, 10H, aromatic & CH=C).MS (70 eV, m/z): 340.2[M], 307, 277, 137, 103, 91, 78. FTIR (KBr disk, υ, cm^{-1}):3224, 3016, 1581, 1481, 1489, 1388,1157,1065. Anal. calc. $C_{20}H_{21}N_3S_3$: C, 60.12; H, 5.30; N, 10.52; S, 24.07, found: C, 59.79; H, 5.11; N, 10.26; S, 23.87.

Procedure for the synthesis of 2 - chloro -1-(2,3,4-trihydroxyphenyl) ethan-1- one:

To a cooled solution of stirred of aluminum chloride (24g) dissolved in DCM at 10-15°C, (8g) of pyrogallol in (50mL) DCM was added drop-wisely within 20 min. (5mL) of chloroacetyl chloride was added to the reaction mixture which is still at the same temperature. The temperature of reaction mixture raised up to room temperature and further stirring for

another 20 hours. After that time the reaction was poured onto (100 mL) of dilute hydrochloric acid with stirring for 2 hours at room temperature. The solid material wascollectedby filtration and washed with water, then the solid suspended in dilute acetic acid solution and heated to 85°C. The mixture was-cooled down to room temperature. Theproduct was filtered, washed with water and dried, thenrecrystallized from benzene (scheme 3).

Color: whitepowder, recrystallized from benzene, white powder, recrystallized from benzene, yield: 85%, M.P.: 169-170 °C, ^{1}HNMR (400 MHz, DMSO-d_6, δ ppm): 5.03(s,2H,-CH_2-), 6.44 (d, H, *J*=5 Hz, aromatic),7.3(d, H, *J*=5 Hz, aromatic), 8.77, 10.28, 11.63 (s,3H,-OH),^{13}CNMR (100MHz, DMSO-d_6, δ ppm): 47.3, 109, 112, 123, 133, 152.2, 153.4, 195.2. MS (70 eV, m/z): 202.1[M], 153,125,79,51. FTIR (KBrdisk, υ, cm-^{1}), 3498, 3390, 3095, 2989,1637, 1523.

Procedure for the synthesis of (E)-4-(2-(5-(benzo[d][1,3]dioxol-5-yl)-3-(2 (benzo[d][1,3]dioxol-5-yl) vinyl)-4,5-dihydro-1H-pyrazol-1-yl) thiazol-4-yl) benzene-1,2,3-triol (3):

In the reaction vessel (0.9g, 2.36 mmol) of compound (**1a**), and (0.48g, 2.36 mmol) of compound 2-chloro-1-(2,3,4-trihydroxyphenyl) ethan-1-one dissolved in (20mL) of dimethyl formamide. The reaction mixture was heated under reflux for 6 hours. The solid product was collected by filtration, dried then recrystallized from ethylacetate (scheme 4).

Color: light brown powder, recrystallized from ethanol, yield: 56%, M.P.:260-261°C, ^{1}HNMR (400 MHz, DMSO-d_6, δ ppm): 3.12(dd, H, *J*= 10 Hz, pyrazole ring), 3.84(dd, H, *J*=10Hz, pyrazole ring), 5.58(dd, H, *J*=5Hz, pyrazole ring), 5.98, and 6.05(s,4H, -OCH_2O-), 6.28(d, 1H, *J*=10Hz,CH=C), 6.93(s, 1H, H of thiazole), 6.79-7.17 (m, 8H, aromatic), 7.38(d, 1H, *J*=5Hz, CH=C) 8.06 (s, H,-OH),8.98(s,1H,-OH),10.64 (s, H,-OH).^{13}CNMR(100MHz, DMSO-d_6, δ ppm): 43.1, 64, 101.7, 106.2, 106.3, 107.7, 108.9, 109, 111.1, 116.9 118.4, 119.7, 123.6, 130.9, 133.3, 135.6, 137.5, 145.5, 146.6, 147.2, 148.2, 148.4, 148.5, 149.5, 155.5, 164.MS (70 eV, m/z):543.3[M], 394, 336, 147, 89, 43. FTIR (KBr disk, υ, cm-^{1}), 3537, 3429, 3032, 2908,1604, 1489, 1242, 1087, 1037. Anal. calc. $C_{28}H_{21}N_3O_7S$: C, 61.87; H, 3.89; N, 7.73; S, 5.90, found: C, 61.61; H, 3.67; N, 7.57; S, 5.73.

DPPH Radical Scavenging Assay

The antioxidant activity of synthesized curcuminoids (**1, 1a, 2, 2a, and 3**) were determined by measuring the ability ofscavenging thestable 2,2-diphenyl-1-picrylhydrazyl(DPPH) free radicals according to Blois method[12,13]. The DPPH inhibition activity was measured by spectrophometric method, by mixing (1 mL, 200 µmol/L) of ethanolic solution of DPPH with (1mL)of different concentrations (50, 100, and 200) µmol/L of ethanolic solution of synthesized curcuminoids. The absorbance was read at 517 nm as functional of differenttimes byusing uv-visble spectrophotometer. Inaddition, there was a notable change DPPH color graduate from violet to yellow or colorless. The percentage of inhibition was calculated by the following equation[14, 15].

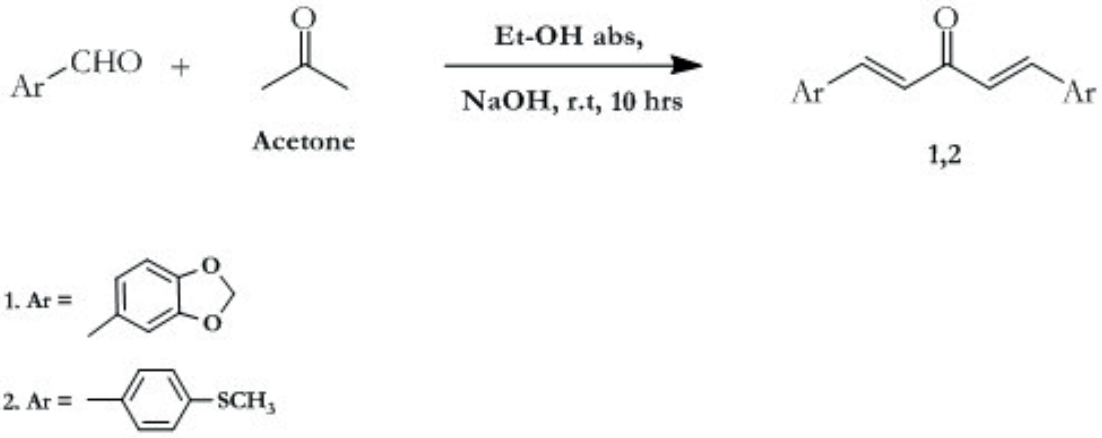
$$\%\text{inhibition percentage} = \frac{A\,c \quad A\,s}{A\,c} \times 100$$

Ac: control absorbance, the absorbance of pure DPPH
As: sample absorbance, the absorbance of DPPH mixed with sample
The liner curve was obtained by plotting inhibitor percentage of radical versus concentrations of compounds.

RESULTS AND DISCUSSION

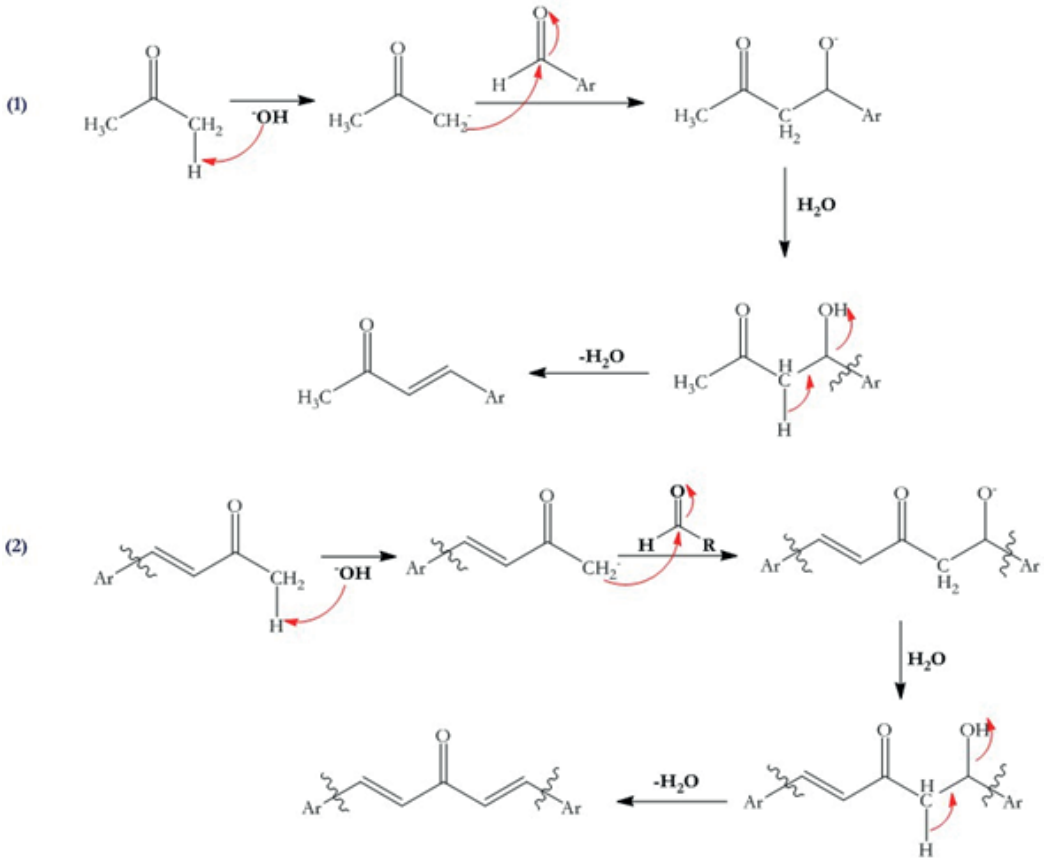
Spectroscopy identification:

The monocarbonyl curcuminoids (MCCs) (**1, and 2**) prepared according to (Scheme1). The proposed structure has confirmed by using spectroscopic techniques such as FTIR, Mass spectrometry, ^{1}H and ^{13}C NMR spectroscopy as well as the elemental analysis.



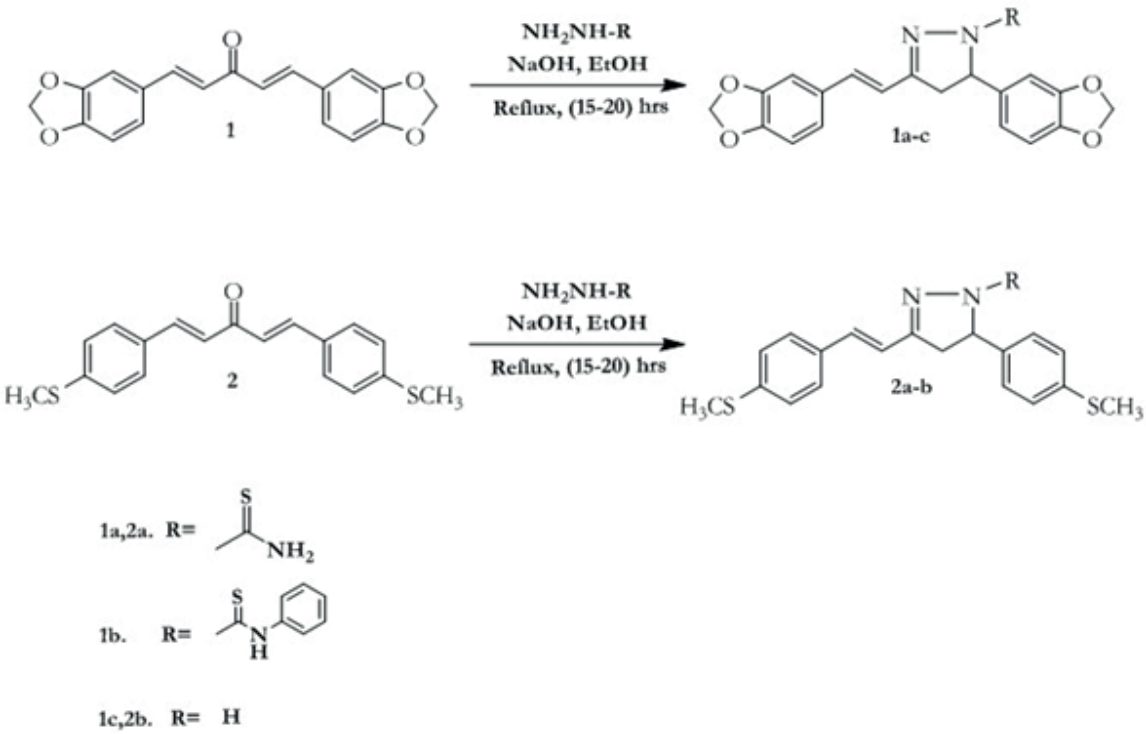
Scheme 1Preparation compound (MCCs).

The (MCCs) prepared according to Claisen–Schmidt condensation reaction between acetone and, aromatic aldehyde, (scheme 2) represents the suggested preposed reaction mechanism.



Scheme 2 Reaction mechanism of (MCCs).

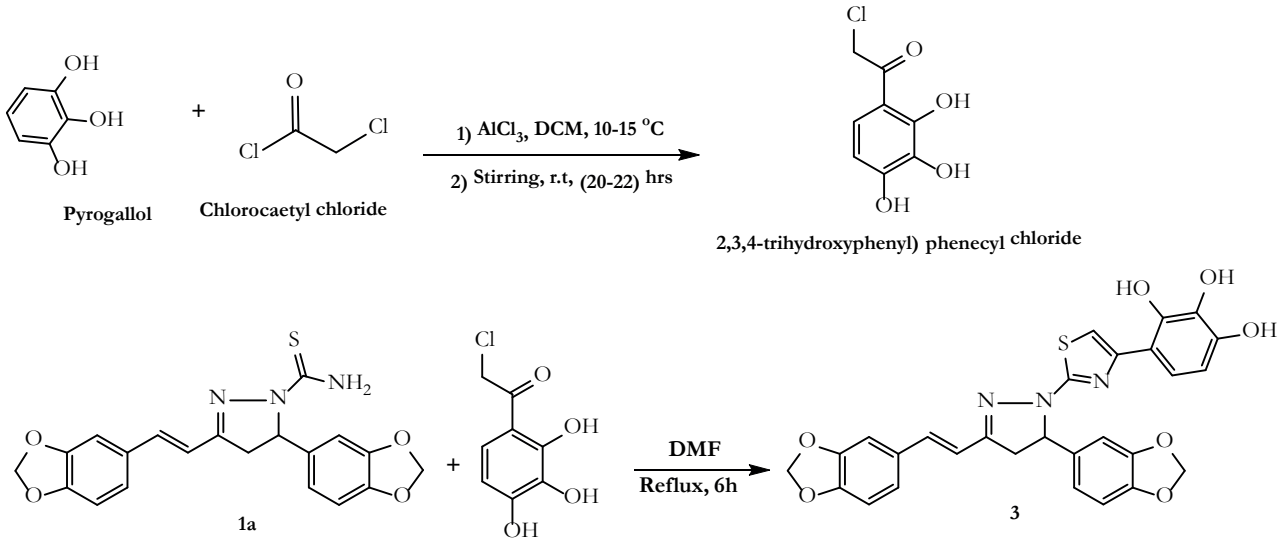
The IR spectra of the prepared compounds exhibit all bands of functionalgroups.The spectra of compound (**1, and 2**) have shown stretching vibration bands at υ (3014, 3016) cm^{-1}, and υ (2912, 2916) cm^{-1}attributed to C-H aliphatic, and C-H aromatic, respectively. The Stretching vibration band appeared at υ(1643, 1643.35)cm^{-1}attributedto ketone group as well as band of C=C group at υ(1598, 1603) cm^{-1}. The ^{1}HNMR spectra analysis for (MCCs) at room temperature in DMSO-d_6 confirmed the proposed structure. Thespectrum of compound (**1**) has shown singlet signal for CH_2-O at δ (6.10) ppm, doublet signals of vinylic proton atδ (7.0, and 7.71) ppm and signals at δ(7.19, 7.26, and 7.45)ppm which attributed to CH-C aromatic. The ^{13}CNMR spectra showedsignal at δ (102) ppm,andδ (188) ppm assigned to CH_2-O and ketone groups,respectively.The pyrazole derivatives of (MCCs) was synthesized from the reaction curcuminoids with hydrazine and their derivatives according to (scheme 3).



Scheme 3 Preparation pyrazols of (MCCs).

The IR spectra of pyrazole compounds show a new band at υ)1620-1627(cm^{-1} attributed to the C=N in pyrazol ring[16], the bands at υ (3066-3014) cm^{-1}related to C-H aromatic and at υ (1604-1598) cm^{-1} assigned of stretching vibration of C=C group.In addition, the band of carbonyl group disappeared inspectra of curcuminoids derivatives (pyrazoles). The ^{1}HNMR spectra analysis for pyrzoles show new signals due to the interaction between neighbor protons in pyrazole ring, two doublet of doublet signals at δ (2.49- 2.97) ppm, and δ (3.68- 4.0)ppm attributed to C-CH_2-C of pyrazol ring as well as doublet of doublet signal at δ (5.05-5.85) ppm assigned of CH=N of pyrazol ring[17]. In addition exhibitedsignals attributed to the aliphatic, aromatic, and vinylic protons.The ^{13}CNMR spectra of pyrazoles display signals of the carbon skeleton for pyrazoles. The spectra characterized signals attributed to aliphatic carbon, vinylic carbon, aromatic carbon, and C=N of pyrazol ring. Mass spectra (EI)results showthe proposed formula. The elemental analysis was used to determine the molecular formula of the prepared

compounds. In all cases, the differences in values of elemental percentage between measured and calculated formula are within acceptable values. Thecompound (**3**)was prepared from the reaction of compound (**1a**) with 2-chloro-1-(2,3,4-trihydroxyphenyl) ethan-1-one, according to (scheme 4).



Scheme 4 preparation thiazolo thiazole of (MCCs).

The compound 2-chloro-1-(2,3,4-trihydroxyphenyl) ethan-1-one was prepared according to Friedel–Crafts reaction. The proposed structure was confirmed by using spectroscopic techniques. The IR spectrum shows strong band at υ(3390) cm^{-1} and band at υ(1637) cm^{-1} attributed to hydroxyl group, and carbonyl group, respectively.The ^{1}HNMR spectrum shows signal at δ(5.03) ppm, doublet signals at δ (6.44, and 7.3) ppm attributed to aromatic proton as well as three singlet signals at δ (8.77,10.28, and 11.63) assigned to phenolic proton. The ^{13}CNMR spectrum shows eight signals one of them at δ (196) ppm attributed to carbonyl carbon. The Mass spectrum results improved the proposed formula. The pyrazolo thiazol derivatives characterized by spectroscopic techniques, the IR spectrum shows bands at υ(3527) cm^{-1}, υ(3032) cm^{-1}, υ(2908) cm^{-1}, υ(1621) cm^{-1}, υ(1604) cm^{-1} and υ(1087, 1037) cm^{-1} attributed to C-OH, C-H aromatic, C-H aliphatic, C=N, C=C, and O-CH_2-O groups. The ^{1}HNMR spectrum shows signals at δ (10.46, 8.98, and 8.06) ppm attributed to phenolic proton, signals at δ (6.23-7.38) ppm attributed to olefinic and aromatic protons, as well as signal at δ (6.28) ppm assigned to O-CH_2-O proton and three doublet of doublet signals at δ (3.12, 3.84, and 5.58) ppm attributed to protons of pyrazol ring. The elemental analysis was used to determine the molecular formula of prepared compounds. In all cases, the differences in values of elemental percentage between measured and calculated formula are within the acceptable values.

Antioxidant activity assay

The *in-vitro* free radical inhibition activity of (MCCs) and some derivatives were analyzed by the DPPH method, the percentage of inhibition activity and the result of IC_{50} are gathered in (Table1), and (figure 7). The inhibition percentage activity of synthesized compounds (**1, 1a, 2, 2a, and 3**) concentration (50-200) μmol/L are measured by the decreasing of DPPH absorbance at 517 nm with time (figures 1-6). The compounds showed lower in scavenging activity in comparison with ascorbic acid, expect the compound (**3**) whichshowed higherinhibition activity of 66.8% at 50 μmol/L, 78.57% at 100 μmol/L, and 95% at 200 μmol/L. The other compounds (**1, 1a,**

2, and 2a) showed lower inhibition at 200 µmol/L. Therefore the compound 3 showed a high inhibition activity due to the phenolic OH groups[18]that able to scavenge the radicals. The scavenge of radicals activity of compounds (**1, 1a, 2, 2a, and 3**) will be in the order of:3 > 2a>1a>2> 1. As well as half maximal inhibitory concentration (IC_{50}) between (17.35-135.2) µmol/L.

Figure 2: DPPH free radical scavenging activity of compounds (1)at 50-200 µmol/L concentrations showing percentage inhibition.

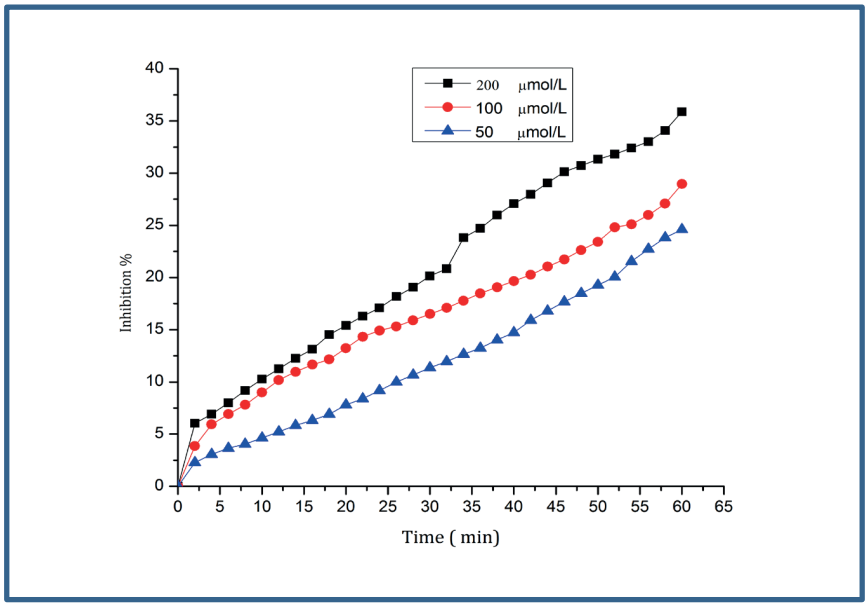


Figure 3: DPPH free radical scavenging activity of compounds (1a) at 50-200 µmol/L concentrations showing percentage inhibition.

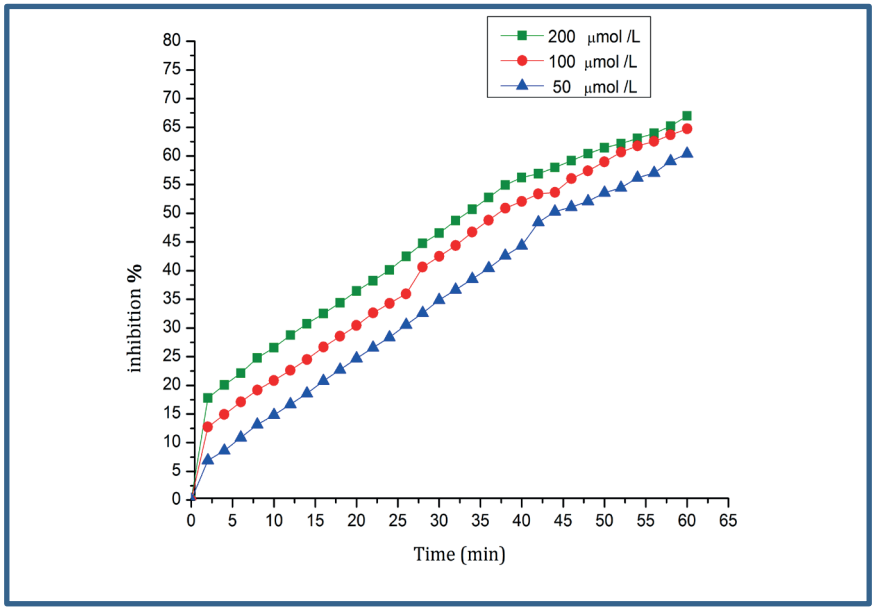


Figure 4: DPPH free radical scavenging activity of compounds (2) at 50-200 µmol/L concentrations showing percentage inhibition.

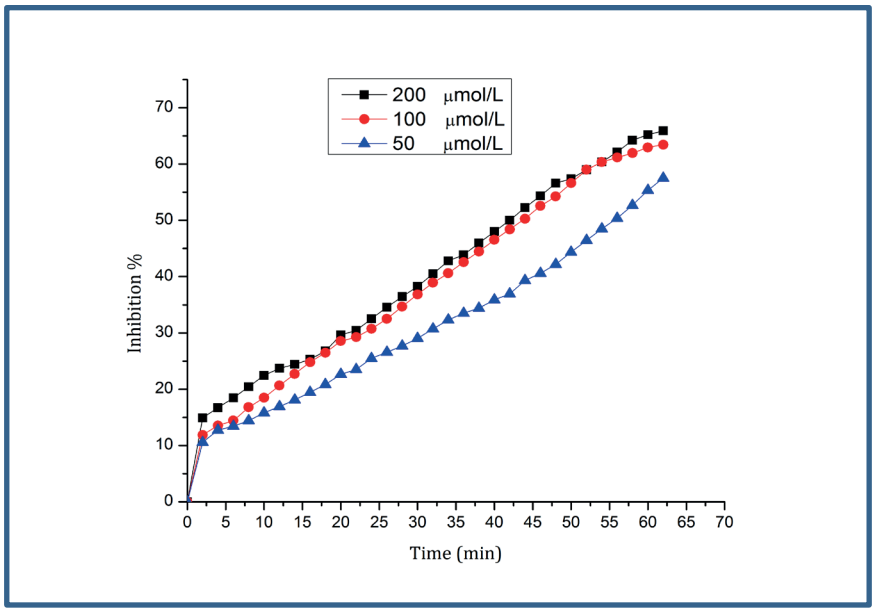


Figure 5: DPPH free radical scavenging activity of compounds (2a) at 50-200 µmol/L concentrations showing percentage inhibition.

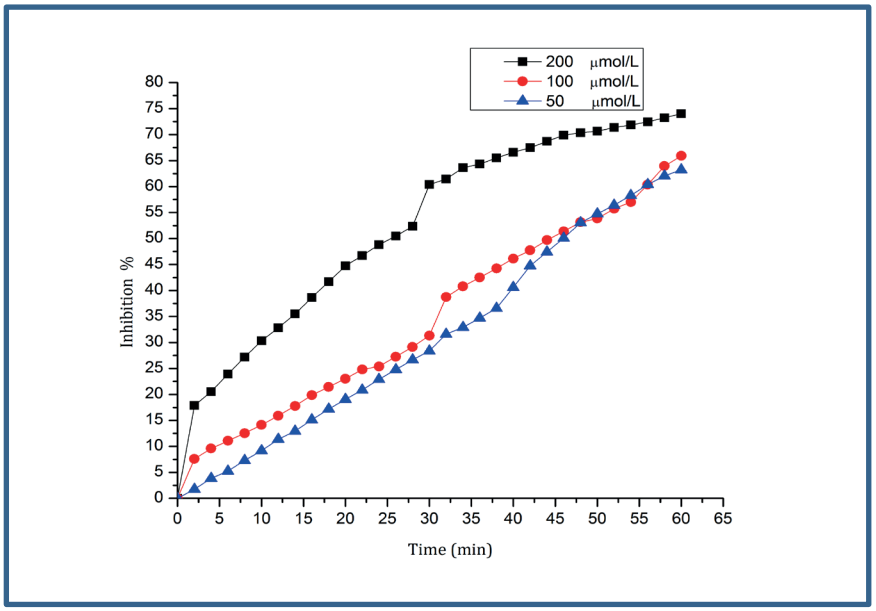


Figure 6: DPPH free radical scavenging activity of compounds (3) at 50-200 µmol/L concentrations showing percentage inhibition.

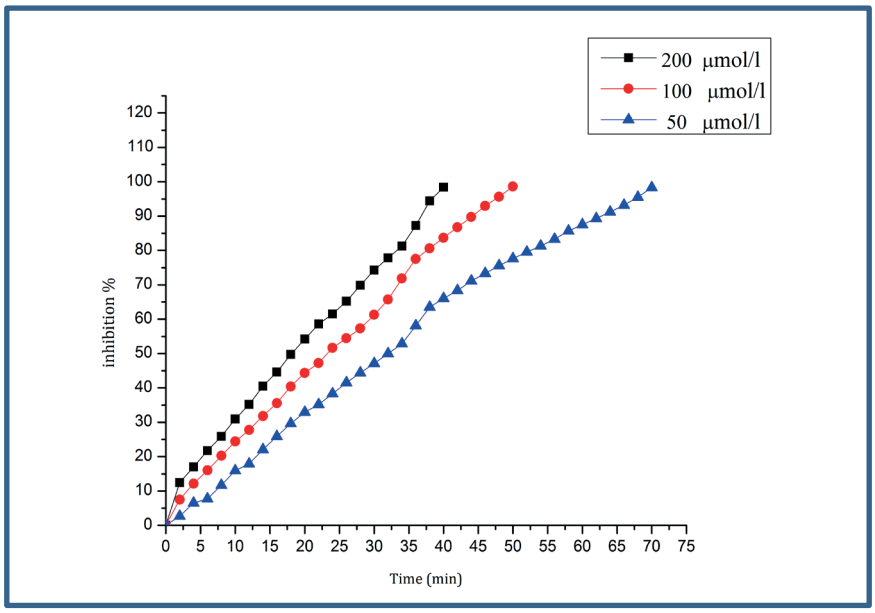


Figure 7: DPPH free radical scavenging activity of ascorbic acid at 200 µmol/L concentrations showing percentage inhibition.

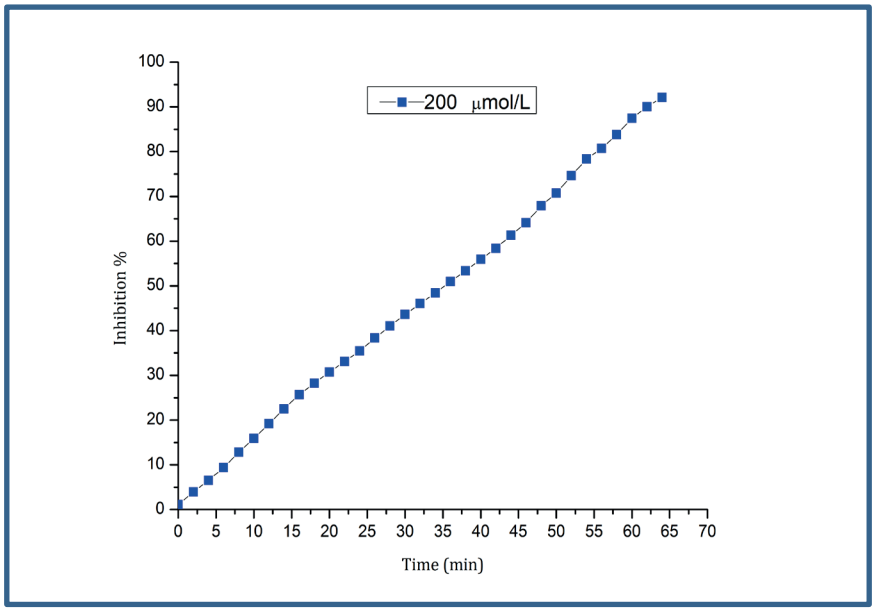


Figure 8: The percentage inhibition of DPPH free radical scavenging activity of compounds (1, 1a, 2, 2a, 3, andVit.C) at 50-200 µmol/L concentrations.

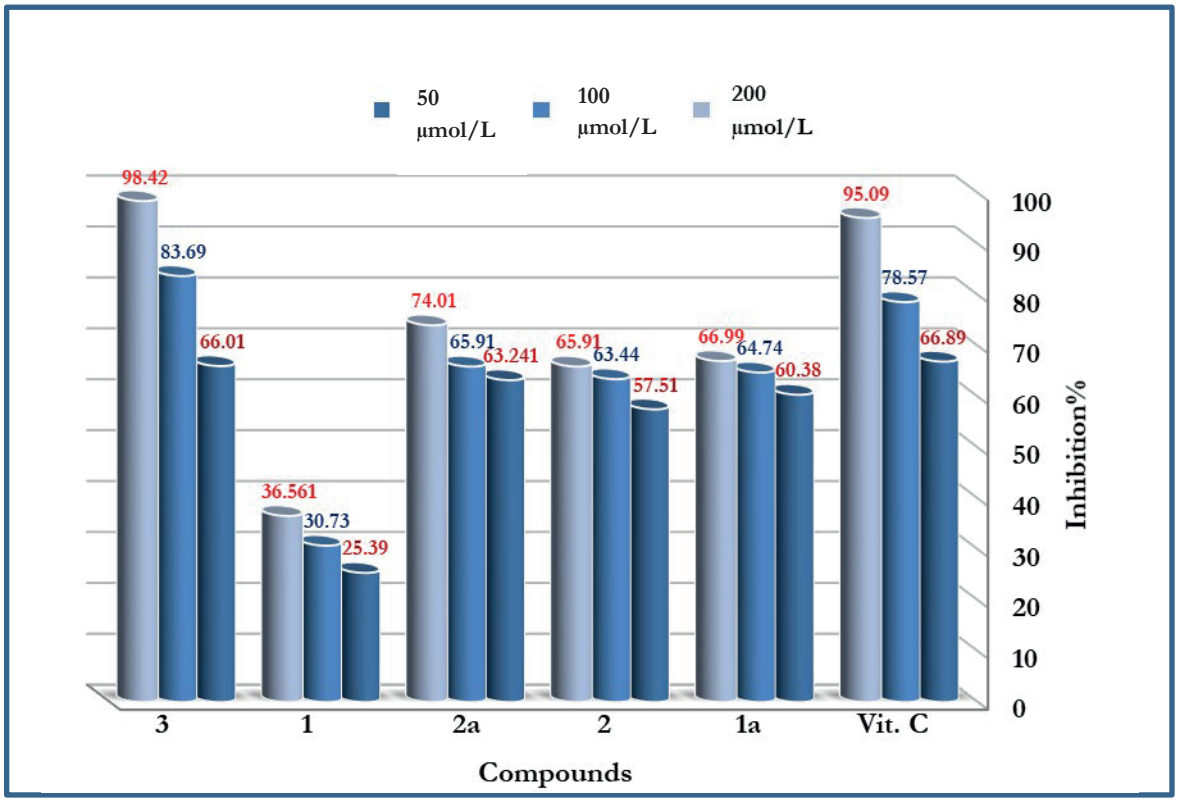


Tabla 1: In-*vitro* antioxidant activities of compounds (1, 1a, 2, 2a, and 3).

Compounds	Percentage of Inhibition			
	50 µmol/L	100 µmol/L	200 µmol/L	IC 50 µmol/L
Ascorbic acid	66.89	78.57	95.09	18.74
1a	60.38	64.74	66.99	60.12
2	57.51	63.44	65.91	20.97
2a	63.241	65.91	74.01	31.59
1	25.39	30.73	36.561	135.2
3	66.01	83.69	98.42	17.35

CONCLUSIONS

In this study, the monocarbonyl curcuminoids (MCCs) was synthesized according to Claisen–Schmidt condensation reaction between acetone and aromatic aldehydes, followed by synthsis of their derivatives. The IR, ^{1}HNMR, ^{13}CNMR, and Mass spectra as well as elemental analysis of the studied-compounds are considered as the essential identification. The antioxidant activity of curcuminoids were studied by using DPPH as a source of radicals. The higher activity of compounds can be attributed to present the phenolic OH group. IC_{50} value between (17.35-135.2) µmol/L.

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