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Synthesis and antioxidant study of new hydrazones derived from bisdemethoxycurcumin pyrazole

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ABSTRACT

The antioxidant activity of new hydrazones derived from bisdemethoxycurcumin pyrazole was investigated. The study was divided into two main parts: The first one includes the synthesis and characterization of the target compounds from bisdemethoxycurcumin (BDMC), while the second step is devoted to the investigation of their antioxidant activities. In the first step of synthesis, the curcumin-pyrazole (2) was synthesized by the reaction of BDMC with hydrazine hydrate. Later, the obtained product treated with ethyl 2-chloroacetate to produce curcumine ester (3), then the product was converted to hydrazide (4) by the reaction of curcumin ester (3) with hydrazine hydrate. Finally, curcumine hydrazones (5a-f) were synthesized from the reaction of hydrazide (4) with substituted aromatic aldehydes. All compounds were characterized with the aid of suitable spectroscopic techniques. The antioxidant activity of the prepared compounds was studied against the stable radical α,α-diphenyl-β-picrylhydrazyl. The study showed that only the phenolic OH-containing compounds (2, 5b and 5f) have antioxidant activity.

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1. Introduction

Curcumine is a pigment isolated from Turmeric (*Curcuma Longa* L) rhizome [1]. The pigment contains three isomers of curcuminoids (Figure 1) with curcumine as the major isomer with abundance of about 77%, while demethoxycurcumine (DMC) and bisdemethoxycurcumine constitute about 17 and 3%, respectively [2-4].

Turmeric has been used as a colour of food and flavouring [5,6] as well as a traditional medicine. Curcuminoids have a large variety of activities such as antioxidant to the reactive oxygen species (ROS) [7-9], anti-viral [10], anti-bacterial [11], diminishing the blood cholesterol level [12], the ability to treat Alzheimer's disease [13], the inhibition of a wide types of tumour cells, such as lung cancer, bladder cancer, prostate cancer, breast cancer and leukaemia cancer [14-17]. Curcumin has no toxicity and is extremely safe at high dose. Also, curcumine binds with metals, albumin and other molecules such as *p*-glycoprotein (p-gp) [18]. These properties give the curcuminoids a medical potency. But, their activities are limited due to their limited solubility in water and their short half-life, therefore, the researcher dream is to synthesize a super curcumin by the modification of the structure of curcumin to increase the activity [19,20].

In the present study, BDMC pyrazole-hydrazone derivatives were prepared and characterized by various spectroscopic techniques, then evaluated for their antioxidant activity.

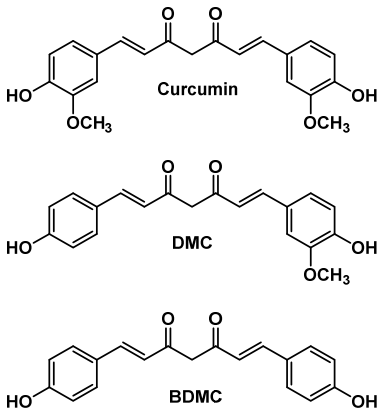

Figure 1. Structures of curcuminoids.

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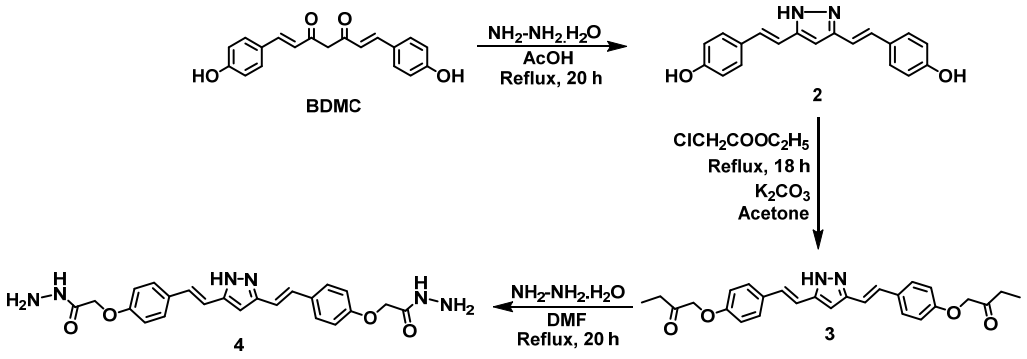
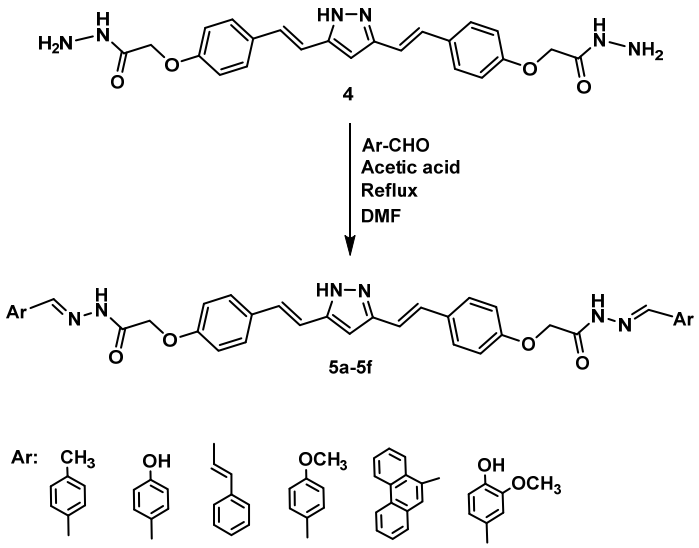


Scheme 1



Scheme 2

2. Experimental

2.1. Instrumentation

IR spectra were recorded using Shimadzu FT-IR spectrophotometer in the region 4000-400 cm^{-1} in KBr pellets. The mass spectra were scanned by the EI technique at 70 eV with an Agilent Technologies 5975 Cs spectrometer. The experimental values of ^{1}H and ^{13}C NMR spectra for the studied compounds were scanned on a Bruker 500 MHz spectrometer operating at 500 MHz for proton observation and 125 MHz for carbon observation using TMS as the internal standard. DMSO-d_6 was used as solvent. Elemental analysis (CHNS) measured by using elementar Vario MICRO. UV-Visible spectra were measured using a PG-instrument T80+ spectrophotometer.

2.2. Synthesis

BDMC pyrazole-hydrazone was synthesized from BDMC pyrazole in four steps (Scheme 1 and 2).

2.2.1. Synthesis of BDMC, 1,7-bis(4-hydroxyphenyl)hepta-1,6-diene-3,5-dione (1)

Acetylacetone (5 g, 0.046 mol) and boric oxide (2.4 g, 0.034 mol) was stirred for 1 hour. A mixture of *p*-hydroxy benzaldehyde (11.2 g, 0.092 mol) in dry dimethylacetamide (DMA) (70 mL), heated in water bath at 80 °C, and trimethyl borate (10 g, 0.092 mol) was added to the previousmixture. The reaction was stirred for 5 min followed by a dropwise addition of a solution of *n*-butylamine (1.5 g, 0.02 mol) in DMA over a period of 1 h. The mixture was stirred for further 3 h. The solution was set aside overnight. Acetic acid (5 N, 120 mL) at 80 °C was then added, and the mixture stirred for 1 h. The mixture cooled and the solid product was collected by filtration, and then washed by hot water twice, dried then recrystallized from ethanol. Color: Yellow needles. Yield: 56%. M.p.: 221-223 °C. FT-IR (KBr, ν, cm^{-1}): 3217 (OH), 3039 (H-Ar), 1622 (C=O), 1600 (C=C), 1562, 1512 (C-C), 1448 (C-O-H), 1240, 1141 (C-O). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 5.87 (s, 2H, vinylic-H), 6.81 (d, 2H, *J* = 16.2 Hz, C*H*=C), 7.09 (d, 4H, *J* = 7.8 Hz, Ar-H), 7.20 (d, 4H, *J* = 8.4 Hz, Ar-H), 7.82 (d, 2H, *J* = 16.2 Hz, C*H*=C), 9.93 (s, 2H, OH).

2.2.2. Synthesis of4,4'-((1H-pyrazole-3,5-diyl)bis(ethene-2, 1-diyl))diphenol (2)

BDMC (2 g, 6.24 mmol) was dissolved in 20 mL of glacial acetic acid for which 1 g of hydrazine monohydrate was added. The mixture heated under reflux for 20 h, then cooled and poured into ice water. The product collect by filtration and dried then recrystallized from *n*-hexane:ethylacetate (*v*:*v*, 7:3). Color: White powder. Yield: 74%. M.p.: 273-275 °C. FT-IR (KBr, ν, cm^{-1}): 3280 (OH), 3022(C-H Ar), 1647 (C=N), 1604 (C=O), 1554, 1512 (C-C), 1448 (C-O-H), 1240, 1008 (C-O), 823 (1,4-disubstituted ring). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 6.68

(s, 1H, CH-pyrazole ring), 6.82 (d, 2H, *J* = 16.2 Hz, C*H*=C), 6.95 (d, 4H, *J* = 7.8 Hz, Ar-H), 7.10 (d, 4H, *J* = 8.4 Hz, Ar-H), 7.40 (d, 2H, *J* = 16.2 Hz, C*H*=C), 9.65 (2H, s, OH). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 99.6, 112.9, 116.1, 116.9, 118.6, 128.1, 130, 142.6, 151.9, 152.1.

2.2.3. Synthesis of 1,1'-((((1H-pyrazole-3,5-diyl)bis(ethene-2,1-diyl))bis(4,1-phenylene))bis(oxy))bis(butan-2-one) (3)

In a round bottomed flask was added 20mL acetone, compound **2** (2 g, 6.6 mmol) and potassium carbonate (1.84 g, 13.2 mmol), then ethyl 2-chloro acetate (1.6 g, 13.2 mmol) was added. The mixture was heated under reflux with stirring for 18 h, cooled then poured into ice water, the solid product filtered and recrystallized from hexane:ethylacetate (*v*:*v*, 4:6). Color: White powder. Yield: 57.6%. M.p.: 71-72 °C. FT-IR (KBr, ν, cm^{-1}): 3307 (NH), 3037 (C-H, Ar), 2923 (C-H, aliph), 1665 (C=O), 1660 (C=N), 1604 (C=C), 1531, 1508 (C-O), 1242, 1060 (C-O), 823 (1,4-disubstituted ring). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 1.21 (t, 6H, CH_2CH_3), 3.96 (q, 4H, CH_2CH_3), 4.17 (s, 4H, OCH_2), 6.40 (s, 1H, CH-pyrazole ring), 6.92 (d, 2H, *J* = 16.2 Hz, C*H*=C), 7.11 (d, 4H, *J* = 7.8 Hz, Ar-H), 7.51 (d, 4H, *J* = 8.4 Hz, Ar-H), 7.59 (d, 2H, *J* = 16.2 Hz, C*H*=C). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 14.5, 61.1, 65.1, 99.5, 115.2, 113, 130, 128, 129, 141.6, 150.2, 158.1, 157.8.

2.2.4. Synthesis of2,2'-((((1H-pyrazole-3,5-diyl)bis(ethene-2,1-diyl))bis(4,1-phenylene))bis (oxy))di(acetohydrazide) (4)

The mixture of a solution of compound **3** (2 g, 4.2 mmol) in 20 mL ethanol and 0.5 g of hydrazine hydrate was heated under reflux with stirring for 3 h. The mixture then cooled and poured into ice water (100 mL), to get a white solid product which then dried and recrystallized from ethanol:DMF mixture (8:2, *v*:*v*). Color: White powder. Yield: 67%. M.p.: 238-239 °C. FT-IR (KBr, ν, cm^{-1}): 3307, 3237 (NH_2), 3034 (C-H, Ar), 2931 (C-H, aliph), 1678 (C=O), 1664 (C=N), 1600 (C=C), 1531, 1508 (C-O), 1242, 1060 (C-C), 823 (1,4-disubstituted ring). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 4.22 (s, 4H, NH_2), 4.40 (s, 4H,OCH_2), 6.50 (s, 1H, CH-pyrazole ring), 7.01 (d, 2H, *J* = 16.2 Hz, C*H*=C), 7.05 (d, 4H, *J* = 7.8 Hz, Ar-H), 7.56 (d, 4H, *J* = 8.4 Hz, Ar-H), 7.61 (d, 2H, *J* = 16.2 Hz, C*H*=C), 9.42 (s, 2H, NH-C=O). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 66.7, 99.4, 111.0, 111.2, 115.4, 127.9, 128.2, 129.1, 130.2, 141.6, 149.1, 150.3, 157.0, 166.9, 167.8. MS (EI, *m/z*): 448.4 [M]$^+$. Anal. calcd. for $C_{23}H_{24}N_6O_4$: C, 61.60; H, 5.39; N, 18.74. Found: C, 61.09; H, 5.48; N, 18.21%.

2.2.5. Synthesis of compounds 5a-h

To a clear solution of compound **4** (1 g, 2.23 mmol) in 10 mL DMF, the appropriate aldehyde (4.46 mmol) was added with few drops of AcOH. The mixture was heated under reflux with stirring for 3-7 h, then cooled and the solid product was collected by filtration, dried and recrystallized from chloroform:ethylacetate (*v*:*v* ,7:3).

2, 2'-((((1H-Pyrazole-3, 5-diyl) bis(ethene-2, 1-diyl)) bis(4, 1-phenylene)) bis(oxy)) bis(N'-(4-methylbenzylidene)acetohydrazide) (**5a**): Color: White powder. Yield: 51%. M.p.: 148-150 °C. FT-IR (KBr, ν, cm^{-1}): 3309 (N-H), 3037 (C-H, Ar), 2945 (C-H, alipha), 1674 (C=O), 1663 (C=N), 1601 (C=C), 1531, 1508 (C-O), 1443 (CH_2, bend), 1241, 1062 (C-C), 823 (1,4-disubstituted ring). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 1.22 (s, 6H, CH_3), 4.19 (s, 4H, CH_2O), 6.51 (s, 1H, CH-pyrazole ring), 6.91 (d, 2H, *J* = 16.2 Hz, CH=C), 7.08-7.66 (m, 16H, Ar-H), 7.95 (d, 2H, *J* = 16.2 Hz, CH=C), 8.30 (s, 2H, CH=N), 9.64 (s, 2H, NHCO). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 21.5, 65.3, 115.3, 121.3, 127.5, 128.5, 129.9, 131.7, 140.2, 140.5, 144.5, 148.4, 158.7, 164.4, 168.8. MS (EI, *m/z*): 656.3 [M]$^+$. Anal. calcd. for $C_{39}H_{36}N_6O_4$: C, 71.76; H, 5.56; N, 12.87. Found: C, 71.29, H, 5.48, N, 12.21%.

2, 2'-((((1H-Pyrazole-3, 5-diyl) bis(ethene-2, 1-diyl)) bis(4, 1-phenylene))bis(oxy)) bis(N'-(4-hydroxybenzylidene)acetohydrazide) (**5b**): Color: White powder. Yield: 56%. M.p.: 176-179 °C. FT-IR (KBr, ν, cm^{-1}): 3203 (N-H), 3062 (C-H, Ar), 2949 (C-H, alipha), 1681 (C=O), 1670(C=N), 1604 (C=C), 1541, 1508 (C-O), 1438 (CH_2, bend), 1274, 1076 (C-C), 837 (1,4-disubstituted ring). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 4.17 (s, 4H, CH_2O), 6.50 (s, 1H, CH-pyrazol ring), 6.91 (d, 2H, *J* = 16.2 Hz, CH=C), 6.90-7.60 (m, 16H, Ar-H), 7.92 (d, 2H, *J* = 16.2 Hz, olefinic proton), 8.23 (s, 2H, CH=N) 9.41 (s, 2H,NHCO), 9.91 (s, 2H,OH). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 65.1, 116.0, 125.4, 125.5, 127.5, 127.8, 128.3, 128.8, 129.1, 129.3, 144.6, 148.7, 151.7, 162.7, 168.5, 169.0. Anal. calcd. for $C_{37}H_{32}N_6O_6$: C, 67.67; H, 4.91; N, 12.80.Found: C, 67.19; H, 4.48; N, 12.27%.

2, 2'-((((1H-Pyrazole-3, 5-diyl) bis(ethene-2, 1-diyl)) bis(4, 1-phenylene))bis(oxy))bis(N'-(3-phenylallylidene)acetohydrazide) (**5c**): Color: White powder. Yield: 48%. M.p.: 170-173 °C. FT-IR (KBr, ν, cm^{-1}): 3264 (N-H), 3042 (C-H, Ar), 2978 (C-H, alipha), 1686 (C=O), 1673 (C=N), 1602 (C=C), 1583 (C-O), 1435 (CH_2, bend), 1270, 1083 (C-C), 827 (1,4-disubstituted ring). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 4.66 (s, 4H,CH_2O), 6.53 (s, 1H,CH-pyrazole ring), 7.01 (d, 2H, *J* = 16.2 Hz, CH=C), 7.00-7.83 (m, 22H, Ar-H and CH=C), 7.92 (d, 2H, *J* = 16.2 Hz, CH=C), 8.31 (s, 2H, CH=N), 9.43 (s, 2H, NHCO). Anal. calcd. for $C_{41}H_{36}N_6O_4$: C, 72.76; H, 5.36; N, 12.42. Found: C, 72.09; H, 5.31; N, 12.67%.

2, 2'-((((1H-Pyrazole-3, 5-diyl) bis(ethene-2, 1-diyl)) bis(4, 1-phenylene))bis(oxy)) bis(N'-(4-methoxybenzylidene)acetohydrazide) (**5d**): Color: White powder. Yield: 52.7%. M.p.: 128-130 °C. FT-IR (KBr, ν, cm^{-1}): 3207 (N-H), 3035 (C-H, Ar), 2953 (C-H, alipha), 1683 (C=O), 1639 (C=N), 1604 (C=C), 1573, 1508 (C-O), 1456 (CH_2, bend), 1251, 1170, 1076 (C-C), 829 (1,4-disubstituted ring). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 3.80 (s, 6H, OCH_3), 4.36 (s, 4H, CH_2O),6.53 (s, 1H, CH-pyrazole ring), 6.91 (d, 2H, *J* = 16.2 Hz, CH=C), 6.94-7.71 (m, 16H, Ar-H), 7.98 (d, 2H, *J* = 16.2 Hz, CH=C), 8.28 (s, 2H, CH=N), 9.33 (s, 2H, NHCO). Anal. calcd. for $C_{39}H_{36}N_6O_6$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.09; H 5.08; N, 12.21%. MS (EI, *m/z*): 684.5 [M]$^+$.

2, 2'-((((1H-pyrazole-3, 5-diyl) bis(ethene-2, 1-diyl)) bis(4, 1-phenylene)) bis(oxy)) bis(N'-(phenanthren-9-ylmethylene)acetohydrazide) (**5e**): Color: Pale yellow powder. Yield: 66.2 %. M.p.: 169-172 °C. FT-IR (KBr, ν, cm^{-1}): 3217 (N-H), 3015 (C-H, Ar), 1683 (C=O), 1647 (C=N), 1604 (C=C), 1529, 1508 (C-O), 1450 (CH_2, bend), 1230, 1074 (C-C), 819 (1,4-disubstituted ring). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 4.78 (s, 4H, CH_2O), 5.68 (s, 1H, CH-pyrazole ring), 6.96-8.11 (m, 30H, Ar-H and CH=C), 8.32 (s, 2H, CH=N), 9.03 (s, 2H, NHCO). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 67.2, 115.3, 123.4, 124.0, 125.5, 127.6, 128.5, 128.7, 129.8, 130.2, 130.7, 130.9, 144.8, 148.7, 162.7, 168.9. Anal. calcd. for $C_{53}H_{40}N_6O_4$: C, 77.17; H, 4.89; N, 10.19. Found: C, 77.09; H, 4.48; N, 10.53%.

2, 2'-((((1H-Pyrazole-3, 5-diyl) bis(ethene-2, 1-diyl)) bis(4, 1-phenylene)) bis(oxy)) bis(N'-(4-hydroxy-3-methoxybenzylidene) acetohydrazide) (**5f**): Color: White powder. Yield: 45 %. M.p.: 168-171 °C. FT-IR (KBr, ν, cm^{-1}): 3217 (N-H), 3039 (C-H, Ar), 2902 (C-H, alipha), 1683 (C=O), 1654 (C=N), 1602 (C=C), 1558, 1508 (C-O), 1456 (CH_2, bend), 1284 (C-C), 821 (1,4-disubstituted ring). ^{1}H NMR (500 MHz, DMSO-d_6, δ, ppm): 3.82 (s, 6H, OCH_3), 4.10 (s, 4H,CH_2O),6.46 (s, 1H, CH-pyrazole ring), 6.83 (d, 2H, *J* = 16.2 Hz, CH=C), 6.91-7.61 (m, 16H, Ar-H and CH=C), 8.22 (s, 2H, CH=N), 9.50 (s, 2H,NHCO), 10.27 (s, 2H, OH). ^{13}C NMR (125 MHz, DMSO-d_6, δ, ppm): 56.0, 65.2, 109.5, 115.9, 121.7, 122.6, 125.9, 128.4, 144.7, 148.5, 149.6, 162.7, 169.0. Anal. calcd. for$C_{39}H_{36}N_6O_8$: C, 65.35; H, 5.06; N, 11.73. Found: C, 65.09; H, 5.48; N, 11.22%.

2.3. α,α-Diphenyl-β-picrylhydra (DPPH) radical scavenging assay

Table 1. *In-vitro* antioxidant activities of compounds **2**, **5b**, **5d**, **5e** and **5f**.

Compounds	Percentage of inhibition				IC_{50} µmol/L
	25 µmol/L	50 µmol/L	100 µmol/L	200 µmol/L	
2	23	39	63	91	80.32
5b	30	41	64	95.4	78.79
5d	15.4	26	39	63	84.54
5e	20	29	48	75	83.75
5f	21	39	63	94	82.96

The antioxidant activity of the synthesized curcuminoids (**2**, **5b**, **5d**, **5e** and**5f**) was determined by the ability to scavenge the stable DPPH free radical according to Blois method [21]. Briefly 1mL of various concentration 25, 50, 100 and 200 µmol/L of each compounds in ethanol solution mixed with 1 mL of 200 µmol/L DPPH at room temperature. The absorbance was read at 517 nm after 60 min. The colour of DPPH changed from violet to yellow or colourless due to the curse of the reaction. The percentage of inhibition was calculated by the following equation [22].

$$\% \text{ Inhibition percentage} = \frac{Ac - As}{As} \times 100 \quad (1)$$

Ac = Control absorbance, the absorbance of DPPH without sample.

As = Sample absorbance, the absorbance of DPPH with sample.

The IC_{50} was calculated by using XY scattered plot, the liner curve was obtained by plotting inhibitor percentage of radical versus concentrations of compounds. IC_{50} it is mean the value of the concentration of inhibitor able to scavenging 50% DPPH radical.

3. Results and discussion

3.1. Spectroscopic identification

The compounds prepared according to Scheme 1 and 2, and their proposed structures were confirmed by the aid of spectroscopic techniques such as, FT-IR, ^{1}H and ^{13}C NMR, Mass spectra as well as the elemental analysis. The elemental analysis showed acceptable differences between the measured and the calculated percentages of the elements which supports the validity of the proposed structures of the prepared compounds.

The FT-IR spectra of the prepared compounds exhibited all the expected bands. Comparing the IR spectra of BDMC with compound **2**, shows a new band at ν 1647 cm^{-1} which is attributed to the C=N in pyrazole ring [23], while IR spectrum of BDMC has a band at 1622 cm^{-1} attributed to the carbonyl group of the central chelated ring. The IR spectrum of compound **3** showed new band at 1685 cm^{-1} which is assigned to the ester carbonyl group. Meanwhile, when this compound converted to hydrazide (compound B), a new band was appeared 1678 cm^{-1}. All IR spectra of compounds **5a**-**5f** show a strong band at the range 1670-1639 cm^{-1} which is assigned to the azomethan (N=CH) group as well as bands at the range 1683-1674 cm^{-1} which are attributed to the N=C stretching vibration in the pyrazole ring. That is in addition to bands at 1604-1601 cm^{-1} which are assigned to the stretching vibration of the C=C group.

The ^{1}H and ^{13}C NMR spectra in DMSO-d_6 confirmed their proposed structures. BDMC characterized by four main signals; avinylic proton at δ 5.87 ppm, the two signals of the olefinic protons at δ 6.81 and 7.82 ppm, the signals of the aromatic proton appear at δ 7.20-7.09 ppm and the singlet of the phenolic proton at δ 9.93 ppm. Curcuminpyrazole (compound **2**) shows a new signal at δ 6.68 ppm attributed to the CH proton of the pyrazole ring [22]. The phenolic proton disappears in the spectrum of compound **3** accompanied with the appearance of new signal due to CH_2O at δ 4.17 ppm, and two signals of the ester group ($CO\text{-}CH_2CH_3$) at δ 1.21 ppm (CH_3) and at δ 3.96 ppm (CH_2). The spectrum of compound **4** shows two singlets at δ 9.42 and 4.22 ppm, due to the protons of NH and NH_2, respectively. The ^{1}H NMR spectra of compounds **5a-f** show a singlet due to the azomethan proton within the range δ 8.22 and 8.33 ppm [24]. They also display a singlet near δ 9.39 ppm attributed to the NH-C=O proton. The ^{13}C NMR spectra of compounds **5a-f** display signals of carbon skeleton of compounds, the spectra were characterized by six kind of signals, the aliphatic, the vinylic signals of pyrazol ring, the aromatic signals, the azomethan signal, the C=N of pyrazole ring signal and the signal of C=O. The Mass spectra (EI), supported the proposed formulae of the prepared compounds

3.2. Antioxidant activity assay

The *in-vitro* free radical inhibition activity of the synthesized compounds was investigated by the DPPH method. The result of IC_{50} and the percentage of inhibition activity are gathered in Table 1. The value of scavenging activity of the synthesized compounds (**2**, **5b**, **5d**, **5e**, **5f**) at concentration 25-200 µmol/L were determined by the decrease of DPPH absorbance at 517 nm with the time (Table 1 and Figure 2).

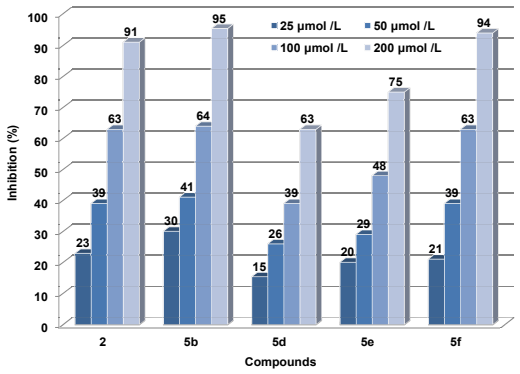


Figure 2. DPPH free radical scavenging activity of compounds **2**, **5b**, **5d**, **5e** and **5f** at concentrations 25-200 µmol/L showing percentage of inhibition.

Compound **2** showed inhibition activity of 23% at 25 µmol/L, 39% at 50 µmol/L, 63% at 100 µmol/L and 91% at 200 µmol/L. Compounds **5b** and **5f** showed high inhibition of 95.4% and 94% at 200 µmol/L, respectively. On the other hand compounds **5d** and **5e** were not so active and their percentages of inhibition are63.4 and 75% at 200 µmol/L, respectively.

The reduction of DPPH indicates the activity of the synthesized compounds against the free radical of DPPH according to the following equations.

$$DPPH^{\bullet} + RH \rightarrow DPPH\text{-}H + R^{\bullet} \quad (1)$$

$$DPPH^{\bullet} + R^{\bullet} \rightarrow DPPH\text{-}R \quad (2)$$

The high activity of the compounds **5b**, **5f** and **2** can be attributed to the phenolic OH group [24]. Therefore, the scavenge of radical activity of compounds **2**, **5b**, **5d**, **5e**and **5f** is in the order: **5b** > **5f** > **2** > **5e** > **5d**, and the IC_{50} of the scavenge activity at the range 78.79-83.75 µmol/L.

4. Conclusion

In this study, bisdemethoxycurcumin pyrazole derivatives were prepared by four steps and characterized by FT-IR, ^{1}H NMR, ^{13}C NMR, Mass spectra and elemental analysis techniques. The antioxidant activities of some compounds are also studied by using DPPH as a source of radical. The high activity of compounds can be attributed to the phenolic -OH group.

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