Asian Journal of Chemistry; Vol. 27, No. 4 (2015), 1489-1494

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2015.18529

Synthesis, Characterization and Antioxidant Studies of Curcumin Derivatives

R. REVATHI[1,*], D. ARUL ANANTH[2], A. RAMESHKUMAR[2] and T. SIVASUDHA[2]

[1]Department of Science and Humanities, Sri Ramakrishna Institute of Technology, Coimbatore-641 010, India
[2]Department of Environmental Biotechnology, Bharathidasan University, Tiruchirappalli-620 024, India

*Corresponding author: E-mail: revathigr09@gmail.com

Received: 29 July 2014; *Accepted*: 14 November 2014; *Published online*: 4 February 2015; AJC-16821

Three curcumin derivatives having modification in active methylene group (1, 3) and keto groups (2) were successfully synthesized and characterized by ^{1}H NMR and FT-IR spectroscopic techniques. The substitution on the active methylene site of curcumin increases the antioxidant behaviour but it is decreased on modifications in the carbonyl group. The observed results suggest that the structural modifications will help in tuning the antioxidant behaviour of curcumin. While comparing compound **1** which have strong donating group than compound **3**, the former shows higher scavenging activity. This implies the electron donating strength also plays an important role in determining the antioxidant activity. The observed results will aid in developing new curcumin derivatives for better antioxidant properties.

Keywords: Curcumin, Antioxidant activity.

INTRODUCTION

Reactive oxygen species which comprises free radicals such as superoxide anion radicals ($O_2^{\bullet-}$), hydroxyl radicals ($OH^{\bullet}$) and non-free radical species such as hydrogen peroxide (H_2O_2) and singlet oxygen ($^1O_2$)[1,2], damages nucleic acids, lipids, proteins, carbohydrates and DNA which leads to mutation and several diseases. Hence scavenging the free radicals is important to prevent numerous diseases. Antioxidants are the compounds which have the ability to trap free radicals, they could be either synthetic or natural, scavenge the free radicals, such as peroxide, hydroperoxide or lipid peroxides and thus inhibit the oxidative mechanisms that lead to degenerative diseases. Several synthetic compounds with good antioxidant behaviour have been found in literature[3-7]. In recent decades, the interest has increased considerably in finding naturally occurring antioxidants in foods or medicinal plants to replace synthetic antioxidants, which are being restricted due to their side effects such as inflammation and carcinogenicity etc. Natural antioxidants can protect the human body from free radicals and retard the progress of many chronic diseases. Several previous literatures show large number of plants that can be used against diseases, in which reactive oxygen species and free radical play important role. Turmeric which contains curcumin (*Curcuma longa*) is a natural tropical plant that has been used since ancient times as a spice, as a beauty care agent and as a traditional medicine[8]. Curcumin is the major active polyphenol compound and this agent has been extensively investigated for its pharmacological activities that include anticancer, antiinflammatory, antioxidant, antiulcer, immunomodulatory, antiviral, antifungal, wound healing, antibacterial, neuroprotective and antiaging effects. Encompassing investigation over the last five decades has indicated that curcumin reduces blood cholesterol and thus has a potential against various malignant diseases, diabetes, allergies, arthritis, Alzheimer's disease and other chronic illnesses[9-12]. The significant antioxidant activity of curcumin to be mainly due to the phenolic –OH group, although a small fraction may be due to the CH_2 site[13-15]. The antioxidative properties of curcumin act not only against lipid peroxidation but also prevent DNA damage. Further studies revealed that the antioxidant properties of curcumin positively influenced antioxidant and phase-II metabolizing enzyme activity in mice and more over diminished iron-induced oxidative damage of lipids and DNA *in vitro* and in mice treated with ferric nitrilo triacetate (Fe-NTA). Thus curcumin was able to prevent Fe-NTA-induced lipid peroxidation, DNA damage and protein carbonylation in the kidney of these mice[16].

By considering all the literature applications of curcumin, we have concluded the antioxidant activity of curcumin to be mainly from the phenolic -OH group and a small fraction due to the CH_2 site. Hence, the modification of the curcumin in the active methylene site and keto site will have impact in its antioxidant behaviour. Herein we report the synthesis of three curcumin derivatives having modification in active methylene group and keto groups and investigated the effect of these structural modifications on antioxidant behaviour.

EXPERIMENTAL

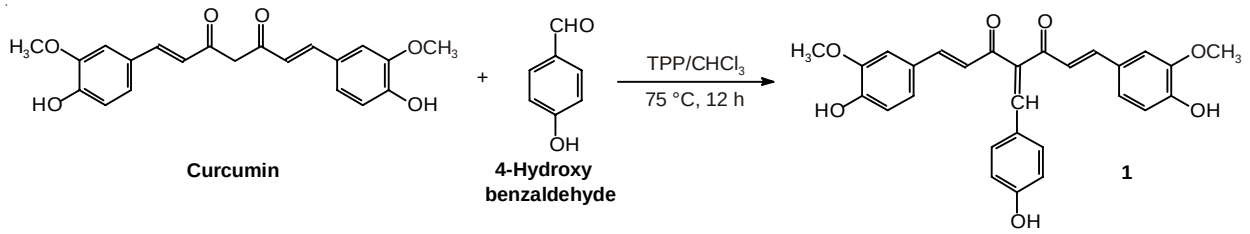
Curcumin, triphenyl phosphine, *N*,*N*-dimethylamino benzaldehyde, piperidine, 4-amino phenol, 4-hydroxy benzaldehyde, 2,2'-diphenyl-1-picrylhydrazyl (DPPH), 2,2'-azino-*bis*-3-ethyl benzthiazoline-6-sulphonic acid (ABTS), calcium chloride, silica gel for column (200-400 mesh), silica gel for TLC (350 mesh) potassium bromide, potassium persulphate, paraffin wax, acetone, distilled water, methanol, ethanol, chloroform, petroleum ether, ethyl acetate are were procured commercially.

Synthesis of curcumin derivatives

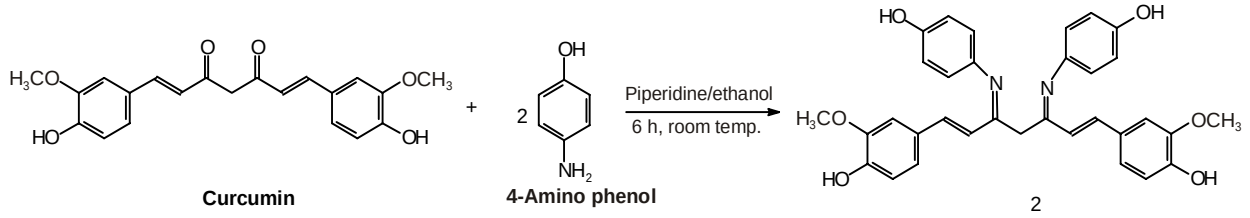
Synthesis of 4-(4-hydroxybenzylidene)-1,7-*bis*(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene-3,5-dione (1): Curcumin (0.2210 g, 0.6 mmol) and 4-hydroxy benzaldehyde (0.8616 g, 0.6 mmol) (1:1 equivalent) were taken in 100 mL round-bottom flask along with triphenyl phosphine (0.1836 g, 0.70 mmol) in 30 mL of chloroform. The reaction mixture was stirred at 75 °C for 12 h in an oil bath. The progress of the reaction was continuously monitored using thin layer chromatographic technique and the completion of the reaction was confirmed by R_f values. The reaction mixture was evaporated to dryness at room temperature, the resultant compound was extracted repeatedly with chloroform-water mixture. The organic layer was separated and dried to get yellow coloured solid as product (**Scheme-I**). Further the product was purified by column chromatography by using petroleum ether/ethyl acetate mixture (1:1) as eluent. Yield: 69.4 % (0.752 g); Yellow solid. m.f.: $C_{28}H_{24}O_7$; m.w.: 472.49; m.p.: 70 °C. IR (KBr, ν_{max}, cm^{-1}): 3392 (O-H), 3051 (C-H) (aromatic ring) 2920 ν_{as}(C-H) (methyl), 2800 ν_s(C-H) (methyl), 1621 ν_s(C=O), 1584 ν(C=C), 1511, 1435 ν(aromatic C=C) 1282 ν_{as}(C-O-C), 1206 ν(C-O) (phenolic hydroxyl group), 814 δ(C-H), 693 ρ(C-H); ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 3.95 (s, 6H, Ar-OCH_3[a]), 6.47 (d, 2H, Ar [c]CH), 6.84 (d, 2H, Ar [d]CH-OCH$_3$), 6.91 (d, 2H, Ar eCH), 7.05 (d, 2H, Ar [f]CH), 7.12 (s, 2H, [g]CH), 7.61 (d, 2H, [h]CH), 7.76 (d, 2H, [i]CH), 8.98 (s, 1H, [j]CH(CO)).

Synthesis of 3,5-*bis*-(4-hydroxy-phenyl)-imido-1,7-*bis*(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene (2): The compound **2** was synthesized by the literature procedure[18,19]. Curcumin (0.2210 g, 0.6 mmol) and 4-amino phenol (0.1308 g, 1.2 mmol) (1:2 equivalent) were taken in a 100 mL round-bottom flask along with piperidine (catalytic amount) as the proton scavenger in 30 mL of methanol. The reaction mixture was stirred at room temperature for 6 h. The progress of the reaction was monitored by TLC. TLC (R_f): 0.0465 (ethyl acetate: petroleum ether -1: 0.5). After the completion of the reaction, the reaction mixture was concentrated by evaporation using water bath and the resulting residue was dried under vacuum overnight. The yellowish brown color solid was recrystallized from ethanol (**Scheme-II**). Yield: 56.9 % (0.292 g); Yellowish brown solid, m.f: $C_{33}H_{30}N_2O_6$; m.w.: 550.61; m.p.: 100 °C. IR (KBr, ν_{max}, cm^{-1}): 3369 ν(O-H), 2929 ν_{as}(C-H), 2800 ν_s(C-H), 1577 ν(C=N) and ν(C=C), 1514, 1458, 1430 ν(aromatic C=C), 1379 ν(C-N), 1274 ν_s(C-O-C), 1206 ν(C-O) (phenolic hydroxyl group), 846 δ(C-H), 758 ρ(C-H); ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 3.50 (s, 2H, =N-[a]CH_2-N=), 3.94 (s, 6H, Ar-OCH_3[b]), 5.80 (s, 4*H*, -OH[c]), 6.47 (d, 2*H*, [d]C*H*), 6.92-7.14 (m, 14*H*, Ar [e-j]CH), 7.61 (d, 2H, [k]C*H*).

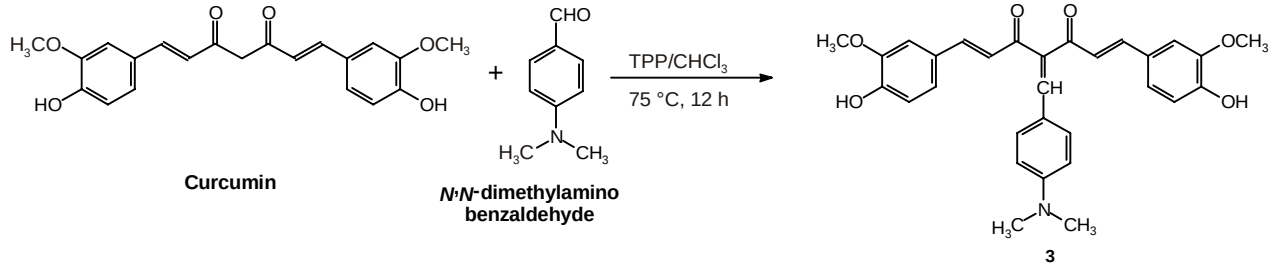
Synthesis of 4-[4-(dimethylamino)benzylidene]-1,7-*bis*(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene-3,5-dione (3): Curcumin (0.2210 g, 0.6 mmol) and *N*,*N*-dimethylamino benzaldehyde (0.0894 g, 0.6 mmol) (1:1 equivalent) were taken in 100 mL round-bottom flask in the presence of triphenyl phosphine (0.1836 g, 0.70 mmol) in chloroform (50 mL) (**Scheme-III**). The



Scheme-I: Synthesis of 4-(4-hydroxybenzylidene)-1,7-*bis*(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione (**1**)



Scheme-II: Synthesis of 3,5-*bis*-(4-hydroxy-phenyl)-imido-1,7-*bis*(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene (**2**)



Scheme-III: Synthesis of 4-(4-(dimethylamino) benzylidene)-1,7-*bis*(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene-3,5-dione (**3**)

reaction mixture was stirred at 75 °C for 12 h in an oil bath. The progress of the reaction was continuously monitored using thin layer chromatographic technique and the completion of the reaction was confirmed by R_f values. The reaction mixture was evaporated to dryness at room temperature, the resultant compound was extracted repeatedly with chloroform-water mixture. The organic layer was separated and dried to get yellow colored solid as product. Further the product was purified by column chromatography by using petroleum ether/ethyl acetate mixture (1:1) as eluent. Yield: 60.2 % (0.378 g); Yellow colour solid; m.f.: $C_{30}H_{29}NO_6$; m.w.: 499.56; m.p.: 120 °C. IR (KBr, ν_{max}, cm^{-1}): 3380 ν(O-H), 2923 ν_{as}(C-H), 2800 ν_s(C-H), 1512 ν(C=C), 1374 ν(C-N), 963 δ(C-H), 725 ρ(C-H); ^{1}H NMR (400 MHz, $CDCl_3$) ppm: 3.09 (s, 6H, Ar-N-(^{a}CH_3)$_2$), 3.95 (s, 6H, Ar-OCH_3^b), 6.45 (d, 2H, Ar ^{d}CH), 6.49 (d, 2H, Ar ^{e}CH), 6.69 (s, 2*H*, Ar ^{f}CH), 6.92 (d, 2*H*, Ar ^{g}C*H*), 7.05 (d, 2*H*, Ar ^{h}CH), 7.11 (d, 2H, ^{i}CH), 7.76 (d, 2*H*), 8.73 (s, 1*H*).

Antioxidant studies

DPPH scavenging activity: The radical scavenging activity of the synthesized curcumin derivatives towards 2,2'-diphenyl-1-picrylhydrazyl (DPPH) free radical was monitored according to the earlier reported procedure[20]. One mL of 0.135 mM DPPH prepared in methanol was mixed with 1.0 mL of sample solutions of compounds **1**, **2** and **3** with various concentrations ranging from 50-250 mg/mL. The reaction mixture was vortexed thoroughly and left in dark at room temperature for 0.5 h. The absorbance was measured spectrophotometrically at 517 nm. The percentage of inhibition activity of DPPH by the synthesized curcumin derivatives was calculated from the following equation:

$$\text{DPPH scavenging activity (\%)} = [(A_{control} - A_{sample})]/(A_{control})] \times 100$$

where A control is the absorbance of DPPH + methanol.

A sample is the absorbance of DPPH radical + sample (*i.e.*, standard or curcumin derivatives).

ABTS scavenging activity: The antioxidant properties of the synthesized curcumin derivatives (**1**, **2** and **3**) are determined by the ABTS scavenging activity. The working standard solution was prepared by mixing two stock solutions of 7 mM ABTS solution and 2.4 mM potassium persulphate solution in equal amount and allowed to react for 12 h at room temperature in the dark. 1 mL of the resulting solutions was allowed to react with 1 mL of the curcumin derivative with different concentration ranging from 50 to 250 mg/mL and the reaction mixture was vortexed and absorbance was measured at 734 nm after 6 min interval. The percentage of inhibition capacity of ABTS by the synthesized curcumin derivatives are calculated from the following equation;

$$\text{ABTS scavenging activity (\%)} = [(A_{control} - A_{sample})]/(A_{control})] \times 100$$

where A control is the absorbance of ABTS + methanol. A sample is the absorbance of ABTS radical + sample (*i.e.*, standard or curcumin derivative).

RESULTS AND DISCUSSION

Characterization of 4-(4-hydroxybenzylidene)-1,7-*bis*-(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione (1): The infrared spectrum of compound **1** showed the broad absorption band at 3392 cm^{-1} corresponding to ν(O-H) vibration of hydroxyl group. The absorption band at 3051 cm^{-1} is assignable to ν(C-H) vibration of aromatic ring. The absorption bands at 2920 and about 2800 cm^{-1} are due to the ν_{as}(C-H) and ν_s(C-H) vibrations, respectively of the methyl group. The absorption band at 1621 cm^{-1} is assignable to the ν_s(C=O) vibration of the carbonyl group. The absorption band at 1584 cm^{-1} is attributed to the aliphatic ν(C=C) vibration of alkene group. The absorption bands at 1511 and 1435 cm^{-1} are due to the ν_s(C=C) vibrations of the aromatic ring. The absorption bands at 1282 and 1024 cm^{-1} are attributed to the ν_{as}(C-O-C) and ν_s(C-O-C) vibrations, respectively of the methoxy group. The absorption band at 1206 cm^{-1} is due to ν(C-O) vibration of phenolic hydroxyl group. The absorption bands at 814 and 693 cm^{-1} are due to δ(C-H) and ρ(C-H) vibrations, respectively[17].

The ^{1}H NMR spectrum of compound **1** in $CDCl_3$ contains signals for ten different kinds of proton environments. The signal at 3.95 ppm (6H, s) is assignable to the methoxy protons of the curcumin (Ar-OCH_3^a). The resonance for the hydroxyl protons is not observed in the spectrum since the -O*H*^{b} protons may undergo very fast exchange with the deuterated solvent. The signal at 6.47 ppm (2H, d) is assignable to the aromatic ^{c}CH protons adjacent to -OH group of curcumin. The signal at 6.84 ppm (2H, d) is attributed to the ^{d}C*H* aromatic methine protons adjacent to -OCH_3 group of curcumin. The signal at 6.91 ppm (2H, d) is due to the aromatic ^{e}CH methine protons adjacent to the -OH group of 4-hydoxy benzaldehyde functionality. The resonance at 7.05 ppm (2H, d) is attributed to the ^{f}C*H* aromatic methine protons of the curcumin functionality. The singlet at 7.12 ppm (2H, s) is assignable to the ^{g}C*H* aliphatic methine proton adjacent to the carbonyl group. The doublet at 7.61 ppm (2H, d) is assignable to the ^{h}C*H* aromatic methine proton of the 4-hydoxy benzaldehyde functionality. The resonance at 7.76 ppm (2H, d) is due to the ^{i}C*H* aliphatic methine proton adjacent to the aromatic ring. The signal at 8.98 ppm (1H, s) is due to the ^{j}CH aliphatic methine proton adjacent to the carbonyl group[11].

Characterization of 3,5-*bis*-(4-hydroxy-phenyl)-imido-1,7-*bis*-(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene (2): Infrared spectrum showed the broad absorption band at 3369 cm^{-1} corresponding to the ν(O-H) vibration of the hydroxyl group. The absorption band at 2929 cm^{-1} is due to the ν_{as}(C-H) vibration of methyl group. The absorption band at about 2800 cm^{-1} is assignable to the ν_s(C-H) vibration of methyl group. The absorption band at 1577 cm^{-1} is assignable to the ν(C=N) vibration and which is merged with the ν(C=C) vibrational absorption band of alkene group. The absorption bands at 1514, 1458 and 1430 cm^{-1} are attributed to the ν(C=C) vibrations of the aromatic ring. The absorption band at 1379 cm^{-1} is due to the ν(C-N) vibration and δ_s(C-H) vibration of methoxy methyl group. The absorption bands at 1274 and 1028 cm^{-1} are due to the ν_s(C-O-C) and ν_{as}(C-O-C) vibrations of methoxy group. The absorption band at 1206 is due to the ν(C-O) vibration of phenolic hydroxyl group. The absorption band at 846 and 758 cm^{-1} are due to the δ(C-H) and ρ(C-H) vibrations, respectively of methylene group[17].

The ^{1}H NMR spectrum of compound **2** in $CDCl_3$ contains signals for eleven different kinds of proton environments. The

signal at 3.50 ppm (2H, s) is assignable to the centre methylene protons (=N-^{a}CH_2-N=) which are in between two methine groups of curcumin. The resonance at 3.94 ppm (6 H, s) is attributed to the methoxy protons (Ar-OCH_3^{b}) of the curcumin. The signal at 5.80 ppm (4H, s) is due to the hydroxyl protons (-OH^{c}). The doublet at 6.47 ppm (2H, d) is attributed to the aliphatic ^{d}C*H* protons. The signals between 6.92 to 7.14 ppm (14H, m) are due to the compound **e-j** aromatic methine protons of both curcumin and 4-aminophenol functionalities. The doublet at 7.61 ppm (2H, d) is assignable to the aliphatic ^{k}C*H* protons adjacent to the aromatic ring of curcumin functionality[11].

Characterization of 4-(4-(dimethylamino)benzylidene)-1,7-*bis*-(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione (3): The infrared spectrum showed the broad absorption band at 3380 cm^{-1} corresponding to the ν(O-H) vibration of hydroxyl group. The absorption band at 2923 cm^{-1} is due to the ν_{as}(C-H) vibration of methyl group. The absorption band at ≈ 2800 cm^{-1} is assignable to the ν_{s}(C-H) vibration of methyl group. The absorption band at 1594 cm^{-1} is assignable to the ν(C=O) vibration of the carbonyl group which is merged with the ν(C=C) vibrational absorption band of alkene group. The absorption bands at 1512, 1509 and 1425 cm^{-1} are attributed to the ν(C=C) vibration of the aromatic ring. The absorption band at 1374 cm^{-1} is due to the ν(C-N) vibration of tertiary amine and δ_s(C-H) vibration of methyl group. The absorption bands at 1271 and 1028 cm^{-1} are due to the ν_{as}(C-O-C) and ν_{s}(C-O-C) vibrations, respectively of the methoxy group. The absorption band at 963 cm^{-1} is due to δ(C-H) vibration of alkene. The absorption band at 725 cm^{-1} is due to the ρ(C-H) vibration of the methyl group[17].

The ^{1}H NMR spectrum of compound **3** in $CDCl_3$ contains signals for eleven different kinds of proton environments. The signal at 3.09 ppm (6H, s) is assignable to the methyl protons (Ar-N-(CH_3^{a})$_2$) attached to the nitrogen atom of dimethyl amino benzaldehyde. The resonance at 3.95 ppm (6H, s) is attributed to the methoxy protons (Ar-OCH_3^{b}) of the curcumin. The signal for the hydroxyl protons (-OH^{c}) is not observed in the spectrum since these labile protons will undergo very fast exchange with the deuterated solvent. The signals at 6.45 (2H, d), 6.49 (2H, d), 6.69 (2H, s), 6.92 (2H, d) and 7.05 (2H, d) are due to the aromatic $^{d\text{-}h}$C*H* methine protons. The signal at 7.11 ppm (2H, d) is due to the ^{i}C*H* aliphatic methine protons adjacent to the carbonyl group. The resonance at 7.76 ppm (2H, d) is attributed to the ^{j}C*H* aliphatic methine proton of curcumin which is adjacent to the aromatic ring. The singlet at 8.73 ppm (1H, s) is assignable to the ^{k}C*H* aliphatic methine proton which is in between methylene group of curcumin and aromatic ring of benzaldehyde[11].

DPPH and ABTS radical inhibition activity studies

DPPH radical inhibition activity studies: DPPH scavenging activity of curcumin derivatives were investigated by comparing curcumin as the reference sample. Figs. 1-3 show the comparison of scavenging activities of curcumin derivatives (**1**, **2** and **3**) with curcumin. The results reveals the fact that the modification of curcumin structure on the active methylene group increases the scavenging activity but the modification on two carbonyl groups decrease the percentage of inhibition.

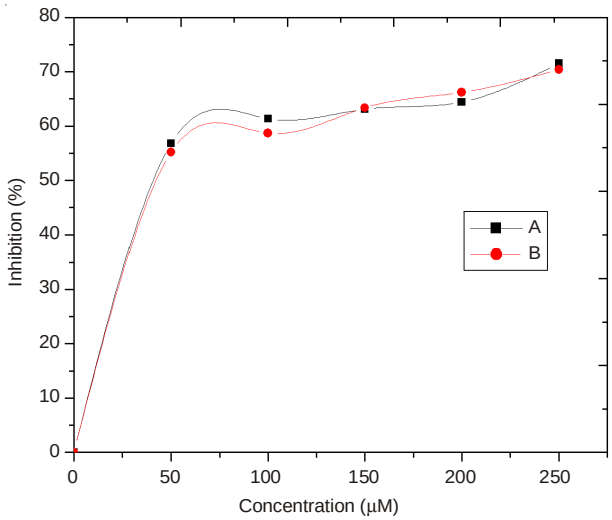


Fig. 1. Plot of % of inhibition *vs.* concentration of 4-(4-hydroxybenzylidene)-1,7-*bis*-(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione (**1**) (curve B) and curcumin (curve A) by DPPH scavenging activity study

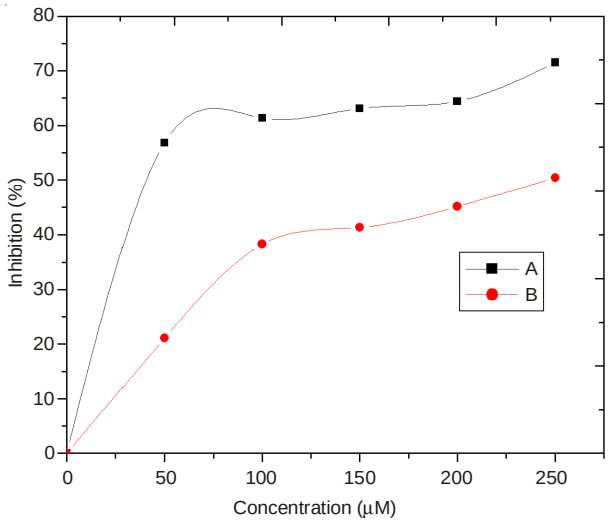


Fig. 2. Plot of % of inhibition *vs.* concentration of 3,5-*bis*-(4-hydroxyphenyl)-imido-1,7-*bis*-(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene (**2**) (curve B) and curcumin (curve A) by DPPH scavenging activity study

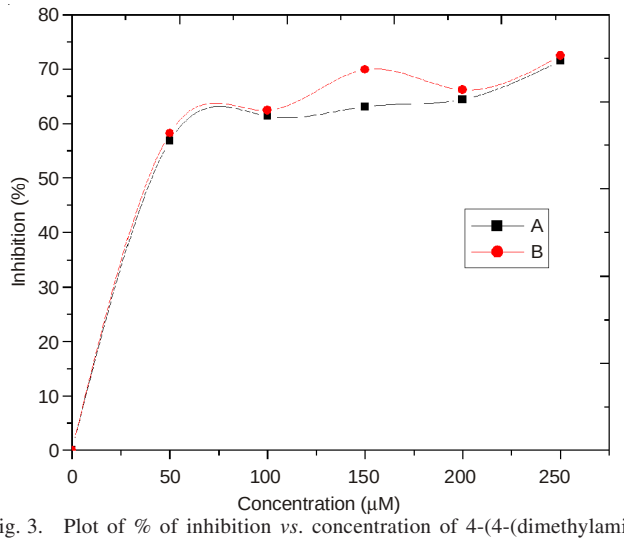


Fig. 3. Plot of % of inhibition *vs.* concentration of 4-(4-(dimethylamino)benzylidene)-1,7-*bis*-(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione (**3**) (curve B) and curcumin (curve A) by DPPH scavenging activity study

The percentage of inhibition of compound **1** is higher than curcumin around 200 mM concentrations, while the curcumin have better inhibition with other concentrations. The inhibition rate was higher for the compound **3** than curcumin in all concentrations. At 150 µM concentration the inhibition was 70 % for compound **3** whereas curcumin shows 70 % inhibition at 250 µM only. The only structural difference between the compounds **1** and **3** is as follows; the compound **1** has electron donating hydroxyl group while **3** has *N*,*N*'-dimethyl electron donating group. Hence, the results suggest that by introducing more electron donating groups will lead to better percentage of inhibition. While for the compound **2**, the percentage of inhibition is only around 45 % at higher concentration. Although the compound has two phenolic -OH groups which is expected to increase the antioxidant behaviour of curcumin, but the decrease in activity suggests the importance of two keto groups in curcumin moiety for antioxidant behaviour. Hence the modification on active methylene group with electron donating groups will produce better percentage of inhibition which in turn increases the antioxidant property of the compound than modifying keto groups in curcumin.

The IC_{50} value of curcumin is achieved at less than 50 µM concentration. For the compounds **1** and **3** also the IC_{50} value found to be less than 50 µM concentration. But, for compound **2** the IC_{50} value was not achieved even at higher concentration (250 µM). This further supports the dramatic negative effect of antioxidant activity on modifying the two keto groups in curcumin derivatives.

ABTS radical inhibition activity studies: ABTS scavenging activity of curcumin derivatives (**1**, **2** and **3**) were analyzed by comparing curcumin as the reference sample. Figs. 4-6 show the comparison of scavenging activity of curcumin derivatives (**1**, **2** and **3**) with curcumin. The inhibition activities of the synthesized derivatives are similar to the results obtained from DPPH radical inhibition studies. The compound **2** has lower scavenging activity compared to that of the compounds **1** and **3**. These results also reveal the fact that the modification on the active methylene group of curcumin increases the scavenging activity but the modification on two carbonyl groups decreases the percentage of inhibition. The concentration required to the reach IC_{50} value in ABTS study was very much lower than the concentration needed for DPPH scavenging activity. For curcumin derivatives **3** and **1**, the IC_{50} value reaches at a very low concentration of around 0-5 µM. But for the compound **2** the IC_{50} value reaches only at 25 µM solution. The percentage of inhibition of the compound **3** is higher than the curcumin in all the concentrations, while the compound **1** has lower inhibition property than that of curcumin standard. Finally, the scavenging properties of the curcumin derivatives (**1**, **2** and **3**) from both DPPH and ABTS studies suggest that the effect of structural modifications in curcumin on antioxidant abilities. The order of the radical scavenging activity of curcumin and the curcumin derivatives (**1**, **2** and **3**) is given above.

Conclusion

Three curcumin derivatives with different substituents were synthesized and characterized by ^{1}H NMR and FT-IR spectroscopic techniques. The antioxidant behaviours of the synthesized derivatives were compared with curcumin which is taken as standard by DPPH and ABTS scavenging activity studies. Interestingly it is observed that the scavenging activity of the curcumin is increased when the substitution is carried out in active methylene site. But the conversion of keto group in to imine moiety decreases the scavenging activity. The

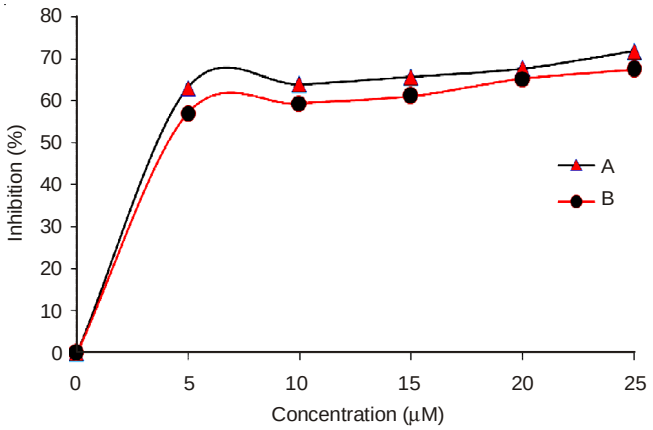


Fig. 4. Plot of % of inhibition *vs*. concentration of 4-(4-hydroxybenzylidene)-1,7-*bis*-(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione (**1**) (curve B) and curcumin (curve A) by ABTS scavenging activity study

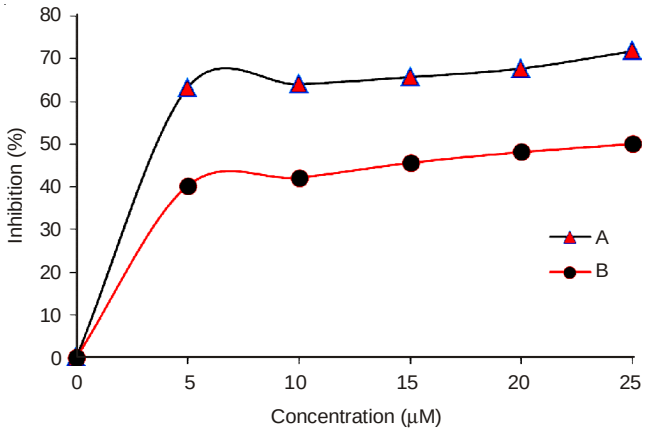


Fig. 5. Plot of % of inhibition *vs*. concentration of 3,5-*bis*-(4-hydroxyphenyl)-imido-1,7-*bis*-(4-hydroxy-3-methoxyphenyl) hepta-1,6-diene (**2**) (curve B) and curcumin (curve A) by ABTS scavenging activity study

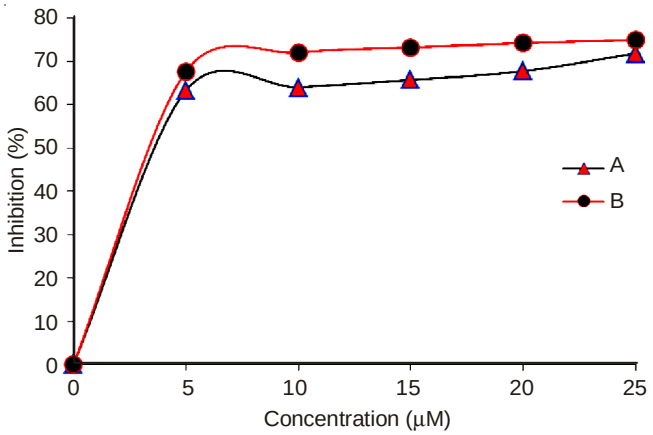
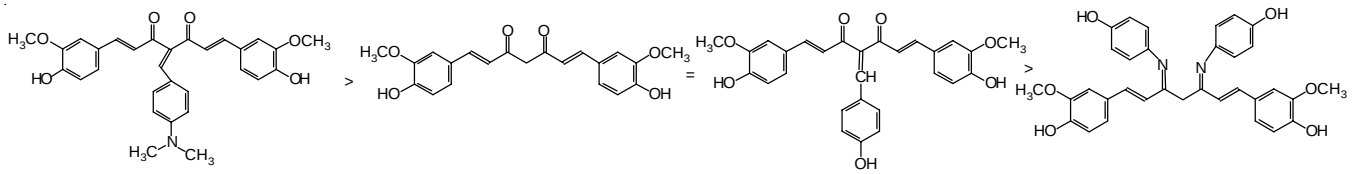


Fig. 6. Plot of % of inhibition *vs*. concentration of 4-(4-(dimethylamino) benzylidene)-1,7-*bis*(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione (**3**) (curve B) and curcumin (curve A) by ABTS scavenging activity study



3 > Curcumin = **1** > **2**

results suggest that the two carbonyl moieties in the curcumin derivatives have significant effect in the radical scavenging properties. The results were further supported by the IC_{50} value. Compared to the compounds **1** and **3** with strong donating strength shows higher scavenging activity. This shows that the strength of electron donating group also has impact in antioxidant activity of curcumin. All these results will provide basic insights in future designing of curcumin derivatives for better antioxidant properties.

REFERENCES

1. L. Barros, M.J. Ferreira, B. Queirós, I.C.F.R. Ferreira and P. Baptista. *Food Chem*., **103**, 413 (2006).
2. (a) A.J.A. Petrus, *Asian J. Chem.*, **26**, 4929 (2014); (b) Ý. Gülçin, *Life Sci.*, **78**, 803 (2006).
3. D. Shahwar, U. Sana and N. Ahmad, *Turk. J. Chem.*, **37**, 262 (2013).
4. (a) G. Rajasekhar Reddy, A.B. Morais and N.N. Gandhi, *Asian J. Chem.*, **25**, 9249 (2013); (b) X.Y. Shang, Y. Zhang, Y.L. Bai, C.L. Xu, W.N. Niu and C.G. Qin, *Asian J. Chem.*, **25**, 9092 (2013); (c) Y. Jin, Y. Xuan, M. Chen, J. Chen, Y. Jin, J. Piao and J. Tao, *Asian J. Chem.*, **25**, 8901 (2013).
5. D. Yasuda, K. Takahashi, T. Ohe, S. Nakamura and T. Mashino, *Bioorg. Med. Chem.*, **21**, 7709 (2013).
6. A.R. Garrett, E.G. Weagel, A.D. Martinez, M. Heaton, R.A. Robison and K.L. O'Neill, *Food Chem.*, **158**, 490 (2014).
7. (a) S. Baytas, E. Kapcak, T. Coban and H. Ozbilge, *Turk. J. Chem.*, **36**, 867 (2012); (b) J.P. Raval, T.N. Akhaja, D.M. Jaspara, K.N. Myangar and N.H. Patel, *J. Saudi Chem. Soc.*, **18**, 101 (2014).
8. M. Cousins, J. Adelberg, F. Chen and J. Rieck, *Ind. Crops Prod.*, **25**, 129 (2007).
9. B.B. Aggarwal, I.D. Bhatt, H. Ichikawa, K.S. Ahn, G. Sethi, S.K. Sandur, N. Chitra, N. Seeram and S. Shishodia, Curcumin Biological and Medicinal Properties, In: Turmeric: The Genus Curcuma, CRC Press, New York, vol. 45, p. 297 (2006).
10. S. Shishodia, G. Sethi and B.B. Aggarwal, *Ann. N.Y. Acad. Sci*., **1056**, 206 (2005).
11. B.B. Aggarwal, C. Sundaram, N. Malani and H. Ichikawa, *Adv. Exp. Med. Biol*., **595**, 1 (2006).
12. F.L. Yen, T.H. Wu, C.W. Tzeng, L.T. Lin and C.C. Lin, *J. Agric. Food Chem.*, **58**, 7376 (2010).
13. K.I. Priyadarsini, D.K. Maity, G.H. Naik, M.S. Kumar, M.K. Unnikrishnan, J.G. Satav and H. Mohan, *Free Radic. Biol. Med.*, **35**, 475 (2003).
14. S.V. Jovanovic, C.W. Boone, S. Steenken, M. Trinoga and R.B. Kaskey, *J. Am. Chem. Soc.*, **123**, 3064 (2001).
15. S. Mishra, U. Narain, R. Mishra and K. Misra, *Bioorg. Med. Chem.*, **13**, 1477 (2005).
16. M. Kelkel, C. Jacob, M. Dicato and M. Diederich, *Molecules*, **15**, 7035 (2010).
17. R.M. Silverstein and F.X. Webster, Spectrometric Identification of Organic Compounds, John Wiley & Sons, New Delhi, edn 5 (2005).
18. S. Sumathi, P. Tharmaraj, C.D. Sheela and R. Ebenezer, *J. Coord. Chem.*, **65**, 506 (2012).
19. J. Lal, S.K. Gupta, D. Thavaselvam and D.D. Agarwal, *Eur. J. Med. Chem.*, **64**, 579 (2013).
20. A. Rameshkumar and T. Sivasudha, *Asian Pacific J. Trop. Biomed.*, **2**, S895 (2012).