Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2016, 8(8):6-11
(http://derpharmachemica.com/archive.html)

Synthesis of bioactive furan derivatized pyrazole carboxamides: Studies on their antimicrobial and antioxidant activities

Pavithra Gurunanjappa and Ajay Kumar Kariyappa*

Department of Chemistry, Yuvaraja College, University of Mysore, Mysuru, India

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ABSTRACT

*In search of new antimicrobial and antioxidant agents, a series of novel pyrazole carboxamides bearing furan moiety have synthesized by simple and assessable procedure. The method involves base catalyzed cyclocondensation reaction of chalcones **3a-e** and semicarbazide hydrochloride **4** in ethanol under optimum temperature. The reaction yielded 3-(furan-2-yl)-4,5-dihydro-5-aryl-pyrazole-1-carboxamides **5a-g** in good yields. The synthesized new compounds were characterized by spectral studies and elemental analysis, and were evaluated in vitro for their antimicrobial and antioxidant susceptibilities.*

Key words: Antimicrobial, antioxidant, chalcone, cyclocondensation, furanoyl, semicarbazone.

INTRODUCTION

Exploring new antimicrobial agents are still remains a worldwide problem because of the enlargements in gaining resistance to older antimicrobial drugs and their possible side effects. The development of novel antimicrobial drugs with different mechanisms of action to the currently available antimicrobial drugs is still demand [1-2]. Antioxidants are the agents; they prevent the deleterious effects caused by free radicals in the human body. Free radicals are associated with multiple diseases conditions such as carcinogenesis, inflammation, mutagenesis, arthritis, cancer and genotoxicity.

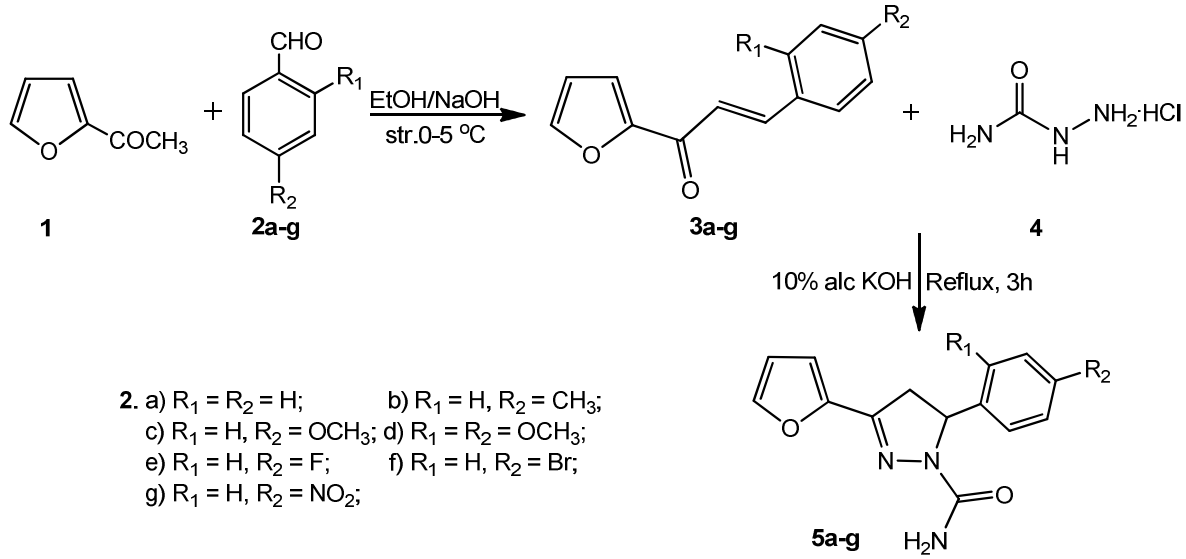
Furan derivatives are an important class of heterocycles that own various biological properties. Furan moiety was considered as common structural motif in many natural products. Furan derivatives showed interesting biological activities such as antioxidant [3], antimicrobial [4], anti-inflammatory [5], antitumor and antiviral [6]. Pyrazoles are an imperative class of five membered heterocycles, which occupies a prime position in the new drug design and discovery [7]. Pyrazoles are versatile lead molecules which have known for their biological activities such as antimicrobial [8], insecticidal and fungicidal [9], analgesic, anticancer, and anti-inflammatory properties [10].

Encouraged by the above facts and in continuation of our interest in the field of pyrazole derivatives, we anticipated that the introduction of pyrazole core to the furan nucleus might generate a new group of biologically active compounds that may be potent antimicrobial and antioxidant agents.

METERIALS AND METHODS

All the reagents and chemicals used are of analytical grade. Melting points were determined by open capillary method and are uncorrected. The ^{1}H NMR and ^{13}C NMR spectra were recorded on Agilent-NMR 400 MHz and 100 MHz spectrometer respectively in $CDCl_3$ as solvent. Chemical shifts are expressed in δ ppm. Mass spectra were obtained on SynaptG2 spectrometer in TOF mode. Elemental analysis was performed on a Thermo Finnigan Flash EA 1112 CHN analyzer. Chromatographic separations were carried out on silica gel (70-230 mesh, Merck) column using hexane: ethyl acetate (4:1) as eluent.

General procedure for the synthesis of 5-aryl-3-(furan-2-yl)-4,5-dihydro-1*H*-pyrazole-1-carboxamides, 5a-g: A mixture of substituted chalcones (**3a-g**) (0.001 mol) and thiosemicarbazide hydrochloride (**4)** (0.001mol) and potassium hydroxide (0.02 mol) in ethyl alcohol (20 mL) was refluxed on a water bath for 3-4 hrs. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured into ice cold water, the solid separated was filtered, washed with ice cold water and recrystallised from ethyl alcohol to obtain target molecules (**5a-g**) in good yields. The synthetic reaction pathway is depicted in **Scheme-1**.



2. a) $R_1 = R_2 = H$; b) $R_1 = H$, $R_2 = CH_3$;
c) $R_1 = H$, $R_2 = OCH_3$; d) $R_1 = R_2 = OCH_3$;
e) $R_1 = H$, $R_2 = F$; f) $R_1 = H$, $R_2 = Br$;
g) $R_1 = H$, $R_2 = NO_2$;

Scheme-1: Reaction pathway for the synthesis of pyrazole carboaxamides

***3-(Furan-2-yl)-4,5-dihydro-5-phenylpyrazole-1-carboxamide*, 5a:** Yield 88%, m. p. 112-113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.18-3.23 (dd, *J*= 12.8, 13.2 Hz, 1H, C_4-H_a), 3.65-3.71 (dd, *J*= 4.8, 12.8 Hz, 1H, C_4-H_b), 5.13-5.19 (dd, *J* = 4.8, 13.2 Hz, 1H, C_5-H_c), 6.41-6.44 (t, 1H, $C_{4'}$-H), 6.66-6.67 (d, 1H, $C_{3'}$-H), 6.92-7.21 (m, 5H, Ar-H), 7.38 (s, 2H, -NH_2), 7.42-7.45 (d, 1H, $C_{5'}$-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 37.6 (1C, C-4), 58.6 (1C, C-5), 110.7 (1C, C-3'), 111.8 (1C, C-4'), 125.4 (1C, C-4"), 127.6 (2C, C-2", C-6"), 128.9 (2C, C-3", C-5"), 138.4 (1C, C-1"), 142.8 (2C, C-2', C-4'), 151.1 (1C, C-3), 156.6 (1C, $CONH_2$). MS (*m/z*): 255 (M+1). Anal. Calcd. for $C_{14}H_{13}N_3O_2$ (%): C, 65.87; H, 5.13; N, 16.46. Found: C, 65.64; H, 5.28; N, 16.27.

***3-(Furan-2-yl)-4,5-dihydro-5-p-tolylpyrazole-1-carboxamide*, 5b:** Yield 82%, m. p. 145-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 1.84 (s, 3H, CH_3), 3.25-3.31 (dd, *J* = 12.6, 13.5 Hz, 1H, C_4-H_a), 3.62-3.67 (dd, *J* = 5, 12.6 Hz ,1H, C_4-H_b), 5.14-5.18 (dd, *J* = 5, 13.5 Hz, 1H, C_5-H_c), 6.42-6.43 (t, 1H, $C_{4'}$-H), 6.67-6.68 (d, 1H, $C_{3'}$-H), 7.01-7.04 (d, 2H, $C_{3"}$-H, $C_{5"}$-H), 7.16-7.19 (d, 2H, $C_{2"}$-H, $C_{6"}$-H), 7.39 (s, 2H, -NH_2), 7.68-7.70 (d, 1H, $C_{5'}$-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 23.2 (1C, CH_3), 39.4 (1C, C-4), 55.1 (1C, C-5), 108.1 (1C, C-3'), 108.5 (1C, C-4'), 123.6 (1C, C-2" C-6"), 127.4 (2C, C-3", C-5"), 132.5 (1C, C-4"), 139.5 (1C, C-1"), 141.3 (2C, C-2' C-4'), 147.2 (1C, C-3), 150.9 (1C, $CONH_2$). MS (*m/z*): 270 (M+1). Anal. Calcd. for $C_{15}H_{15}N_3O_2$ (%): C, 66.90; H, 5.61; N, 15.60. Found: C, 66.78; H, 5.85; N, 15.83.

***3-(Furan-2-yl)-4,5-dihydro-5-(4-methoxyphenyl)pyrazole-1-carboxamide*, 5c:** Yield 86%, m. p. 120-121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.05-3.10 (dd, *J* = 12.9, 13.8 Hz, 1H, C_4- H_a), 3.68-3.73 (dd, *J* = 2.9, 12.9 Hz,

1H, C_4- H_b), 3.85 (s, 3H, OCH_3), 5.42-5.47 (dd, *J*= 2.9, 13.8 Hz, 1H, C_5- H_c), 6.48-6.49 (t, 1H, $C_{4'}$-H), 6.66-6.67 (d, 1H, $C_{3'}$-H), 6.83-6.85 (d, 2H, $C_{3''}$-H, $C_{5''}$-H), 7.15-7.18 (d, 2H, $C_{2''}$-H, $C_{6''}$-H), 7.25 (s, 2H, -NH_2), 7.51-7.52 (d, 1H, $C_{5'}$-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 42.6 (1C, C-4), 55.2 (1C, OCH_3), 59.2 (1C, C-5), 111.8 (1C, C-3'), 111.8 (1C, C-4'), 114.2 (2C, C-3", C-5"), 126.7 (2C, C-2", C-6"), 134.3 (1C, C-1"), 143.4 (1C, C-3), 144.3 (2C, C-2', C-4'), 154.9 (1C, $CONH_2$), 159.0 (1C, C-4''). MS (*m/z*): 286 (M+1). Anal. Calcd. for $C_{15}H_{15}N_3O_3$ (%): C, 63.15; H, 5.30; N, 14.73. Found: C, 63.41; H, 5.18; N, 14.55.

***3-(Furan-2-yl)-4,5-dihydro-5-(2,4-dimethoxyphenyl)pyrazole-1-carboxamide*, 5d:** Yield 87%, m. p. 160-161 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.18-3.23 (dd, *J* = 13.2, 13.9 Hz, 1H, C_4- H_a), 3.54-3.59 (dd, *J* = 4.8, 13.2 Hz, 1H, C_4- H_b), 3.72 (s, 6H, $2OCH_3$), 4.98-5.03 (dd, *J* = 4.8, 13.9 Hz, 1H, C_5- H_c), 6.22-7.41 (m, 6H, Ar-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 39.8 (1C, C-4), 55.9 (2C, $2OCH_3$), 57.1 (1C, C-5), 106.6 (2C, C-3", C-5"), 109.2 (2C, C-3', C-4'), 123.4 (1C, C-1"), 128.6 (1C, C-6"), 141.9 (2C, C-2', C-4'), 148.5 (1C, C-3), 154.8 (1C, $CONH_2$), 156.1 (2C, C-2", C-4"). MS (*m/z*): 316 (M+1). Anal. Calcd. for $C_{16}H_{17}N_3O_4$ (%): C, 60.94; H, 5.43; N, 13.33. Found: C, 60.75; H, 5.65; N, 14.52.

***5-(4-Fluorophenyl)-3-(Furan-2-yl)-4,5-dihydropyrazole-1-carboxamide*, 5e:** Yield 78 %, m. p. 118-119 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.11-3.17 (dd, *J* = 12.2, 13.5 Hz, 1H, C_4- H_a), 3.33-3.39 (dd, *J* = 3.5, 12.2 Hz, 1H, C_4- H_b), 5.10-5.15 (dd, *J* = 3.5, 13.5 Hz, 1H, C_5- H_c), 6.42-6.44 (t, 1H, $C_{4'}$-H), 6.66-6.67 (d, 1H, $C_{3'}$-H), 6.96-6.98 (d, 2H, $C_{3''}$-H, $C_{5''}$-H), 7.16-7.18 (d, 2H, $C_{2''}$-H, $C_{6''}$-H), 7.35 (s, 2H, -NH_2), 7.54-7.56 (d, 1H, $C_{5'}$-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 37.1 (1C, C-4), 58.5 (1C, C-5), 109.1 (1C, C-3'), 109.4 (1C, C-4'), 118.7 (2C, C-3", C-5"), 124.3 (1C, C-2", C-6"), 138.4 (1C, C-1"), 142.1 (2C, C-2', C-4'), 148.3 (1C, C-3), 152.2 (1C, $CONH_2$), 160.1 (1C, C-4"). MS (*m/z*): 274 (M+1). Anal. Calcd. for $C_{14}H_{12}FN_3O_2$ (%): C, 61.53; H, 4.43; N, 15.38; Found: C, 61.75; H, 4.28; N, 15.60.

***5-(4-Bromophenyl)-3-(Furan-2-yl)-4,5-dihydropyrazole-1-carboxamide*, 5f:** Yield 78 %, m. p. 153-154 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.12-3.17 (dd, *J* = 12.6, 13.5 Hz, 1H, C_4- H_a), 3.34-3.39 (dd, *J* = 4.8, 12.6 Hz, 1H, C_4- H_b), 5.01-5.06 (dd, *J* = 4.8, 13.5 Hz,1H, C_5- H_c), 6.42-6.44 (t, 1H, $C_{4'}$-H), 6.66-6.67 (d, 1H, $C_{3'}$-H), 7.16-7.18 (d, 2H, $C_{2''}$-H, $C_{6''}$-H), 7.22-7.26 (d, 2H, $C_{3''}$-H, $C_{5''}$-H), 7.37 (s, 2H, -NH_2), 7.46-7.48 (d, 1H, $C_{5'}$-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 37.1 (1C, C-4), 58.6 (1C, C-5), 108.1 (1C, C-3'), 108.5 (1C, C-4'), 122.4 (1C, C-4"), 128.1 (2C, C-3", C-5"), 129.4 (1C, C-2", C-6"), 139.5 (1C, C-1"), 142.2 (2C, C-2', C-4'), 150.1 (1C, C-3), 154.4 (1C, $CONH_2$). MS (*m/z*): 335 (M+1). Anal. Calcd. for $C_{14}H_{12}BrN_3O_2$ (%): C, 50.32; H, 3.62; N, 12.57; Found: C, 50.54; H, 3.45; N, 12.79.

***3-(Furan-2-yl)-4,5-dihydro-5-(4-nitrophenyl)pyrazole-1-carboxamide*, 5g:** Yield 78 %, m. p. 175-176 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.22-3.26 (dd, *J* = 12.8, 13.6 Hz,1H, C_4- H_a), 3.35-3.39 (dd, *J* = 5, 12.8 Hz, 1H, C_4-H_b), 5.01-5.06 (dd, *J* = 5, 13.6 Hz, 1H, C_5-H_c), 6.34-6.36 (t, 1H, $C_{4'}$-H), 6.66-6.67 (d, 1H, $C_{3'}$-H), 7.27-7.32 (d, 2H, $C_{2''}$-H, $C_{6''}$-H), 7.38 (s, 2H, -NH_2), 7.54-7.56 (d, 1H, $C_{5'}$-H), 7.96-6.99 (d, 2H, $C_{3''}$-H, $C_{5''}$-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 38.1 (1C, C-4), 58.6 (1C, C-5), 111.3 (1C, C-3'), 111.8 (1C, C-4'), 119.1 (2C, C-3", C-5"), 126.4 (1C, C-2", C-6"), 141.3 (1C, C-1"), 143.1 (2C, C-2', C-4'), 147.1 (1C, C-4"), 150.8 (1C, C-3), 154.9 (1C, $CONH_2$). MS (*m/z*): 301 (M+1). Anal. Calcd. for $C_{14}H_{12}N_4O_4$ (%): C, 56.00; H, 4.03; N, 18.66. Found: C, 56.23; H, 4.28; N, 18.50.

RESULTS AND DISCUSSION

The structure proof of the products **5a-g** was provided by ^{1}H NMR, ^{13}C NMR, MS studies and elemental analysis. The structural assignments were made by ^{1}H NMR analysis by considering **5a** as the representative compound. In ^{1}H NMR spectra, compound **5a** showed three doublet of doublets for H_a, H_b and H_c protons of the pyrazole ring. C_4- H_a proton resonate with both C_4- H_b proton and C_5- H_c proton and appearing as doublet of doublet at δ 3.18-3.23 ppm (*J*= 12.8, 13.2 Hz); C_4- H_b proton resonate with both C_4- H_a proton and C_5- H_c proton and appearing as doublet of doublet at δ 3.65-3.71 ppm (*J*= 4.8, 12.8 Hz); and C_5- H_c proton resonate with both C_4- H_b proton and C_4- H_a proton and appearing as doublet of doublet at δ 5.132-5.197 ppm (*J*= 4.8, 13.2 Hz). Coupling constant (J) values of C_4- H_a and C_4- H_b protons suggested that the two methylene protons of C-4 atom are of diastereotopic nature. Among H_a, H_b and H_c protons, H_c is the most deshielded due to its close proximity to a benzene ring and electronegative nitrogen atom of the pyrazole ring. The NH_2 protons deshielded due to adjacent C=O group and appearing as singlet at δ 7.38 ppm. Further the compound showed the signals due to methoxy substitution, aromatic and thiophene ring protons in the expected region. All the series of synthesized compounds showed the similar ^{1}H NMR spectra.

In ^{13}C NMR, compound **5a** showed signals due to C-3-atom at δ 151.1ppm, for C-4 atom at δ 37.6 ppm. The C-5 atom signal appeared at δ 58.6 ppm. An intense signal appeared at δ 156.6 ppm was due to C=O carbon atom. Further, it showed the signals due to methoxy substitution, aromatic and thiophene ring carbons in the expected region. The synthesized compounds **5a-g** showed the similar consistent pattern signals in their ^{13}C NMR spectra, which strongly favors the formation of the products. All new compounds showed M+1 molecular ion peaks as base peak. The satisfactorily elemental analysis further supports the structure of the products.

Antimicrobial activity

Microbial studies of synthesized compounds were assessed by minimum inhibitory concentration (MIC) by serial dilution method [11]. The compounds were screened for their antimicrobial activities against Gram-negative bacteria species *Escherichia coli, Pseudomonas aeruginosa,* Gram-positive bacteria *Staphylococcus aureus,* fungi species *Aspergillus nigar, Aspergillus flavus* and *Candila albicans.* The experiments were carried out in triplicate; the results were taken as a mean of three determinations. Known antibiotics ciprofloxacin and fluconazole were used as standards for antibacterial and antifungal studies respectively. The results of MIC's were summarized in **Table 1.**

Table 1: Minimum inhibitory concentrations (MIC) in µg/mL* of the test compounds 5a-g against bacterial and fungal species

Compound	*S. aureus*	*E. coli*	*P. aeruginosa*	*A. niger*	*A. flavus*	*C. albicans*
5a	25±0.56	25±0.23	25±0.65	50±0.21	50±0.91	50±0.43
5b	50±0.76	25±0.47	25±0.20	25±0.56	25±0.36	75±0.75
5c	75±0.26	75±0.25	50±0.76	50±0.71	75±0.83	75±0.76
5d	100±0.97	75±0.14	50±0.54	50±0.51	50±0.95	75±0.40
5e	25±0.76	6.25±0.22	12.5±0.53	12.5±0.10	12.5±0.33	25± 0.65
5f	12.5±0.98	12.5±0.73	25±0.20	12.5±0.76	25±0.61	25±0.34
5g	75±0.12	100±0.09	50±0.54	75±0.33	50±0.84	100±0.55
cipro[a]	25±0.45	25±0.23	12.5±0.65	----	----	----
fluc[b]	----	----	----	25±0.81	25±0.66	50±0.32

** Values are mean ±SD of three replicates; [a] ciproafloxacin was used as a positive control against bacteria species; [b] fluconazole was used as a positive control against fungi species*

All the synthesized compounds exerted a wide range of modest *in vitro* antibacterial activity having minimum inhibitory concentration (MIC) values ranging from 6.25-100 µg/mL. Compounds **5e** and **5f** having F and Br substitution showed excellent bacterial activity by inhibiting spore germination of all the tested organisms. Compound **5a** having no substitution in the phenyl ring showed activity as potent as the standard. Remaining compounds **5b, 5c, 5d** and **5g** having methyl, methoxy, dimethoxy and nitro substitution exhibited poor inhibitory effect on the organisms.

The synthesized pyrazole derivatives exerted modest antifungal activity having minimum inhibitory concentration (MIC) value 12.5-100 µg/mL. Fluro and Bromo substitution in compounds **5e** and **5f** demonstrated excellent antifungal activity against the organisms tested. However, compound **5b** having methyl substitution showed moderate activity against *A. niger* and *A. flavus*. Compound **5a** having no substitution in the phenyl ring showed activity similar to that shown by the standard only at *C. albicans*. Remaining compounds **5c**, **5d** and **5g** having methoxy and nitro substitution exhibit lesser activity against all the organisms tested.

DPPH radical scavenging activity

The capacity to scavenge the stable free radical 2, 2-diphenyl-1-picrylhydrazyl (DPPH) was monitored according to the Blois method [12]. A freshly prepared DPPH solution shows a deep purple color with an absorption maximum at 517 nm. When the purple color changes to yellow, it leads to decreased absorbance. This is because of the antioxidant molecule reducing the DPPH free radical through donation of hydrogen atom. Instantaneously or concomitant decrease in absorbance would be indicative of potent antioxidant activity by the compound. The free radical scavenging potential was calculated as a percentage (I %) of DPPH decoloration using the equation

$$I\% \text{ of scavenging} = (A_0\text{-}A_1/A_0) \times 100$$

Where A_0 is the absorbance of the control reaction mixture excluding the test compounds, and A_1 is the absorbance of the test compounds. Tests were carried out in triplicate and the results are expressed as I% ± Standard Deviations and were summarized in **Table 2**.

Table 2: DPPH Radical Scavenging activity (measured in %) of the compounds 5a-g

Compound	25 (µg/mL)	50 (µg/mL)	75 (µg/mL)	100 (µg/mL)
5a	26.98±0.66	32.43±0.60	36.25±0.54	45.54±0.90
5b	20.65±0.31	26.87±0.32	28.09±0.76	31.87±0.32
5c	21.65±0.98	28.61±1.21	31.21±0.13	36.92±0.82
5d	21.02±0.40	28.76±0.82	32.43±0.58	36.43±0.55
5e	30.54±0.98	35.23±0.72	41.32±0.21	48.12±0.76
5f	33.12±0.09	35.97±0.60	42.65±0.12	50.12±0.76
5g	18.65±0.76	22.32±0.97	28.06±0.63	34.32±0.22
Ascorbic acid	28.75±0.15	33.12±0.21	37.87±0.77	46.54±0.73

Based on the experimental results, compounds **5e** and **5f** having fluro and bromo substitution showed antioxidant activity better than the standard ascorbic acid. Compound **5a** having no substitution showed antioxidant properties closer to the standard. Remaining compounds **5b**, **5c, 5d** and **5g** having methyl, methoxy, dimethoxy and nitro substitution showed less activity compared with the standard ascorbic acid.

Hydroxyl radical scavenging assay

The hydroxyl radical is a highly reactive free radical formed in biological systems and it is capable of damaging biomolecule found in living cells [13]. The hydroxyl radical has the ability to break DNA and cause strand breakage, which contributes to carcinogenesis, mutagenesis and cytotoxicity. The experiment was carried out in triplicate and the results were expressed as I% ± standard deviations and were summarized in **Table 3**.

Table 3: Hydroxyl radical scavenging activity (measured in %) of the compounds 5a-g

Compound	25 (µg/ml)	50 (µg/ml)	75 (µg/ml)	100 (µg/ml)
5a	6.97±0.76	11.94±0.65	22.04±0.32	31.95±0.76
5b	6.04±0.54	10.43±0.76	16.76±0.32	22.65±0.43
5c	6.54±0.15	11.87±0.08	20.65±0.32	28.93±0.65
5d	6.76±0.33	11.67±0.52	21.53±0.52	27.18±0.21
5e	11.21±0.65	15.62±0.87	27.32±0.05	35.05±0.92
5f	12.43±0.76	17.87±0.43	26.32±0.21	36.66±0.44
5g	05.54±0.76	09.43±0.54	15.32±0.21	21.65±0.70
BHA	7.11±0.24	12.98±0.38	22.65±0.20	32.98±0.71

In this method, compounds **5(a-g)** were found to be possess stronger to weak hydroxyl radical scavenging activity. Among the compounds studied, fluro and bromo substitution in compounds **5e** and **5f** exhibited remarkable capacity for scavenging hydroxyl radical significantly higher than that of the standard BHA. However compound **5a** having no substitution exhibit moderate activity. Methyl, methoxy, dimethoxy and nitro substitution present in the compounds **5b**, **5c, 5d** and **5g** exhibits weak radical scavenging activity.

CONCLUSION

An accessible procedure for the synthesis of pyrazoline carbothiomides was reported. The antimicrobial and antioxidant activity was significantly affected by the substitution present on the phenyl ring. The electron donating groups in the *ortho* and *para* positions of the phenyl ring were found to be more active. The rest of the compounds showed moderate activity with respect to standard drug against the test strains.

Acknowledgements

The authors are grateful for the IOE Instrumentation facility, University of Mysore, for recording NMR and mass spectra of the compounds reported. One of the author Pavithra G is grateful to the UGC for awarding NON-NET Fellowship (Order No. DV9/192/NON-NETFS/2013-14, Dated 11-11-2013).

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