ORIGINAL RESEARCH



# Synthesis of some new indolo[2,3-c]isoquinolinyl pyrazoles, -1,3,4oxadiazoles and their biological activities

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Received: 19 March 2012/Accepted: 13 November 2012/Published online: 9 December 2012 © Springer Science+Business Media New York 2012

Abstract A new series of novel compounds [10-substituted 6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]carbohydrazides (**3a–c**), 1-[10-substituted 6H, 7H-indolo[2, 3-c]isoquinolin-5-one-6-y]]fomy]-, -3',5'-dimethylpyrazoles (4a-c), -3',5'-diphenylpyrazoles (5a-c), -3'-methylpyrazol-5'-ones (**6a–c**) and -1',3',4'-oxidiazole-2'-thiones (**7a–c**) linked to indoloisoquinoline at position-6 through formyl bridge was prepared. The structures of these newly synthesized compounds were confirmed by their spectral studies and elemental analysis. These compounds have been screened for their antimicrobial and antioxidant activities. Compounds 4a, 4b, 5a, 5b, 5c, 6b, 7a, and 7c exhibited the maximum zone of inhibition against A. niger, A. flavus, and A. fumigatus. Compounds 4a, 5a, 5c, 6b, 6c, 7a, and 7b showed good antibacterial activity. Compounds 4b, 4c, 5b, 5c, 6a, 6b, 7a, 7b, and 7c showed good radical scavenging activity compared with standards.

**Keywords** Indolo[23-c]isoquinoline · Pyrazole · Pyrazolone · Oxadizole · Antimicrobial · Antioxidant

**Electronic supplementary material** The online version of this article (doi:10.1007/s00044-012-0366-6) contains supplementary material, which is available to authorized users.

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#### Introduction

Pyridoindoles (Carbolines) are known for their wide spectrum of biological activities, viz., anticoagulant (Cohen and Cattanach, 1967), anticonvulsant (Saxena et al., 1969), antidepressant (Garmaise and Parks, 1973), anti-inflammatory, antibacterial (Winter et al., 1979), antitumor (Ishizumi and Katsube, 1980; Sumitomo, 1983), and antihistaminic (Kosuge et al., 1973). However, there are few reports on the antimicrobial activities of  $\alpha$ -carbolines (Azimvand, 2012; Thakur et al., 2010), and recently we have reported the antioxidant and antimicrobial activities (Saundane et al., 2012) of compounds containing this system. Apart from this, pyrazole and its derivatives have been found to exhibit antimicrobial, anthelmintic, oxytocic (Hiremath et al., 1993; 1995; 1997), anti-inflammatory, analgesic (Saundane et al., 1998a), ulcerogenic, and lipid peroxidation (Amir and Kumar 2005) activities. Some of the pyrazole analogs were reported as antimicrobial (Sridhar et al., 2004; Bondock et al. 2010), fungicides (Chen et al., 2000; Vicentini et al., 2007), and antioxidant (Burgute et al., 2007) activities. In addition, 1,3,4-oxadiazoles are also known for their biologic importance, viz., anticancer (Rajyalakshmi et al., 2011), antifungal (Abdel-Rahman, 2004), antibacterial (Padmavathi et al., 2009), and antioxidant (Padmavathi et al., 2010) activities. The aim of the present study was both to explore the effect of the synthesized compounds on the tested pathogens and to find lead compounds having potent antimicrobial and/or antioxidant activity. Hence, in the continuation of our work on the synthesis of biologically important α-carbolines, we are reporting the synthesis, antimicrobial and antioxidant activities of the title compounds in the present communication.

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# **Results and discussion**

The reaction sequence employed for the synthesis of title compounds is illustrated in Scheme 1. The starting compounds 10-substituted 6H, 7H-indolo[2,3-c]isoquinolin-5-ones (1a-c), ethyl[10-substituted 6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]formates (2a-c) and [10-substituted 6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]carbohydrazides (3a-c) were prepared according to the reported method (Hiremath et al., 1995). The hydrazide (3a) were subjected to cyclocondensation with acetyl acetone or dibenzoyl methane or ethyl acetoacetate in dry methanol containing catalytic amount of conc. hydrochloric acid under reflux temperature to yield 1'-[10-chloro-6H, 7H-indolo[2,3-c] isoquinolin-5-one-6-yl]formyl-, -3',5'-dimethylpyrazole (4a), -3',5'-diphenylpyrazole (5a) and -3'-methylpyrazol-5'-one (6a), respectively.

Compound (3a) on reaction with carbon disulfide and potassium hydroxide in dry methanol under reflux conditions afforded 5'-[10-chloro-6H, 7H-indolo[2, 3-c]isoquinolin-5-one- 6-yl]-1', 3', 4'-oxidiazol-2'-thione (7a). Similarly, other derivatives in the series were prepared and structures of these compounds were confirmed by their spectral studies and elemental analysis.

## **Biological activities**

Literature survey reveals that most of the synthesized compounds contain the biologically active pharmacophores -N-CO-N-, -N-CO-N-CO- and oxdiazoles which exhibited the wide range of activities such as, antimicrobial (Dhansay et al., 2010; Jaiswal et al., 2012; Latthe et al., 2006; Patel et al., 2007; Aanandhi et al., 2011), antioxidant (George et al., 2008; Aanandhi et al., 2010; Amornraksa et al., 2009), anti-inflammatory (Amir Mohd et al., 2007), and anticancer (Aboraia et al., 2006), etc. Therefore, based on these observations, the synthesized compounds have been screened for their antimicrobial and antioxidant activities.

### Antimicrobial activity

The newly synthesized compounds (4-7) were screened for their antimicrobial activity by Cup-plate method (Indian pharmacopoeia, 1985; Saundane et al., 1998b). Escherichia coli, Bacillus subtilis, and Pseudomonas putida were used for antibacterial activity. Antifungal activity was evaluated against Asperigillus niger, Asperigillus flavus, and Asperigillus fumigatus. For the screening, nutrient agar medium



Table 1 Antimicrobial activity of synthesized compounds (4-7)

Compd. no	Antibacterial activity (zone of inhibition in mm)			Antifungal activity (zone of inhibition in mm)		
	E. coli	B. subtilis	P. putida	A. niger	A. flavus	A. fumigatus
4a	09	11	19	16	11	15
4b	13	11	10	08	16	11
4c	11	08	10	10	08	04
5a	10	13	18	04	09	15
5b	05	09	13	15	13	04
5c	11	11	17	09	17	15
6a	07	10	15	06	09	13
6b	10	08	18	12	14	15
6c	17	10	10	09	07	04
7a	18	19	20	17	16	17
7b	11	11	19	08	13	10
7c	13	10	07	10	10	15
$S_1$	19	20	22	-	-	-
$S_2$	-	-	-	18	19	18

Where, S<sub>1</sub> Streptomycin (Standard), S<sub>2</sub> Fluconazole (Standard)

and potato dextrose agar medium were used for antibacterial and antifungal activity. The compounds were tested at 1 mg/ml concentration. Streptomycin and fluconazole were used as standards for antibacterial and antifungal activities, respectively. The results are reported in (Table 1).

The investigation of antibacterial screening revealed that compounds **6c** and **7a** exhibited maximum zone of inhibition against *E. coli*. Compound **7a** exhibited maximum inhibitory zone against *B. subtilis*. Whereas, compounds **5a**, **5c**, **6b**, **7a**, and **7b** exhibited maximum zone of inhibition against *P. putida*.

In the case of antifungal activity, compounds **4a**, **5b**, and **7a** showed maximum zone of inhibition against *A. niger*. Compounds **4b**, **5c**, and **7a** exhibited good activity against *A. flavus*. Compounds **4a**, **5a**, **5c**, **6b**, **7a**, and **7c** showed good activity against *A. fumigatus*. Rest of the compounds showed either lower activity or inactive against the organisms tested. From the results of antimicrobial activities, it could be assumed that the majority of synthesized compounds having chloro and methoxy substituents exhibited better activity.

# Antioxidant activity

1, 1-Diphenyl-2-picryl hydrazyl (DPPH) radical scavenging activity (RSA)

DPPH has an odd electron and has strong absorption band at 517 nm. The reduction capability of DPPH radical was determined by decrease in its absorption at 517 nm induced by antioxidant. The RSA of the newly synthesized compounds (4-7) was carried out by following literature procedure (Hatano et al., 1988) using ascorbic acid (AA), 2-tert-butyl-4-methoxy phenol (butylated hydroxy anisole, BHA), and 2-(1,1-dimethylethyl)-1,4-benzenediol (tertiary butylated hydroquinone, TBHQ) as standards. The RSA of test compounds in methanolic solution at 25, 50, 75, and 100 ug/ml concentrations containing freshly prepared DPPH solution (0.004 % w/v) was carried out and compared with those of standards AA, BHA, and TBHQ. All the test analyses were performed on three replicates and results were averaged. The results in percentage were expressed as the ratio of absorption decrease in the presence of test compounds and absorption of DPPH solution in the absence of test compounds at 517 nm on Elico SL 171 Mini Spec spectrophotometer. The results are shown in the Figs. 1 and 2.

The analysis of results indicated that compounds **5b**, **5c**, **6a**, **6b**, **7a**, **7b**, and **7c** exhibited good radical scavenging activity (56.21, 60.05, 67.45, 57.98, 68.35, 57.69, and 60.75 %) at 25 µg/ml concentration, respectively. Compounds **5b**, **6b**, **7a**, **7b**, and **7c** showed radical scavenging ability (56.86, 64.20, 69.82, 65.38, and 67.75 %) at 50 µg/ml concentration, respectively. While compounds **4c**, **6b**, and **7a** showed radical scavenging ability (53.84,



Fig. 1 Antioxidant activity of compounds (4-5)



Fig. 2 Antioxidant activity of compounds (6-7)

56.50, and 57.98) at 75  $\mu$ g/ml concentration, respectively. The compounds **4b** and **7a** exhibited RSA (64.74 and 68.93 %) at 100  $\mu$ g/ml concentration, respectively. Compound **7a** showed maximum RSA may be due to presence of chloro and methoxy group. However, none of the compounds exhibited better RSA than the standards.

# Conclusion

The present study revealed that the compounds having chloro and methoxy substituents exhibited good antimicrobial and antioxidant activities.

## **Experimental procedure**

Chemistry

### Materials and methods

All the reagents were obtained commercially and used by further purification. Melting points were determined by an open capillary method and are uncorrected. Purity of the compounds was checked by TLC using silica gel-G coated alumininum plates (Merck) and spots were visualized by exposing the dry plates in iodine vapors. The IR (KBr) spectra were recorded using a Perkin-Elmer Spectrum on FT-IR spectrometer. The <sup>1</sup>H NMR (DMSO) spectra recorded using Marcy Plus (Varian 400 MHz) and the chemical shifts were expressed in ppm ( $\delta$  scale) and <sup>13</sup>C NMR (125 MHz, DMSO) spectra recorded on Bruker NMR. Mass spectra were recorded using a ILS-CHU-C-41-VBV4 MS mass spectrometer.

General procedure for the synthesis of 10-substituted 6H, 7H-indolo[2,3-c]isoquinolin-5-ones (**1a-c**), ethyl [10substituted 6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl] formates (**2a-c**) and [10-substituted 6H, 7H-indolo[2,3-c] isoquinolin-5-one-6-yl]carbohydrazides (**3a-c**). These compounds were prepared by reported literature methods (Hiremath et al., 1995).

General procedure for the synthesis of 1'-[10-substituted 6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]formyl-, -3',5'dimethylpyrazoles (4a-c), -3',5'-diphenylpyrazoles (5a-c) and -3'-methylpyrazole-5'-ones (6a-c). A mixture of hydrazides (3a-c) (0.001 mol) and acetyl acetone or dibenzoyl methane or ethyl acetoacetate (0.001 mol) in dry methanol containing 4–5 drops of conc. HCl was refluxed for 4 h on steam bath. The excess of solvent was distilled off under reduced pressure and the residue was cooled to room temperature. The separated solid was filtered off, washed with cold methanol (5-7 mL), dried, and recrystallized from ethanol to furnish pure **4a–c**, **5a–c** and **6a–c**.

*l'-[10-chloro-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]* formyl-3',5'-dimethylpyrazole (4a) Yield: 72 %, mp > 300 °C; Rf, 0.65 ethyl acetate:acetone (6:4) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,278 (Indole NH); 1,654 (C=O); 1,630 (C=O); 1,620 (C=N); <sup>1</sup>H NMR (DMSO-*d<sub>6</sub>*, δ, ppm), 10.90 (s, 1H, indole NH); 7.20–8.40 (m, 7H, Ar–H); 6.10 (s, 1H, Pyrazole-H); 3.50 (s, 3H, CH<sub>3</sub>); 2.33 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C-NMR (DMSO-*d<sub>6</sub>*, 125 MHz, δ), 162.8, 161.0, 145.5, 139.1, 138.8, 136.1, 134.6, 132.9, 132.4, 130.9, 130.7, 130.2 129.7, 128.6, 126.1, 125.4, 122.0, 120.9, 120.3, 22.8, 20.6; MS (EI) *m/z* 390 (M<sup>+</sup>); 392 (M<sup>+</sup>+2). Anal. % C<sub>21</sub>H<sub>15</sub>N<sub>4</sub>O<sub>2</sub>Cl: C, 64.54; H, 3.87; N, 14.34. Found: C, 64.41; H, 3.82; N, 14.29.

*l'-[10-methyl-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]* formyl-3',5'-dimethylpyrazole (**4b**) Yield: 68 %, mp > 300 °C; Rf, 0.71 ethyl acetate:acetone (6:4) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,388 (Indole NH); 1,700 (C=O); 1,658 (C=O); 1,623 (C=N); <sup>1</sup>H NMR (DMSO- $d_6$ ,  $\delta$ , ppm) 11.09 (s, 1H, indole NH); 7.00–8.06 (m, 7H, Ar–H); 6.10 (s, 1H, Pyrazole-H); 2.58 (s, 3H, CH<sub>3</sub>); 2.52 (s, 3H, CH<sub>3</sub>); 2.21 (s, 3H, CH<sub>3</sub>); Anal. % C<sub>22</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub>: C, 71.34; H, 4.90; N, 15.13. Found: C, 71.31; H, 4.82; N, 15.29.

*l'-[10-methoxy-6H, 7H-indolo*[2,3-*c*]*isoquinolin-5-one-6-yl]* formyl-3',5'-dimethylpyrazole (4c) Yield: 70 %, mp > 300 °C; Rf, 0.45 ethyl acetate:acetone (6:4) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,300 (Indole NH); 1,684 (C=O); 1,650 (C=O); 1,630 (C=N); <sup>1</sup>H NMR (DMSO- $d_6$ ,  $\delta$ , ppm) 11.82 (s, 1H, indole NH); 7.10–8.23 (m, 7H, Ar–H); 6.22 (s, 1H, Pyrazole-H); 3.67 (s, 3H, OCH<sub>3</sub>); 2.35 (s, 3H, CH<sub>3</sub>); 2.25 (s, 3H, CH<sub>3</sub>); Anal. % C<sub>22</sub>H<sub>18</sub>N<sub>4</sub>O<sub>3</sub>: C, 68.38; H, 4.70; N, 14.50. Found: C, 68.41; H, 4.82; N, 14.39.

*l'-[10-chloro-6H, 7H-indolo*[2,3-*c*]*isoquinolin-5-one-6-yl]* formyl-3',5'-diphenylpyrazole (5a) Yield: 72 %, mp > 300 °C; Rf, 0.65 ethyl acetate:acetone (6:4) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,214 (indole-NH); 1,739 (C=O); 1,700 (C=O); 1,630 (C=N); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, δ, ppm), 11.00 (s, 1H, indole NH); 7.05–8.21 (m, 17H, Ar–H); 6.10 (s, 1H, Pyrazole-H); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>, 125 MHz, δ), 163.0, 160.8, 146.3, 140.4, 135.8, 135.3, 135.1, 134.3, 133.9, 131.3, 129.8, 129.3, 129.2, 129.1, 128.8, 128.7, 128.3, 128.5, 128.2, 127.4, 127.3, 127.2, 127.1, 126.4, 126.3, 126.2, 126.1, 126.0, 121.8, 121.4, 121.3; MS (EI) *m/z* 514 (M<sup>+</sup>); 516 (M<sup>+</sup>+2). Anal. % C<sub>31</sub>H<sub>19</sub>N<sub>4</sub>O<sub>2</sub>Cl: C, 72.30; H, 3.72; N, 10.88. Found: C, 72.21; H, 3.82; N, 10.71. *l'-[10-methyl-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl] formyl-3',5'-diphenylpyrazole* (*5b*) Yield: 72 %, mp 298–99 °C; Rf, 0.72 ethyl acetate:acetone (6:4) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,385 (indole-NH); 1,721 (C=O); 1,700 (C=O); 1,628 (C=N); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>,  $\delta$ , ppm), 11.82 (s, 1H, indole NH); 7.19–8.08 (m, 17H, Ar–H); 6.24 (s, 1H, Pyrazole-H); 2.48 (s, 3H, CH<sub>3</sub>); Anal. % C<sub>32</sub>H<sub>22</sub>N<sub>4</sub>O<sub>2</sub>: C, 77.72; H, 4.48; N, 11.33. Found: C, 77.75; H, 3.78; N, 10.68.

*l'-[10-methoxy-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]* formyl-3',5'-diphenylpyrazole (5c) Yield: 72 %, mp 265-66 °C; Rf, 0.52 ethyl acetate:acetone (6:4) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,306 (indole-NH); 1,725 (C=O); 1,700 (C=O); 1,630 (C=N); <sup>1</sup>H NMR (DMSO- $d_6$ ,  $\delta$ , ppm), 11.82 (s, 1H, indole NH); 7.19-8.08 (m, 17H, Ar–H); 6.38 (s, 1H, Pyrazole-H); 3.46 (s, 3H, OCH<sub>3</sub>); Anal. % C<sub>32</sub>H<sub>22</sub>N<sub>4</sub>O<sub>3</sub>: C, 75.28; H, 4.34; N, 10.97. Found: C, 75.20; H, 4.28; N, 11.25.

*l'-[10-chloro-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]* formyl-3'-methylpyrazole-5'-one (**6a**) Yield: 66 %, mp > 300 °C; Rf, 0.70 ethyl acetate:methanol (9:1) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,290 (indole-NH); 1,700 (C=O); 1,660 (C=O); 1,655 (C=O); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>,  $\delta$ , ppm), 11.00 (s, 1H, indole NH); 7.41–8.40 (m, 7H, Ar–H); 3.09 (s, 2H, CH<sub>2</sub>); 2.21 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>, 125 MHz,  $\delta$ ), 163.3, 160.4, 158.0, 148.1, 139.8, 139.1, 135.8, 133.1, 132.4, 131.9, 130.1, 129.8, 129.1, 128.9, 126.3, 125.8, 122.5, 120.9, 120.1, 39.50, 19.6; MS (EI) *m/z* 392 (M<sup>+</sup>); 394 (M<sup>+</sup>+2). Anal. % C<sub>20</sub>H<sub>13</sub>N<sub>4</sub>O<sub>3</sub>Cl: C, 61.16; H, 3.34; N, 14.26. Found: C, 62.00; H, 3.22; N, 14.18.

*l'-[10-methyl-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl] formyl-3'-methylpyrazole-5'-one* (*6b*) Yield: 82 %, mp 288–89 °C; Rf, 0.52 ethyl acetate:methanol (9:1) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,330 (indole-NH); 1,700 (C=O); 1,682 (C=O); 1,664 (C=O); <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>, δ, ppm), 11.84 (s, 1H, indole NH); 7.00–8.25 (m, 7H, Ar–H); 3.10 (s, 2H, CH<sub>2</sub>); 2.58 (s, 3H, CH<sub>3</sub>); 2.18 (s, 3H, CH<sub>3</sub>); Anal. %  $C_{21}H_{16}N_4O_3$ : C, 67.73; H, 4.33; N, 15.05. Found: C, 67.82; H, 4.28; N, 15.18.

*l'-[10-methoxy-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]* formyl-3'-methylpyrazole-5'-one (**6***c*) Yield: 58 %, mp > 300 °C; Rf, 0.63 ethyl acetate:methanol (9:1) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,300 (indole-NH); 1,713 (C=O); 1,700 (C=O); 1,682 (C=O); <sup>1</sup>H NMR (DMSO- $d_6$ ,  $\delta$ , ppm), 11.68 (s, 1H, indole NH); 7.10–8.20 (m, 7H, Ar–H); 3.25 (s, 2H, CH<sub>2</sub>); 3.58 (s, 3H, OCH<sub>3</sub>); 2.18 (s, 3H, CH<sub>3</sub>); Anal. % C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>O<sub>4</sub>: C, 64.94; H, 4.15; N, 14.43. Found: C, 65.11; H, 4.28; N, 14.38. General procedure for the synthesis of 5'-[10-substituted 6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl]-1',3',4'-oxidiazole-2'-thiones (7a-c). A mixture of hydrazides (3a-c) (0.005 mol), KOH (0.005 mol), and CS<sub>2</sub> (5 ml) in methanol (50 ml) was refluxed on a steam bath until the evolution of H<sub>2</sub>S ceased (45–48 h). The solvent was then evaporated and residue dissolved in ice-cold water. The resulting clear solution was filtered and the filtrate was acidified with dilute HCl. The separated solid was filtered, washed with water, dried, and recrystallized from ethanol to furnish pure 7a-c.

5'-[10-chloro-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl] -1',3',4'-oxidiazole-2'-thione (7a) Yield: 62 %, mp > 300 °C; Rf, 0.62 ethyl acetate:methanol (9:1) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,283 (indole-NH); 3,154 (NH); 1,658 (C=O); 1,201 (C=S); <sup>1</sup>H NMR (DMSO- $d_6$ ,  $\delta$ , ppm) 11.32 (s, 1H, indole NH); 9.21 (s, 1H, NH); 7.23–8.12 (m, 7H, Ar–H); <sup>13</sup>C-NMR (DMSO- $d_6$ , 125 MHz,  $\delta$ ), 176.2, 163.5, 158.1, 148.3, 139.2, 137.1, 136.7, 136.1, 129.8, 129.1, 128.9, 128.5, 127.3, 127.1, 121.4, 121.2, 120.9; MS (EI) *m/z* 368 (M<sup>+</sup>); 370 (M<sup>+</sup>+2). Anal. % C<sub>17</sub>H<sub>9</sub>N<sub>4</sub>O<sub>2</sub>SCI: C, 55.36; H, 2.46; N, 15.19. Found: C, 55.41; H, 2.40; N, 15.11.

5'-[10-methyl-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl] -1',3',4'-oxidiazole-2'-thione (7b) Yield: 60 %, mp 244–45 °C; Rf, 0.52 ethyl acetate:methanol (9:1) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,333 (indole-NH); 3,282 (NH); 1,700 (C=O); 1,213 (C=S); <sup>1</sup>H NMR (DMSO- $d_6$ ,  $\delta$ , ppm), 11.74 (s, 1H, indole NH); 9.00 (s, 1H, NH); 7.03–8.00 (m, 7H, Ar–H); 2.18 (s, 3H, CH<sub>3</sub>); Anal. % C<sub>18</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub>S: C, 62.06; H, 3.47; N, 16.08. Found: C, 61.86; H, 3.40; N, 16.11.

5'-[10-methoxy-6H, 7H-indolo[2,3-c]isoquinolin-5-one-6-yl] -1',3',4'-oxidiazole-2'-thione (7c) Yield: 56 %, mp 295– 96 °C; Rf, 0.45 ethyl acetate:methanol (9:1) mixture; FTIR (KBr) cm<sup>-1</sup>: 3,315 (indole-NH); 3,245 (NH); 1,701 (C=O); 1,210 (C=S); <sup>1</sup>H NMR (DMSO- $d_6$ ,  $\delta$ , ppm), 11.59 (s, 1H, indole NH); 8.75 (s, 1H, NH); 7.00–8.12 (m, 7H, Ar–H); 3.68 (s, 3H, OCH<sub>3</sub>); Anal. % C<sub>18</sub>H<sub>12</sub>N<sub>4</sub>O<sub>3</sub>S: C, 59.33; H, 3.32; N, 15.38. Found: C, 60.06; H, 3.40; N, 15.31.

Acknowledgments The authors are thankful to the Chairman, Department of Chemistry, Gulbarga University, Gulbarga, for providing laboratory facilities and Chairman, Department of Microbiology, Gulbarga University, Gulbarga, for providing facilities to carry out antimicrobial activity. We are also thankful to Director, Indian Institute of Technology, Madras, Chennai, for providing spectral data.

#### References

- Aanandhi MV, Hashim Mansoori M, Shanmugapriya S, George S, Shanmugasundaram P (2010) Synthesis and *In-vitro* antioxidant activity of substituted Pyridinyl 1, 3, 4 oxadiazole derivatives. Res J Pharm Biol Chem Sci 1(4):1083–1090
- Aanandhi MV, Mishra PS, George S, Chaudhary R (2011) Synthesis, antimicrobial and sedative hypnotic activity of cinnamoyl ureas. Int J PharmTech Res 3(1):99–103
- Abdel-Rahman AHF (2004) Synthesis, reaction and microbial activity of some new indolyl- 1,3,4-oxadiazol, triazole and pyrazole derivatives. J Chin Chem Soc 51:147–156
- Aboraia SA, Rahman-abdel MH, Mahouz MN (2006) Novel 5-(2 hydroxyphenyl)-3-substituted-2,3-dihydro-1,3,4-oxadiazole-2thione derivatives: promising anticancer agents. Bioorg Med Chem 14:1236–1246
- Amir M, Kumar Shikha (2005) Synthesis and anti-inflammatory, analgesic, ulcerogenic and lipid peroxidation activities of 3, 5-dimethyl pyrazoles, 3-methyl pyrazol-5-ones and 3, 5-disubstituted pyrazolines. Indian J Chem 44B:2532–2537
- Amir Mohd, Javed SA, kumar Harish (2007) Synthesis of some 1,3, 4-oxadiazole derivatives as potential anti-inflammatory agents. 46B:1014-1019
- Amornraksa K, Worachartcheewan A, Prachayasittikul V (2009) Facile synthesis of *N*-aroylurea analogs as potential antioxidants. Eur J Sci Res 31(4):510–518
- Azimvand J (2012) Synthesis of some new derivatives of N-phenyl-2-chloro-9H-pyrido[2,3-b]indole-3-ylmethanimines using Vilsmeir-Hacck reagent. J Chem Pharm Res 4(8):3909–3913
- Bondock S, Fadaly W, Metawally MA (2010) Synthesis and antimicrobial activity of some new thiazole, thiophene and pyrazole derivatives containing benzothiazole moiety, Eur J Med Chem. 45(9): 3692–3701
- Burgute A, Pontiki E, Hadjipavlou-Litina D, Villar R, Vicente E, Solano B, Ancizu S, Perezsilanes S, Aldana I, Monge A (2007) Synthesis and anti-inflammatory/antioxidant activities of some new ring 3-phenyl-1-(1,4-di-N-oxide quinolin-2-yl)-2-propen-1-one derivatives and of their 4,5-dihydro-1(1H)-pyrazole analogues. Bioorg Med Chem Lett 17:6439–6443
- Chen HS, Li ZM, Han YF (2000) Synthesis and fungicidal activity against Rhizoctonia solani of 2-alkyl (alkylthio)-5-pyrazolyl-1,3, 4-oxadiazoles (thiadiazoles). J Agric Food Chem 48:5312–5315
- Cohen A (1967) 2-Methyl-7-alkoxy-1, 2, 3, 4,-tetrahydro-5H-pyrido [4,3-b]indoles. US Pat. 3,316,271. Chem Abstr 67:21900s
- Dhansay D, Pandey Alok, Sivakumar T, Rajavel R, Dubey RD (2010) Synthesis of some novel 2, 5- disubstituted1, 3, 4-oxadiazole and its analgesic, anti-Inflammatory, anti-bacterial and anti-tubercular activity. Int J ChemTech Res 2(3):1397–1412
- Garmaise DL, Parks GV (1973) 2-Aralkyl-8-fluoro-1, 2, 3, 4-tertrahydro-5-propionyl-pyrido[3,4-b]indoles. US Pat. 3,705,901. Chem Abstr 78:72103
- George S, Parameswaran M, Chakraborty AR, Thengungal KR (2008) Synthesis and evaluation of the biological activities of some 3-\_[5-(6-methyl-4-aryl-2-oxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1,3,4-oxadiazol-2-yl]-imino\_-1,3-dihydro-2*H*-indol-2-one derivatives. Acta Pharm 58:119–129
- Hatano T, Kanawa H, Yasuhara T, Okuda (1988) Two new flavonoids and other constituents in licorice root: their relative astringency and radical scavenging effects. Chem Pharm Bull 36:2090–2097
- Hiremath SP, Saundane AR, Swamy HKS, Mruthyunjayaswamy BHM (1993) Synthesis and biological evaluation of some substituted 5H, 6H, 7H-indolo[2,3-c]isoquinoline-5-thiones and their derivatives. Indian J Heterocycl Chem 3:37–42
- Hiremath SP, Saundane AR, Mruthyunjayaswamy BHM (1995) Synthesis of [10-substituted 6H, 7H-indolo[2,3-c]isoquinolin-

5-one-6-yl]acetyl-3, 5-disubstituted-pyrazoles/pyrazolones and 5-[10-substituted 6*H*, 7*H*-indolo[2,3-c]isoquinolin-5-one-6-yl] methyl-1,3,4-oxadiazole-2-thiones. J Indian Chem Soc 72(10): 735–738

- Hiremath SP, Saundane AR, Mruthyunjayaswamy BHM (1997) Synthesis and biological studies of some new bridgehead nitrogen heterocycles containing indoloisoquinoline nucleus. Orient J Chem 13(2):173–176
- Indian pharmacopoeia, Government of India (1985) 3rd Ed. New Delhi Appendix IV, 90
- Ishizumi K, Katsube J (1980) Indoloisoquinolines and process for producing them. Brit. Pat., 2, 025,932, Chem. Abstr, 93: 186322e
- Jaiswal N, Singh AK, Singh D, Ahmad T (2012) A comphrensive review on antimicrobial activity of 1, 3, 4-oxadiazole derivatives. Int Res J Pharm 3(3):83–89
- Kosuge T, Zenda H, Tamamoto H, Torigoe Y (1974) Japan Kokai, Jap. Pat (1973) Harmans from tar of defatted soybean. 7391,210, Chem Abstr 80: 112616p
- Latthe PR, Shinge PS, Badami BV, Patil PB, Holihosur SN (2006) Curtius rearrangement reactions of 3-(4-azidocarbonyl)phenylsydnone. Synthesis of 4-(sydnon-3-yl) phenyl carbamates, N-aryl-N¢-[4-(sydnon-3-yl)] phenyl ureas and their antimicrobial and insecticidal activities. J Chem Sci 118(3): 249–256
- Sumitomo Chemical Co.Ltd, Jpn Kokai Tokkyo Hoho, Jap.Pant. (1983) Indoloisoquinolines 5869,882 (8369, 882). Chem Abstr, (1983) 99: 88182p
- Padmavathi V, Reddy GS, Padmaja A, Kondaiah P, Shazia A (2009) Synthesis, antimicrobial and cytotoxic activities of 1,3,4-oxadiazole, 1,3,4-thiadiazoles and 1,2,4-triazoles. Eur J Med Chem 44:2106–2112
- Padmavathi V, Nagi Reddy S, Dinneswara Reddy G, Padmaja A (2010) Synthesis and bioassay of aminosulfonyl-1, 3, 4-oxadiazole and their interconversion to 1, 3, 4-oxadiazole. Eur J Med Chem 45(9):4246–4251
- Patel RB, Chikhalia KH, Pannecouque C, Clercq ED (2007) Synthesis of novel PETT analogues 3,4-dimethoxy phenyl ethyl 1,3, 5-triazinyl thiourea derivatives and their antibacterial and anti-HIV study. J Braz Chem Soc 18(2):312–321
- Rajyalakshmi G, Rama NRA, Narsimha RY, Sarangapani M (2011) Synthesis, characterization and anticancer activity of certain 3-{4-(5- mercapto-1,3,4-oxadiazole-2-yl)phenylimino}indolin-2-one derivatives. Saudi Pharm J. doi:10.1016/j.jsps.2011. 03.002Reference:SPJ70
- Saundane AR, Ranganath SH, Prayagrai G, Rudresh K, Satyanayana ND (1998a) Synthesis and Pharmacological studies of some new [11H-indolo[3,2-c]isoquinoline-5ylthio]acetylthiosemicarbazide and derivatives. Orient J Chem 14(2):251–254
- Saundane AR, Rudresh K, Satyanarayan ND, Hiremath SP (1998b) Phamacological Screening of 6H, 11H-indolo[3,2-c]isoquinoline-5-ones and their derivatives. Indian J Pharm Sci 60(6):379–383
- Saundane AR, Vaijinath AV, Vijaykumar K (2012) Synthesis, antimicrobial and antioxidant activities of some new 1'-(10-substituted 5H, 6H, 7H-indolo[2,3-c]isoquinolin-5-ylthio)formyl-3',5'-disubstituted pyrazoles, -3'-methylpyrazol-5'-ones and -1',3',4'-oxidiazol-2'-thiones. Heterocyclic Lett 2(3):333–348
- Saxena VC, Bapat SK, Dhawan BN (1969) An experimental evaluation of the anticonvulsant activity of some antihistaminic drugs, Jpn J Pharmacol, 19: 477–484
- Sridhar R, Perumal PJ, Etti S, Shanmugam G, Ponnuswamy MN, Prabavathy VR, Mathivanan N (2004) Design, synthesis and antimicrobial activity of 1H-pyrazole carboxylate. Bioorg Med Chem Lett 14:6035–6040
- Thakur AS, Jha AK, Verma P, Deshmukh R, Devangan D, Chandy A (2010) Synthesis and evaluation of some new quinoline and

pyrido[2,3-b]indole derivatives. Internat J Compressive Pharm 3(13):1–4

- Vicentini CB, Romangnoli C, Reotti E, Mares D (2007) Synthetic pyrazole derivatives as growth inhibitors of some phytopathogenic fungi. J Agric Food Chem 55(25):10331–10338
- Winter G, Dimola N, Berti M, Ariali V (1979) Synthesis and biological activities of some indolo[2,3-c]isoquinoline derivatives. Farmaco Ed Sci 34(6):507–517