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SYNTHESIS AND BIOLOGICAL ACTIVITIES OF SOME INDOLE ANALOGUES CONTAINING PYRIDINE, PYRIDOPYRIMIDINE AND PYRANONAPHTHYRIDINE SYSTEMS[#]

Saundane Anand R*, Katkar Vijaykumar, Yarlakatti Manjunatha, Prabhaker Walmik and Vaijinath A. Varma.

Department of Postgraduate Studies and Research in Chemistry,
Gulbarga University, Gulbarga-585 106, Karnataka, India.
E-mail:arsaundane@rediffmail.com

Abstract

The reaction of 5-substituted 2-phenylindol-3-carboxaldehydes **1** with aromatic ketones followed by cyclocondesation of resulting chalcones **2** with malononitrile and ammonium acetate afforded the key intermediates 2-amino-3-cyano-4-(5'-substituted 2'-phenylindol-3'-yl)-6-aryl pyridines **3**. Compounds **3** underwent cyclocondesation reactions with commercially available reactants to afford new heterocycles containing the pyrano[2,3-b]naphthyridines **4**, pyrido[2,3-d]pyrimidin-2-(1H)-ones **5** and pyrido[2,3-d]pyrimidin-2-(1H)-thiones **6** linked to the position-3 of indole nucleus. The structures of all these previously unknown compounds were confirmed by their spectral studies and elemental analysis. These compounds were tested for their antibacterial, antifungal and antioxidant activities.

Keywords: Indole analogues, Pyridine, Pyridopyrimidine, Pyranonapthyridine, Antimicrobial activity, Antioxidant activity.

Introduction

Nitrogen containing heterocyclic compounds is one of the most fruitful and extensively developing fields of heterocyclic chemistry. These compounds exhibit various kinds of biological activities. The biological activities of several analogues of indole such as, anticancer[1], antidiabetic[2], anti-inflammatory[3], anti-HIV[4], antimalerial[5], antimicrobial[6] and antioxidant[7,8] were well documented. Many of the pyridine, pyrimidine and napthyridine analogues have been evaluated pharmacologically and found to exhibit anticancer[9], antimalerial[10] and antituberculosis[11], antituberculostatic[12] and antibacterial[12] activities. Compounds containing fused pyrimidine ring have attracted much attention due to their wide range of biological activities particularly in cancer and virus research[13]. Also pyrimidine substituted with an amino group at position-2 or -4 are known pharmacophores in several structure based drug design

* Author for correspondence.

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approaches in medicinal chemistry[14,15]. In view of these findings and in continuation of our ongoing search for new heterocycles[16-18] of biological importance, we have prepared several analogues of indole in which pyridine, pyridopyrimidine and pyranonapthyridine moieties are linked to position-3 of the indole nucleus and screened them for antimicrobial and antioxidant activities.

Results and Discussion

The starting material 5-substituted 2-phenylindol-3-carboxyaldehydes **1** were prepared according to the reported procedure[19]. Reaction of compounds **1** with 4-substituted acetophenones in ethylene glycol containing catalytic amount of piperidine at reflux temperature afforded 2-phenyl-3-(2'-benzoylethylen-1'-yl)indoles **2**. Cyclocondensation of compounds **2** with a mixture of malononitrile and ammonium acetate at 120-130^{0}C afforded 2-amino-3-cyano-6-aryl-4-(5'-substituted 2'-phenylindol-3'-yl)pyridines **3** (Scheme-1). The IR spectrum of **3a** exhibited three characteristics absorption bands at 3350, 3050 and 2193 cm^{-1} due to NH/ NH_2 and CN functions, respectively. The ^{1}H NMR spectrums revealed characteristics signals (D_2O exchangeable) at δ 5.85 assigned to NH_2 protons (Spectral data of other compounds are given in Table-2).

Compounds **3** when subjected to heterocyclization with ethyl cyanoacetate in presence of a catalyst triethylamine in refluxing ethanol yielded 3-cyano-4,5-diamino-6-(5'-substituted 2'-phenylindol-3'-yl)-8-aryl-2-oxo-2(1H)-pyrano[2,3-b][1,8]napthyridines[20] **4** (Scheme-2). The structures of **4** were confirmed by their spectral data and elemental analysis. Compound **4a** in its IR spectrum exhibited characteristics absorption bands at 3410, 3300, 3059, 2230, 1736, 1667 and 1261 cm^{-1} due to NH/ NH_2, NH_2, CN, C=O, C=N and C-O-C functions, respectively. In its ^{1}H NMR spectrum, signals resonated at δ 3.80 accounting for the two protons of amino group of pyrone ring, whereas protons of amino group of napthyridine system were resonated along with aromatic protons. The mass spectrum of **4a** exhibited isotopic molecular ion peak at m/e 554, 556 with a base ion peak at m/e 240 (Spectral data of other compounds are given in Table-2).

On the other hand, compound **3** when refluxed with urea or thiourea in ethanol afforded 4-amino-5-(5'-substituted 2'-phenylindol-3'-yl)-7-aryl-pyrido [2,3-d]pyrimidin-2(1H)-ones/thiones **5** and **6**, respectively. The IR spectrum of **5a** showed three characteristics absorption peaks at 3325, 1598 and 1530 cm^{-1} due to pyrimidine NH, C=O, and C=N functions, respectively, whereas, absorption due to CN functions at 2193 cm^{-1} was missing. In its ^{1}H NMR, the characteristics singlet at δ 3.40 integrating for two protons was assigned to the amino group of pyrimidine ring, whereas the downfield broad singlet at δ 8.20 accounting for one proton was attributed to pyrimidine NH. The mass spectrum exhibited the isotopic molecular ion peak at m/e 462 and 464, which is also a base ion peak. The above spectral data are in conformity with the structure assigned to **5a** (Spectral data of other compounds are given in Table-2).

Similarly, in the IR spectrum of **6a** characteristics absorption peaks due to NH_2, NH, C=N and C=S were observed at 3352, 3325, 1599 and 1027 cm^{-1}, respectively. The absorption

at 2193 cm^{-1} due to CN function was missing. Its ^1H NMR spectrum exhibited the characteristics signals at δ 3.50 and 8.10 due to two protons of amino group of pyrimidine ring and NH of pyrimidine ring, respectively. The mass spectrum of **6a** exhibited the isotopic molecular ion peak at m/e 479 and 481.This spectral data is in good agreement with the structure of **6a** (Spectral data of other compounds are given in Table-2).

Antioxidant activity: 1, 1-diphenyl-2-picryl hydrazyl (DPPH) radical scavenging activity (RSA).

The scavenging of the stable DPPH radical model is widely used method to evaluated antioxidant activities in relatively short time compared with other methods. DPPH is a stable free radical that can accept an electron or hydrogen radical and must thus be converted to a stable diamagnetic molecule[21]. DPPH has an odd electron and so 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. All compounds were tested for their interaction with the stable free radical DPPH. This interaction indicates radical scavenging activity in an iron free system following Hatano's method[22] using 2-tert-butyl-4-methoxy phenol (butylated hydroxy anisole, BHA) and 2-(1, 1-dimethylethyl)-1,4-benzenediol(tertiary butylated hydroxy quinone, TBHQ) as standards. The radical scavenging activity (RSA) of test compounds in methanolic solution at concentration 25, 50, 75 and 100 µg/ml containing freshly prepared DPPH solution (0.004% w/v) was carried out and compared with those of standards BHA and TBHQ. All the test analyses were performed on three replicates and result were averaged. The results in percentage are expressed as the ratio of absorption decrease in the presence of test compounds and

$$\% \text{ DPPH radical scavenging} = \frac{(\text{Absorbance of control- Absorbance of test sample})}{(\text{Absorbance of controls})} \text{X100}$$

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 fig-1-4. Percent scavenging activity of the DPPH free radical was measured using the following equation.

The analysis of results indicated that compounds **3a** and **5b** exhibited the good radical scavenging activity (63% and 64.3%) at 50 µg/ml, respectively. Compounds **4i** and **6c** showed radical scavenging ability (60.47% and 59.88%) at 100 µg/ml, respectively. Whereas **4d** and **5a** caused instantaneous decrease in the absorption of DPPH indicating the strong radical scavenging activity of these compounds. The scavenging activity of compounds **3-6** was perhaps due to the presence of NH_2 or NH group in the compounds, which can donate hydrogen atom to DPPH radical. After donating a hydrogen atom, compounds **3-6** exist in a radical form and radical could be delocalised by conjugated systems. All other compounds exhibited either moderate or poor radical scavenging activities than the standards.

Antimicrobial activity

All the newly synthesised compounds **3-6** were evaluated for their antibacterial and antifungal activity by cup-plate method at a concentration of 1mg/ml following reported procedure[23]. The zone of inhibition was compared with the standard gentamycin and flucanazole for antibacterial and antifungal activity, respectively. The investigation of antibacterial screening

revealed that, compound **3b** exhibited the maximum zone of inhibition against *S.aureus.* Compounds **3d, 3e, 3h, 4d, 4e, 4i, 5d, 5h, 6a, 6d, 6f** and **6g** showed maximum zone of inhibition against *E.coli.* Compounds **3e** and **6a** exhibited maximum zone of inhibition against *K.pneumonia.* The only compound **4d** showed maximum zone of inhibition against *P.aeruginosa.*

In case of antifungal screening, the compounds **3c, 3d, 3h, 4c, 4d, 4i, 5a, 5d, 6a, 6c** and **6d** exhibited promising activity against *A.niger,* whereas compounds **6a** and **6d** exhibited maximum zone of inhibition against *A.oryzae.* Compounds **6d** and **6g** showed maximum zone of inhibition against *A.terrus.* The only compound **5a** exhibited maximum zone of inhibition against *A.flaves.*

Experimental Section

All the reagents were obtained commercially and used by further purification. Physical constant were determined by an open capillary method and are uncorrected. Analytical TLC was performed on Merk percolated $^{60}F_{254}$ silica gel plates. Visualization was done by exposing to iodine vapour. The IR (KBr pellet) spectra were recorded with a FT IR (Perkin-Elmer Spectrum ONE) spectrometer and absorption positions ν_{max} were expressed in cm^{-1}. The ^{1}H NMR (DMSO, d_6) spectra recorded with an AMX-400 AV III solid NMR. The chemical shifts are expressed in ppm (δ-scale) downfield from TMS as an internal standard. Mass spectral measurements were carried out by EI Method on a JEOL JMC-300 spectrometer at 70 eV. Elemental analyses were carried out using flash EA112 series elemental analyzer.

General procedure for the synthesis of 2-phenyl indol-3-carboxyaldehydes (1a-c):

These compounds were prepared by following literature procedure[19].

General procedure for the synthesis of 2-phenyl indol-3-(2'-benzoyl ethylene-1'-yl)indoles (2a-i):

These compounds were prepared by following literature procedure[24].

General procedure for the synthesis of 2-amino-3-cyano-4-(5'-substituted 2'-phenyl indol -3'-yl) -6-(4-substituted phenyl)pyridines (3a-i):

Method-1: To a solution of **2** (0.05 mol) in acetic acid, malononitrile (0.05 mol) and ammonium acetate (0.05 mol) were added, and reaction mixture was refluxed for 5 hrs. The reaction mixture was then cooled and decomposed in ice- cold water. The solid thus separated was filtered off, dried and recrystallized from ethanol to furnish **3**.

Method-2: A mixture of compound **2** (0.05 mol), malononitrile (0.05 mol) and ammonium acetate (0.05 mol) was heated at 120-130^0 C in oil bath. After standing overnight, the solid mass was dissolved in methanol and poured in water. The crude product separated was filtered off, dried and recrystallized from ethanol to furnish **3**. Physical data were tabulated in Table-1.

General Procedure for the synthesis of 3-cyano-4,5-diamino-6-(5'-substituted 2'-phenyl indol-3'-yl)-8-(4-substituted phenyl)-2-oxo-2H-pyrano[2,3-b][1,8]napthyridines (4a-i):

To a mixture of **3** (0.01 mol) and ethyl cyanoacetate (0.01 mol) in absolute ethanol (30 ml), triethylamine (0.5 ml) was added. The reaction mixture was refluxed for 2 hrs, excess of ethanol was removed under vacuum to about one third of its original volume and left overnight at room temperature. To the clear solution thus obtained few drops of conc. HCl were added, whereby the precipitate formed was filtered off and washed thoroughly with diethyl ether. The crude product crystallized from ethanol to afford **4**. Physical data were tabulated in Table-1.

General procedure for the synthesis of 4-amino-5-(5'-substituted 2'-phenylindol-3'-yl)-7-(4-substituted phenyl) pyrido[2, 3-d]pyrimidin-2(1H)-ones/thiones (5a-i) and (6a-i):

A solution of **3** (0.01 mol) and urea or thiourea (0.01 mol) in ethanol was heated under refluxed for 5 hrs. At the end of this period, the solution was cooled to room temperature and poured into ice cold water. The separated solid was filtered off and recrystallized from ethanol. Physical data were tabulated in Table-1.

Conclusion

The present study revealed that the chloro substituted compounds were founds to be good antimicrobial agents whereas antioxidant activity results suggested that, compounds **5a**, **5b** and **6c** were the most active among the series exhibiting good radical scavenging activity compared to other compounds. This activity may be due to the better radical stabilizing ability of pyridopyrimidine system **5** and **6** compared to pyranonapthyridine system **4** in which the electron withdrawing cyano group attached to position-3 may be responsible for the destabilization of free radical formed after donating an electron and/or hydrogen atom to the stable DPPH free radical. Thus compounds **5** and **6** acts as good hydrogen and/or electron donors as compared to compound **4**.

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Table 1: Physical data of synthesized compounds (3-6).

Comp. No.	Substitution		Molecular formula	Yield (%)	M.P. (^{0}C)	Elemental Analysis. Calculated(found)		
	R	R'				C	H	N
3a	Cl	H	$C_{26}H_{17}N_4Cl$	53	255-56	74.29(74.36)	4.05(4.18)	13.33(13.26)
3b	CH_3	H	$C_{27}H_{20}N_4$	66	178-80	81.00(81.24)	5.00(5.26)	14.00(13.85)
3c	H	Cl	$C_{26}H_{17}N_4Cl$	49	164-65	74.29(74.32)	4.05(4.19)	13.33(13.46)
3d	Cl	Cl	$C_{26}H_{16}N_4Cl_2$	71	171-72	68.72(68.58)	3.52(3.42)	12.33(12.15)
3e	CH_3	Cl	$C_{27}H_{19}N_4Cl$	65	155-56	74.66(74.79)	4.38(4.44)	12.90(12.75)
3f	H	CH_3	$C_{27}H_{20}N_4$	79	192-93	81.00(80.85)	5.00(4.98)	14.00(14.11)
3g	Cl	CH_3	$C_{27}H_{19}N_4Cl$	75	180-81	74.66(74.43)	4.38(4.42)	12.90(12.78)
3h	CH_3	CH_3	$C_{28}H_{22}N_4$	70	178-80	81.16(81.29)	5.31(5.46)	13.52(13.38)
3i	H	H	$C_{26}H_{18}N_4$	70	174-75	80.83(80.65)	4.67(4.73)	14.50(14.35)
4a	Cl	H	$C_{32}H_{19}N_6O_2Cl$	54	185-86	69.31(69.52)	3.43(3.63)	15.16(15.28)
4b	CH_3	H	$C_{33}H_{22}N_6O_2$	45	151-52	74.15(74.31)	4.11(4.29)	15.73(15.83)
4c	H	Cl	$C_{32}H_{19}N_6O_2Cl$	42	192-93	69.31(68.52)	3.43(3.58)	15.16(15.32)
4d	Cl	Cl	$C_{32}H_{18}N_6O_2Cl_2$	38	155-56	65.30(65.52)	3.06(3.21)	14.28(14.46)
4e	CH_3	Cl	$C_{33}H_{21}N_6O_2Cl$	57	175-76	69.71(69.58)	3.69(3.73)	14.79(14.59)
4f	H	CH_3	$C_{33}H_{22}N_6O_2$	70	152-53	74.15(74.29)	4.11(4.32)	15.73(15.82)
4g	Cl	CH_3	$C_{33}H_{21}N_6O_2Cl$	63	144-45	69.71(69.83)	3.69(3.75)	14.79(14.93)
4h	CH_3	CH_3	$C_{34}H_{24}N_6O_2$	61	155-56	74.45(74.68)	4.38(4.56)	15.32(15.23)
4i	H	H	$C_{32}H_{20}N_6O_2$	61	147-48	73.84(73.63)	3.85(3.62)	16.15(16.28)
5a	Cl	H	$C_{27}H_{18}N_5OCl$	67	190-91	69.98(70.15)	3.89(4.08)	15.11(15.28)
5b	CH_3	H	$C_{28}H_{21}N_5O$	45	142-43	75.84(75.81)	4.74(4.58)	15.80(15.68)
5c	H	Cl	$C_{27}H_{18}N_5OCl$	76	191-92	69.97(70.17)	3.89(4.19)	15.11(15.25)
5d	Cl	Cl	$C_{27}H_{17}N_5OCl_2$	45	195-96	65.19(65.29)	3.42(3.23)	14.08(14.21)
5e	CH_3	Cl	$C_{28}H_{20}N_5OCl$	42	164-65	70.44(70.65)	4.19(4.32)	14.68(14.48)
5f	H	CH_3	$C_{28}H_{21}N_5O$	54	163-64	75.84(75.69)	4.74(4.95)	15.80(15.66)
5g	Cl	CH_3	$C_{28}H_{20}N_5OCl$	85	172-73	70.44(70.56)	4.19(4.32)	14.67(14.85)
5h	CH_3	CH_3	$C_{29}H_{23}N_5O$	54	162-63	76.14(76.29)	5.03(5.35)	15.32(15.59)
5i	H	H	$C_{27}H_{19}N_5O$	76	141-42	75.52(75.32)	4.42(4.66)	16.31(16.27)
6a	Cl	H	$C_{27}H_{18}N_5SCl$	55	169-70	67.64(67.86)	3.75(3.85)	14.61(14.56)
6b	CH_3	H	$C_{28}H_{21}N_5S$	56	154-55	73.20(73.45)	4.57(4.76)	15.25(15.36)
6c	H	Cl	$C_{27}H_{18}N_5SCl$	79	175-76	67.64(67.88)	3.75(3.92)	14.61(14.85)
6d	Cl	Cl	$C_{27}H_{17}N_5SCl_2$	64	213-14	63.15(63.02)	3.31(3.49)	13.64(13.48)
6e	CH_3	Cl	$C_{28}H_{20}N_5SCl$	45	141-42	68.15(68.36)	4.06(4.25)	14.19(14.23)
6f	H	CH_3	$C_{28}H_{21}N_5S$	78	142-43	73.20(73.43)	4.57(4.78)	15.25(15.36)
6g	Cl	CH_3	$C_{28}H_{20}N_5SCl$	49	162-63	68.15(68.36)	4.05(4.27)	14.19(14.38)
6h	CH_3	CH_3	$C_{29}H_{23}N_5S$	85	190-91	73.57(73.77)	4.86(4.67)	14.79(14.58)
6i	H	H	$C_{27}H_{19}N_5S$	53	145-46	72.80(73.88)	4.27(4.48)	15.73(15.59)

Table 2: Spectral data of synthesized compounds (3-6).

Comp.	IR(KBr) cm^{-1}	^{1}HNMR ($CDCl_3$+DMSO) δ ppm	MS m/z[M^+]
3a	3350, 3050 (NH/NH_2), 2193 (CN), 1604 (C=N).	10.78 (s, 1H, indole NH), 7.00-7.56 (m, 14H, Ar-H), 5.85 (s, 2H, NH_2).	422[M^+ +2]
3b	3331, 3100 (NH/NH_2), 2214 (CN), 1605 (C=N).	10.92 (s, 1H, indole NH), 6.70-7.45 (m, 14H, Ar-H), 5.32 (s, 2H, NH_2), 2.11(s, 3H, CH_3).	
3c	3291, 3129 (NH/NH_2), 2214 (CN), 1565 (C=N).	11.00 (s, 1H, indole NH), 6.71-7.65 (m, 14H, Ar-H), 5.49 (s, 2H, NH_2),	
3d	3291, 3115 (NH/NH_2), 2194 (CN), 1582 (C=N)	11.10 (s, 1H, indole NH), 6.70-7.62 (m, 13H, Ar-H), 5.21 (s, 2H, NH_2).	
3e	3325, 3100 (NH/NH_2), 2200 (CN), 1595 (C=N).	10.72 (s, 1H, indole NH), 6.61-7.85 (m, 13H, Ar-H), 5.34 (s, 2H, NH_2), 2.15 (s, 3H, CH_3).	
3f	3291, 3100 (NH/NH_2), 2175 (CN), 1529(C=N).	10.72 (s, 1H, indole NH), 6.72-7.61 (m, 14H, Ar-H), 5.13 (s, 2H, NH_2), 2.21 (s, 3H, CH_3).	
3g	3295, 3110 (NH/NH_2), 2210 (CN), 1602 (C=N).	11.00 (s, 1H, indole NH), 6.62-7.32 (m, 13H, Ar-H), 5.25 (s, 2H, NH_2), 2.21 (s, 3H, CH_3).	
3h	3312, 3110 (NH/NH_2), 2179 (CN), 1569 (C=N).	11.21 (s, 1H, indole NH), 6.72-7.56 (m, 13H, Ar-H), 5.32 (s, 2H, NH_2), 2.08 (s, 6H, 2-CH_3).	
3i	3309, 3110 (NH/NH_2), 2194 (CN), 1614 (C=N).	10.89 (s, 1H, indole NH), 6.85-7.67 (m, 15H, Ar-H), 5.15 (s, 2H, NH_2).	
4a	3410 (indole NH), 3300 (napthyridine NH_2), 3059 (pyrano NH_2), 2230 (CN), 1736 (C=O of lactone ring), 1667 (C=N), 1261 (C-O-C).	11.12 (s, 1H, indole NH), 6.65-7.20 (m, 14H, Ar-H and naphthyridine NH_2), 3.80 (s, 2H, pyrano NH_2)	556[M^+ +2]
4b	3329 (indole NH), 3010 (napthyridine NH_2), 2912 (pyrano NH_2), 2135 (CN), 1711(C=O of lactone ring), 1608 (C=N), 1251 (C-O-C).	11.02 (s, 1H, indole NH), 6.75-7.52 (m, 14H, Ar-H and naphthyridine NH_2), 4.35 (s, 2H, pyrano NH_2), 2.21 (s, 3H, CH_3).	
4c	3321 (indole NH), 3000 (napthyridine NH_2), 2952 (pyrano NH_2), 2232 (CN), 1724 (C=O of lactone ring), 1601 (C=N), 1230 (C-O-C).	11.80 (s, 1H, indole NH), 6.62-7.25 (m, 14H, Ar-H and naphthyridine NH_2), 4.22 (s, 2H, pyrano NH_2).	
4d	3401 (indole NH), 3333 (napthyridine NH_2), 3015 (pyrano NH_2), 2232 (CN), 1743 (C=O of lactone ring), 1598 (C=N), 1214 (C-O-C).	10.91 (s, 1H, indole NH), 6.65-7.4 (m, 13H, Ar-H and naphthyridine NH_2), 3.90 (s, 2H, pyrano NH_2).	

4e	3375 (indole NH), 3048 (napthyridine NH_2), 2921 (pyrano NH_2), 2232 (CN), 1743 (C=O of lactone ring), 1599 (C=N), 1242 (C-O-C).	11.00 (s, 1H, indole NH), 6.62-7.40 (m, 13H, Ar-H and naphthyridine NH_2), 3.95 (s, 2H, pyrano NH_2), 2.22 (s, 3H, CH_3).	
4f	3345 (indole NH), 3125 (napthyridine NH_2), 3000 (pyrano NH_2), 2241 (CN), 1743 (C=O of lactone ring), 1597 (C=N), 1258 (C-O-C).	10.95 (s, 1H, indole NH), 6.72-7.45 (m, 14H, Ar-H and naphthyridine NH_2), 4.41 (s, 2H, pyrano NH_2), 2.21 (s, 3H, CH_3).	
4g	3432 (indole NH), 3312 (napthyridine NH_2), 3125 (pyrano NH_2), 2222 (CN), 1740 (C=O of lactone ring), 1604 (C=N), 1215 (C-O-C).	11.01 (s, 1H, indole NH), 6.72-7.45 (m, 13H, Ar-H and naphthyridine NH_2), 4.32 (s, 2H, pyrano NH_2), 2.31 (s, 3H, CH_3).	
4h	3401(indole NH), 3349 (napthyridine NH_2), 3050 (pyrano NH_2), 2200 (CN), 1748 (C=O of lactone ring), 1608 (C=N), 1232 (C-O-C).	10.85 (s, 1H, indole NH), 6.45-7.21 (m, 13H, Ar-H and naphthyridine NH_2), 4.42 (s, 2H, pyrano NH_2), 2.21 (s, 6H, 2-CH_3).	
4i	3390 (indole NH), 3295 (napthyridine NH_2), 3059 (pyrano NH_2), 2214 (CN), 1730 (C=O of lactone ring), 1602 (C=N), 1235 (C-O-C).	11.12 (s, 1H, indole NH), 6.65-7.20 (m, 15H, Ar-H and naphthyridine NH_2), 3.85 (s, 2H, pyrano NH_2).	
5a	3408 (indole NH), 3365 (NH_2), 3325 (pyrimidine NH),1598 (C=O), 1530 (C=N).	10.85 (s, 1H, indole NH), 8.20 (s, 1H, pyrimidine NH), 6.40-7.4 (m, 14H, Ar-H), 3.40 (s, 2H, NH_2).	465[M^+ +2]
5b	3418 (indole NH), 3310 (NH_2), 3208(pyrimidine NH), 1662 (C=O), 1558 (C=N).	10.95 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.91-7.65 (m, 14H, Ar-H), 3.96 (s, 2H, NH_2), 2.21 (s, 3H, CH_3).	
5c	3345 (indole NH), 3300 (NH_2), 3212 (pyrimidine NH),1660 (C=O), 1576 (C=N).	11.11 (s, 1H, indole NH), 8.25 (s, 1H, pyrimidine NH), 6.41-7.41(m, 14H, Ar-H), 4.32 (s, 2H, NH_2),	
5d	3450 (indole NH), 3292 (NH_2), 3215 (pyrimidine NH),1662 (C=O), 1600 (C=N).	10.82 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.41-7.41 (m, 13H, Ar-H), 4.42 (s, 2H, NH_2).	
5e	3445 (indole NH), 3275 (NH_2), 3210 (pyrimidine NH),1660 (C=O), 1521 (C=N).	11.00 (s, 1H, indole NH), 8.18 (s, 1H, pyrimidine NH), 6.45-7.24 (m, 13H, Ar-H), 4.21 (s, 2H, NH_2), 2.11 (s, 3H, CH_3).	
5f	3430 (indole NH), 3215 (NH_2), 3158 (pyrimidine NH),1662 (C=O), 1553 (C=N).	10.75 (s, 1H, indole NH), 8.31 (s, 1H, pyrimidine NH), 6.31-7.25 (m, 14H, Ar-H), 3.91 (s, 2H, NH_2), 2.11 (s, 3H, CH_3).	

5g	3425 (indole NH), 3242 (NH_2), 3198 (pyrimidine NH),1662 (C=O), 1559 (C=N).	10.72 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.45-7.31(m, 13H, Ar-H), 4.28 (s, 2H, NH_2), 2.11 (s, 3H, CH_3).	
5h	3445 (indole NH), 3242 (NH_2), 3200 (pyrimidine NH),1660 (C=O), 1552 (C=N).	10.88 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.81-7.55 (m, 15H, Ar-H), 4.11 (s, 2H, NH_2), 2.21 (s, 6H, 2-CH_3).	
5i	3444 (indole NH), 3295 (NH_2), 3200 (pyrimidine NH),1662 (C=O), 1558 (C=N).	10.90 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.91-7.45 (m, 15H, Ar-H), 3.89 (s, 2H, NH_2).	
6a	3401(indole NH), 3352 (NH_2), 3325 (pyrimidine NH),1599 (C=N), 1027 (C=S).	10.81 (s, 1H, indole NH), 8.10 (s, 1H, pyrimidine NH), 7.00-7.65 (m, 14H, Ar-H), 3.50 (s, 2H, NH_2).	481[M^+ +2]
6b	3414 (indole NH), 3295 (NH_2), 3214 (pyrimidine NH),1576 (C=N), 1025 (C=S).	10.92 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.91 -7.45 (m, 14H, Ar-H), 3.95 (s, 2H, NH_2), 2.12 (s, 3H, CH_3).	
6c	3435 (indole NH), 3312 (NH_2), 3210 (pyrimidine NH),1576 (C=N), 1015 (C=S).	10.95 (s, 1H, indole NH), 8.15 (s, 1H, pyrimidine NH), 6.92-7.45 (m, 14H, Ar-H), 4.22 (s, 2H, NH_2).	
6d	3401 (indole NH), 3315 (NH_2), 3210 (pyrimidine NH),1553 (C=N), 1010 (C=S).	11.00 (s, 1H, indole NH), 8.22 (s, 1H, pyrimidine NH), 6.55-7.46 (m, 13H, Ar-H), 4.21 (s, 2H, NH_2).	
6e	3425 (indole NH), 3300 (NH_2), 3210 (pyrimidine NH),1562 (C=N), 1015 (C=S).	10.88 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.60-7.31 (m, 13H, Ar-H), 4.58 (s, 2H, NH_2), 2.11 (s, 3H, CH_3).	
6f	3415 (indole NH), 3300 (NH_2), 3215 (pyrimidine NH),1558 (C=N), 1031 (C=S).	11.20 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.82-7.46 (m, 14H, Ar-H), 3.88 (s, 2H, NH_2), 2.12 (s, 3H, CH_3).	
6g	3415 (indole NH), 3300 (NH_2), 3210 (pyrimidine NH),1554 (C=N), 1015 (C=S).	11.11 (s, 1H, indole NH), 8.14 (s, 1H, pyrimidine NH), 6.60-7.65 (m, 13H, Ar-H), 4.31 (s, 2H, NH_2), 2.25 (s, 3H, CH_3).	
6h	3400 (indole NH), 3325 (NH_2), 3175 (pyrimidine NH),1576 (C=N), 1020 (C=S).	10.82 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.35 -7.21 (m, 13H, Ar-H), 4.98 (s, 2H, NH_2), 2.12 (s, 6H, 2-CH_3).	
6i	3400 (indole NH), 3300 (NH_2), 3210 (pyrimidine NH),1551 (C=N), 1010 (C=S).	11.00 (s, 1H, indole NH), 8.21 (s, 1H, pyrimidine NH), 6.81 -7.55 (m, 15H, Ar-H), 4.11 (s, 2H, NH_2).	

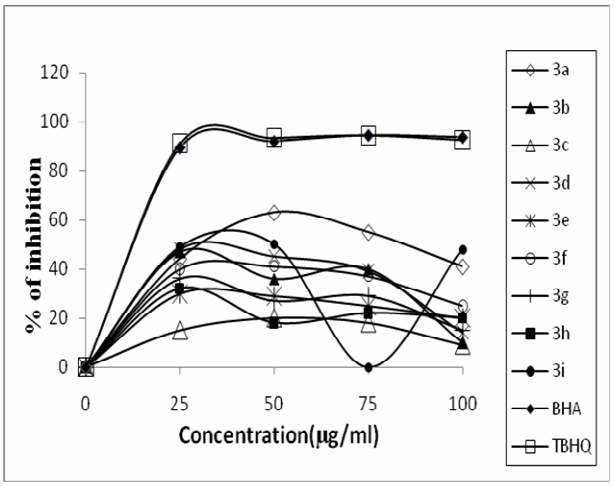


Fig-1: Antioxidant activity of compounds (3a-i)

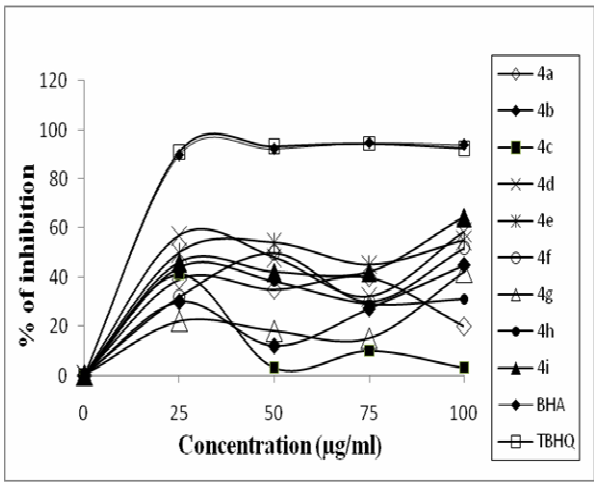


Fig-2: Antioxidant activity of compounds (4a-i)

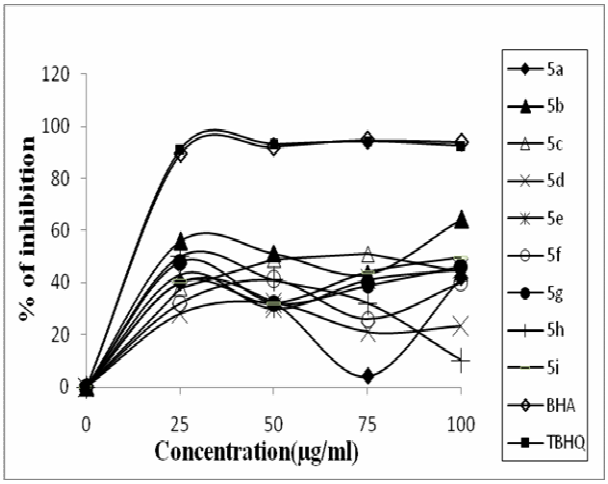


Fig-3: Antioxidant activity of compounds (5a-i)

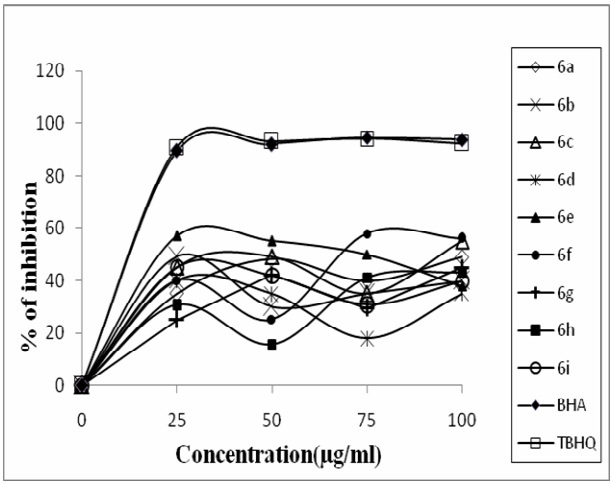
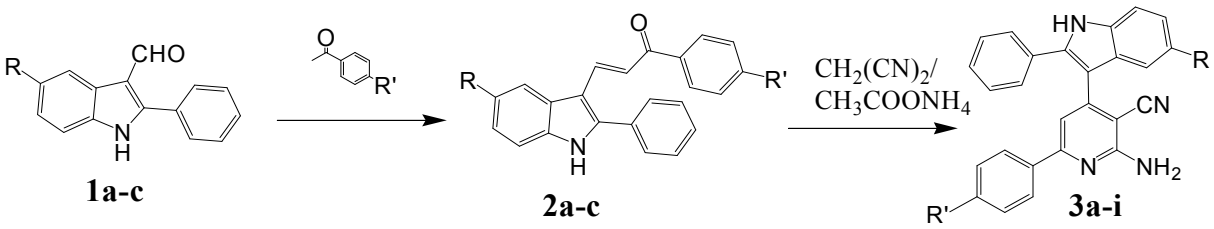


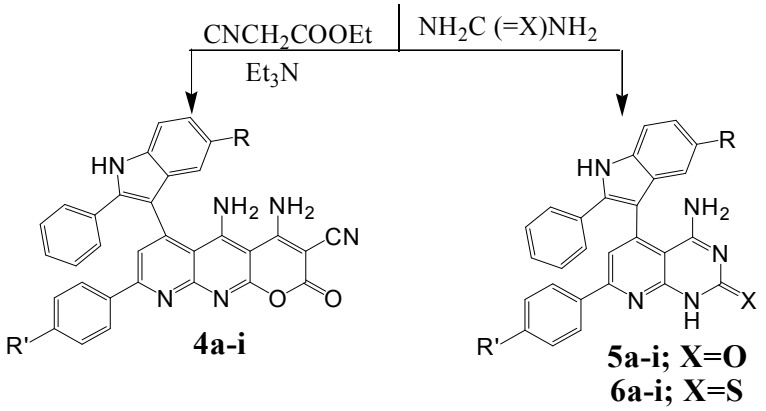
Fig-4: Antioxidant activity of compounds (6a-i)



	a,	b,	c,	d,	e,	f,	g,	h,	i
R=	Cl,	CH_3,	H,	Cl,	CH_3,	H,	Cl,	CH_3,	H
R'=	H,	H,	Cl,	Cl,	Cl,	CH_3,	CH_3,	CH_3,	H

Scheme-1

3a-i



	a,	b,	c,	d,	e,	f,	g,	h,	i
R=	Cl,	CH_3,	H,	Cl,	CH_3,	H,	Cl,	CH_3,	H
R'=	H,	H,	Cl,	Cl,	Cl,	CH_3,	CH_3,	CH_3,	H

Scheme-2