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Synthesis and antiparkinsonian activity of different pyrazolinylpyridinyl indole derivatives

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2-Methyl/ethyl-5-methoxy/ethoxy-3-(2-benzofuran-2-yl)-3-((2-substitutedphenylazo) pyrazolin-4-yl)indoles **3a-l** have been prepared by the reaction of 2-methyl/ethyl-5-methoxy/ethoxy-3-((2-benzofuran-2-yl)-pyrazolin-4-yl)indoles **2a-d** with various substituted benzenediazonium chlorides in presence of sodium acetate. Compounds **3a-l** on reaction with different 4-aminopyridine and formaldehyde yield 2-methyl/ethyl-5-methoxy/ethoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-substitutedphenylazo)-pyrazolin-4-yl)indoles **4a-l**. All the newly synthesized compounds **3a-l** and **4a-l** have been screened for their antiparkinsonian activity**.** Structures of all the compounds are established by elemental and spectral (IR, ^{1}H NMR and mass spectroscopic) analysis.

Keywords: Indoles, pyrazolinylindoles, pyrazolinylpyridinylindoles, antiparkinsonian activity, acute toxicity

Parkinson's disease is a terminal late onset neurodegenerative disorder characterized by a progressive and relatively selective degeneration of dopaminergic neurons in the substantia nigra[1]. Indole derivatives have been reported to possess different biological and pharmacological activities like anti-parkinsonian[2-4], anticonvulsant[5], anti-inflammatory[6] and antipsychotic[7]. Furthermore, various derivatives of benzofuran and pyrazoline have been reported to exhibit antiparkinsonian activity[8,9]. Moreover, different derivatives of pyridine have been shown to possess wide range of biological properties including antiparkinsonian[10-12] and anticonvulsant activity[13]. In the light of above discussion, various derivatives of indole have been synthesized by incorporating benzofuran, pyrazoline and pyridine moieties with the hope to get better antiparkinsonian agents.

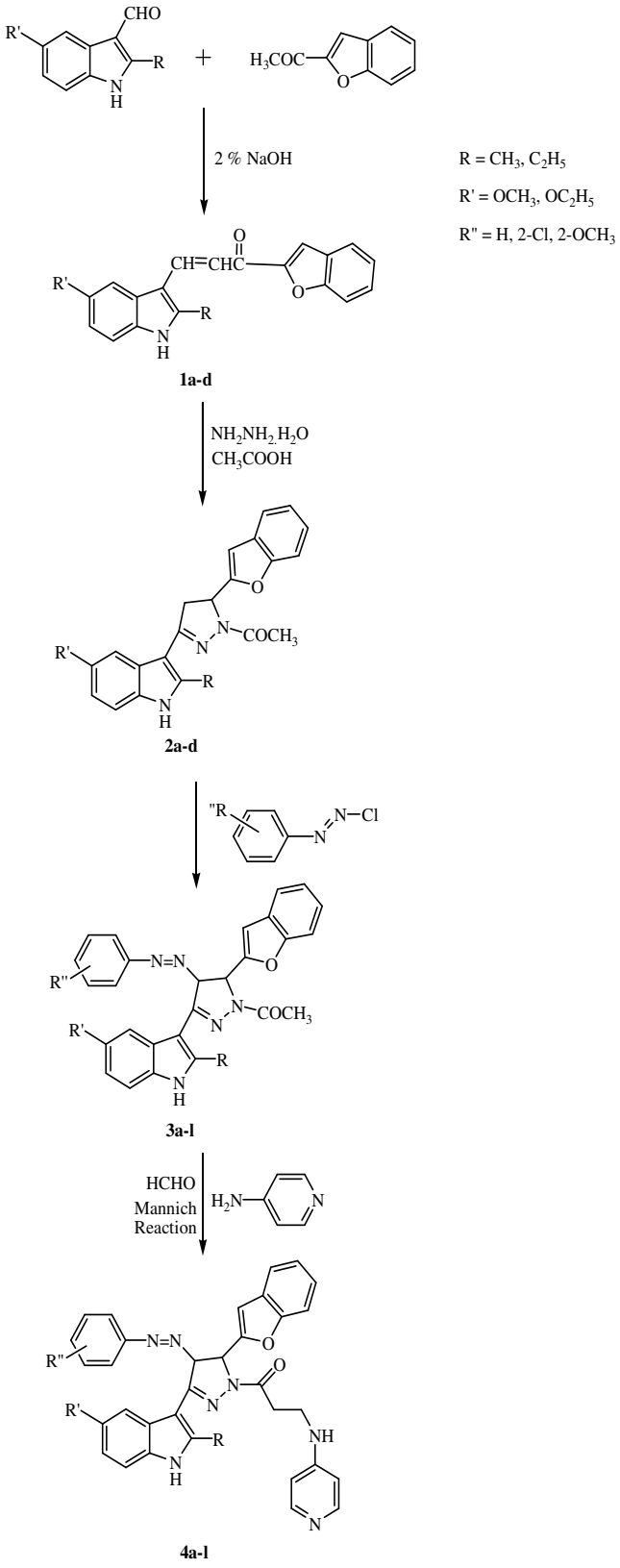
Results and Discussion

Synthetic routes of indole derivatives are outlined in **Scheme I**. 2-Acetylbenzofuran was reacted with different substituted indole-3-aldehydes to give 2-methyl/ethyl-5-methoxy / ethoxy-3-(2-benzofuran-2-yl-chalconyl)indoles **1a-d**, which on cyclization with hydrazine hydrate in presence of glacial acetic acid yielded 2-Methyl/ethyl-5-methoxy/ethoxy-3-((2-benzo-furan-2-yl)-pyrazolin-4-yl)indoles **2a-d**. Compounds **2a-d** on reaction with different substituted benzene diazoniumchlorides afforded 2-methyl/ethyl-5-methoxy/ethoxy-3-(2-benzofuran-2-yl)- 3-(2-substituted-phenylazo) pyrazolin-4-ylindoles **3a-l** which on Mannich reaction with 4-aminopyridine and formal-dehyde gave 2-methyl/ethyl-5-methoxy/ethoxy-3-((2-benzofuran-2-yl)- 1 -(pyridinylamino)methyl-3-substi-tutedphenyl-azo)-pyrazolin-4-yl) indoles **4a-l**. The homogeneneity of all synthesized compounds was determined by thin layer chromatography using several solvent systems of different polarity.

Material and Methods

Antiparkinsonian activity: All the newly synthesized compounds have been evaluated for their antiparkinsonian activity. The study was carried out on albino rats weighing 100-200 g and mice 20-30 g of either sex. The animals were provided feed and allowed water *ad libidum*. The number of animals in each group was 5. All the compounds were administered in a dose of 100 mg/kg i.p.

Tremors: This activity was conducted by the method of D M Coward and M S Dogges[14]. Tremors were induced by oxotremorine (OT) (0.5 mg/kg i.p) in mice 45 min after pretreatment with the test compounds. After 5 min of OT injection, tremors were assessed visually and scored as: 0 = no tremor; 1 = occasional tremor; 2 = intermittent tremors;



Scheme I

3 = continuous tremors. Each animal of a group was scored and tremor index (mean score for each group) determined.

Rigidity: Reserpine (5 mg/kg i.p.) was administered in rats to produce rigidity and after 15 min, test compounds were injected. Rigidity was measured 1 hr after reserpine administration. To measure rigidity, rats were grasped immediately below forelimbs and slight pressure was applied upward against the hind limbs. The degree of resistance was scored according to Goldstein *et al*[15]. : 0 = no resistance; 1= normal resistance; 2 = complete resistance. A score of 2 was selected as criterion for rigidity and expressed as percentage of animals showing rigidity (score 2) in a group.

Hypokinesia: This was performed according to the method of Morpugo[16]. It was produced by reserpine (5 mg/ kg i.p.) in rats. Locomotor activity was measured after 2 hr by placing each group of rats in a photoactometer for 15 min and total counts were recorded. The test compounds were administered 15 min after reserpine administration. The percent increase of decrease in counts was calculated on the basis of counts of untreated groups.

Acute toxicity study: The compounds which showed significant antiparkinsonian activity were investigated for their acute toxicity study in mice (25-30g) of their sex. The compounds were given orally at graded doses to separated groups of animals. After 24 hr of administration, percent mortality in each group was observed from the data obtained. LD_{50} values were calculated by the method of Smith[17].

Experimental Section

All reagents and solvents used in the study were of analytical grade and procured locally. The progress of the reaction was monitored by TLC and the products were purified by recrystalization and homogeneity of the compounds was checked by thin layer chromatography (TLC) performed on silica gel G coated plate of 0.5 mm thickness. The elemental analysis, spectral studies, IR, and ^{1}H NMR were determined by standard methods. Infrared (IR) spectra were recorded in KBr on Perkin-Elmer-spectrum RX-I instrument and ν_{max} was recorded in cm^{-1}. The ^{1}H NMR spectra were recorded in $CDCl_3$ and DMSO-d_6 on Brucker DRX-300 FTNMR instrument. ^{13}C NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer using solvent peak as internal standard. Mass spectra were determined on VG-70-S instrument.

General procedure for preparation of 2-methyl/ethyl-5-methoxy/ethoxy - 3-(2-benzofuran-2-yl-chalconyl)-indoles, 1a-d.

A solution of 2-methyl/ethyl-5-methoxy/ethoxyindol-3-aldehyde (1.5 mol) in absolute methanol (100 mL) in 2% NaOH and 2-acetylbenzofuran (1.5 mol) was refluxed for 10 hr, concentrated, cooled and poured onto ice. The solid thus obtained was filtered, washed with water and purified by recrystallization from appropriate solvent to obtained compounds **1a-d**.

2-Methyl-5-methoxy-3-(2-benzofuran-2-yl-chalconyl)indole, 1a: Yield 75% (Methanol); m.p. 132°C. IR (KBr): 1035 (C-O-C), 1615 (C=C of aromatic ring), 1715 (C=O, COCH), 3352 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.38 (s, 3H, CH_3), 3.40 (s, 3H, OCH_3), 5.60 (d, 1H, *J* = 9.0 Hz, COC*H*=CH), 6.70 (d, 1H, *J* = 9.1 Hz, COCH=C*H*Ar), 6.85-7.89 (m, 8H, Ar-H), 8.72 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.9, 55.8, 104.8, 111.5, 112.1, 112.2, 105.9, 116.6, 120.9, 123.3, 124.7, 127.2, 127.3, 127.5, 127.8, 131.1, 145.1, 154.0, 155.2, 160.5, 177.8; MS: $[M]^+$ at *m/z* 331.36. Anal. Calcd for $C_{21}H_{17}NO_3$: C, 76.12; H, 5.17; N, 4.23. Found: C, 76.11; H, 5.19; N, 4.25%.

2-Methyl-5-ethoxy-3-(2-benzofuran-2-yl-chalconyl)-indole, 1b: Yield 71% (Methanol); m.p. 138°C. IR (KBr): 1038 (C-O-C), 1618 (C=C of aromatic ring), 1714 (C=O, COCH), 3355 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.38 (s, 3H, CH_3), 2.36 (t, 3H, *J* = 7.1 Hz OCH_2CH_3), 3.90 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 5.63 (d, 1H, *J* = 9.0 Hz, COC*H*=CH), 6.72 (d, 1H, *J* = 9.1 Hz, COCH=C*H*Ar), 6.88-7.87 (m, 8H, Ar-H), 8.70 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$) : δ 14.8, 15.9, 64.6, 104.9, 105.9, 153.4, 111.5, 111.7, 116.6, 117.1, 117.8, 120.9, 123.3, 124.7, 126.8, 127.3, 127.8, 131.1, 145.1, 155.2, 160.5; MS: $[M]^+$ at *m/z* 345.39. Anal. Calcd for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found: C, 76.52; H, 5.52; N, 4.09%.

2-Ethyl-5-methoxy-3-(2-benzofuran-2-yl-chalconyl)-indole, 1c: Yield 72% (Ethanol); m.p. 133°C. IR (KBr): 1039 (C-O-C), 1613 (C=C of aromatic ring), 1718 (C=O, COCH), 3357 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.32 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.82 (q, 2H, *J* = 7.1 Hz, CH_2CH_3), 3.46 (s, 3H, OCH_3), 5.63 (d, 1H, *J* = 9.0 Hz, COC*H*=CH), 6.72 (d, 1H, *J* = 9.1 Hz, COCH=C*H*Ar), 6.78-7.87 (m, 8H, Ar-H), 8.71 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.1, 22.4, 55.8, 104.8, 105.9, 111.5, 112.1, 112.2, 116.6, 120.9, 123.3, 124.7, 127.2, 127.3, 127.5, 127.8, 137, 145.1, 154.0, 155.2, 160.5, 177.8; MS: $[M]^+$ at *m/z* 345.39. Anal. Calcd. for $C_{22}H_{19}NO_3$: C, 76.50; H, 5.54; N, 4.06. Found: C, 76.54; H, 5.53; N, 4.10%.

2-Ethyl-5-ethoxy - 3-(2-benzofuran-2-yl-chalconyl)-indole, 1d: Yield 71% (Methanol); m.p. 140°C. IR (KBr): 1040 (C-O-C), 1614 (C=C of aromatic ring), 1715 (C=O, COCH) 3356 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.27 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.35 (t, 3H, *J* = 7.2 Hz OCH_2CH_3), 3.84 (q, 2H, *J* = 7.3 Hz, CH_2CH_3), 3.86 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 5.63 (d, 1H, *J* = 9.0 Hz, COC*H*=CH), 6.72 (d, 1H, *J* = 9.1 Hz, COCH=C*H*Ar), 6.98-7.89 (m, 8H, Ar-H), 8.78 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.1, 14.8, 22.4, 104.9, 105.9, 111.5, 111.7, 115.5, 116.6, 117.1, 120.9, 123.3, 124.7, 126.8, 127.3, 127.8, 137, 145.1, 153.4, 155.2, 160.5, 177.8; MS: $[M]^+$ at *m/z* 359.42. Anal. Calcd for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.89; N, 3.90. Found: C, 76.84; H, 5.93; N, 3.92%.

General procedure for preparation of 2-methyl/ethyl-5-methoxy/ethoxy-3-(2-benzofuran-2-yl)-pyrazolin-4-yl)indoles, 2a-d.

To a solution of **1a-d** (0.4 mol) in methanol, hydrazine hydrate (99%) (0.4 mol) and a few drops of glacial acetic acid were added. The reaction mixture was refluxed for 8-10 hr, the solvent distilled out the reaction mass cooled. The separated solid was filtered, washed with water and purified by recrystallization from suitable solvent to furnish compounds **2a-d**.

2-Methyl-5-methoxy-3-((2-benzofuran-2-yl)-pyrazolin-4-y)indole, 2a: Yield 70% (Methanol); m.p. 145°C. IR (KBr): 1042 (C-O-C), 1294 (N-N of pyrazoline ring), 1584 (C=N), 1616 (C=C of aromatic ring), 1710 (C=O, $COCH_3$), 3358 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.32 (s, 3H, CH_3), 3.42 (s, 3H, OCH_3), 3.61 (s, 3H, N-$COCH_3$), 3.75 (d, 2H, *J* = 9.0 Hz, CH_2 of pyrazoline ring), 5.75 (t, 1H, *J* = 9.35 Hz, CH of pyrazoline ring), 6.85-7.89 (m, 8H, Ar-H), 8.72 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.9, 23.4, 42.4, 51.4, 55.8, 103, 104.8, 111.5, 112.1, 112.2, 115.6, 119.2, 123.3, 124.7, 127.2, 127.5, 129.8, 131.1, 141.4, 151.7, 154.0, 155.1, 168.5; MS: $[M]^+$ at *m/z* 387.43. Anal. Calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85. Found: C, 71.28; H, 5.44; N, 10.84%.

2-Methyl-5-ethoxy-3-((2-benzofuran- 2-yl)-pyrazolin-4-yl)indole, 2b: Yield 68% (Acetone); m.p. 149°C. IR (KBr): 1046 (C-O-C), 1290 (N-N of

pyra-zoline ring), 1583 (C=N), 1612 (C⎓C of aromatic ring), 1714 (C=O, $COCH_3$), 3356 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.42 (s, 3H, CH_3), 2.36 (t, 3H, *J* = 7.3 Hz OCH_2CH_3), 2.87 (q, 2H, *J* = 7.2 Hz, OCH_2CH_3), 3.65 (s, 3H, N-$COCH_3$), 3.75 (d, 2H, *J* = 9.0 Hz, CH_2 of pyrazoline ring), 5.75 (t, 1H, *J* = 9.30 Hz, CH of pyrazoline ring), 6.88-7.87 (m, 8H, Ar-H), 8.70 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.8, 15.9, 23.4, 42.4, 51.4, 64.6, 103, 104.9, 111.5, 111.7, 115.6, 117.1, 119.2, 123.3, 124.7, 126.8, 129.8, 131.1, 137, 141.4, 151.7, 153.4, 155.1, 168.5; MS: $[M]^+$ at *m/z* 401.46. Anal. Calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47; Found: C, 71.79; H, 5.75; N, 10.45%.

2-Ethyl-5-methoxy-3-((2-benzofuran-2-yl)-pyrazolin-4-y)indole, 2c: Yield 72% (Petroleum ether); m.p. 141°C. IR (KBr): 1041 (C-O-C), 1292 (N-N of pyrazoline ring), : 1584 (C=N), 1615 (C⎓C of aromatic ring), 1711 (C=O, $COCH_3$), 3356 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.34 (t, 3H, *J* = 7.1 Hz, CH_2CH_3), 2.78 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.46 (s, 3H, OCH_3), 3.62 (s, 3H, N-$COCH_3$), 3.75 (d, 2H, *J* = 9.0 Hz, CH_2 of pyrazoline ring), 5.75 (t, 1H, *J* = 9.35 Hz, CH of pyrazoline ring), 6.88-7.87 (m, 8H, Ar-H), 8.72 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 22.4, 23.4, 42.4, 51.4, 55.8, 103, 104.8, 111.5, 112.1, 112.2, 115.6, 119.2, 123.3, 124.7, 127.2, 127.5, 129.8, 137, 141.4, 151.7, 154.0, 155.1, 168.5; MS: $[M]^+$ at *m/z* 401.46. Anal. Calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47. Found: C, 71.81; H, 5.78; N, 10.46%.

2-Ethyl-5-ethoxy-3-((2-benzofuran-2-yl)-pyrazolin-4-yl)indole, 2d: Yield 67% (Methanol); m.p. 146°C. IR (KBr): 1044 (C-O-C), 1290 (N-N of pyrazoline ring), 1586 (C=N), 1617 (C⎓C of aromatic ring), 1714 (C=O, $COCH_3$), 3353 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.30 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.38 (t, 3H, *J* = 7.3 Hz OCH_2CH_3), 2.78 (q, 2H, *J* = 7.0 Hz, CH_2CH_3), 3.52 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 3.68 (s, 3H, N-$COCH_3$), 3.75 (d, 2H, *J* = 9.0 Hz, CH_2 of pyrazoline ring), 5.75 (t, 1H, *J* = 9.31 Hz, CH of pyrazoline ring), 6.88-7.87 (m, 8H, Ar-H), 8.72 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 11.7, 13.7, 14.8, 22.4, 23.4, 42.4, 51.4, 64.6, 103, 104.9 111.5, 115.6, 117.1, 119.2, 123.3, 124.7, 126.8, 129.8, 137, 151.7, 153.4, 141.4, 151.4, 155.1, 168.5; MS: $[M]^+$ at *m/z* 405.21. Anal. Calcd for $C_{25}H_{25}N_3O_3$: C, 72.27; H, 6.06; N, 10.11. Found: C, 71.25; H, 6.08; N, 10.13 %.

General procedure for preparation of 2-methyl/ethyl-5-methoxy/ethoxy-3-((2-benzofuran-2-yl)-3-(2-substituted phenylazo) pyrazolin-4-yl indoles, 3a-l.

Aryldiazonium salt solution of different anilines (0.1 mol) was added drop wise with stirring to the ethanolic solution of compounds **2a-d** (0.1 mol) containing sodium acetate (0.1 mol) at 0-5^{0}C. The reaction mixture was kept at RT for 2 hr and poured onto ice cold water. The solid thus obtained was washed several times with water filtered and then purified by recrystalization from suitable solvents to afford compounds **3a-l**.

2-Methyl-5-methoxy-3-((2-benzofuran-2-yl)-3-(phenylazo)pyrazolin-4-yl)indole 3a: Yield 65% (Ethanol); m.p. 172°C. IR (KBr): 1050 (C-O-C), 1292 (N-N of pyrazoline ring), 1421 (N=N), 1584 (C=N), 1613 (C⎓C of aromatic ring), 1716 (C=O, $COCH_3$), 3354 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.34 (s, 3H, CH_3), 3.48 (s, 3H, OCH_3), 3.74 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.85 (s, 3H, N-$COCH_3$), 5.77 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.78-7.99 (m, 13H, Ar-H), 8.82 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.9, 23.4, 38.6, 55.8, 70.4, 103, 104.8, 112.1, 112.1, 111.5, 115.6, 119.2, 122.6, 123.3, 124.7, 125.7, 127.2, 127.5, 129.2, 129.8, 131.1, 141.4, 150.9, 154.0, 155.1, 155.6, 168.5; MS: $[M]^+$ at *m/z* 491.54. Anal. Calcd for $C_{29}H_{25}N_5O_3$: C, 70.86; H, 5.13; N, 14.25. Found: C, 70.88; H, 5.12; N, 14.24%.

2-Methyl-5-methoxy- 3 -((2-benzofuran-2-yl)-3-(2-chlorophenylazo)pyrazolin-4-yl) indole, 3b: Yield 74% (Acetone); m.p. 168°C. IR (KBr): 750 (C-Cl), 1058 (C-O-C), 1294 (N-N of pyrazoline ring), 1425 (N=N), 1587 (C=N), 1617 (C⎓C of aromatic ring), 1718 (C=O, $COCH_3$), 3357 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.38 (s, 3H, CH_3), 3.53 (s, 3H, OCH_3), 3.71 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.86 (s, 3H, N-$COCH_3$), 5.72 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.85-7.79 (m, 12H, Ar-H), 8.89 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.9, 23.4, 38.6, 55.8, 70.4, 103, 104.8, 111.5, 112.1, 112.2, 115.6, 119.2, 123.3, 124.0, 124.7, 127.1, 127.2, 127.3, 127.5, 128.1, 129.3, 129.8, 131.1, 141.4, 151.1, 154.0, 155.1, 155.6, 168.5; MS: $[M]^+$ at *m/z* 525.99. Anal. Calcd for $C_{29}H_{24}ClN_5O_3$: C, 66.22; H, 4.60; N, 13.31. Found: C, 66.24; H, 4.58; N, 13.32%.

2-Methyl-5-methoxy-3-((2-benzofuran-2-yl)-3-(2-methoxyphenylazo)pyrazolin-4-yl)indole, 3c: Yield 70% (Methanol); m.p. 178°C. IR (KBr): 1056 (C-O-C), 1292 (N-N of pyrazoline ring), 1422 (N=N),

1588 (C=N), 1619 (C⎓C of aromatic ring), 1715 (C=O, $COCH_3$), 3352 cm^{-1} (NH). ^1H NMR ($CDCl_3$): δ 1.40 (s, 3H, CH_3), 3.56 (s, 6H, 2 × OCH_3), 3.76 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.80 (s, 3H, N-$COCH_3$), 5.70 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.87-7.89 (m, 12H, Ar-H), 8.93 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.9, 23.4, 38.6, 55.8, 70.4, 103, 104.8, 112.1, 112.2, 114.8, 115.6, 119.2, 121.5, 121.7, 122.8, 123.3, 123.6, 124.7, 127.2, 127.5, 129.8, 131.1, 141.4, 152.8, 154.0, 155.1, 155.6, 168.5; MS: $[M]^+$ at *m/z* 521.57. Anal. Calcd for $C_{30}H_{27}N_5O_4$: C, 69.08; H, 5.22; N, 13.43. Found: C, 69.09; H, 5.20; N, 13.45%.

2-Methyl-5-ethoxy-3-((2-benzofuran-2-yl)-3-(phenylazo)pyrazolin-4-yl)indole, 3d: Yield 77% (Methanol); m.p. 170°C. IR (KBr): 1058 (C-O-C), 1295 (N-N), 1426 (N=N), 1589 (C=N), 1620 (C⎓C of aromatic ring), 1717 (C=O, $COCH_3$), 3358 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.30 (s, 3H, CH_3), 1.92 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 3.84 (q, 2H, *J* = 7.1 Hz, OCH_2CH_3), 3.76 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.81 (s, 3H, N-$COCH_3$), 5.69 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.87-7.78 (m, 13H, Ar-H), 8.95 (s, 1H, indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.8, 15.9, 23.4, 38.6, 55.8, 64.6, 70.4, 103, 104.9, 111.5, 111.7, 114.8, 115.6, 117.1, 119.2, 121.5, 121.7, 122.8, 123.3, 123.6, 124.7, 126.8, 129.8, 126.8, 131.1, 141.4, 152.8, 153.4, 155.1, 155.6, 168.5; MS: $[M]^+$ at *m/z* 505.57. Anal. Calcd for $C_{30}H_{27}N_5O_3$: C, 71.27; H, 5.38; N, 13.85. Found: C, 71.28; H, 5.39; N, 13.82%.

2-Methyl-5-ethoxy- 3 -((2-benzofuran-2-yl)-3-(2-chlorophenylazo) pyrazolin-4-yl) indole, 3e: Yield 69% (Ethanol); m.p. 187°C. IR (KBr): 756 (C-Cl), 1056 (C-O-C), 1292 (N-N), 1422 (N=N), 1590 (C=N), 1625 (C⎓C of aromatic ring), 1722 (C=O, $COCH_3$), 3352 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.35 (s, 3H, CH_3), 1.88 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 3.89 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 3.79 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.81 (s, 3H, N-$COCH_3$), 5.67 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.77-7.88 (m, 12H, Ar-H), 8.98 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.8, 15.9, 22.8, 46.6, 64.6, 67.5, 102.0, 103, 104.9, 111.7, 117.1, 126.8, 111.5, 120.9, 123.3, 124.0, 124.7, 126.8, 126.9, 127.1, 127.3, 128.1, 129.3, 131.1, 151.1, 153.4, 154.1, 155.6, 159.6, 168.5; MS: $[M]^+$ at *m/z* 540.01. Anal. Calcd for $C_{30}H_{26}ClN_5O_3$: C, 66.72; H, 4.85; N, 12.97. Found: C, 66.70; H, 4.86; N, 12.96%.

2-Methyl-5-ethoxy-3-((2-benzofuran-2-yl)-3-(2-methoxyphenylazo)pyrazolin-4-yl)indole, 3f: Yield 71% (Methanol); m.p. 190°C. IR (KBr): 1056 (C-O-C), 1293 (N-N), 1425 (N=N), 1593 (C=N), 1623 (C⎓C of aromatic ring), 1727 (C=O, $COCH_3$), 3356 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.29 (s, 3H, CH_3), 2.34 (t, 3H, *J* = 7.0 Hz, OCH_2CH_3), 2.92 (q, 2H, *J* = 7.2 Hz, OCH_2CH_3), 3.55 (s, 3H, OCH_3), 3.70 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.75 (s, 3H, N-$COCH_3$), 5.69 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.97-7.79 (m, 12H, Ar-H), 8.92 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.8, 15.9, 22.8, 46.6, 55.8, 64.6, 67.5, 102.0, 103, 104.9, 111.5, 111.7, 114.8, 117.1, 120.9, 121.5, 121.1, 122.8, 123.3, 123.6, 126.8, 126.9, 131.1, 152.8, 153.4, 154.1, 155.6, 159.6, 168.5; MS: $[M]^+$ at *m/z* 535.59. Anal. Calcd for $C_{31}H_{29}N_5O_4$: C, 69.52; H, 5.46; N, 13.08. Found: C, 69.50; H, 5.47; N, 13.06%.

2-Ethyl-5-methoxy- 3 -((2-benzofuran-2-yl)-3-(phenylazo)pyrazolin-4-yl)indole, 3g: Yield 72% (Petroleum ether); m.p. 183°C. IR (KBr): 1049 (C-O-C), 1295 (N-N), 1426 (N=N), 1585 (C=N), 1622 (C⎓C of aromatic ring), 1720 (C=O, $COCH_3$), 3349 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.37 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.74 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.59 (s, 3H, OCH_3), 3.74 (d, 1H, *J* = 7.4 Hz, CH of pyrazoline ring), 3.80 (s, 3H, N-$COCH_3$), 5.69 (d, 1H, *J* = 7.4 Hz, CH of pyrazoline ring), 6.97-7.79 (m, 13H, Ar-H), 8.98 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 22.4, 22.8, 46.4, 55.8, 67.5, 102.0, 103, 104.8, 111.5, 112.1, 112.2, 120.9, 122.6, 123.3, 124.7, 125.7, 126.9, 127.2, 127.5, 129.2, 137, 150.9, 154.0, 154.1, 155.6, 159.6, 168.5; MS: $[M]^+$ at *m/z* 505.57. Anal. Calcd for $C_{30}H_{27}N_5O_3$: C, 71.27; H, 5.38; N, 13.85. Found: C, 71.26; H, 5.39; N, 13.84%.

2-Ethyl-5-methoxy-3-((2-benzofuran-2-yl)-3-(2-chlorophenylazo)pyrazolin-4-yl)indole, 3h: Yield 75% (Petroleum ether); m.p. 194°C. IR (KBr): 752 (C-Cl), 1053 (C-O-C), 1290 (N-N), 1424 (N=N), 1629 (C⎓C of aromatic ring), 1593 (C=N), 1718 (C=O, $COCH_3$), 3357 cm^{-1} (NH). ^1H NMR ($CDCl_3$): δ MS: 2.34 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.85 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.53 (s, 3H, OCH_3), 3.72 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.75 (s, 3H, N-$COCH_3$), 5.62 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.87-7.89 (m, 12H, Ar-H), 8.91 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 22.4, 22.8, 46.6, 55.8, 67.5, 102.0, 103, 104.8, 111.5, 112.1, 112.2, 120.9, 123.3, 124.0, 124.7, 126.9, 127.1, 127.3, 127.5, 128.1, 129.3, 137, 154.1, 155.6, 159.6, 127.2,

154.0, 168.5; $[M]^+$ at *m/z* 540.01. Anal. Calcd for $C_{30}H_{26}ClN_5O_3$: C, 66.72; H, 4.85; N, 12.97. Found: C, 66.71; H, 4.86; N, 12.95%

2-Ethyl-5-methoxy-3-((2-benzofuran-2-yl)-3-(2-methoxyphenylazo)pyrazolin-4-yl)indole, 3i: Yield 74% (Methanol); m.p. 199°C. IR (KBr): 1056 (C-O-C), 1294 (N-N), 1424 (N=N), 1594 (C=N), 1624 (C⎓C of aromatic ring), 1721 (C=O, $COCH_3$), 3351 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.37 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.81 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.59 (s, 6H, 2 × OCH_3), 3.74 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.87 (s, 3H, N-$COCH_3$), 5.69 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.97-7.69 (m, 12H, Ar-H), 8.93 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 22.4, 22.8, 46.6, 55.8, 67.5, 102.0, 103, 104.8, 111.5, 112.1, 112.2, 114.8, 120.9, 121.5, 121.7, 122.8, 123.3, 123.6, 124.7, 126.9, 127.2, 127.5, 137, 152.8, 154.0, 154.1, 155.6, 159.6, 168.5; MS: $[M]^+$ at *m/z* 535.59. Anal. Calcd for $C_{31}H_{29}N_5O_4$: C, 69.52; H, 5.46; N, 13.08. Found: C, 69.50; H, 5.47; N, 13.06%.

2-Ethyl-5-ethoxy-3-((2-benzofuran-2-yl)-3-(phenylazo)pyrazolin-4-yl)indole, 3j: Yield 70% (Ethanol); m.p. 175°C. IR (KBr): 1062 (C-O-C), 1292 (N-N), 1422 (N=N), 1590 (C=N), 1625 (C⎓C of aromatic ring), 1722 (C=O, $COCH_3$), 3357 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.30 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.33 (t, 3H, OCH_2CH_3), 2.90 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.54 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 3.78 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.82 (s, 3H, N-$COCH_3$), 5.66 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.69-7.69 (m, 13H, Ar-H), 8.90 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 14.8, 22.4, 22.8, 46.6, 64.6, 67.5, 102.0, 103, 104.9, 111.5, 111.7, 117.1, 120.9, 122.6, 123.3, 124.7, 125.7, 126.8, 126.9, 129.2, 137, 150.9, 153.4, 154.1, 155.6, 159.6, 168.5; MS: $[M]^+$ at *m/z* 519.59. Anal. Calcd for $C_{31}H_{29}N_5O_3$: C, 71.66; H, 5.63; N, 13.48. Found: C, 71.65; H, 5.64; N, 13.47%.

2-Ethyl-5-ethoxy-3-((2-benzofuran-2-yl)-3-(2-chlorophenylazo)pyrazolin-4-yl)indole, 3k: Yield 70% (Methanol); m.p. 186°C. IR (KBr): 753 (C-Cl), 1054 (C-O-C), 1294 (N-N), 1425 (N=N), 1595 (C=N), 1630 (C⎓C of aromatic ring), 1730 (C=O, $COCH_3$), 3354 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.29 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.37 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3), 2.94 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.54 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 3.78 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.83 (s, 3H, N-$COCH_3$), 5.64 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.66-7.66 (m, 12H, Ar-H), 8.89 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 14.8, 22.4, 22.8, 46.6, 64.6, 67.5, 102.0, 103, 104.9, 111.5, 111.7, 117.1, 120.9, 123.3, 124.0, 124.7, 126.8, 126.9, 127.1, 127.3, 128.1, 129.3, 137, 151.1, 153.4, 154.1, 155.6, 159.6, 168.5; MS: $[M]^+$ at *m/z* 554.04. Anal. Calcd for $C_{31}H_{28}ClN_5O_3$: C, 67.20; H, 5.09; N, 12.64. Found: C, 67.21; H, 5.10; N, 12.66%.

2-Ethyl-5-ethoxy-3-((2-benzofuran-2-yl)-3-(2-methoxyphenylazo)pyrazolin-4-yl)indole, 3l: Yield 71% (Methanol); m.p. 197°C. IR (KBr): 1057 (C-O-C), 1294 (N-N), 1423 (N=N), 1593 (C=N), 1623 (C⎓C of aromatic ring), 1725 (C=O, $COCH_3$), 3352 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.32 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.41 (t, 3H, *J* = 7.3 Hz OCH_2CH_3), 2.90 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.60 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 3.72 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.75 (s, 3H, N-$COCH_3$), 3.55 (s, 3H, OCH_3), 5.62 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.79-7.99 (m, 12H, Ar-H), 8.90 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 14.8, 22.4, 22.8, 46.6, 55.8, 64.6, 67.5, 102.0, 103, 104.9, 111.5, 111.7, 114.8, 117.1, 120.9, 121.5, 121.7, 121.8, 122.8, 123.3, 123.6, 124.7, 126.8, 126.9, 137, 152.8, 153.4, 154.1, 155.6, 159.6, 168.5; MS: $[M]^+$ at *m/z* 549.24. Anal. Calcd for $C_{32}H_{31}N_5O_4$: C, 69.93; H, 5.69; N, 12.74. Found: C, 69.95; H, 5.67; N, 12.76%.

General procedure for preparation of 2-methyl/ethyl-5-methoxy/ethoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-substitutedphenylazo)-pyrazolin-4-yl)indoles, 4a-l.

To the solution of compound **3a-l** (0.03 mol) in methanol, formaldehyde (0.06 mol) and different anilines (0.02 mol) were added and refluxed for 4-6 hr. The resultant mixture was concentrated, cooled and poured onto ice. Separated solid was filtered and purified by recrystallization from suitable solvents to yielded compounds **4a-l**.

2-Methyl-5-methoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(phenylazo) pyrazolin-4-yl)indole, 4a: Yield 60% (Ethanol); m.p. 242°C. IR (KBr): 1039 (C-O-C), 1292 (N-N), 1422 (N=N), 1590 (C=N), 1625 (C⎓C of aromatic ring), 1722 (C=O, $COCH_3$), 3355 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.45 (s, 3H, CH_3), 3.12 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.16 (q, 2H, *J* = 7.2 Hz, CH_2NH), 3.54 (s, 3H, OCH_3), 3.74 (d, 1H, *J* = 7.4 Hz, CH of pyrazoline ring), 5.40 (brs, 1H, $NHCH_2$ exchangeable with D_2O), 5.77 (d, 1H, *J* = 7.4 Hz, CH of pyrazoline ring), 6.78-7.99 (m, 17H,

Ar-H), 8.82 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.9, 34.7, 39.0, 46.9, 55.8, 67.5, 102.0, 103, 104.8, 107.3, 111.5, 112.1, 112.2, 120.9, 122.6, 123.3, 124.7, 125.7, 127.2, 127.5, 129.2, 129.6, 126.9, 131.1, 154.0, 150.2, 150.9, 154.1, 154.9, 155.6, 159.6, 171.7. MS: $[M]^+$ at *m/z* 597.67. Anal. Calcd for $C_{35}H_{31}N_7O_3$: C, 70.34; H, 5.23; N, 16.40; Found: C, 69.35; H, 5.22; N, 16.42%.

2-Methyl-5-methoxy-3-((2-benzofuran-2-yl-1-(pyridinylamino)methyl)-3-(2-chlorophenylazo) pyrazolin-4-yl)indole, 4b: Yield 70% (Acetone); m.p. 232°C. IR (KBr): 756 (C-Cl), 1044 (C-O-C), 1291 (N-N), 1426 (N=N), 1589 (C=N), 1625 (C⋯C of aromatic ring), 1730 (C=O), 3346 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.49 (s, 3H, CH_3), 3.15 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.20 (q, 2H, *J* = 7.2 Hz, CH_2NH), 3.53 (s, 3H, OCH_3), 3.71 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 5.48 (brs, 1H, $NHCH_2$ exchangeable with D_2O), 5.72 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.85-7.79 (m, 16H, Ar-H), 8.89 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.9, 34.7, 39.0, 46.9, 55.8, 67.5, 102.0, 102.9, 103,104.8, 107.3, 112.1, 112.2, 111.5, 123.3, 124.0, 124.7, 126.9, 127.1, 127.2, 127.3, 127.5, 128.1, 129.3, 131.1, 150.2, 151.1, 154.0, 154.1, 154.9, 159.6, 155.6, 171.7; MS: $[M]^+$ at *m/z* 632.11. Anal. Calcd for $C_{35}H_{30}ClN_7O_3$: C, 66.50; H, 4.78; N, 15.51. Found: C, 66.50; H, 4.76; N, 15.53%.

2-Methyl-5-methoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(2-methoxyphenyl azo)-pyrazolin-4-yl)indole, 4c: Yield 67% (Acetone); m.p. 248°C. IR (KBr): 1039 (C-O-C), 1293 (N-N), 1426 (N=N), 1590 (C=N), 1629 (C⋯C of aromatic ring), 1735 (C=O), 3352 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.43 (s, 3H, CH_3), 3.10 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.28 (q, 2H, *J* = 7.2 Hz, CH_2NH), 3.56 (s, 6H, 2 × OCH_3), 3.76 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 5.42 (brs, 1H, $NHCH_2$ exchangeable with D_2O), 5.70 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.87-7.89 (m, 16H, Ar-H), 8.93 (ss, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.9, 22.4, 34.7, 39.0, 46.9, 55.8, 67.5, 102.0, 103, 104.8, 111.5, 112.1, 112.2, 107.3, 120.9, 122.6, 123.3, 124.7, 125.7, 126.9, 127.2, 127.5, 129.2, 137, 150.2, 150.9, 154.0, 154.1, 154.9, 155.6, 159.6, 171.7; MS: $[M]^+$ at *m/z* 627.69. Anal. Calcd for $C_{36}H_{33}N_7O_4$: C, 68.88; H, 5.30; N, 15.62. Found: C, 68.86; H, 5.31; N, 15.63%.

2-Methyl-5-ethoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(phenylazo)pyrazolin-4-yl)-indole, 4d: Yield 74% (Petroleum ether); m.p. 257°C. IR (KBr): 1047 (C-O-C), 1290 (N-N), 1424 (N=N), 1594 (C=N), 1632 (C⋯C of aromatic ring), 1733 (C=O), 3338 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.47 (s, 3H, CH_3), 2.38 (t, 3H, *J* = 7.3 Hz OCH_2CH_3), 3.16 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.26 (d, (q, 2H, *J* = 7.2 Hz, CH_2NH), 3.76 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.92 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 5.46 (brs, 1H, $NHCH_2$ exchangeable with D_2O), 5.69 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.87-7.78 (m, 17H, Ar-H), 8.95 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 22.4, 34.7, 39.0, 46.9, 55.8, 67.5, 102.0, 103, 104.8.107.3, 112.1, 112.2, 111.5, 120.9, 122.6, 123.3, 124.7, 125.7, 126.9, 127.2, 127.5, 129.2, 137, 150.2, 150.9, 154.0, 154.1, 154.9, 159.6, 155.6, 171.7; MS: $[M]^+$ at *m/z* 611.69. Anal. Calcd for $C_{36}H_{33}N_7O_3$: C, 70.69; H, 5.44; N, 16.03. Found: C, 70.67; H, 5.45; N, 16.05%.

2-Methyl-5-ethoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(2-chlorophenylazo) pyr-azolin-4-yl)indole, 4e: Yield 65% (Methanol); m.p. 260°C. IR (KBr): 759 (C-Cl), 1042 (C-O-C), 1292 (N-N), 1421 (N=N), 1590 (C=N), 1626 (C⋯C of aromatic ring), 1734 (C=O), 3356 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 1.43 (s, 3H, CH_3), 2.34 (t, 3H, *J* = 7.2 Hz OCH_2CH_3), 3.12 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.23 (q, 2H, *J* = 7.2 Hz, CH_2NH), 2.85 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 3.79 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 5.50 (brs, 1H, $NHCH_2$ exchangeable with D_2O); 5.67 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.77-7.88 (m, 16H, Ar-H), 8.98 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 22.4, 34.7, 39.0, 46.9, 55.8, 67.5, 102.0, 103, 104.8, 107.3, 111.5, 112.1, 112.2, 120.9, 123.3, 124.0, 124.7, 126.9, 127.1, 127.2, 127.3, 127.5, 128.1, 129.3, 137, 150.2, 151.1, 154.0, 154.1, 154.9, 155.6, 159.6, 171.7; MS: $[M]^+$ at *m/z* 646.14. Anal. Calcd for $C_{36}H_{32}ClN_7O_3$: C, 66.92; H, 4.99; N, 15.17. Found: C, 66.94; H, 4.97; N, 15.19%.

2-Methyl-5-ethoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(2-methoxyphenylazo) pyrazolin-4-yl)indole, 4f: Yield 67% (Methanol); m.p. 239°C. IR (KBr): 1035 (C-O-C), 1295 (N-N), 1428 (N=N), 1591 (C=N), 1625 (C⋯C of aromatic ring), 1723 (C=O), 3349 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.39 (t, 3H, *J* = 7.3 Hz, CH_2CH_3), 3.10 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.33 (q, 2H, *J* = 7.2 Hz, CH_2NH), 2.87 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.59 (s, 6H, 2 × OCH_3), 3.74 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 5.43 (brs, 1H, $NHCH_2$ exchangeable with D_2O), 5.69 (d,

1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.97-7.79 (m, 16H, Ar-H), 8.98 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 22.4, 34.7, 39.0, 46.9, 55.8, 67.5, 102.0, 103, 104.8, 107.3, 111.5, 112.1, 112.2, 114.8, 120.9, 121.5, 121.7, 122.8, 123.3, 123.6, 124.7, 126.9, 127.2, 127.5, 137, 150.2, 152.8, 154.0, 154.1, 154.9, 155.6, 159.6, 171.7; MS: $[M]^+$ at *m/z* 641.72. Anal. Calcd for $C_{37}H_{35}N_7O_4$: C, 69.25; H, 5.50; N, 15.28. Found: C, 69.22; H, 5.52; N, 15.30%.

2-Ethyl-5-methoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(phenylazo) pyrazolin-4-yl)indole, 4g: Yield 70% (Methanol); m.p. 270°C. IR (KBr): 1039 (C-O-C), 1290 (N-N), 1428 (N=N), 1590 (C=N), 1629 (C⎓C of aromatic ring), 1733 (C=O), 3356 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.37 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 3.17 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.31 (q, 2H, *J* = 7.2 Hz, CH_2NH), 2.88 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.59 (s, 3H, OCH_3), 3.74 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 5.46 (brs, 1H, $NHCH_2$ exchangeable with D_2O), 5.69 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.97-7.79 (m, 17H, Ar-H), 8.98 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.8, 15.9, 34.7, 39.0, 46.9, 64.6, 67.5, 102.0, 103, 104.9, 107.3, 111.5, 117.1, 111.7, 120.9, 122.6, 123.3, 124.7, 125.7, 126.8, 126.9, 128.6, 129.2, 131.1, 124.7, 126.9, 150.2, 150.9, 153.4, 154.1, 154.9, 155.6, 159.6, 171.7; MS: $[M]^+$ at *m/z* 611.69. Anal. Calcd for $C_{36}H_{33}N_7O_3$: C, 70.69; H, 5.44; N, 16.03. Found: C, 70.67; H, 5.45; N, 16.01%.

2-Ethyl-5-methoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(2-chlorophenylazo) pyrazolin-4-yl)indole, 4h: Yield 68% (Ethanol); m.p. 260°C. IR (KBr): 761 (C-Cl), 1040 (C-O-C), 1295 (N-N), 1420 (N=N), 1592 (C=N), 1626 (C⎓C of aromatic ring), 1720 (C=O), 3350 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.34 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 3.13 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.30 (q, 2H, *J* = 7.2 Hz, CH_2NH), 2.82 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.53 (s, 3H, OCH_3), 3.76 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 5.42 (brs, 1H, $NHCH_2$ exchangeable with D_2O), 5.62 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.87-7.89 (m, 16H, Ar-H), 8.96 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.8, 15.9, 34.7, 39.0, 46.9, 64.6, 67.5, 102.0, 103, 104.9, 107.3, 111.5, 111.7, 117.1, 120.9, 123.3, 124.0, 124.7, 126.8, 126.9, 127.1, 127.3, 128.1, 129.3, 131.1, 150.2, 151.1, 153.4, 154.9, 154.1, 155.6, 159.6, 171.7; MS: $[M]^+$ at *m/z* 646.14. Anal. Calcd for $C_{36}H_{32}ClN_7O_3$: C, 66.92; H, 4.99; N, 15.17. Found: C, 66.94; H, 4.97; N, 15.19%.

2-Ethyl-5-methoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(2-methoxyphenyl azo) pyrazolin-4-yl)indole 4i: Yield 72% (Methanol); m.p. 268°C. IR (KBr): 1039 (C-O-C), 1294 (N-N), 1423 (N=N), 1592 (C=N), 1628 (C⎓C of aromatic ring), 1726 (C=O), 3347 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.37 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 3.10 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.27 (q, 2H, *J* = 7.2 Hz, CH_2NH), 2.86 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 3.59 (s, 6H, 2 × OCH_3), 3.74 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 5.45 (brs, 1H, $NHCH_2$ exchangeable with D_2O), 5.69 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.97-7.69 (m, 16H, Ar-H), 8.93 (s, 1H, NH of indole exchangeable with D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 14.8, 15.9, 34.7, 39.0, 46.9, 55.8, 64.6, 67.5, 102.0, 103, 104.9, 107.3, 111.5, 114.8, 111.7, 117.1, 120.9, 121.5, 121.7, 122.8, 123.3, 123.6, 124.7, 126.8, 126.9, 131.1, 150.2, 154.9, 152.8, 153.4, 154.1, 155.6, 159.6, 171.7; MS: $[M]^+$ at *m/z* 641.72. Anal. Calcd for $C_{37}H_{35}N_7O_4$: C, 69.25; H, 5.50; N, 15.28; Found: C, 69.24; H, 5.48; N, 15.27%.

2-Ethyl-5-ethoxy - 3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(phenylazo) pyrazolin-4-yl indole, 4j: Yield 74% (Acetone); m.p. 255°C. IR (KBr): 1039 (C-O-C), 1292 (N-N), 1421 (N=N), 3353 (NH), 1593 (C=N), 1625 (C⎓C of aromatic ring), 1724 (C=O), 3346 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.41 (t, 3H, *J* = 7.3 Hz OCH_2CH_3), 2.30 (t, 3H, *J* = 7.3 Hz, CH_2CH_3), 3.05 (t, 2H, *J* = 6.0 Hz, CH_2CH_2), 3.25 (q, 2H, *J* = 7.2 Hz, CH_2NH), 2.92 (q, 2H, *J* = 7.2 Hz, CH_2CH_3), 5.46 (brs, 1H, $NHCH_2$ exchangeable with D_2O), 3.95 (q, 2H, *J* = 7.3 Hz, OCH_2CH_3), 3.78 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 5.66 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.69-7.69 (m, 17H, Ar-H), 8.90 (s, 1H, indole exchangeable With D_2O); ^{13}C NMR (400 MHz, $CDCl_3$): δ 13.7, 14.8, 22.4, 34.7, 39.0, 46.9, 64.6, 67.5, 102.0, 103, 107.3, 104.9.111.5, 111.7, 117.1, 120.9, 122.6, 123.3, 124.7, 125.7, 126.8, 126.9, 129.2, 137.0, 150.2, 150.9, 153.4, 154.1, 154.9, 155.6, 159.6, 171.7; MS: $[M]^+$ at *m/z* 611.69. Anal. Calcd for $C_{37}H_{35}N_7O_3$: C, 70.69; H, 5.44; N, 16.03. Found: C, 70.68; H, 5.45; N, 16.05%.

2-Ethyl-5-ethoxy-3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(2-chlorophenyl azo) pyrazolin-4-yl)indole, 4k: Yield 63% (Methanol); m.p. 271°C. IR (KBr): 766 (C-Cl), 1036 (C-O-C), 1292 (N-N), 1426 (N=N), 1594 (C=N), 1627 (C⎓C of aromatic ring), 1722 (C=O, $COCH_3$), 3356 cm^{-1} (NH); ^1H NMR ($CDCl_3$): δ 2.32 (t, 3H, *J* = 7.0 Hz, CH_2CH_3), 2.37 (t, 3H, *J* = 7.3 Hz OCH_2CH_3), 2.92 (q, 2H, *J* = 7.2

Table I — Antiparkinsonian activity of compounds **3a-l** and **4a-l**

Compd.	R	R′	R″	Oxotremorine induced tremors in mice (0.5 mg/kg)	Reserpine induced (5 mg/kg)		LD_{50} mg/kg i.p.
					Rigidity (%)	Hypokinesia (% counts)	
Control	-	-	-	3.0 ± 0	100	14.06	
L-Dopa	-	-	-	2.60 ± 0.26	80	30.39	
3a	CH_3	OCH_3	H	2.15 ± 0.28	80	53.80	1000
3b	CH_3	OCH_3	2-Cl	2.36 ± 0.21	40	67.10	1000
3c	CH_3	OCH_3	2-OCH_3	2.39 ± 0.26	50	56.25	1000
3d	CH_3	OC_2H_5	H	2.17 ± 0.24	50	60.60	1000
3e	CH_3	OC_2H_5	2-Cl	2.19 ± 0.35	40	74.50	1000
3f	CH_3	OC_2H_5	2-OCH_3	2.53 ± 0.15	60	64.10	1000
3g	C_2H_5	OCH_3	H	2.20 ± 0.27	80	49.80	1000
3h	C_2H_5	OCH_3	2-Cl	2.51 ± 0.26	30	70.10	1000
3i	C_2H_5	OCH_3	2-OCH_3	2.28 ± 0.12	50	56.30	1000
3j	C_2H_5	OC_2H_5	H	2.23 ± 0.10	60	73.60	1000
3k	C_2H_5	OC_2H_5	2-Cl	2.49 ± 0.14	40	74.20	1000
3l	C_2H_5	OC_2H_5	2-OCH_3	2.28 ± 0.26	50	73.70	1000
4a	CH_3	OCH_3	H	2.32 ± 0.28	70	54.06	1000
4b	CH_3	OCH_3	2-Cl	2.15 ± 0.25	30	70.39	1000
4c	CH_3	OCH_3	2-OCH_3	2.26 ± 0.21	50	63.80	1000
4d	CH_3	OC_2H_5	H	2.39 ± 0.26	60	57.10	1000
4e	CH_3	OC_2H_5	2-Cl	2.21 ± 0.24	30	76.20	1000
4f	CH_3	OC_2H_5	2-OCH_3	2.19 ± 0.35	30	79.60	1000
4g	C_2H_5	OCH_3	H	2.23 ± 0.10	40	64.50	1000
4h	C_2H_5	OCH_3	2-Cl	2.10 ± 0.27	10	90.10	1600
4i	C_2H_5	OCH_3	2-OCH_3	2.31 ± 0.23	50	69.80	1000
4j	C_2H_5	OC_2H_5	H	2.26 ± 0.23	80	80.20	1000
4k	C_2H_5	OC_2H_5	2-Cl	2.38 ± 0.10	40	76.30	1000
4l	C_2H_5	OC_2H_5	2-OCH_3	2.25 ± 0.20	50	73.60	1000

Hz, C*H*$_2$CH$_3$), 3.15 (t, 2H, *J* = 6.0 Hz, C*H*$_2$CH$_2$), 3.24 (q, 2H, *J* = 7.2 Hz, CH$_2$NH), 3.90 (q, 2H, *J* = 7.3 Hz, OC*H*$_2$CH$_3$), 3.78 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 5.52 (brs, 1H, NHCH$_2$ exchangeable with D$_2$O), 5.64 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.66-7.66 (m, 16H, Ar-H), 8.89 (s, 1H, NH indole exchangeable With D$_2$O); ^{13}C NMR (400 MHz, CDCl$_3$): δ 13.7, 14.8, 22.4, 34.7, 39.0, 46.9, 64.6, 67.5, 102.0, 103, 104.9, 107.3, 111.5, 111.7, 117.1, 120.9, 123.3, 124.0, 124.7, 126.8, 126.9, 127.1, 127.3, 128.1, 129.3, 137.0, 150.2, 151.1, 153.4, 154.1, 154.9, 155.6, 159.6, 171.7; MS: [M]$^+$ at *m/z* 660.16. Anal. Calcd for $C_{37}H_{34}ClN_7O_3$: C, 67.32; H, 5.19; N, 14.85. Found: C, 67.34; H, 5.21; N, 14.86%.

2-Ethyl-5-ethoxy - 3-((2-benzofuran-2-yl)-1-(pyridinylamino)methyl-3-(2-methoxyphenyl azo)-pyrazolin-4-yl)indole, 4l: Yield 66% (Petroleum ether); m.p. 262°C. IR (KBr): 1048 (C-O-C), 1290 (N-N), 1426 (N=N), 1595 (C=N), 1629 (C⎓C of aromatic ring), 1729 (C=O, COCH$_3$), 3362 cm^{-1} (NH); ^{1}H NMR (CDCl$_3$): δ 1.62 (t, 3H, *J* = 7.0 Hz, CH$_2$C*H*$_3$), 2.36 (t, 3H, *J* = 7.3 Hz OCH$_2$C*H*$_3$), 2.87 (q, 2H, *J* = 7.2 Hz, C*H*$_2$CH$_3$), 3.10 (t, 2H, *J* = 6.0 Hz, C*H*$_2$CH$_2$), 3.28 (q, 2H, *J* = 7.2 Hz, CH$_2$NH), 3.55 (s, 3H, OCH$_3$), 3.72 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 3.92 (q, 2H, *J* = 7.3 Hz, OC*H*$_2$CH$_3$), 5.57 (brs, 1H, NHCH$_2$ exchangeable with D$_2$O), 5.62 (d, 1H, *J* = 7.5 Hz, CH of pyrazoline ring), 6.79-7.99 (m, 16H, Ar-H), 8.90 (s, 1H, indole exchangeable With D$_2$O); ^{13}C NMR (400 MHz, CDCl$_3$): δ 13.7, 14.8, 22.4, 34.7, 39.0, 46.9, 55.8, 64.6, 67.5, 102.0, 103, 104.9, 107.3, 111.5, 111.7, 117.1, 114.8, 120.9, 121.5, 121.7, 122.8, 123.3, 123.6, 124.7, 126.8, 126.9, 137.0, 150.2, 152.8, 153.4, 154.1, 154.9, 155.6, 159.6, 171.7. MS: [M]$^+$ at *m/z* 655.74. Anal. Calcd for $C_{38}H_{37}N_7O_4$: C, 69.60; H, 5.69; N, 14.95. Found: C, 69.58; H, 5.68; N, 14.93%.

Conclusion

The antiparkinsonian activities of the synthesized compounds were determined by *in vivo test*. The experimental data of all the compounds of this series have been reported in **Table Ia**,

Anti-tremor activity

Among all the compounds, compounds **3b, 3c, 3k, 4a, 4d,** and **4k** showed moderate antitremor activity.

Furthermore, compounds **3g, 3j, 4c, 4e, 4g, 4j** and **4l** exhibited good antitremor activity. The compounds **3a, 3d, 3e, 4b** and **4f** showed interesting response against oxotremorine induced tremors. Moreover, compound **4h** (having 2-chlorophenyl moiety) have shown maximum anti-tremor activity (2.10 ± 0.10 score).

Antirigidity activity

Compounds **4b, 4e** and **4f** significantly antagonized the reserpine induced rigidity. Furthermore, compounds **3b-3e, 3i, 3k, 3l, 4c, 4g, 4i, 4k** and **4l** showed good activity *i.e.* 50-60%. The compound **4h** has shown 90% response against reserpine induced rigidity.

Antihypokinetic Activity

The compounds **3a, 3c, 3i, 4a** and **4d** showed moderate antihypokinetic activity, while compounds **3b, 3d, 4c, 4g** and **4i** exhibited good antihypokinetic activity. The compounds **3e, 3h, 3j, 3k, 3l, 4b, 4e, 4f, 4j, 4k,** and **4l** showed interesting activity. Moreover, compounds **4h** showed most potent (*i.e*, 90.10%) antihypokinetic activity.

Acute Toxicity

The newly synthesized compounds were also tested for lethal dose LD_{50} and were found to exhibit a high value of LD_{50} *i.e.* more than 1000 mg/kg i.p. except compound **4h** which exhibited LD_{50} of more than 1600 mg/kg i.p. (maximum dose tested). Therefore, all these compounds have shown high value of LD_{50} thus indicating good safety margin.

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