IJPSR (2014), Vol. 5, Issue 8 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 07 February, 2014; received in revised form, 11 April, 2014; accepted, 26 May, 2014; published 01 August, 2014

SYNTHESIS OF SOME 3, 5- DIPHENYL -Δ^1 –PYRAZOLINE AND 5-(2′′-FURYL)-Δ^1-PYRAZOLINE DERIVATIVES AND THEIR SCREENING FOR ANTIDEPRESSANT AND ANTICONVULSANT ACTIVITY

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Keywords:
Pyrazoline, Antidepressant, Anticonvulsant, Maximal Electroshock Seizure (MES), Porosolt's behavioral despair test.

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ABSTRACT: Sixteen 1-(substituted) phenyl, 1- thiocarbamoyl -3-phenyl-5-(2′′-Furyl) / Phenyl- Δ^1-pyrazoline derivatives were synthesized. The chemical structures were confirmed by IR, H^1 –NMR and analysis. The antidepressant activities of the compounds were investigated by Porosolt's behavioral despair test on albino mice. 3-phenyl-5-(2′′-chlorophenyl)-4,5-dihydro-1H-pyrazole-carbothioamide **(2_f),**1-(2,4-dinitrophenyl)-3-(3′-hydroxy-phenyl)-5-(2′′-methoxy phenyl)-4,5-di- hydro-1H-pyrazole **(2_k),** 1-(2,4-dinitro phenyl)-3-(3′ -hydroxyl phenyl)-5-furyl - 4,5-dihydro-1H-pyrazole **(2_m)** significantly reduced the duration of immobility times by 23.58-25.76% at 25mg kg^{-1} dose level using imipramine as standard reference. Anticonvulsant activities of the compounds were examined by Maximal Electroshock Seizure (MES) using Phenytoin as standard reference, and neurotoxicity were determined by Rotarod toxicity test on albino mice. 1-(2, 4-dinitrophenyl)-3-phenyl-5-(2′′chlorophenyl)-4,5-dihydro-1H-pyrazole**(2_e)**, 1-(2,4-dinitro phenyl) -3-(3′ -nitro phenyl)-5-furyl- 4, 5-dihydro-1H-pyrazole**(2_o),** and 3-(3′ -nitro phenyl)-5-furyl-4,5-dihydro-1H-pyrazole–thiocarbamide **(2_p)** had good protection against the Maximal Electroshock Seizure (M.E.S) at 20 mg kg^{-1} dose levels. These compounds (**2_f 2_k, 2_m, 2_e, 2_o, 2_p)** did not show any neurotoxicity in the Rotarod test at 20mg kg^{-1} dose levels.

INTRODUCTION: Recent research works in synthetic chemistry have suggested that pyrazoline derivatives possess significant biological activity such anticonvulsant [1], antidepressant [2], anti-hypertensive [3], anti-inflammatory [4-7], analgesic [6], anticancer [6-9], antimicrobial [9-14], antimycobacterial [15, 16], antiamoebic [17, 18], antimalarial [19] activities.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.5(8).3226-34

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.5(8).3226-34

Monoamine oxidase (MAO) inhibitors represent useful role in the treatment of several psychiatric and neurological diseases. Reversible and selective MAO-A inhibitors are used as antidepressant and anti anxiety drugs while MAO-B have been found to be useful as conjuvants in the treatment of Parkinson's disease and Alzheimer's disease [20].

The compounds having a great variety of substituted hydrazine behave like as MAO inhibitors [21-23]. Monoamine oxidase inhibitor (MAO) having hydrazide, hydrazine, and amino moieties such as isocarboxazide, phenelzine and

meclobemide have shown profound antidepressant activity in human. The structures of the synthesized 2-pyrazoline derivatives are very similar to those of isocarboxazide [24]. The studies by Parmal et al[2] demonstrated monoamine oxidase inhibitory activity of some 1,3,5-triphenyl -2-pyrazolines,1-thiocarbamoyl-3,5-diphenyl-2-pyrazolines and bicyclic pyrazoline in behavioral despair test. Again Bilgin *et al* [25] demonstrated the antidepressant and anticonvulsant activities of some 3-(2-furyl)-pyrazoline derivatives using despair and MES test respectively. Previously, Prasad *et al* [24] investigated antidepressant activities of some 1, 3, 5-triphenyl-2-pyrazoline and 3-(2-hydroxynaphthalene-1-yl)-1,5-diphenyl-2-pyrazolines by using Despair test. Hence researchers have tried to investigate MAO and other amine oxidase inhibition activity of 2-pyrazoline and found promising results [26-29].

The discovery of such class of drugs has led to a considerable increase in modern drug development. It has also pointed out the biological activity arising from structural modification of prototype drug molecule.

In present work some new 3, 5-diphenyl-2-pyrazoline derivatives and 5-(2'-furyl)-2-pyrazoline derivatives have been synthesized, and then evaluated for their antidepressant and anticonvulsant activities. The antidepressant activity of the synthesized compound was done by using Porosolt Behavioural Despair (force swimming) test. Anticonvulsant activity of the synthesized compounds was performed by Maximal Electroshock (MES) and subcutaneous Pentylene tetrazole test. The neurotoxicity was determined by Rota rod toxicity test.

MATERIALS AND METHODS:

Chemistry: All chemical used in this studies were supplied by E. Merck, Aldrich Chemical Co, and Fluka AG. All the reactions were monitored by TLC using silica gel G. The melting point determinations were done by using in open glass capillary using Kjeldahl flask containing liquid paraffin. IR spectra were recorded on the (Biored FTs) FTIR-spectrophotometer using KBr pellets. ^{1}H NMR spectra were recorded on Bruker model DRX-400 MHz NMR spectrometer in DMSO-d_6 using tetra methyl silane (TMS) as internal reference.

1. **Synthesis of chalcone derivatives:** Chalcone derivatives [1, 3-diphenyl prop-2-ene-1-ones **(I_{a-h})** and 3-furyl-1-phenylprop-2-ene-1-ones **(I_{i-k})**] were synthesized by condensing appropriate acetophenone and benzaldehyde derivatives and furfuryl aldehyde derivatives respectively in ethanolic sodium hydroxide at ice cold temperature according to Claisen - Schmidt condensation [30-32]. The solid which separated out was washed with water, dried and recrystalized with ethanol. The purity was checked by TLC in solvent system T.E.F(toluene: ethyl acetate: formic acid=5:4:1).

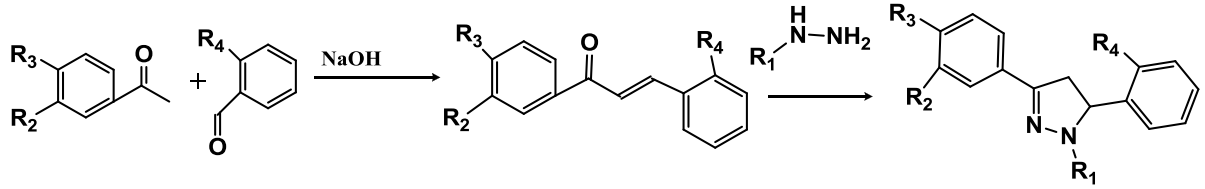
2. **Synthesis of 1, 3, 5-triphenyl-2-pyrazoline derivatives (2_a , 2_c ,2_d , 2_e,2_g ,2_i ,2_k and 2_l):** To a solution of appropriate chalcone (0.001mole) in absolute ethanol (20mL), appropriate hydrazine (such as 2, 4- dinitro phenyl hydrazine, phenyl hydrazine or hydrazine) was added. The reaction mixture was heated under reflux for 48 hrs and then cooled and poured into crushed ice. The solid pyrazoline product so obtained was filtered, washed with water, dried, and recrystalized from ethanol.

3. **Synthesis of 3,5 –diphenyl -4,5-dihydro-1-h-pyrazole- thio carbamide derivatives (2_b , 2_f ,2_h ,2_j)**: To a solution of appropriate chalcone (0.001ml) in absolute ethanol (40 mL), semi thio carbazide was added. The reaction mixture was heated under reflux for 24 hrs and then cooled, poured into crushed ice. The solid pyrazoline product was filtered, washed, and recrystallized from ethanol.

4. **Synthesis of 3-phenyl-5-(2′-furyl)-2-pyrazoIine derivatives. (2_m , 2_n , 2_o and 2_p):** To a solution of a appropriate chalcone (0.00 1mol) in absolute ethanol (20 mL), 2- dinitro phenyl hydrazine or thiosemicarbazide (wherever required) was added. The reaction mixture was reflux for 30 hrs and then cooled, poured into crushed ice. The solid so obtained was filtered, washed, and recrystallized from ethanol.

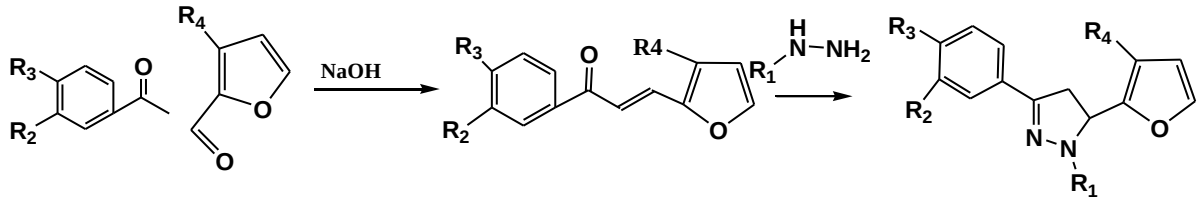
REACTIONS:

A)

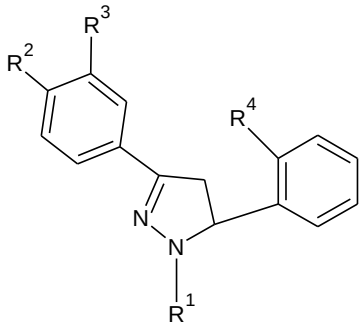


Compounds $\mathbf{2_{a-l}}$

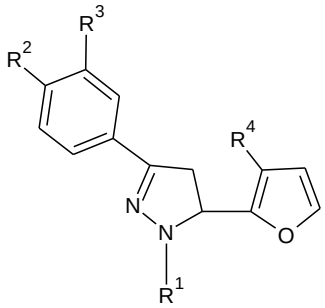
B)



Compounds 2 $_{\mathbf{m-p}}$



Compounds $\mathbf{2_{a-l}}$



Compounds $\mathbf{2_{m-p}}$

Pharmacology: Albino male rats/ mice of Wistar strain (150±10 g), 4–6-week-old, were obtained from Central Animal House of Hamdard University, New Delhi. They were housed in polypropylene cages in groups of 5 rats per cage and kept in a room maintained at 25±2°C with a 12-h light/dark cycle. They were allowed to acclimatize for one week before the experiments and were given free access to standard laboratory feed (Amrut Laboratory, rat and mice feed, Navmaharashtra Chakan Oil Mills Ltd, Pune, India) and water *ad libitum*.

Approval to perform the animal experiment was obtained from Institutional Animal Ethics Committee (IAEC) registered under the Committee for the Purpose of Control and Supervision of Experimental Animals (173/ CPCSEA).

1. **Antidepressant activity:** The antidepressant activity of the synthesized compound was performed using Porosolt's Behavioral Despair (forced swimming) test [33]. Male albino mice were used in the Despair test. The mice were randomly divided into ten groups of six mice each. The reference compound used in this biological screening was imipramine. The synthesized compounds (25 mg kg^{-1}) and imipramine 25 mg kg^{-1} were suspended in propylene glycol. Imipramine and propylene glycol were administered intra-peritoneally in a volume of 0.5ml/kg body weight 1hr prior to test. Imipramine and propylene glycol were administered intra- peritoneally in a volume of 0.5ml/kg body weight 1hr prior to test. Then the mice were placed into the vertical Plexiglas cylinder filled with water, maintained at 25C, for 15 minute.

5-6 minute later the immobility reaches plateau where the mice remain immobile for approximately 80% of the time. The mice was judge immobile if it floats in the water in an upright position and made only slight movement in order to prevent sinking. The duration of immobility was recorded during the 5 minute test. The antidepressant drug reduced duration of immobility.

2. **Anticonvulsant activity:** Stimulator, constant current unit, and corneal electrode (manufactured by Hicon) were used for the evaluation of anticonvulsant activity. The Rota rod used in the neurotoxicity test was made by Hicon. The E. Merck Company provided phenytoin, which was used as a standard drug in the MES test.

a. **Maximal Electroshock seizure (MES)** [34]**:** Anticonvulsant activity of the synthesized compound was also screened by using MES (Maximal Electro Shock) test method. Male albino mice were used in the MES test. The mice were randomly divided into ten groups of six mice each.

The Albino mice were kept under condition at an ambient temperature of 25±2 ºC. Food and water were withdrawn prior to the test. The synthesized compounds were suspended in propylene glycol. Phenytoin was used as standard drug. The drugs and the standard compounds were administered intraperitoneally in a standard volume of 0.5ml/20g body weigh at a dose of 20 mg/kg. Supra maximal electro shock of 54 mA, 60 Hz was given to mice for 0.2 sec through corneal electrodes. The abolition of the hind limb tonic extensor spasm was recorded as an increased anticonvulsant activity.

3. **Neurotoxicity** [35]**:** The neurotoxicity of the synthesized compounds was investigated by using Rota rod Tread mill mouse test (U. Basile). The mice were placed on a rotating rod (24rpm) and observed for 5min .The skeletal muscle relaxation induced by a test compound can be evaluated by testing the ability of mice or rats to remain on a revolving rod. The dose which impairs the ability of 50% of the mice to remain on the revolving rod is considered as the end point. The synthesized compound were administered by i p route at a dose of 20 mg/kg body weight and neurotoxicity was measured after 30 minute.50% or more passed the neurotoxicity testing, when the compounds did not show neurological deficit.

RESULT AND DISCUSSION: The structures, yields and melting points of the compounds have been given in the **table 1**. Melting points of the synthesized compounds were sharp indicating that the compounds were pure; the yield value of the compounds also suggested that the chemical methods were reliable for the synthesis of the compound. All spectral data were in accordance with assumed structures (Table 2). The IR spectra of the compounds containing pyrazoline unit exhibited the absorption bands for C=N stretching (1518-1527 cm^{-1}), C^4-H deformation, C^5-N stretching (1054-1077 cm^{-1}), methoxyl group, –O-C stretching (1180-1190cm^{-1}), thiocarbamoyl group, N-H stretching (3420-3450 cm^{-1}) and phenyl group –O-H stretching (3610-3640 cm^{-1}). In the ^1H NMR spectra (**Table 2**) of the compounds H_A, H_B and H_X protons of pyrazoline ring were observed as double doublet at 2.90-3.04 (J_{AB} : 17.23-17.76 Hz) , δ 3.56-3.82 (J_{BX} : 11.44-1171 Hz) and δ 5.91-5.99 (J_{AX} : 11.52-11.70 Hz)respectively. N-H proton of the thiocarbamoyl group was observed at δ 8.22-8.51. The protons of phenyl groups, benzene, hydroxyl group and methoxyl group, furan ring were observed at their expected ppm values.

The despair test was used to determine the efficacy of anti depressant activity. For predicting the activity of a large number of anti depressants such as MAO inhibitors and atypical antidepressant, the forced swimming test is generally used. It is a reliable test by which the antidepressant potency in human can be predicted more precisely [33]. The data obtained on the anti depressant activity of the compounds and references are given in the **table 2.** In our study 3-phenyl-5-(2″-chlorophenyl)-4,5-dihydro-1H-pyrazole-carbothioamide **(2_f),** 1-(2,4-dinitro phenyl)-3-(3′-hydroxy- phenyl)-5-(2″-methoxyphenyl)-4,5-di- hydro-1H-pyrazole**(2_k),** 1-(2,4-dinitrophenyl)-3-(3′-hydroxyphenyl)-5-furyl-4,5-dihydro-1H-pyrazole **(2_m)** significantly reduced the duration of immobility when compared to control ($p<0.05$, Table 2).

TABLE 1: PHYSICOCHEMICAL PARAMETERS OF THE COMPOUNDS

Compounds	R^1	R^2	R^3	R^4	Yield (%)	Melting point (^{0}C)
2_a	Phenyl	H	H	$-OCH_3$	48	182-184
2_b	$-CSNH_2$	H	H	$-OCH_3$	45	121-123
2_c	2,4-dinitro phenyl	H	H	$-OCH_3$	56	161-164
2_d	H	H	H	$-OCH_3$	67	176-178
2_e	2,4-dinitrophenyl	H	H	-Cl	40	179-182
2_f	$-CSNH_2$	H	H	-Cl	55	132-134
2_g	2,4-dinitrophenyl	$-OCH_3$	$-OCH_3$	-Cl	70	181-182
2_h	$-CSNH_2$	$-OCH_3$	OCH_3	$-OCH_3$	73	128-130
2_i	24-dinitrophenyl	H	-OH	-Cl	56	211-213
2_j	$-CSNH_2$	H	-OH	--Cl	65	197-200
2_k	2,4-dinitrophenyl	H	-OH	$-OCH_3$	56	167-169
2_l	2,4-dinitrophenyl	H	$-NO_2$	$-OCH_3$	70	133-135
2_m	2,4-dinitrophenyl	H	-OH	-H	56	128-130
2_n	$-CSNH_2$	H	-OH	-H	63	121-124
2_o	2,4-dinitrophenyl	H	$-NO_2$	-H	68	143-145
2_p	$-CSNH_2$	H	$-NO_2$	-H	64	156-159

TABLE 2: SPECTRAL DATA OF THE SYNTHESIZED COMPOUNDS

Compounds	FTIR (KBr, cm^{-1})	H^1 NMR ($CDCl_3$,ppm)[a]
2_a	1600 (C=C_{str} aromatic);1520(C=N_{str}) 1180(O-CH_3); 1065(C-N_{str}).	2.98 (1H;dd;$H_{,}$ J_{AB}:17.57Hz, J_{AX}:3.71Hz), 3.72 (1H;dd;$H_{B,}$ J_{AB}: 17.57Hz , J_{AX}:11.63Hz), 3.83 (3H, s, OCH_3) ,5.98 (1H;dd;$H_{X,}$ J_{AX}:3.68Hz, J_{BX}: 11.66Hz) 7.10-7.55 (Benzene)
2_b	3450 (N-H_{str} , in NH_2);1680(-C=S_{str}) 1610 (C=C_{str} aromatic); 1525(C=N_{str}); 1187(O-CH_3); 1057(C-N_{str})	2.90 (1H;dd;$H_{A,}$ J_{AB}:17.65Hz,J_{AX}:3.48Hz), 3.72 (1H;dd;$H_{B,}$ J_{AB}: 17.65Hz , J_{AX}:11.67Hz), 3.79 (3H, s, OCH_3),5.93(1H;dd;$H_{X,}$ J_{AX}:3.35Hz, J_{BX}: 11.70Hz), 7.00-7.55 (Benzene), 8.24 (2H ,s, NH_2)
2_c	1605 (C=C_{str} aromatic). 1523(C=N_{str})1480,1510(-NO_2) ; 1183(O-CH_3); 1070(C-N_{str});	3.01 (1H;dd;$H_{A,}$ J_{AB}:17.70Hz,J_{AX}:3.58Hz),3.65 (1H; dd;$H_{B,}$ J_{AB}:17.57Hz, J_{AX}:11.63Hz), 3.83 (3H, s, OCH_3),5.98 (1H;dd;$H_{X,}$ J_{AX}:3.68Hz, J_{BX}: 11.66Hz), 7.10-7.55 (Benzene) ,7.61(1H; d;H^{10}), 7.79 (1H;d; H^{11}) , 8.22 (1H;s;H^8),
2_d	3475(N-H $_{str}$). 1600 (C=C_{str} aromatic); 1520(C=N_{str});1180(O-CH_3); 1065(C-N_{str})	2.98(1H;dd;$H_{A,}$ J_{AB}:17.61Hz,J_{AX}:3.45Hz), 3.70 (1H;dd;$H_{B,}$ J_{AB}: 17.55Hz , J_{AX}:11.71Hz), 3.85 (3H, s, OCH_3) ,5.93 (1H;dd;$H_{X,}$ J_{AX}:3.39Hz, J_{BX}: 11.61Hz), 6.25 (1H;d;H_Y, J_{XY}:14.43Hz) ,7.00 -7.55 (Benzene),7.99 (1H;s; N=N-H)
2_e	1605 (C=C_{str} aromatic). 1520(C=N_{str}); 1480,1510(-NO_2) ; 1070(C-N_{str}); 855 (-C-Cl_{str})	2.96(1H;dd;$H_{A,}$ J_{AB}:17.64Hz,J_{AX}:3.61Hz),3.69 (1H; dd; $H_{B,}$ J_{AB}:17.64Hz, J_{AX}:11.56Hz),5.93(1H; dd;H_X; J_{AX}:3.67Hz, J_{BX}: 11.52 Hz) ,7.10-7.55 (Benzene), 7.63(1H; d;H^{10}),7.78 (1H;d; H^{11}),8.32 (1H ;s;H^8)
2_f	3428 (N-H_{str} , in NH_2);1690(-C=S_{str}) 1605 (C=C_{str} aromatic). 1520(C=N_{str}); 1070(C-N_{str}); 855 (-C-Cl_{str})	3.04(1H;dd;$H_{A,}$ J_{AB}:17.57Hz,J_{AX}:3.55Hz), 3.75 (1H;dd;$H_{B,}$ J_{AB}:17.67Hz , J_{AX}:11.71Hz),5.93(1H;dd; $H_{X,}$ J_{AX}:3.35Hz, J_{BX}:11.70Hz),7.25-7.55 (Benzene), 8.22(2H ,s, NH_2)
2_g	1605 (C=C_{str} aromatic). 1520(C=N_{str}); 1480(-NO_2 *at C-7&9)* ; 1180(O-CH_3); 1070(C-N_{str}); 855 (-C-Cl_{str})	3.01 (1H;dd;$H_{A,}$ J_{AB}:17.70Hz,J_{AX}:3.58Hz), 3.65 (1H;dd;$H_{B,}$ J_{AB}:17.57Hz, J_{AX}:11.63Hz), 3.95 (3H, s, OCH_3 *at C-15*) , 4.10 (3H, s, OCH_3 *at C-16*) 5.98 (1H;dd;$H_{X,}$ J_{AX}:3.68Hz, J_{BX}:11.66Hz), 7.10-7.55 (Benzene) ,7.65(1H; d;H^{10}),7.81 (1H;d; H^{11}) ,8.25 (1H; s, H^8)
2_h	3450 (N-H_{str} , in NH_2);1685(-C=S_{str}) 1607 (C=C_{str} aromatic); 1521(C=N_{str}); 1185(O-CH_3); 1054(C-N_{str})	2.96 (1H;dd;$H_{A,}$ J_{AB}:17.72Hz,J_{AX}:3.45Hz), 3.67 (1H;dd ;$H_{B,}$ J_{AB}:17.57Hz , J_{AX}:11.54Hz), 3.79 (3H, s, OCH_3 *at C-19*) ,3.89(3H, s, OCH_3 *at C-16*), 4.10 (3H, s, OCH_3 *at C-17*) , 5.97 (1H; dd; $H_{X,}$ J_{AX}:3.41Hz, J_{BX}: 11.62Hz), 7.10-7.50 (Benzene), 8.22 (2H,s,NH_2)

2_i	3610 (-O-H_{str}) 1605 (C=C_{str} aromatic). 1520(C=N_{str});1480,1510(-NO_2) ; 1072(C-N_{str}); 857 (-C-Cl_{str})	2.96 (1H;dd;H_A, J_{AB}:17.67Hz,J_{AX}:3.62Hz),3.56 (1H;dd;H_B, J_{AB}: 17.65Hz, J_{AX}:11.57Hz),5.98 (1H;dd;H_X, J_{AX}:3.68Hz, J_{BX}: 11.66Hz), 6.31(1H;s; *phenolic –OH at C- 14*) 7.10-7.55 (Benzene) ,7.61(1H; d;H^{10}),7.79 (1H;d; H^{11}) ,8.25 (1H; s, H^8),
2_j	3630 (-O-H_{str}) ;3440 (N-H_{str} , in NH_2); 1680(-C=S_{str})1612 (C=C_{str} aromatic). 1521(C=N_{str}); 1073(C-N_{str}); 858 (-C Cl_{str})	2.94(1H;dd;H_A, J_{AB}:17.23Hz,J_{AX}:3.87Hz), 3.78 (1H;dd;H_B, J_{AB}: 17.53Hz , J_{AX}:11.65Hz), 5.57(1H;s ; *phenolic –OH at C- 10*),5.93 (1H; dd; H_X,J_{AX}:3.43Hz, J_{BX}:11.54Hz), 7.15-7.55 (Benzene),8.37(2H ,s; NH_2),
2_k	3625(-O-H_{str}) 1613 (C=C_{str} aromatic). 1520(C=N_{str});1490,1515(-NO_2) ; 1190(O-CH_3); 1076(C-N_{str});	2.96 (1H;dd;H_A, J_{AB}:17.75Hz,J_{AX}:3.54Hz), 3.67 (1H;dd;H_B, J_{AB}: 17.59Hz, J_{AX}:11.56Hz), 3.78 (3H, s, OCH_3) 5.54(1H;s ; *phenolic –OH at C- 14*),5.94 (1H;dd;H_X, J_{AX}:3.63Hz, J_{BX}:11.61Hz), 7.23-7.45 (Benzene) ,7.68(1H; d;H^{10}),7.82 (1H;d; H^{11}) , 8.26 (1H;s; H^8)
2_l	1619 (C=C_{str} aromatic). 1527(C=N_{str}); 1523(-NO_2*at C-7,C-9 &C-14*) ; 1185(O-CH_3); 1070(C-N_{str});	2.99(1H;dd;H_A, J_{AB}:17.73Hz,J_{AX}:3.61Hz), 3.57 (1H;dd;H_B, J_{AB}: 17.55Hz, J_{AX}:11.67Hz), 3.84 (3H, s, OCH_3) ,,5.94 (1H;dd;H_X, J_{AX}:3.63Hz, J_{BX}: 11.61Hz), 7.21-7.44 (Benzene) ,7.64 (1H;d;H^{10}), 7.81 (1H;d;H^{11}) , 8.28 (1H;s; H^8)
2_m	3625 (-O-H_{str}), 1611 (C=C_{str} Bz). 1573(C=C_{str}Furan) 1518(C=N_{str}); 1487,1512(-NO_2) ; 1068(C-N_{str});	2.97(1H;dd;H_A, J_{AB}:17.76Hz,J_{AX}:3.68Hz), 3.65 (1H;dd;H_B, J_{AB}: 17.64Hz, J_{AX}:11.57Hz), 5.54(1H;s ; *phenolic –OH at C- 14*) ,5.91 (1H;dd; H_X, J_{AX}:3.67 Hz, J_{BX}: 11.56 Hz) ,6.41 (1H;m;Furan H^3), 6.67 (1H; d;J_{AB}:3.48 Furan H^4),7.23-7.45(Furan H^2 Benzene) ,7.63(1H; d;H^{10}),7.85 (1H;d; H^{11}) , 8.27 (1H;s; H^8)
2_n	3640 (Ar-O-H_{str}) ;3420 (N-H_{str} , in NH_2); 1670(-C=S_{str}) 1605 (C=C_{str} Bz). 1564(C=C_{str} Furan) 1524(C=N_{str}); 1077(C-N_{str});	2.98(1H;dd;H_A, J_{AB}:17.33Hz,J_{AX}:3.93Hz), 3.82(1H; dd;H_B, J_{AB}: 17.56Hz , J_{AX}:11.59Hz), 5.61(1H;s ; *phenolic –OH at C- 17*),5.97 (1H; dd; H_X, J_{AX}:3.53 Hz, J_{BX}:11.67Hz), 6.45(1H;m; Furan H^3) ,6.62 (1H;d; J_{AB}:3.52 Furan H^4) 7.08-7.45 (Furan H^2 Benzene), 8.49 (2H ,s; NH_2),
2_o	1615 (C=C_{str}).1570(C=C_{str}Furan) 1518(C=N_{str});1487,1512(-NO_2) ; 1063(C-N_{str});	2.89(1H;dd;H_A, J_{AB}:17.69Hz,J_{AX}:3.63Hz), 3.67 (1H;dd;H_B, J_{AB}: 17.64Hz, J_{AX}:11.44Hz), 3.82 (3H, s, OCH_3) ,5.96 (1H;dd; H_X, J_{AX}:3.62Hz, J_{BX}: 11.56 Hz) , 6.44 (1H;m;Furan H^3),6.57(1H;d;J_{AB}:3.43 Furan H^4) 7.17-7.45 (Furan H^2 Benzene) ,7.54(1H; d;H^{15}),7.85 (1H;d; H^{16}) , 8.27 (1H;s; H^{13})
2_p	3421 (N-H_{str} , in NH_2); 1665(-C=S_{str}) 1607 (C=C_{str} Bz). 1566(C=C_{str}Furan) 1520(C=N_{str}); 1508(-NO_2) 1068(C-N_{str});	2.93(1H;dd;H_A, J_{AB}:17.38Hz,J_{AX}:3.98Hz), 3.79(1H;dd;H_B, J_{AB}: 17.77Hz , J_{AX}:11.54Hz), 5.99 (1H; dd; H_X, J_{AX}:3.59Hz, J_{BX}: 11.62Hz), 6.42 (1H;m; Furan H^3) , 6.66 (1H;d;J_{AB}: 3.52 Furan H^4) 7.06-7.40 (Furan H^2 Benzene), 8.51 (2H ,s; NH_2) ,

s = singlet; d = doublet; dd = double doublet; m = multiple

The anticonvulsant activity of the synthesized compounds was also performed and results obtained from this experiment are shown the **table 3**.

In the M.E.S test , it had been found that the compounds 1-(2, 4-dinitrophenyl)-3-phenyl-5-(2″chlorophenyl) -4, 5- dihydro-1H-pyrazole **(2_e)** , 3-(3′-hydroxyphenyl)-5-furyl-4,5-dihydro-1H-pyrazole-thiocarboamide **(2_n),** 1-(2,4-dinitrophenyl) -3-(3′-nitrophenyl)-5-furyl-4,5-dihydro-1H-pyrazole**(2_o),** and 3-(3′ -nitro phenyl)-5-furyl-4,5-dihydro-1H-pyrazole–thiocarboamide **(2_p)** were found to have protection against the Maximal Electroshock Seizure (M.E.S).

Only three compounds such as 1-phenyl-3-phenyl-5-(2″-methoxyphenyl)-4,5-dihydro-1H-pyrazole**(2_a),** 3-phenyl-5-(2″-methoxy phenyl)-4,5-dihydro-1H-pyrazole-1-carbothioamide**(2_b),**1-(2,4-dinitro-phenyl)-3-phenyl-5-(2″-methoxyphenyl)-4,5-dihydro -1H-pyrazole **(2_c)** showed neuro-toxicity in Rotarod test (**Table 4**).

TABLE 3: ANTIDEPRESSANT ACTIVITIES OF THE COMPOUNDS

Compounds	Immobility time ± S.E.M	% Immobility
2_a	235.9 ± 15.7	100.00
2_b	183.7±8.7	80.23
2_c	195.5±7.6	77.87
2_d	186.4±3.4	79.14
2_e	184.0± 12.1	77.99
2_f	179.9± 5.6	76.26
2_g	198.7± 9.9	84.23
2_h	206.4 ± 10.7	87.57
2_i	185.7 ± 8.9	78.71
2_j	216.6± 12.7	91.77
2_k	176.3± 14.8	74.73
2_l	187.2± 13.7	79.35
2_m	178.6± 9.7	75.71
2_n	197.3±12.8	83.63
2_o	209.8± 17.2	88.93
2_p	189.7± 15.4	80.41
Vehicle	215.0± 13.1	100.00
Imipramine	176.3± 14,9	82.00

Value represent the mean ± S.E.M. (n=6)

TABLE 4: ANTICONVULSANT SCREENING OF THE COMPOUNDS

Compounds	% Protection	Recovery
2_a	66.00	Late
2_b	83.33	Soon
2_c	87.56	Soon
2_d	50.45	Late
2_e	90.34	Very Soon
2_f	78.23	Soon
2_g	73.32	Soon
2_h	89.15	Soon
2_i	56.54	Late
2_j	68.43	Soon
2_k	52.05	Late
2_l	74.67	Soon
2_m	87.76	Soon
2_n	89.57	Very soon
2_o	100.00	Very soon
2_p	100.00	Very soon
Phenytoin	100.00	Very soon

TABLE 5: NEUROTOXIC ACTIVITY OF THE COMPOUNDS

Compounds	Dose(mg/kg)	Result
2_a	20	(-)
2_b	20	(-)
2_c	20	(-)
2_d	20	(+)
2_e	20	(+)
2_f	20	(+)
2_g	20	(+)
2_h	20	(+)
2_i	20	(+)
2_j	10	(+)
2_k	10	(+)
2_l	10	(+)
2_m	10	(+)
2_n	10	(+)
2_o	10	(+)
2_p	10	(+)

The (+) sign indicates 50% or more passed the neurotoxicity testing. The (-) sign indicates 50% or more failed the neurotoxicity testing.

CONCLUSION: Only three of the synthesized compounds (2_f, 2_k and 2_m) have shown significant antidepressant activity. Four synthesized compounds such as 2_e, 2_n, 2_o and 2_p have profound anticonvulsant activity. It has been observed that the synthesized compounds having a furyl substituent at 5th position of pyrazoline ring have notable anticonvulsant activity. Therefore they can be considered to be promising compounds for their anticonvulsant activity. The development of 3, 5-2-pyrazoline and 5-(2′-furyl)-2-pyrazoline may be more active and safe antidepressant and anticonvulsants and are expected as the lead compounds for the future development for the newer compounds.

ACKNOWLEDGEMENT: The authors are thankful to the Head, Department of Pharmaceutical Chemistry, Jamia Hamdard, for providing necessary research facilities and in-charge of animal house for providing animals for conducting biological screening of the compounds and UGC, New Delhi for providing the GATE scholarship for conducting the Present research work.

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How to cite this article:
Rahaman T, Khan MA and Ahmed B: Synthesis of some 3, 5- diphenyl -Δ^1 –pyrazoline and 5-(2″-furyl)-Δ^1-pyrazoline derivatives and their screening for antidepressant and anticonvulsant activity. Int J Pharm Sci Res 2014; 5(8): 3226-34.doi: 10.13040/IJPSR.0975-8232.5(8).3226-34