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SYNTHESIS AND ANTIDEPRESSANT ACTIVITY OF PYRAZOLINE-5-ONE DERIVATIVE

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ABSTRACT

Pyrazoline are prominent nitrogen containing heterocyclic compounds posses various pharmacological activities. In our study we synthesized pyrazoline-5-one derivatives. Synthesized compounds were characterized by using UV, IR and ^{1}H NMR. Characterized compounds were screened for Anti depressant activity was by force swim test method. Compound 2 and 5 posses potent antidepressant activity.

Key words: Pyrazoline-5-one derivatives, Anti depressant activity, force swim test

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INTRODUCTION

Many heterocyclic compounds due to their specific activity are employed in the treatment of many infectious diseases. Their use in the treatment is attributed to their inherent toxicity to various pathogens. The title compound (Pyrazoline) is five-membered heterocyclic having two adjacent nitrogen atoms within the ring. It has only one endocyclic double bond and is basic in nature. It plays a crucial role in the development of theory in heterocyclic chemistry and is also extensively used as useful synthons in organic synthesis. Bulky groups in both the 4- and 5-positions improved both the fluorescence efficiency and the stability to light of the molecule. It

has significance for the design of pyrazoline whitening agents. Aryl group at position-5 is also responsible for spiroconjugated charge transfer quenching of pyrazoline fluorescence. Pyrazolines are well known and important nitrogen containing 5-membered heterocyclic compounds and various methods have been worked out for their synthesis. Numerous pyrazoline derivatives have been found to possess considerable biological activities, which stimulated the research activity in this field.

Pyrazoline are prominent nitrogen containing heterocyclic compounds play important role in medicinal chemistry. Considerable attention has been focused on pyrazoline derivatives due to their interesting biological activities. They have found to possess antifungal (1), antibacterial (2), antidepressant (3), anticonvulsant (4), anti-inflammatory (5) anti-tumor (6), antidiabetic (7), analgesic properties (8). Pyrazole ring is a prominent structural moiety found in numerous pharmacologically active compounds. Hence we aimed to synthesis pyrazoline-5-one derivatives and its antidepressant screening.

MATERIALS AND METHODS

MATERIALS

Aniline, chloroaniline, bromoaniline, toluidine, ethyl acetoacetate, sodium acetate, carbazide, glacial acetic acid, methanol and ethanol were purchased from Merck Spl Ltd, Mumbai.

METHODS

Synthetic method (9)

Aniline and different derivatives were diazotized and diazonium salt solutions were filtered directly into a cold solution of ethyl acetoacetate and sodium acetate, to get Ethyl-2(Substituted Phenyl) Hydrazone-3-Oxobutyrates). The diazotized product and carbazide was dissolved in glacial acetic acid separately and the mixture was refluxed for 4hrs, to get pyrazoline-5-one derivative (Fig-1) and synthesized compounds were characterized by using UV, IR and ^{1}H NMR.

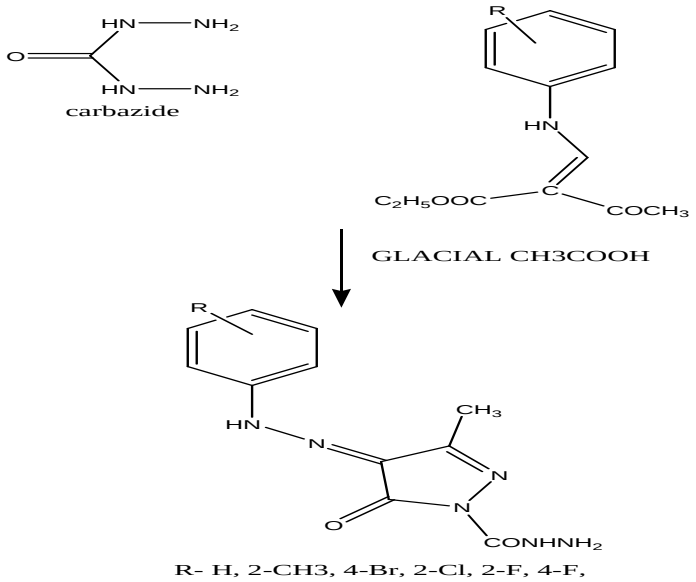

Fig-1 Scheme of synthesis of pyrazoline 5-one

Compound-1: [4-[(Phenyl) hydrazono] 3-methyl-2-pyrazolin-5-one

U V- λmax at 372nm. I.R (KBR pellet) NH (3300cm-1), C=O (1730cm-1), CO (1200cm-1), C=N (1600 cm-1). 1H NMR (CDCl3): d 0.9 (s, 3H, CH3), d 7.0 (s, 1H, NH), d 7.02-7.27 (m, 9H, Ar-H).

Compound-2: [4-[(2-methyl phenyl) hydrazono] 3 methyl -2 pyrazolin-5-one]]

U V- λmax at 434nm. I.R (KBR pellet) NH (3300cm-1), C=O (1730cm-1), CO(1200cm-1), C=N (1600 cm-1). 1H NMR (CDCl3): d 0.9 (s, 3H, CH3), d2.35 (s, 3H, CH3), d 7.0 (s, 1H, NH), d 7.02-7.27 (m, 8H, Ar-H).

Compound-3: [4-[(4-Bromophenyl) hydrazono] 3-methyl-2-pyrazolin-5-one]

U V- λmax at 415nm. I.R (KBR pellet) NH (3300cm-1), C=O (1730cm-1), CO (1200cm-1), C=N (1600 cm-1). 1H NMR (CDCl3): d 0.9 (s, 3H, CH3),d 7.0 (s, 1H, NH), d 7.02-7.27 (m, 8H, Ar-H).

Compound-4: [4-[(2-Chlorophenyl) hydrazono] 3-methyl-2-pyrazolin-5-one]

U V- λmax at 425nm. I.R (KBR pellet) NH (3300cm-1), C=O (1730cm-1), CO(1200cm-1), C=N (1600 cm-1). 1H NMR (CDCl3): d 0.9 (s, 3H, CH3), d 7.0 (s, 1H, NH), d 7.02-7.27 (m, 8H, Ar-H).

Compound-5: [4-[(2-fluorophenyl) hydrazono] 3-methyl- 2-pyrazolin-5-one]

U V- λmax at 412nm. I.R (KBR pellet) NH (3300cm-1), C=O (1730cm-1), CO(1200cm-1), C=N (1600 cm-1). 1H NMR (CDCl3): d 0.9 (s, 3H, CH3), d 7.0(s, 1H, NH), d 7.02-7.27 (m, 8H, Ar-H).

Compound-6: [4-[(4-fluorophenyl) hydrazono] 3-methyl-2-pyrazolin-5-one]

U V-λmax at 428 nm. I.R (KBR pellet) NH (3300cm-1), C=O (1730cm-1), CO (1200cm-1), C=N (1600 cm-1). 1H NMR (CDCl3): d 0.9 (s, 3H, CH3), d 7.0 (s, 1H, NH), d 7.02-7.27 (m, 8H, Ar-H).

Determination of median lethal doses (LD_{50})

Animal's Swiss albino mice (20-25gm) and Male Sprague - Dawley rats (160-180) were maintained at standard diet and *ad libido*. The experiment protocol was approved from institutional ethical committee. The test compounds were dissolved in 3 % DMSO administered orally to different groups with increasing doses. Six animals were taken in each group. Mortality was determined after 24 hours of treatment. The dose, at which the 50 % mice survived, was considered as LD50 value of the compound (10).

Anti depressant activity

Male Sprague - Dawley rats weighing 160-180 grams were divided into eight groups of six animals each. The test groups received orally 20 mg/kg of each sample. The reference group received imipramine (5 mg/kg, p.o) while the control group received vehicle (1 % CMC). Naïve rats are individually forced to swim inside a vertical Plexiglas cylinder (height : 40 cm ; diameter : 18 cm ; containing 15 cm of water maintained at 25 ^{o}C). Floating behaviour during this 5 minutes period has been determined in different groups of rats. The percentage inhibition was calculated by the formula (11).

$$\text{Percentage Inhibition} = \frac{\text{Before treatment} - \text{After treatment}}{\text{Before treatment}} \times 100$$

RESULTS AND DISCUSSION

Synthetic procedures of compounds are given in the scheme. Synthesized compounds were characterized by using U V, I R and 1H NMR spectra. I.R spectrum of compound showed NH stretching peak at 3300cm-1, C=O stretching peak at 1730cm-1 ,C-O peak at 1200cm-1 , C=N peak at 1600 cm-1. 1H NMR spectra showed singlet peak at d 0.9 and d 7.0 for methyl and NH group and multiplet peak at d 7.02-7.27 for aromatic hydrogen. Anti depressant activity was evaluated by force swim test method, the animals which are immobile for less time considered as active. The results are given the table-1.

Table-1 Results of *in vivo* anti depressant activity of pyrazoline-5-one derivatives

S. No	Treatment	Immobile response in 5 minutes		Percentage response (%)
		Before treatment	After treatment	
1	Group-I Control (1% CMC)	3.25	3.25	-
2	Group-II Standard (Imipramine 5mg/kg.b.wt)	3.54	1.23	65
3	Group-III Compound-1(20mg/kg.b.wt)	3.69	2.27	45
4	Group-IV Compound-2 (20mg/kg.b.wt)	3.44	1.34	64
5	Group-V Compound-3 (20mg/kg.b.wt)	3.65	2.17	47
6	Group-VI Compound-4 (20mg/kg.b.wt)	3.55	2.54	35
7	Group-VII Compound-5 20mg/kg.b.w	3.47	1.45	62
8	Group-VIII Compound-6 20mg/kg.b.wt	3.57	2.67	31

CONCLUSION

Pyrazoline-5-one derivatives were synthesized. Synthesized compounds were screened for antidepressant activity. Compound 2 and compound 5 possess good antidepressant activity when compared to that of standard control (Imipramine). Further research is required to explore the possible mechanism of action of the synthesized compounds.

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