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RESEARCH ARTICLE

ANTI-INFLAMMATORY AND CNS ACTIVITIES OF (E)-4-(4-HYDROXY-3-METHOXYBENZYLIDENEAMINO) 1-5-DIMETHYL-2-PHENYL-1H-PYRAZOL-3(2H)-ONE.

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Abstract

The Schiff base (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one was prepared from 4-aminoantipyrine and 4-hydroxy-3-methoxybenzaldehyde by microwave oven method using standard procedure. Anti-inflammatory and CNS activities of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one were studied using albino rats of both the sexes. Animals were divided into four groups, each consisting of four animals. Group 1 served as control and Group 2 received standard drug. Group 3 received 200mg/kg of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one and Group 4 received 400mg/kg of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one. For the determination of anti-inflammatory activity, inflammation was induced used 1% Carrageenan. CNS depressant activity of the compound was measured by placing the rat individually in the Locomotor for 15min. The results obtained showed that the Schiff base was found to exhibited anti-inflammatory and CNS activities. The Anti-inflammatory activity determination showed that (E)-4-(4-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one (400mg/kg) was found to exhibit higher anti-inflammatory activity (90.82%) as that of standard diclofenac sodium(48.48%). The CNS depressant activity of (E)-4-(4-hydroxy-3-ethoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one exhibited closer CNS depressant activity (97.96%) as that standard chlorpromazine(98.01%).

Introduction

Various literature reviews the importance of Schiff bases [1]. The Schiff bases play a vital role and find its use in analytical chemistry, agriculture, dyes and polymer industries besides their utility as model systems in the field of bio-inorganic chemistry [2]. Schiff bases are the important compound owing to their wide range of biological activities and industrial application. They have been found to possess the pharmacological activities such as antimalarial[3], anticancer[4], antibacterial[5], antifungal[6], antitubercular[7], anti-inflammatory[8], analgesic[9], antiviral[10] and CNS[11] depressant etc. They also serve as a back bone for the synthesis of various heterocyclic compounds. In view of these above biological importance of Schiff base, we plan to synthesis (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one by standard procedure. The present work focus on the synthesis of the Schiff base by condensation method from 4-aminoantipyrine and 4-hydroxy -3-methoxybenzaldehyde in ethanol for thirty second in microwave oven. The

pharmacological activities like anti-inflammatory and CNS depressant activities were studied.

Material and Methods

Materials used

The chemical such as 4-aminoantipyrine, 4-hydroxy -3-methoxybenzaldehyde of E.merck grade and distilled ethanol were used.

Drugs

Diclofenac sodium(standard for anti-inflammatory) and Cholpromazine(standard for CNS) were chosen for our work.

Animals used

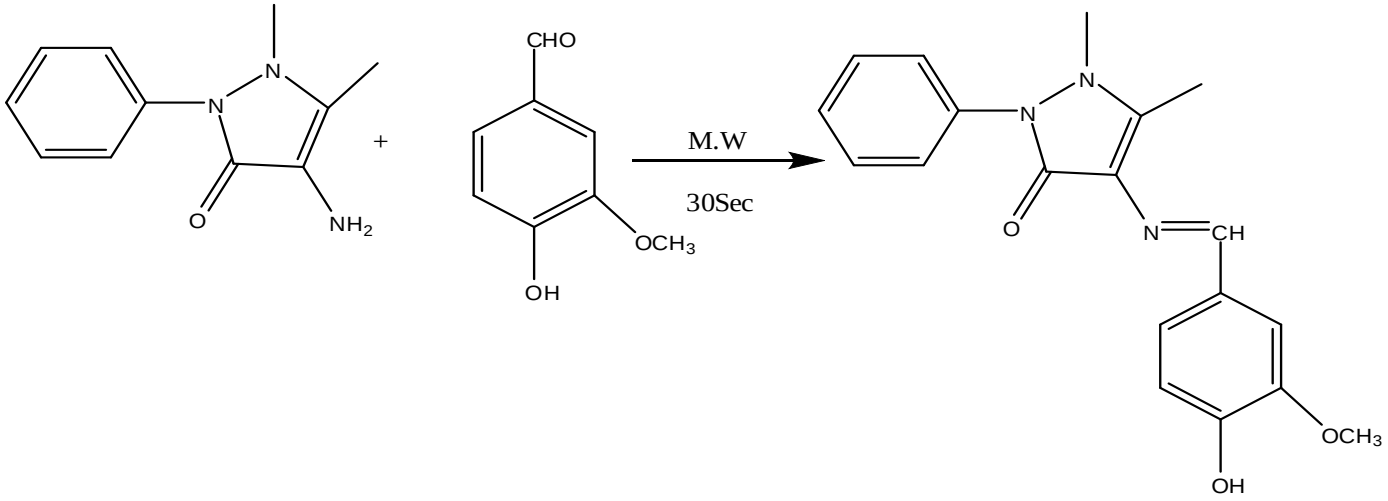
For the anti-inflammatory and CNS depressant activity studies twenty four albino rates of both sexes of weight 100-165g were used for each studies

Methods used

Preparation of Schiff bases

The 4-aminoantipyrine and 4-hydroxy -3-methoxybenzaldehyde were taken in a equimolar ratio of 0.005mol in ethanol (5ml). The reaction mixture was placed on microwave oven for thirty second. The product was isolated and crystallized from absolute ethanol. The yield and the melting point were noted. The melting point was determined using melting point apparatus

Yield – 92% M.pt-203°C



DETERMINATION OF ANTI-INFLAMMATORY ACTIVITY [12-13]

Carrageenan induced paw edema

Carrageenan-induced hind paw edema is the standard experimental model of acute inflammation. The animals were divided into four groups as *Control, Standard, group3 and group4.* Acute inflammation was produced by sub plantar injection of 0.1 ml of 1% suspension of carrageenan in normal *Saline*, in the right hind paw of the rats, one hour after oral administration of the drugs. The paw diameter was measured with the aid of a verniar caliper at 0, 15, 30 and 60mts after the injection of carrageenan. The difference between the readings at time zero mts(minutes) and the different time intervals were taken as the thickness of edema. With Diclofenac sodium (5mg/kg) as standard, *Group 3 and Group 4* were treated orally with (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one of 200 and 400 mg/kg dose levels of drugs by feeding needle and the paw diameter were measured at 0, 15, 30 and 60mts after the injection of the *standard,* (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one and the recorded values were given in **Table-1**. Percentage inhibition of paw edema was calculated by comparing the controls. The percentage inhibition of inflammation was calculated for each dose at different hours.

Percentage inhibition = 1- Vt / Vc *100

Where Vc = volume of paw edema in control animals

Vt = volume of paw edema in treated animals

CNS DEPRESSANT ACTIVITY [14]

CNS depressant activity-determination

Locomotor methods were employed to determine the CNS depressant activity.

Preparation of the drug for the experimental study:

Extracts and the standard drugs were administered in the form of suspension in water with 1% Sodium Carboxy Methyl Cellulose (SCMC) as suspending agent.

Effect on locomotor activity

Locomotor activity was recorded with a using a digital activity cage(Actophotometer). The animals were divided into four groups (n = 4). Each rat was individually placed in the actophotometer for 10 min. animals of Group 1was treated orally with Caffeine (30 mg/kg) (p.o.), group 2 was intraperitoneally treated with Chlorpramazine 3 mg/kg (i.p.). Group3 (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one of 200 mg/kg dose levels of drug. Group 4 was treated orally with (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one of 400 mg/kg dose levels of drug.

Basal reaction time was noted before and 30 mts after the administration of treatment. A count was recorded when the beam of light falling on the photocell of actophotometer was cut off by rat Sample 1 received reference standard Chlorpramazin at a dose of 3 mg/kg (i.p.) 30 min before the test. Mean change in the locomotor activity was recorded for each group. The recorded values were listed in **Table-2**

Anti-inflammatory and CNS depressant activities were determined at SB College of Pharmacy, Anaikuttam, Virudhunagar district.

Table- 1, Anti-inflammatory activity of (E)-4-(4-hydroxy-3- methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one

Treatment	Dose	Mean time (in second) ± SEM		
		15mts	30mts	60mts
Control	Saline 5mg/kg	5.5±0.2897	7.095±0.2521	8.86±0.3305
Standard	Diclofenac Sodium 100mg/kg	3.7275±0.9244 (32.22)	2.78±1.0071 (60.81)	1.515±0.8727 (82.90)
Schiff base	200mg/kg	2.25±0.5855 (59.09)	0.935±0.7035 (86.82)	0.265±0.2647 (97.00)
Schiff base	400mg/kg	1.81±0.3852 (67.09)	0.255±0.8703 (96.40)	0.797±0.9702 (91.00)

One way ANOVA

F	7.77	17.83	40.58
DF	(3,12)	(3,12)	(3,12)
P	0.003802	0.000102	<.0001

Table-2, Locomotor activity of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one

Treatment	Dose	Locomotor activity(score in 10 min)		
		Before treatment	After treatment	% change in activity
Caffeine	(30 mg/kg(p.o.)	41.5±0.6455	67.25±0.4781	98.86
Chlorpramazin	3 mg/kg (i.p.)	52±0.8165	17±0.4052	98.01
Schiff base	(200mg/kg p.o)	58.25±0.4787	43.75±1.4361	97.94
Schiff base	(400mg/kg p.o)	42.25±0.8539	20±0.4082	97.96

One way ANOVA

F	127.59	837.9
DF	(3,12)	(3,12)
P	<.0001	<.0001

RESULT AND DISCUSSION

Anti-inflammatory activity

The anti-inflammatory activity determination showed that dose dependent increase in the size of the edema range from 3.7275±0.92 to 1.515±0.872 for Standard Diclofenac Sodium 100mg/kg and from 2.25±0.585 to 0.265±0.264 for 200mg/kg and 1.81±0.3852 to 0.797±0.9702 for 400mg/kg of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one. The result showed that 200mg/kg of this compound after sixty minutes exhibited higher anti-inflammatory activity with the probability <.0001. 400 mg/kg of this compound after thirty minutes exhibited 96.4% anti-inflammatory activity with the probability <.0001.

CNS depressant activity

The results obtained for the dose dependent depression in the locomotor activity was 17±0.4052 for standard chlorpromazine. For 200 mg/kg of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one was 43.75±1.4361 and 20±0.4082 for 400mg/kg of this compound. Both 400mg/kg and 200mg/kg exhibited similar CNS depressant activity with the probability of <.0001.

CONCLUSION

The Schiff base (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one was prepared from 4-aminoantipyrine and 4-hydroxy-3-methoxybenzaldehyde exhibit anti-inflammatory and CNS activities.

200mg/kg of the (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one exhibited 97% of anti-inflammatory activity after sixty minutes whereas 400mg/kg of (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one showed 96.4% of anti-inflammatory activity after thirty minutes with the probability <.0001.

The dose dependant depression in the locomotor activity was measured for caffeine, chlorpromazine and (E)-4-(4-hydroxy-3-methoxybenzylideneamino)-1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H)-one. 200 and 400mg/kg of this compound have showed approximately closer CNS depressant activity (97.94% and 97.96%) after drug administration when compared to standard chlorpromazine (98.01%) with a probability <.0001.

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