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Der Pharmacia Lettre, 2018, 10 [10]: 19-24
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ISSN 0975-5071
USA CODEN: DPLEB4

Anti-Inflammatory Activity of 5-(Substituted-Phenyl)-3-(Furan-2-Yl)-4,5-Dihydro-1h-Pyrazole Derivatives

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ABSTRACT

A novel series of 5-(Substituted-phenyl)-3-(furan-2-yl)-4,5-dihydro-1H-pyrazole were already prepared from the reaction of hydrazine hydrate with many chalcone in the presence of ethanol. All novel compounds were screened for their In-vitro anti-inflammatory activity by using egg albumin/ protein denaturation method at various concentrations. On the bases of structure-activity relationship (SAR) study it was found that amongst to all other compounds, 4-(3-(furan-2-yl)-4,5-dihydro-1H-pyrazol-5-yl)aniline (7) found to be the most potent with the IC50 value of 419.05 µg/ml as compared with standard drug Diclofenac sodium.

Keywords: Pyrazole, In-vitro anti-inflammatory activity.

INTRODUCTION

Prostaglandins are dominant potent mediators of inflammation due to, they are endogenous substances involved in different processes of physiological nature. During the metabolism of the arachidonic acid, various prostanoids are produced prostaglandins are also produced together with them. The oxidative conversion of arachidonic acid into prostaglandin H2, is catalyzed by cyclooxygenase (COX). The enzyme (COX) exists at least as two isoforms form, (COX-1) and (COX-2) [1-4]. The (COX-1) are present in the kidneys, in the gastrointestinal tract and in blood platelets. The (COX-2) isoform is a type of inducible enzyme which synthesized when numerous of cell types upon disclosure to cytokines, mitogens and endotoxins released during injury [5,6]. Since, COX-2 is a catalyst enzyme to synthesis the prostaglandins, when COX-2 is overexpressed at the spot of injury they cause inflammation and pain at the injury site [6]. Most of the non-steroidal anti-inflammatory drugs (NSAIDs decreases the bio synthesis of prostaglandin via inhibition of the COX reaction [7-9]. The anti-inflammatory and analgesic effects of NSAIDs associated to inhibition of COX-2 enzyme while gastrointestinal irritation and ulcerative effects of NSAIDs have been associated with inhibition of COX-1 enzyme [10].

MATERIAL AND METHODS

In continuous of my work novel 5-(Substituted-phenyl)-3-(furan-2-yl)-4,5-dihydro-1H-pyrazole were already synthesized and screened for their *In-vitro* anti-inflammatory activity by using egg albumin/ protein denaturation method. The synthesis of 5-(Substituted-phenyl)-3-(furan-2-yl)-4,5-dihydro-1H-pyrazole, Spectral data and Physicochemical characterization of all synthesized compounds are already described in previous article [11] (Figure 1).

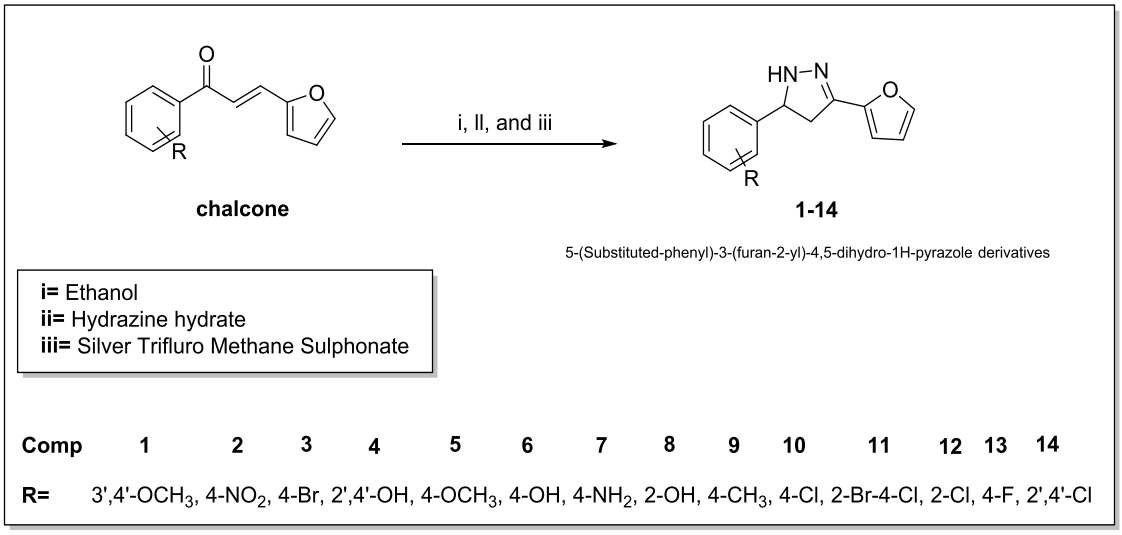

Figure 1: Determination of *in-vitro* anti-inflammatory activity.

The newly synthesized compounds were screened for *in-vitro* anti-inflammatory activity according to Sangita, Chavan and Hosamani [12,13] with slightly modification at four different concentration of 0.25 mg/mL, 0.5 mg/mL, 0.75 mg/mL, 1 mg/m [14]. From fresh hen egg 0.2 ml of albumin was taken and 2.8 ml of phosphate buffer saline with pH of 6.4 and 2 ml of varying concentration of sample were taken so that final reaction mixture 5 ml. Solvent without any drug served as control [15]. Then our mixture samples were incubated in BOD at 37 ℃ for 20 min then heated for 70 ℃ for 5 min. After the cooling the reaction mixture absorbance was determined at 660 nm (UV-1800EN240V SOFT, SHIMADZU, FR. Germany). Diclofenac sodium uses as reference drug with concentration of 0.25 mg/mL, 0.5 mg/mL, 0.75 mg/mL, 1 mg/mL. The percentage of inhibition with their IC_{50} values given in Table 1 and the percentage of inhibition was calculated by given formula:

$$\%\ inhibition = \left(Abs\ control - Abs\ sample \right) * 100 / Abs\ control$$

Preparation of Phosphate Buffer Saline

A solution mixture of disodium hydrogen phosphate 1.79 g, potassium dihydrogen phosphate 1.36 g and sodium chloride 7.02 g were dissolved in sufficient water up to 1000 ml and maintained the pH of solution [16].

RESULTS AND DISCUSSION

The aim of present study is to explore in-*vitro* anti-inflammatory activity of 5-(Substituted-phenyl)-3-(furan-2-yl)-4,5-dihydro-1H-pyrazole derivatives. All the synthesized compounds were tested for *in-vitro* anti-inflammatory activity by inhibition of egg albumin/ protein denaturation method. The percentage of inhibition with their IC_{50} values given in Table 1 and Figure 2.

Table 1: *In-vitro* inflammatory activity.

Variables		Absorbance at 660 nm				% Denaturation activity				
S. no	**Comp**	**250 µg/ml**	**500 µg/ml**	**750 µg/ml**	**1000 µg/ml**	**250 µg/ml**	**500 µg/ml**	**750 µg/ml**	**1000 µg/ml**	**IC_{50} µg/ml**
1	1	0.118	0.132	0.134	0.155	26.33	41.32	43.46	65.95	743.49
2	2	0.097	0.101	0.104	0.123	3.85	8.13	11.34	31.79	1666.09
3	3	0.099	0.103	0.112	0.127	5.99	10.27	19.91	35.97	1428.64
4	4	0.12	0.137	0.139	0.156	28.47	46.68	48.82	67.02	673.03
5	5	0.113	0.131	0.133	0.153	20.98	40.25	42.39	63.81	938.3
6	6	0.125	0.147	0.149	0.16	33.83	57.38	59.92	71.3	502.82

7	7	0.127	0.151	0.157	0.163	**35.97**	**61.67**	**68.09**	**74.51**	**419.05**
8	8	0.122	0.141	0.144	0.158	30.62	50.96	54.17	69.16	599.62
9	9	0.109	0.129	0.131	0.152	16.7	38.11	40.25	62.74	813.1
10	10	0.105	0.119	0.123	0.143	12.41	27.4	31.69	53.1	998.811
11	11	0.101	0.106	0.114	0.132	8.13	13.49	22.26	41.43	1283.67
12	12	0.103	0.113	0.117	0.138	10.27	20.98	25.26	47.75	1137.36
13	13	0.107	0.121	0.128	0.148	14.56	29.55	37.04	58.45	895.69
14	14	0.104	0.118	0.12	0.142	11.34	26.33	28.47	52.03	1036.41
15	Control	0.0934	-	-	-	-	-	-	-	

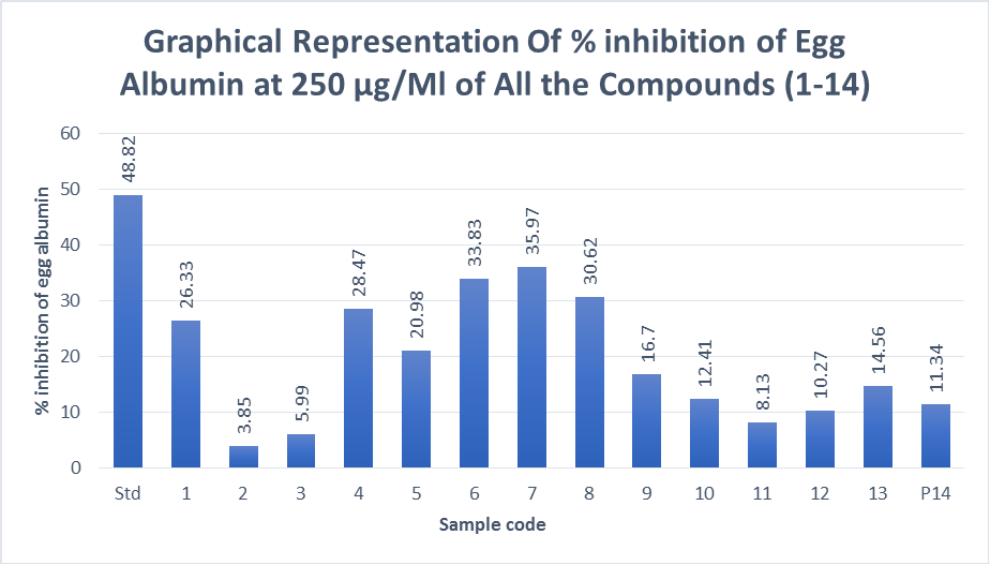

Figure 2: Graphical representation of % inhibition of egg albumin in 250 µg/ml of all the compounds.

The result of *in-vitro* anti-inflammatory studies indicate that compound **7** (**R=** 4-NH_2) showed excellent anti-inflammatory activity against the various concentrations i.e., 1000, 750, 500 and in 250 µg/ml as compared to standard drug Diclofenac sodium with IC_{50} values of 419.05 µg/ml**.**

Structure–Activity Relationship (SAR)

1. It was found that the electron releasing/electron donating group present in the compound increasing the anti-inflammatory activity of the 5-(Substituted-phenyl)-3-(furan-2-yl)-4,5-dihydro-1H-pyrazole derivatives (Figure 3).
2. The electron withdrawing groups such as halogen influences the activity of 5-(Substituted-phenyl)-3-(furan-2-yl)-4,5-dihydro-1H-pyrazole derivatives.

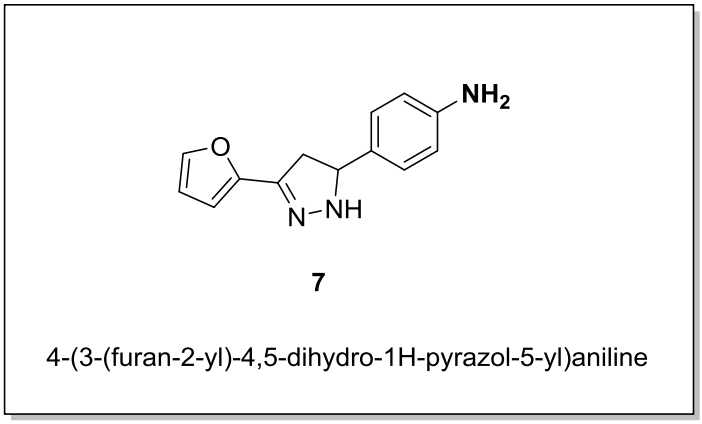

Figure 3: Structure of 4-(3-(furan-2-yl)-4,5-dihydro-1H-pyrazole -5-yl) aniline.

CONCLUSION

Current study describes the *In- Vitro* anti-inflammatory activity of 5-phenyl-3-(furan-2-yl)-4,5-dihydro-1H-pyrazole Derivatives. All newly compounds were screened for there *In-Vitro* anti-inflammatory activity by using protein denaturation method. The results of *In-Vitro* anti-inflammatory activity showed that compound containing electron releasing/electron donating groups were found to be most active compounds. The compound **7** ($R=NH_2$) most active compound of that series.

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