Research Paper | Medical Science | E-ISSN : 2455-295X | Volume : 1 | Issue : 1 | Nov 2015

BIOLOGICAL ACTIVITY OF 3-ARYLIDENE-5(4-SUBSTITUTED PHENYL)-2(3H)-PYRROLONES

Asif Husain

Department of Pharmaceutical Chemistry, Jamia Hamdard (Hamdard University), New Delhi-110062, India.

* Corresponding Author

ABSTRACT

A series of 3-arylidene-5(4-substituted phenyl)-2(3H)-pyrrolones have been evaluated for their in vitro anthelmintic activity against two species of earthworms i.e. Pheretima posthuma and Perionyx excavatus. The anthelmintic activity of seven pyrrolones (1-7) was determined by recording the mean paralyzing and death times of the worms at concentration of 2mg/mL. The screened compounds showed appreciable anthelmintic activities against both types of worms.

Keywords: Nitrogen heterocycles, Pheretima posthuma, Perionyx excavatus, Anthelmintic.

INTRODUCTION

Pyrrolones are nitrogen containing heterocyclic compounds. The chemistry of pyrrolones has attracted much attention during recent years due to their reactivity and important pharmacological activities. Pyrrolones are either either Δ1 or Δ2 five-membered heterocyclic lactams which are present in several biologically active natural compounds [1]. Pyrrolone derivatives have been reported to possess several biological activities - antibacterial, antifungal, antitubercular, anticonvulsant activity, immunosuppressive activity, anticancer activity, analgesic, and anti-inflammatory activity [2-8].

Butenolides or furanones are good starting material for the synthesis of pyrrolones and benzyl-pyrrolones, which show increased biological actions [9,10]. Helminthiasis or worm infestation is one of the major problems in developing countries [11]. Currently available anthelmintic drugs are associated with several side effects in host and many worms have developed resistance to these drugs. In view of these points, it was thought worthwhile to screen the pyrrolone derivatives (1-7) for their in vitro anthelmintic activity.

MATERIALS AND METHODS

Synthesis of 3-arylidene-5-(4-substituted phenyl)-2(3H)-pyrrolones (1-7).

The synthesis, chemistry, anti-inflammatory and antimicrobial activity of these compounds **(1-7)** have already been published by our group **(Figure 1)** [9,10].

Anthelmintic activity

The title compounds **(1-7)** were evaluated for their anthelmintic activities against two species of worms; *Pheretima posthuma* and *Perionyx excavatus,* at a concentration of 2 mg/mL [12]. Collected earthworms were washed with normal saline water to remove soil and fecal matter. Suspensions of samples were prepared by triturating synthesized compounds (100 mg) with 0.5% Tween 80 and normal saline solution and the resulting mixtures were stirred for 30 min. The suspensions were diluted to obtain conc. of 0.2% w/v of the test samples. Suspension of reference drug; Albendazole (0.2% w/v), was prepared in the same manner. Three sets of five earthworms of almost similar sizes (approx. 2 inch in length) were placed in Petri plates of 4 inch diameter containing 50 mL of suspension of test samples and reference drug. Another set of five earthworms was kept as control in 50 mL suspension of distilled water and 0.5% Tween 80. The time taken for paralysis and death of both types of worm were recorded and their mean was calculated for triplicate sets. The anthelmintic activity of the test compounds is compared with the standard drug, Albendazole and is reported as mean±SD (n=5).

RESULTS AND DISCUSSION

The five membered nitrogen-heterocyclic derivatives **(1-7)** showed appreciable anthelmintic activity at 2 mg/mL concentration. The results revealed that all the tested compounds are effective against *Pheretima posthuma* and *Perionyx excavatus* in terms of mean paralyzing and mean lethal time. The mean paralyzing time (min) of tested compounds against *Perionyx excavatus* and *Pheretima posthuma*, was observed to be 17.15-23.65 and 18.8- 26.71 min, respectively, in comparison to 10.13 and 11.53 min, respectively, shown by standard drug, Albendazole **(Table 1)**. Similarly, the mean death time of pyrrolone derivatives against *Perionyx excavatus* and *Pheretima posthuma*, was noted to be 24.23-35.61 and 25.9-35.46 min, respectively. The mean death time taken by Albendazole to kill *Perionyx excavatus* and *Pheretima posthuma* was found to be 15.72 and 17.92 min.

Analysis of results shows that pyrrolone derivatives are more active against P. *posthuma* in comparison to P. *excavatus* in killing the worms. Pyrrolones derived from biphenyl **(1-5)** were less active as compared to the pyrrolones derived from phenoxy-phenyl **(6,7)**. Presence of nitro group in arylidine moiety (7) showed maximum activity among the tested compounds. Also the presence of chloro group at 4th position in arylidine ring (6) showed good activity.

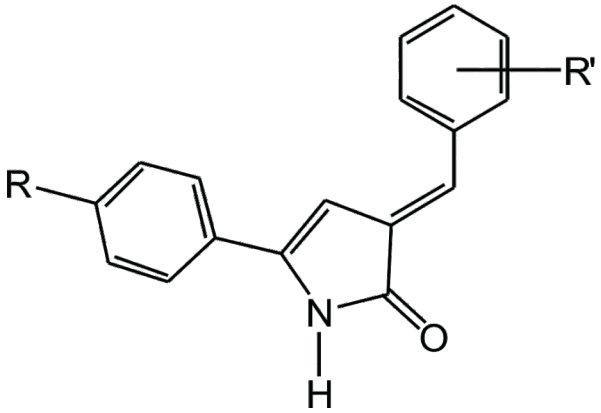

Figure 1: Structure of the title compounds (1-7).

Compound	R	R'
1	C_6H_5-	-H
2	C_6H_5-	2-OH
3	C_6H_5-	3,4-$(OH)_2$
4	C_6H_5-	2,6-$(Cl)_2$
5	C_6H_5-	4-OH; 3-OCH_3
6	C_6H_5O-	4-Cl
7	C_6H_5O-	3-NO_2

Table 1. Anthelmintic activity of 2(3H) pyrrolone derivatives (1-7).

Compound	Earthworm species			
	Perionyx excavatus		Pheretima posthuma	
	Mean paralyzing time (min)[a]	Mean death time (min)[a]	Mean paralyzing time (min)[a]	Mean death time (min)[a]
1	23.65±2.1	35.61±0.21	26.71±0.43	35.46±0.87
2	23.43±1.55	33.56±1.43	23.65±2.32	31.6±1.33
3	19.92±1.62	27.55±3.1	20.54±0.95	26.2±2.5
4	21.50±0.71	35.14±0.39	21.11±0.22	30.09±0.51
5	23.18±0.24	34.84±2.43	25.81±2.45	32.92±1.8
6	18.95±2.32	24.23±2.22	19.2±1.4	27.73±2.5
7	17.15±0.95	25.54±1.22	18.8±2.3	25.9±1.4
Albendazole	10.13±0.69	15.72±0.52	11.23±0.85	17.92±0.59
Control	--	--	--	--

[a]Data are given as mean±S.D (n=5)

CONCLUSION

The present study evaluated the in vitro anthelmintic activity of seven compounds containing pyrrolone ring system. The synthesized 3-arylidene-5(substituted phenyl)-2(3H)-pyrrolones **(1-7)** showed appreciable anthelmintic activity against two types of worms. It is conceivable that further derivation of the active compounds **(6,7)** could result in potential anthelmintic compounds.

CONFLICT OF INTEREST: The author declares that there is no conflict of interest.

REFERENCES

1. Koot WJ, Hiemstra H, Speckamp WN. (R)-1-Acetyl-5-isopropoxy-3-pyrrolin-2-one: a versatile chiral dienophile from (S)-malic acid. J Org Chem., 1992; 57: 1059-61.
2. Husain A, Hasan SM, Lal S, Alam MM. Antibacterial and antifungal activities of 2-arylidene-4-(4-methylphenyl)but-3-en-4-olides and their pyrrolone derivatives. Indian J Pharm Sci., 2006; 68:536-38.
3. Husain A, Khan MSY, Hasan SM, Alam MM. 2-Arylidene-4-(4-phenoxyphenyl) but-3-en-4-olides: synthesis, reactions and biological activity. Eur J Med Chem., 2005;40:1394-1404.
4. Ahmad A, Husain A, Khan SA, Mujeeb M, Bhandari A. Design, synthesis, molecular properties and antimicrobial activities of some novel 2(3H)pyrrolone derivatives. J Saudi Chem Soc., 2015; 19: 340-46.
5. Grunwald C, Rundfeldt C, Lankau HJ, Arnold T, Hofgen N, Dost R, Egerland U, Hofmann HJ, Unverferth K. Synthesis, pharmacology, and structure-activity relationships of novel imidazolones and pyrrolones as modulators of GABA A receptors. J Med Chem., 2006; 49: 1855-66.
6. Alessio RD, Bargiotti A, Carlini O, Colotta F, Ferrari M, Gnocchi P, Isetta A, Mongelli N, Motta P, Rossi A, Rossi M, Tibolla M, Vanotti E. Synthesis and immunosuppressive activity of novel prodigiosin derivatives. J Med Chem., 2000; 43: 2557-65.
7. Alam MM, Husain A, Hasan SM, Suruchi, Anwer T. Synthesis and pharmacological evaluation of 2(3H)-furanones and 2(3H)-pyrrolones, combining analgesic and anti-inflammatory properties with reduced gastrointestinal toxicity and lipid peroxidation. Eur J Med Chem., 2009; 44: 2636-42.
8. Olla S, Manetti F, Crespan E, Maga G, Angelucci A, Schenone S, Bologna M, Botta M. Indolyl-pyrrolone as a new scaffold for Pim1 inhibitors. Bioorg Med Chem Lett., 2009; 19: 1512-16.
9. Khan MSY, Husain A. Syntheses and reactions of some new 2-arylidene-4-(biphenyl-4-yl) but-3-en-4-olides with a study of their biological activity. Pharmazie, 2002; 57: 448-52.
10. Khan MSY, Husain A, Sharma S. Studies on butenolides: 2-arylidene-4-(substituted aryl)but-3-en-4-olides. Indian J Chem., 2002; 41B: 2160-71.
11. Dhar DN, Sharma RL, Bansal GC. (1982). Gastrointestinal nematodes in sheep in Kashmir. Vet Parasitol, 1982; 11: 271-77.
12. Husain A, Varshney MM, Parcha V, Ahmad A, Alam Khan SA. Synthesis and biological evaluation of new hydrazide-Schiff bases. Bangladesh J Pharmacol., 2015;10: 555-61.