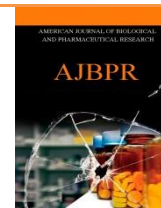




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ANTHELMINTIC ACTIVITY OF 3-ARYLIDENE-5-(BIPHENYL-4-YL)-2(3H)-FURANONES

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ABSTRACT

We report herein the anthelmintic activity of 3-arylidene-5-(biphenyl-4-yl)-2(3H)-furanones against two species of earthworms i.e. *Pheretima posthuma* and *Perionyx excavatus*. The mean paralyzing and death times of the worms due to compounds at concentration 2mg/mL were recorded for the evaluation of anthelmintic activity. Synthesized furanone derivatives exhibited moderate to good anthelmintic activity but among all tested compounds 1d and 1e were found to be promising against *Perionyx excavatus* and *Pheretima posthuma*, respectively. They showed significant anthelmintic activities against both types of worms and the results were comparable to positive control albendazole.

INTRODUCTION

Helminthiasis or worm infestation is a cause of several related diseases and harm humans and animals equally [1]. It is a major health problem especially in developing countries [2]. The worms enter the human body in the form of either egg or larvae acquired by direct contact, eating infected food, via mosquitoes (filarial worms) soil and water [3]. In the market, very few anthelmintic drugs are available to kill and remove all parasitic worms from the infected host body. The regular and continuous use of these compounds has led to the development of drug resistance in many parasitic worms. In addition, some of the widely used anthelmintic drugs such as albendazole causes several side effects in hosts including gastrointestinal symptoms (epigastric pain, diarrhea, nausea, vomiting), headache, dizziness and allergic phenomena reactions [4].

The situation is further worsened due to unavailability of an ideal anthelmintic vaccine [5]. Though research is going on but its delayed development has necessitated the discovery of new anthelmintic compounds that could be used effectively to circumvent the current situation.

A large no of drugs used in clinical practice are of synthetic origin possessing heterocyclic ring in their structure [6]. Santonin was used as an important anthelmintic and ascaricidal agent, since then the physiological activity of the natural lactones is known [7]. The furanone ring system, also known as butyrolactone or butenolide, is a heterocyclic ring system that possesses important biological activities- anti-inflammatory, analgesic, antipyretic [8-10], antifungal [11], antitumor [12], anticonvulsant [13] and antioxidant [14]. As part of our research interest in furanone derivatives, we have previously reported the synthesis, anti-inflammatory and antimicrobial activity of 3-arylidene-5-(biphenyl-4-yl)-2(3H)-furanones [15]. The results of their biological activity were quite encouraging which prompted us to further screen the synthesized compounds for anthelmintic

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activity. Therefore, the present work was aimed at the evaluation of the anthelmintic activity of some 3-arylidene-5-(biphenyl-4-yl)-2(3H)-furanones.

MATERIALS AND METHODS

Synthesis of 3-arylidene-5-(biphenyl-4-yl)-2(3H)-furanones (1a-f).

The compounds were synthesized by reacting 3-(4-phenyl-benzoyl) propionic acid and aromatic aldehydes (Figure 1); their details have already been reported in our previous paper [15].

Anthelmintic activity

The title compounds (1a-f) were evaluated for their anthelmintic activities against two species of worms; *Pheretima posthuma* and *Perionyx excavatus*, at a concentration of 2 mg/mL [16,17]. 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.

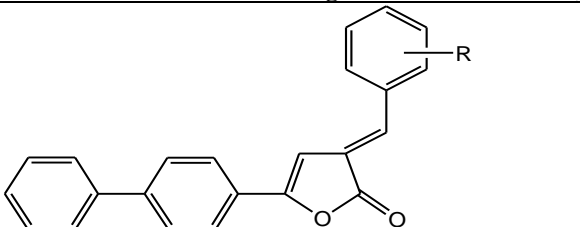
The time taken for paralysis and death of both types of worm were recorded and their mean was calculated for triplicate sets. The anthelmintic activity of the test compounds is compared with the standard drug, albendazole and is reported as Mean \pm SD (n=5).

Table 1. Anthelmintic activity of furanone derivatives (1a- f)

| Compound | Earthworm species | | | |
|-------------|---|------------------------------------|---|------------------------------------|
| | <i>Perionyx excavatus</i> | | <i>Pheretima posthuma</i> | |
| | Mean paralyzing time (min) ^a | Mean death time (min) ^a | Mean paralyzing time (min) ^a | Mean death time (min) ^a |
| 1a | 24.15 \pm 0.76 | 35.14 \pm 0.39 | 19.49 \pm 0.21 | 29.80 \pm 0.22 |
| 1b | 21.50 \pm 0.71 | 28.12 \pm 0.42 | 20.22 \pm 0.12 | 29.99 \pm 0.22 |
| 1c | 20.18 \pm 0.24 | 34.21 \pm 0.51 | 25.29 \pm 0.61 | 33.22 \pm 0.17 |
| 1d | 18.31 \pm 0.48 | 28.65 \pm 0.66 | 23.16 \pm 0.32 | 34.69 \pm 0.41 |
| 1e | 12.15 \pm 0.16 | 17.17 \pm 0.21 | 15.39 \pm 0.11 | 21.14 \pm 0.19 |
| 1f | 19.10 \pm 0.11 | 25.60 \pm 0.76 | 17.84 \pm 0.42 | 25.49 \pm 0.51 |
| Albendazole | 10.13 \pm 0.69 | 15.72 \pm 0.52 | 11.23 \pm 0.85 | 17.92 \pm 0.59 |
| Control | ----- | ----- | ----- | ----- |

^aData are given as mean \pm S.D (n=5).

Figure 1. Structure of 2(3H) furanone derivatives

|  | Compound | R |
|---|----------|-----------------|
| | | 1a |
| | 1b | 4-Chloro |
| | 1c | 3-Nitro |
| | 1d | 2-Thenyl |
| | 1e | Cinnamaldehyde |
| | 1f | 4-Dimethylamino |

RESULTS AND DISCUSSION

Parasitic worms or helminthes are the common cause of parasitic diseases in developing nations having warm, moist environments with poor sanitary conditions. Anthelmintic are those agents that expel parasitic worms from body, by either stunning or killing them, but the extensive use of these drugs has led to the development of resistance [18] and therefore, there is a need of potent and safer anthelmintic agents. Indian earthworms, *Pheretima posthuma* and *Perionyx excavatus*, were used for determining the anthelmintic activity of the synthesized

agents as they have anatomical and physiological resemblance to the intestinal roundworm parasites in humans. The five membered heterocyclic furanone derivatives showed moderate to good anthelmintic activity at 2 mg/mL concentration. The results indicated that all the tested compounds were effective against *Pheretima posthuma* and *Perionyx excavatus*, possessed significant activity in respect 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 13.15-24.15 and 15.39- 25.29 min in comparison to 10.13 and 11.53 min shown by standard drug, albendazole (Table 1). The most and the least potent anthelmintic compound in terms of mean paralyzing time against *Perionyx excavatus* was noted to be 1e (13.15 min) and 1a (24.15 min), while against *Pheretima posthuma*, 1d and 1c had the similar spectrum of activity. The Results were comparable to that of the standard drug. The mean death time observed for Albendazole against *Pheretima posthuma* and *Perionyx excavatus* was 17.92 and 15.72 min. Compounds 1e and 1d were found to be equipotent to standard drug in causing death of nematodes, which took an average time of 19.17 and 22.69 min against *Perionyx excavatus* and *Pheretima posthuma*, respectively. It was observed that presence of an electron withdrawing group in arylidene ring decreases the anthelmintic activity.

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CONCLUSION

The present study evaluated the anthelmintic activity of six 2-arylidene-4-(biphenyl-4-yl) but-3-en-4-olides (1a-f) against two species of earthworms. The results indicated that furanone derivatives have the potential to paralyze and kill the worms. Synthesis of new analogs and derivatives of furanone should be attempted to obtain safer and potent anthelmintic agents based on this heterocyclic moiety.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

