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**INDO AMERICAN JOURNAL OF  
PHARMACEUTICAL SCIENCES**Available online at: <http://www.iajps.com>**Research Article****EVALUATION OF ANTHELMINTIC ACTIVITY OF  
DI/TRISUBSTITUTED 3-ARYLIDENE-5-(BIPHENYL-4-YL)-  
2(3H)-FURANONES**Asif Husain<sup>1\*</sup>, Mohammad Maaz<sup>2</sup>, Aftab Ahmad<sup>3</sup>, Shah Alam Khan<sup>4</sup><sup>1</sup>Dept of Pharmaceutical Chemistry, Jamia Hamdard (Hamdard University), New Delhi-110062, India<sup>2</sup>Faculty of Medicine (Unani), Jamia Hamdard (Hamdard University), New Delhi-110062, India<sup>3</sup>Health Information Technology Department, Jeddah Community College, King Abdulaziz University, Jeddah-21589, KSA<sup>4</sup>Dept of Pharmacy, Oman Medical College, PO Box 620, PC 130, Muscat, Sultanate of Oman**Abstract:**

We describe herein the *in vitro* anthelmintic activity of di/trisubstituted 3-arylidene-5-(biphenyl-4-yl)-2(3H)-furanones against two species of earthworms i.e. *Pheretima posthuma* and *Perionyx excavatus*. The anthelmintic activity was determined by noting the mean paralyzing and death times of the worms due to furanone derivatives at a concentration of 2mg/mL. All the tested compounds displayed moderate to good anthelmintic activity but compounds **1** and **5** were found to be the most potent against *Perionyx excavatus* and *Pheretima posthuma*, respectively. These exhibited significant anthelmintic activities against both types of worms and the results were comparable to reference drug albendazole.

**Keywords:** Furanone, *Pheretima posthuma*, *Perionyx excavatus*, Anthelmintic.

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## INTRODUCTION

A helminthiasis or worm infestation is considered as a major health problem in developing countries [1]. 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 [2]. The infections of helminthes cause several related diseases and thus cause harm to man and animals [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]. Physiological activity of the natural lactones is known ever since santonin was used as an important anthelmintic and ascaricidal agent [7]. The furanone also known as butyrolactone or butenolide is a heterocyclic ring system that exhibits wide range of interesting biological activities such as anti-inflammatory, analgesic, antipyretic [8-10], antifungal [11], antitumor [12], anticonvulsant [13] and antioxidant [14]. As part of our research interest in heterocyclic compounds, we have previously reported the synthesis, anti-inflammatory and antimicrobial activity of 3-arylidene-5-(biphenyl-4-yl)-2(3*H*)-furanones [15]. The results of their biological activity were quite encouraging which prompted us to further screen the synthesized compounds for *in vitro* anthelmintic activity. Therefore, the present work is aimed at the evaluation of the anthelmintic activity of di/trisubstituted-3-arylidene-5-(biphenyl-4-yl)-2(3*H*)-furanones.

## MATERIALS AND METHODS

### Synthesis of di/trisubstituted 3-arylidene-5-(biphenyl-4-yl)-2(3*H*)-furanones (1a-f).

The compounds were synthesized by reacting 3-(4-phenyl-benzoyl) propionic acid and aromatic aldehydes (Fig 1) [15].

## Anthelmintic activity

The title compounds (**1-5**) 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).

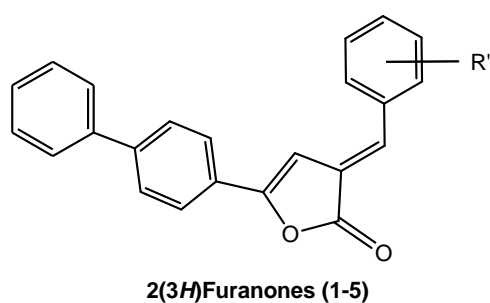
## RESULTS AND DISCUSSION

The helminthes or worms are the common cause of parasitic diseases in developing nations having warm, moist environments with poor sanitary conditions [18]. Anthelmintic agents kill and expel the worms from the infected host body but the extensive use of these drugs has led to the development of resistance and therefore, there is a need to design, synthesize and develop potent and safe anthelmintic agents. Indian earthworms, *Pheretima posthuma* and *Perionyx excavatus*, were used for the evaluation of anthelmintic activity of the synthesized compounds as they bear 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 revealed that all the tested compounds are effective against *Pheretima posthuma* and *Perionyx excavatus*, possessing 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 15.12-23.18 and 14.29- 26.71 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 **1** (15.12 min) and **3** (23.18 min), while against

*Pheretima posthuma*, **5** and **3** had the similar spectrum of activity. The Results were comparable to that of the standard drug, albendazole. The mean death time observed for albendazole against *Pheretima posthuma* and *Perionyx excavatus* was 17.92 and 15.72 min. Compounds **1** and **5** were found to be equipotent to standard drug in causing death of nematodes, which took an average time of 21.14 and 20.74 min against *Perionyx excavatus* and *Pheretima posthuma*, respectively. It was

observed that presence of an electron donating groups in arylidene ring at position 3, 4 increases the anthelmintic activity while electron withdrawing groups decreases the activity. The most potent compound **1** and **5** are having trimethoxy groups at 3,4,5 positions and 3,4 methylene dioxy groups in arylidene ring.



Compd no	R'
1	3,4,5-trimethoxy
2	3,4-diacetoxy
3	2,6-dichloro
4	4-acetoxy-3-ethoxy
5	3,4-methylene-dioxy (piperonal)

**Fig 1: Structure of Di/trisubstituted 2(3H) Furanone Derivatives (1-5)**

**Table 1. Anthelmintic Activity of Furanone Derivatives (1-5)**

Compound number	Earthworm species			
	<i>Perionyx excavatus</i>		<i>Pheretima posthuma</i>	
	Mean paralyzing time (min) <sup>a</sup>	Mean death time (min) <sup>a</sup>	Mean paralyzing time (min) <sup>a</sup>	Mean death time (min) <sup>a</sup>
<b>1</b>	15.12±0.32	21.14±0.39	20.43±0.21	28.10±0.22
<b>2</b>	20.50±0.71	32.43±0.62	18.92±0.12	27.29±0.22
<b>3</b>	23.18±0.24	35.61±0.21	26.71±0.43	39.86±0.87
<b>4</b>	18.31±0.48	28.65±0.54	21.11±0.22	30.09±0.51
<b>5</b>	16.11±0.16	27.17±0.76	14.29±0.61	20.74±0.31
<b>Albendazole</b>	10.13±0.69	15.72±0.52	11.53±0.85	17.92±0.59
<b>Control</b>	-----	-----	-----	-----

<sup>a</sup>Data are given as mean±S.D (n=5)

## CONCLUSION

The present study evaluated the anthelmintic activity of five di/trisubstituted 2-arylidene-4-(biphenyl-4-yl) but-3-en-2-olides (**1-5**) against two types of worms. The results indicated that furanone derivatives have the potential to paralyze and kill the parasitic worms. Synthesis of new analogs and derivatives of furanone should be attempted to obtain safe and potent anthelmintic agents based on this heterocyclic moiety.

**CONFLICT OF INTEREST:** The authors declare that they have no conflict of interest.

## REFERENCES

- Dhar DN, Sharma RL, Bansal GC. Gastrointestinal nematodes in sheep in Kashmir. *Vet Parasitol*, 1982;11: 271-77.
- Srinivasa MV, Jayachandran E. Anthelmintic activity of 8-fluro-9-substituted (1,3)- benzthiazole(5,1- B) – 1,2,4, triazole on *Pheretima posthuma*. *Indian drugs*, 2006;43 (4): 343 – 47.
- 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.
- Selvam TP, Ramu P, Kumar AS. Synthesis, characterization and anthelmintic activity of novel 3-benzyl-2-(4'-substituted phenyl)-4(5H)-(4"-nitrophenyl amino)-1, 3-oxazolidines derivatives. *JPRHC*, 2011;3(1): 9-14.
  - Newton SE, Munn EA. The development of vaccines against gastrointestinal Nematode parasites, particularly *Haemonchus contortus*. *Parasitol Today*, 1999;15(3): 116-22.
  - Bansal RK. (1996). Heterocyclic chemistry-synthesis, reaction and mechanism. 2<sup>nd</sup> Edition, New Delhi, Wiley Eastern Ltd.
  - Shillinger JE Anthelmintic properties of Santonin. *J Agr Res*, 1927;34(9):839-45.
  - Husain A, Khan MSY, Hasan SM, Alam MM. (2005). 2-arylidene-4(4-phenoxy-phenyl) but-3-en-4-olides. *Eur J Med Chem*, 40,1394-1404.
  - 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.
  - Khokra SB, Monga J, Husain A, Vij M, Saini R. Docking studies on butenolide derivatives as Cox-II inhibitors. *Med Chem Res*, 2013;22:5536-44.
  - Husain A, Lal S, Alam MM, Shaharyar M. Antimicrobial activity of some synthetic butenolides & their pyrrolone derivatives. *J Enz Inhib Med Chem*, 2010;25: 54-61.
  - Chimchi S, Boccalini M, Cosimelli B, Viola G, Vedaldi D, Dall' Acqua F. New geiparvarin analogues from 7-(2-oxoethoxy)coumarins as efficient in vitro antitumoral agents. *Tetrahedron Lett*, 2002; 43: 7473-76.
  - Faizul Azam F, Lal S, Prakash O, Ismail A. Synthesis of some novel N4-(naphtha[1,2-d]thiazol-2-yl) semicarbazides as potential anticonvulsants. *Eur J Med Chem*, 2009;44: 203-21.
  - Weber V, Coudert P, Rubat C, Duroux E, Goyet DV, Gardette D, Bria M, Albuissou E, Leal F, Gramain JC, Couquelet J, Madesclaire M. Novel 4,5 diaryl-3-hydroxy-2(5H)-furanones as anti-oxidants and anti-inflammatory agents. *Bioorg Med Chem*, 2002; 10: 1647-58.
  - 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.
  - Dahiya R, Pathak D. Synthetic studies on novel benzimidazolepeptides with antimicrobial, cytotoxic and anthelmintic potential. *Eur J Med Chem*, 2007;42:772-98.
  - Sharma MC, Sahu NK, Kohli DV. Synthesis, characterization and biological evaluation of some 1-(Nicotinylamino-2-substituted azetidine-4-ones as potential antibacterial agents. *Digest J Nanomaterials and Biostructures*, 2009;4:361-67.
  - Sarnim G, Sanjay ST, Roshan A, Vedamurthy AB, Joy HH. *Artemisia indica* extracts as anthelmintic agent against *Pheretima posthuma*. *Int J Pharm Pharm Sci*, 2013;5 (Suppl 3): 259-62.