ejpmr, 2018,5(4), 579-582

SJIF Impact Factor 4.897

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

IN VITRO ANTHELMINTIC ACTIVITY OF NOVEL MANNICH BASES USING

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Article Received on 19/02/2018 **Article Revised on 11/03/2018** **Article Accepted on 31/03/2018**

ABSTRACT

The present study is an attempt to explore the anthelmintic activity of Mannich bases against adult Indian earthworms, Pheretima posthuma. The time taken for each worm for paralysis and death were determined. Mannich condensed derivatives MB-06 show effective activity when compared to orientation of standard drug, Piperazine citrate. The time taken for paralysis and death with mannich base-6 at 80 mg/ml was comparable to standard Piperazine citrate.

KEYWORDS: Anthelmintic Activity, Benzimidazole, O-Phenylene Diamine Docking, Tubulin.

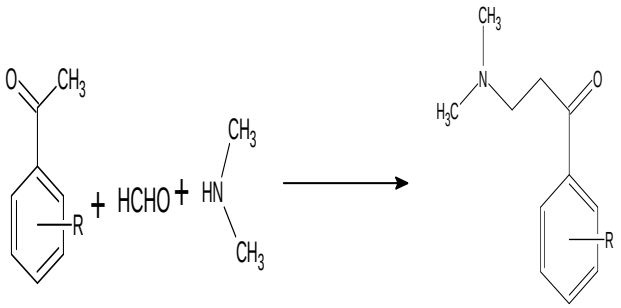
INTRODUCTION

Schiff bases are used as substrates in the preparation of a number of industrial and biologically active compounds via ring closure, cycloaddition and replacement reactions.[1] Moreover, Schiff bases derived from various heterocycles have been reported to possess cytotoxic[2], anticonvulsant[3], antiproliferative[4], antimicrobial[5], anticancer[6], and antifungal activities.[7] Mannich bases have gained importance due to their application in pharmaceutical chemistry. They have been encountered with antibacterial[8], anticancer[9], analgesic and anti-inflammatory[10], anticonvulsant[11], antimalarial[12], antiviral[13], and CNS depressant activities.[14] Isatin, chemically known as 1H-indole-2,3-dione, has become a popular topic due to its various uses. The chemistry of isatin and its derivatives is particularly interesting because of their potential application in medicinal chemistry. Isatins are very important compounds due to their antifungal properties.[15] Schiff and Mannich bases of isatin derivatives are reported to show variety of biological activities like antibacterial[16], antifungal[17], anticonvulsant[18], anti HIV[19], antidepressant[20], and anti-inflammatory[21] activities. Similarly, 1,2,4-triazoles and their derivatives play important roles in medicinal, agricultural and industrial fields.[22-25] N-bridged heterocyclic derivatives derived from 1,2,4-triazoles show varied biological activities such as antimicrobial[26], anticonvulsant[27], anticancer[28], analgesic[29], anti HIV[30] and anti-inflammatory properties.[31]

MATERIALS AND METHODS

Acetophenone derivatives like chloro, bromo, methyl, methoxy, nitro and dimethyl amine, formaldehyde

Reaction



R= H,4-Br.4-OH,4-OCH3, 4-CH3, 3-NO2

Procedure

General procedure.

Ketone **5** (7.5 g, 0.05 mol), paraformaldehyde (3 g, 0.1 mol), dimethy amine hydrochloride (0.05 mol), 0.1 ml conc. HCl and 2-propanol (15–25 ml, depending on the amine) were refluxed with stirring for 4 h. In less than an hour the reactants had dissolved and sometimes the Mannich base hydrochloride started to separate from the reaction mixture as a solid after about 2 h when a small volume of 2-propanol was employed. After the reaction mixture had been kept in a freezer overnight, the crystals were filtered off, washed with acetone (or diethyl ether) and purified by recrystallization from ethanol.

In vitro Anthelmintic activity[32]

Earthworm collection[33]

Earth-worms in moist soil were washed with normal saline and used for the study. The earthworms 3 -5 cm in length and 0.1-0.2 cm width were used due to its anatomical and physiological resemblance with the intestinal roundworm parasites of human beings.[18,19]

Preparation of solutions

Here the synthesised compounds were prepared by using the 5% DMF and saline solutions

In vitro Anthelmintic activity[34-37]

The anthelmintic assay was carried as per the method of Ajaiyeoba et. al.[9] with minor modifications. All the test solutions and standard drug solutions were prepared freshly before starting the experiment. Six groups of earthworms of approximately equal size were released in to 25 ml solutions of three different concentrations (20,40,80 mg/ml) in petri dishes containing 5% of DMF solution. Piperazine citratae was used as reference standard and saline as control. Determination of time of paralysis and time of death of the worm were done. Time for paralysis was noted when no movement of any sort could be observed except when the worms were shaken vigorously. Time for death of worms was recorded after ascertaining that worms neither moved when shaken vigorously nor when dipped in warm water (50oC) followed with fading away of their body colours.

RESULTS AND DISCUSSION

Physical properties of compounds

S. No	Name of the compound	Molecular formula	Relative Mass	M.P	% yield
1	MB-01	$C_{11}H_{15}NO$	177.24	166	94
2	MB-02	$C_{11}H_{14}BrNO$	256.13	174	96
3	MB-03	$C_{11}H_{15}NO2$	193.24	180	84
4	MB-04	$C_{12}H_{17}N02$	207.23	184	76
5	MB-05	$C_{12}H_{17}NO$	191.26	186	84
6	MB-06	$C_{11}H_{14}N_2O_3$	222.22	182	86

Elemental analysis

S. No	Calculated				Observed			
	C	H	N	O	C	H	N	O
MB-01	74.54	8.53	7.90	9.03	74.34	8.52	7.89	9.01
MB-02	51.58	5.51	5.47	6.25	51.48	5.45	5.47	6.21
MB-03	68.37	7.82	7.25	16.56	68.27	7.79	7.22	16.51
MB-04	69.54	8.27	6.76	15.44	69.44	8.22	6.74	15.41
MB-05	75.35	8.96	7.32	8.36	75235	8.91	7.30	8.32
MB-06	59.45	6.35	12.60	21.60	59.35	6.31	12.58	21.58

Anhelmenthetic activity of mannich Derivatives

S. No	Parameter	Concentration (mg/ml)	MB-01	MB-02	MB-03	MB-04	MB-05	MB-06	Piperazine citrate 15 (mg/ml)
1	Time taken for paralysis	80	2.64 ± 0.17	2.55 ± 0.18	2.24 ± 0.15	2.33 ± 0.14	2.01± 0.11	1.87+0.291	41.53 ± 0.13
2		40	3.77 ± 0.13	3.28 ± 0.22	4.09 ± 0.22	4.51± 0.28	4.27 ± 0.12	2.01± 0.31	
3		20	4.25± 0.22	5.11 ± 0.23	6.12 ± 0.21	6.52 ± 0.32	5.87 ± 0.23	3.11 ±0.14	
4	Time taken for Death	80	3.65 ± 0.31	3.44 ± 0.22	3.25 ± 0.22	3.25 ± 0.22	3.12± 0.32	2.02 ± 0.22	45.23 ± 0.22
5		40	5.65±0.24	5.15 ± 0.12	5.85±0.14	5.75 ± 0.15	5.01 ± 0.55	4.12 ± 0.22	
6		20	6.25 ± 0.15	6.15 ± 0.23	6.25 ±0.17	6.65 ± 0.25	6.12 ± 0.18	4.95 ± 0.22	

DISCUSSION

Based on invitro and invivo results, the mannich bases show better Anthelmintic activity. Here the compound Mannich base 6 (3-(dimethylamino)-1-(4-nitrophenyl) propan-1-one shows better activity than other molecules.

CONCLUSION

The compound Mannich base-6 (3-(dimethylamino)-1-(4-nitrophenyl) propan-1-one shows better activity than other molecules.

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