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IN VITRO ANTHELMINTIC ACTIVITY OF 3-(3-CHLOROPHENYL)-5-PHENYL-4, 5-DIHYDRO-1,2-OXAZOLE DERIVATIVES

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ABSTRACT

Novel Isoxazoles are prepared by treating chalcone derivatives from 3-Chloro acetophenone with hydroxyl amine hydro chloride, small amount of sodium acetate and ethanol All the synthesised compounds were characterized by using the IR, H^1 NMR spectroscopy. The Anthelmintic activity of compounds were tested at concentration of 20, 40, 80 mg/ml. In these the compound I-03 (3-(3-chlorophenyl)-5-(4-chlorophenyl)-4,5-dihydro-1,2-oxazole) shows better results than compare with the other compounds.

KEYWORDS: isoxazoles, antihelmentic activity, hydroxyl amine.

INTRODUCTION

Heterocyclic compounds are abundant in nature and are of great significance to life because their structural subunits exist in many natural products such as vitamins, hormones, and antibiotics.[1,2] Hence, they have attracted considerable attention in the design of biologically active molecules[3,4] and advanced organic chemistry.[5,6] Also in the family of heterocyclic compounds nitrogen containing Heterocyclic compounds are an important in the medicinal chemistry and also contributed to the society from biological and industrial point which helps to understand life processes.[7]

Isoxazoline are is the unique molecules possessing the oxygen and nitrogen in the five member ring at 1,2 positions.[8] The nucleus usefulness in drugs designing different types of diseases due it's wide range of pharmacological activities. It has been reported that

isoxazolines possess analgesic, anti-inflammatory[9-12] and antimicrobial.[13-19] Isoxazoline containing different drugs are available in market.

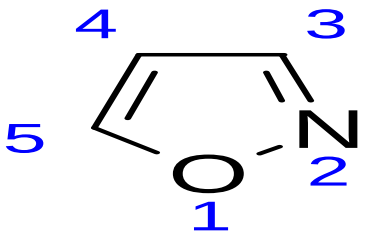

Fig. 1: isoxazole structure.

Experimental work

Materials and methods

(2*E*)-1-(3-chlorophenyl)-3-phenylprop-2-en-1-one derivatives, hydroxyl amine, sodium acetate, glacial acetic acid, conc. HCl, DMSO, DPPH reagent. All the reagents were purchased analytical grade. Melting points were determined on a capillary melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded in the indicated solvent on Bruker WM 400 MHz spectrometer with TMS as internal standard. Infrared spectra were recorded in KBr on Perkin-Elmer AC-1 spectrophotometer. Column chromatography was performed on silica gel (Merck, 60-120 mesh).

General procedure for the synthesis Isoxazolines[20-21]

A mixture of (2*E*)-1-(3-chlorophenyl)-3-phenylprop-2-en-1-one derivatives (0.02 mol), Hydroxyl amine hydrochloride (0.02 mol) and catalytic amount of sodium acetate in ethanol (25 ml) was refluxed for 6 h. The mixture was concentrated by distilling out the solvent under reduced pressure and poured into ice water. The precipitate obtained was filtered, washed and recrystallized from ethanol. The completion of the reaction was monitored by TLC. Similarly various isoxazole derivatives I2-5were prepared.

Scheme of preparation

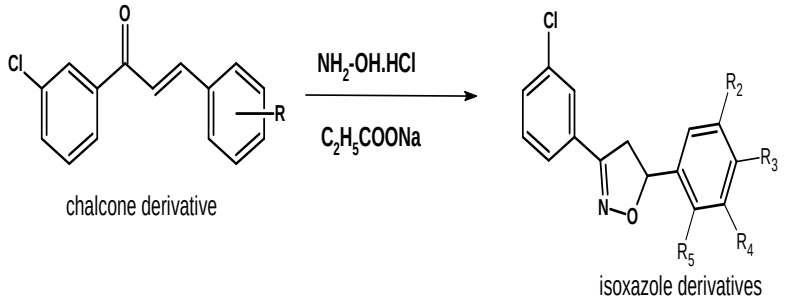

Table 1: List of aldehydes

S. No	R_2	R_3	R_4	R_5
1.	H	H	H	H
2.	H	H	OH	H
3.	H	H	Cl	H
4.	H	H	S-CH_{33}	H
5.	H	OCH_3	OCH_{33}	H

Biological evolution of compounds

Based on the literature, chalcones were reported to possess antimicrobial activity, anti oxidant, anti inflammatory, analgesic, anti cancerous, etc. Therefore the present work performs the anti microbial, anti oxidant activities.

In vitro Anthelmintic activity 22

Earthworm collection 23

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.

Preparation of solutions

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

In vitro Anthelmintic activity 24-27

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 (50^oC) followed with fading away of their body colours.

RESULTS AND DISCUSSION

Table 2: Physical Data.

Compound	R	Molecular Formula	Relative Molecular Mass (RMM)	Melting Point (^{o}C)	Yield %
I-1	H	$C_{15}H_{12}ClNO$	257.7	125	89
I-2	OH	$C_{15}H_{12}ClNO_2$	273.7	115	92
I-3	Cl	$C_{15}H_{11}Cl_2NO$	292.1	122	91
I-4	S-CH_3	$C_{16}H_{14}ClNOS$	303.8	105	94
I-5	DI O-CH_3	$C_{17}H_{16}ClNO_3$	317.7	114	85

Table 3: Elemental composition.

Compound	%Calculated				%Found			
	C	H	CL	O	C	H	Cl	O
I-1	69.91	4.69	13.76	6.21	69.85	4.45	13.55	6.01
I-2	65.82	4.42	12.95	11.69	65.75	4.36	12.85	11.69
I-3	61.67	3.79	24.27	5.48	61.56	3.79	24.25	5.38
I-4	63.25	4.64	11.67	5.27	63.22	4.56	11.56	5.15
I-5	64.26	5.08	11.16	15.10	64.22	5.00	11.05	15.06

Spectral data

3-(3-chlorophenyl)-5-phenyl-4,5-dihydro-1,2-oxazole *(I-1)*

IR(cm-1) 1794.24 (C=O), 1591(C=N), 1097(C-N);3667.07 (C-Cl), 1450 (C=C); 3.366 (1H, s, -C-Cl) 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH

4-[3-(3-chlorophenyl)-4,5-dihydro-1,2-oxazol-5-yl]phenol *(I-2)*

IR(cm-1) 1794.24 (C=O), 1591(C=N), 1097(C-N);667.07 (C-Cl), 1450 (C=C), 3400 (Ar-OH), 3.366 (1H, s, -C-Cl), 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH)

3-(3-chlorophenyl)-5-(4-chlorophenyl)-4,5-dihydro-1,2-oxazole *(I-3)*

IR(cm-1) 1794.24 (C=O), 1591(C=N), 1097(C-N);667.07 (C-Cl), 1450 (C=C), 3.366 (1H, s, -C-Cl), **6.0-9.1 (1H, m,** Ar-H), 7.2-8.4 (5H, s, Ar-OH)

3-(3-chlorophenyl)-5-[4-(methylsulfanyl) phenyl]-4,5-dihydro-1,2-oxazole *(I-4)*

IR(cm-1) 1794.24 (C=O), 1591(C=N), 1097(C-N);667.07 (C-Cl), 1450 (C=C), 3.366 (1H, s, -C-Cl), 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH).

3-(3-chlorophenyl)-5-(3,4-dimethoxyphenyl) -4,5-dihydro-1,2-oxazole *(I-5)*

IR(cm-1) 2568.21 (C-S), 1591(C=N), 1097(C-N);, 667.07 (C-Cl), 1450 (C=C), 2860 (C-O-CH $_3$ P – 153 674.39 (C-Cl), 1614.81 (C=C), 3.366 (1H, s, -C- Cl), 6.0-9.1 (1H, m, Ar-H).

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

DISCUSSION

The spectral data confirm the 1,2 oxazoline derivatives are formed after that The synthesised compounds tested for anthelmintic activity for this compounds were prepared at concentration of 20, 40, 80 mg/ml using saline 5% DMF solvents and compare the results with the standard compound piperazine citrate. In these compounds, I-03 (3-(3-chlorophenyl)-5-(4-chlorophenyl)-4,5-dihydro-1,2-oxazole) shows better results than compare with the other compounds.

CONCLUSION

In these compounds, I-03 (3-(3-chlorophenyl)-5-(4-chlorophenyl)-4,5-dihydro-1,2-oxazole) shows better results than compare with the other compounds

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