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SYNTHESIS, CHARACTERIZATION AND ANTIHELMINTHIC ACTIVITY OF PYRIMIDINENONES DERIVATIVES

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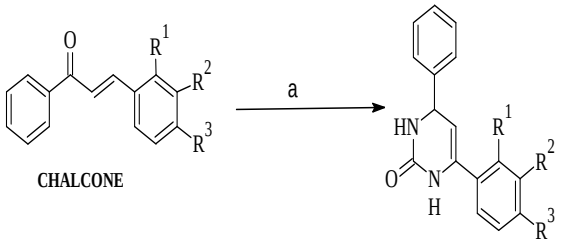
ABSTRACT
The synthesized chalcones compounds were reacted with urea and ethanol upon cyclisation gives pyramidinone derivatives. All these compounds were characterized by means of their IR, ^{1}H NMR spectroscopic data and microanalyses. The antihelminthic activities of compounds were done by using the standard procedure with standard compound piperazine citrate as compound. Here the compound PY-02 shows better activity than the other compounds.

KEYWORDS: Pyrimidinone, urea, Antihelminthic Activity, Piperazine citrate.

INTRODUCTION
Discovery of novel synthetic heterocyclic compounds are the target of organic scientists to cure the diseases. Hence, novel chalcones were synthesized because it is known to exhibit various biological activities. Chalcones have been reported to possess antioxidant antiulcer, antimalarial, antileishmanial, anti-inflammatory, antitumor, antitubercular, antibacterial activity and antifungal activity.[1] The presence of a reactive α,β-unsaturated keto functional group in chalcones is found to be responsible for their antimicrobial and other activities, which may be altered depending on the nature and position of substituent on the aromatic rings of aldehydes and 2-Chloro Acetophenone derivative.[2] In the present communication we report the reaction of 1-(2-chlorophenyl)ethanone with different aromatic aldehydes to afford novel chalcones and the synthesized chalcones compounds were reacted with urea and ethanol upon cyclisation gives Pyrimidinone derivatives. The structures of the various synthesized compounds were assigned on the basis of elemental analysis, IR and ^{1}H NMR spectral data. The antihelminthic activity of compounds were done by using the standard procedure with standard compound piperazine citrate as compound.

Experimental work[3]
Melting points were determined on a capillary melting point apparatus and are uncorrected. 1H NMR spectra was recorded in the indicated solvent on Bruker AV 400 MHz spectrometer using TMS as internal standard. Infrared spectra were recorded in KBr on Perkin-Elmer AC-1 spectrophotometer.

Scheme -I



CHALCONE PYRIMIDINE DERIVATIVES

a) Urea and ethanol and NaOH, reflex 3-4 hrs

i) R^1:R^2 - H, R3: OH, ii) R^1:R^2 - H, R3: Cl, iii) R^1:R^2 - H, R3: SCH_3 iv) R^1:R^2 - H, R3: CH_3 ,V) R^1:R^2 - OCH_3, R3: H

Pyrimidinone Procedure[5]
Chalcones(1eq),urea(1eq), To this mixture 10ml of ethanolic NaoH (1eq) was added at room temperature, reflux for 3-4 hr. The mixture was concentrated by distilling out the solvent under reduced pressure and poured into crushed ice. The obtained solid was purified and recrystallised using mixture of ethanol.

In vitro Anthelmintic activity 6
Earthworm collection 7
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 beings18, 19.

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

In vitro Anthelmintic activity 8-12
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^{o}C) followed with fading away of their body colours.

Spectral Data: 13-14.

4-(2-chlorophenyl)-6-(4-hydroxyphenyl)-3,4-dihydropyrimidin-2(1*H*)- one (PY-1)
IR(cm-1) 1794.24 (C=O), 3515 (N-H), 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)

4-(2-chlorophenyl)-6-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1*H*)- one (PY-2)
IR(cm-1) 1794.24 (C=O), 3515 (N-H), 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)

4-(2-chlorophenyl)-6-(4-methylphenyl)-3,4-dihydropyrimidin-2(1*H*)- one (PY-3)
IR(cm-1) 1794.24 (C=O), 3515 (N-H), 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)

4-(2-chlorophenyl)-6-(2,3-dimethoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (PY-4)
IR(cm-1) 1794.24 (C=O), 3515 (N-H), 667.07 (C-Cl), 1450 (C=C), 2860 (C-O-CH_3),3.366 (1H, s, -C-Cl), 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH)

4-(2-chlorophenyl)-6-[4-(methylsulfanyl)phenyl]-3,4-dihydropyrimidin-2(1*H*)-one(PY-5)
IR(cm-1) 2568.21 (C-S), 147 (S-CH_3), 674.39 (C-Cl), 1614.81 (C=C), 3.366 (1H, s, -C-Cl), 6.0-9.1 (1H, m, Ar-H), 7.2-8.4 (5H, s, Ar-OH), 2.5-2.55 (1H, s, C-S)

Results antihelmentic activity

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

RESULTS AND DISCUSSION
Five novel 1, 3-diphenyl-2-propene-1-one chalcones and pyrimidinones were designed and synthesized by the condensation 1,3-diphenyl-2-propene-1-one with various aromatic aldehydes in dilute ethanolic potassium hydroxide solution at room temperature. And synthesized chalcones upon reaction with urea and sodium hydroxide forms pyrimidinone compounds. The obtained compound structures were characterized by its IR and ^{1}H NMR spectral data.

Based on invitro the bpyridiminone molecules show better Anthelmintic activity. Here the compound PY-02 (4-(2-chlorophenyl)-6-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1H)- one) shows better activity than other molecules.

CONCLUSION
The compound PY-02 (4-(2-chlorophenyl)-6-(4-chlorophenyl)-3, 4-dihydropyrimidin-2(1H)- one) shows better activity than other molecules.

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