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SYNTHESIS AND SCREENING ANTHELMINTIC ACTIVITY OF SOME THIAZOLE DERIVATIVES

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ABSTRACT

Thiazole nucleus frequently occurs in natural products. In the present course of study an attempt is made for synthesis of thiazole derivatives. The thiazole is synthesized by reacting benzil with substituted aldehyde in presence of ammonium thiocynate using the glacial acetic acid as solvent. The synthesized compounds were re-crystallized by ethanol. The structures of the newly synthesized compounds were determined on the basis of their spectroscopic data such as UV, IR and H NMR spectroscopy. The anthelmintic activity of compounds was studied by using the piperazine citrate as standard. Most of the compounds showed a good anthelmintic activity.

Key words: Substituted aldehyde, Thiazole, anthelmintic activity.

INTRODUCTION

Heterocyclic synthesis has emerged as powerful technique for generating new molecules useful for drug discovery. Heterocyclic compounds provide scaffolds on which pharmacophore can arrange to yield potent and selective drugs[1].

Thiazole ring is involved in many of the natural products. The most important naturally occurring thiazole derivative is thiamine (Vitamin B_1) contains both pyrimidine and thiazole ring system. Penicillin's are also important naturally occurring products and contain reduced thiazole ring system. Moreover, a number of thiazole derivatives exhibit pharmacological activities[2]. Some of them are used as medicines. Thiazoles were reported to possess antibiotic, anti-inflammatory, fungicide, anthelmintic, antitubercular, anticonvulsants and cardiotonic activities. Thiazoles have enhanced lipid solubility with hydrophilicity.

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Thiazoles are easily metabolized by routine bio-chemical reactions and are non-carcinogenic in nature[3-7].

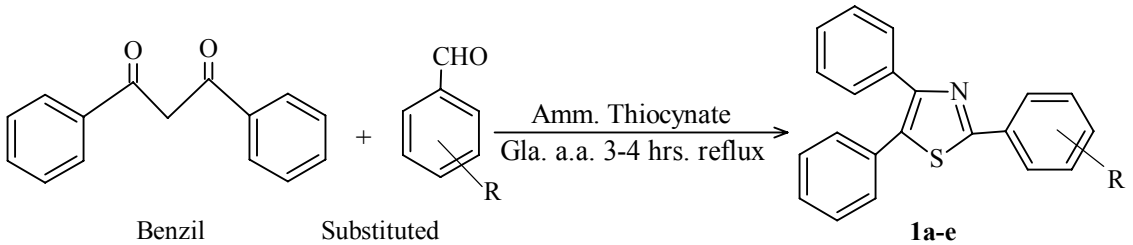
EXPERIMENTAL

Melting points were determined with open capillary and are uncorrected. IR spectra were recorded in KBr pellets by using JASCO FT-IR 300E spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker-400 MHz spectrometer using TMS as an internal standard. UV spectra were recorded on Jasco V-530 UV-Visible spectrometer.

Procedure for synthesis of diphenylthiazol-2-yl derivative (1a-e)

As per procedure reported in literature[7], a mixture of 25 mmole (5.25 g) benzil, 25 mmole of substituted aldehyde and 10 g of ammonium thiocynate were taken in a 250 mL round bottomed flask attached to a reflux condenser and refluxed with 5 mL of glacial acetic acid for 4 hr. The resultant mixture was left overnight and filtered to remove any precipitate. Then 250 mL distilled water was added to the filtrate and precipitate formed was collected. The filtrate was neutralized with ammonium hydroxide and the second crop of the solid was collected. Both solid crops were combined and recrystallized from ethanol.

Characterization data of the synthesized compounds are reported in Table 1.



Benzil Substituted aldehydes **1a-e**

R = -OH (o), -NO_2 (o), -OCH_3 (m), -CH_3 (p), -H
1a 1b 1c 1d 1c

Table 1: Characterization data of compounds

Compound	R	Molecular formula	% Yield	λ_{max} (nm)	M.P. (^{o}C)
1a	OH (o)	$C_{23}H_{17}O_2SN$	89.32%	334	160
1b	NO_2(o)	$C_{21}H_{14}O_2SN$	62.56%	346	158

Cont…

Compound	R	Molecular formula	% Yield	λ_{max} (nm)	M.P. (^oC)
1c	OCH_3(m)	$C_{22}H_{17}OSN$	74.48%	356	170
1d	CH_3(p)	$C_{22}H_{17}SN$	56.42%	346	148
1e	H	$C_{21}H_{15}SN$	69.45%	334	110

2(4, 5 diphenyl 1, 3-Thiazol-2-yl) Phenol (1a):

FTIR: 1437 cm^{-1}(C=C), 1602 cm^{-1} (-C=N-), 2576 cm^{-1} (cyclic S), 3200 cm^{-1} (-OH).

^{1}H NMR (DMSO): δ 5.0 (s, 1H, -OH), 6.88-7.45 (m, 10H, Ar-H), 7.72 (m, 4H, Ar-H).

2-(2-Nitrophenyl)-4, 5-diphenyl-1, 3-Thiazole (1b):

FTIR: 1437 cm^{-1}(C=C), 1604 cm^{-1} (-C=N-), 2647 cm^{-1} (cyclic S), 1504 cm^{-1} (-N=O).

^{1}H NMR (DMSO): δ 6.88-7.45 (m, 10H, Ar-H), 7.5 (m, 4H, Ar-H).

2-(3-methoxyphenyl)-4, 5-diphenyl-1, 3-Thiazole (1c):

FTIR: 1437 cm^{-1} (C=C), 1604 cm^{-1} (-C=N-), 2647 cm^{-1} (cyclic S), 2832 cm^{-1} (-O-CH_3).

^{1}H NMR (DMSO): δ 3.7 (s, 3H, methyl), 7.5 (m, 4H, Ar-H), 6.88-7.45 (m, 10H, Ar-H).

Anthelmintic activity

All the newly synthesized compounds were screened for anthelmintic activity on adult earthworms (*Pheritima posthuma*) [8-12].

Adult earthworm *Pheritima posthuma* were collected (due to its anatomical and physiological resemblance with the intestinal roundworm parasites of human being) from moist soil, obtained from agricultural fields. Three test groups were taken each containing six earth worms of approximately equal size (8 ± 1 cm). Piperazine citrate was taken as standard drug and different concentrations (5 mg/mL, 10 mg/mL, 15 mg/mL, and 20 mg/mL)

were prepared in normal saline containing 1% tween 80. The synthesized compounds of different concentrations were prepared by dissolving in minimum quantity of tween 80 and making up to the final volume with normal saline to obtain 5 mg/mL, 10 mg/mL, 15 mg/mL, and 20 mg/mL concentrations. One of the groups is taken as control group, which was treated with normal saline containing 1% tween 80. Paralysis onset time and death time of individual worms were noted. Paralysis was said to occur when the worms do not revive even in normal saline. Death was concluded when the worms lost their motility followed by fading away of color of worm.

RESULTS AND DISCUSSION

All the above synthesized compounds were screened for anthelmintic activity. The data in Table 2 and Fig. 1, 2 reveals that the synthesized compounds showed significant dose dependent anthelmintic activity compared to the standard. Among the tested compounds, compound **1c** showed most potent activity. The compound **1c** demonstrated paralysis as well as death of worms at a time comparable to piperazine citrate at concentration 5 mg/mL.

Table 2: Anthelmintic activity of synthesized compounds

S. No.	Compound	Concentration (mg/mL)	Paralysis time (min.)	Death time (min.)
1.	Normal saline (control)	-	-	-
2.	Piperazine citrate	5	5.15 ± 0.46	10.08 ± 0.46
3.	1a	5	24.2 ± 2.18	35.22 ± 3.43
		10	8.19 ± 0.70	15.70 ± 2.33
		15	8.30 ± 1.40	15.04 ± 1.20
		20	10.17 ± 0.90	17.42 ± 1.50
4	1b	5	23.12 ± 0.90	46.04 ± 1.00
		10	14.30 ± 0.90	30.46 ± 0.60
		15	9.16 ± 0.70	20.03 ± 0.10
		20	4.41 ± 0.70	14.04 ± 1.00

Cont…

S. No.	Compound	Concentration (mg/mL)	Paralysis time (min.)	Death time (min.)
5.	1c	5	5.03 ± 0.70	10.32 ± 0.50
		10	5.53 ± 1.50	11.40 ± 0.90
		15	5.05 ± 0.90	7.34 ± 1.00
		20	4.02 ± 0.50	7.21 ± 0.40
6.	1d	5	25.34 ± 0.80	44.30 ± 3.10
		10	19.30 ± 0.70	37.28 ± 0.80
		15	15.42 ± 0.80	30.05 ± 0.90
		20	10.51 ± 0.70	23.02 ± 0.90
7	1e	5	17.41 ± 0.60	41.52 ± 0.80
		10	16.16 ± 1.10	30.37 ± 2.40
		15	9.27 ± 0.60	26.42 ± 1.50
		20	6.08 ± 1.00	20.48 ± 0.60

Result are expressed as Mean ± SEM for six observations, when compared with piperazine citrate as standard reference

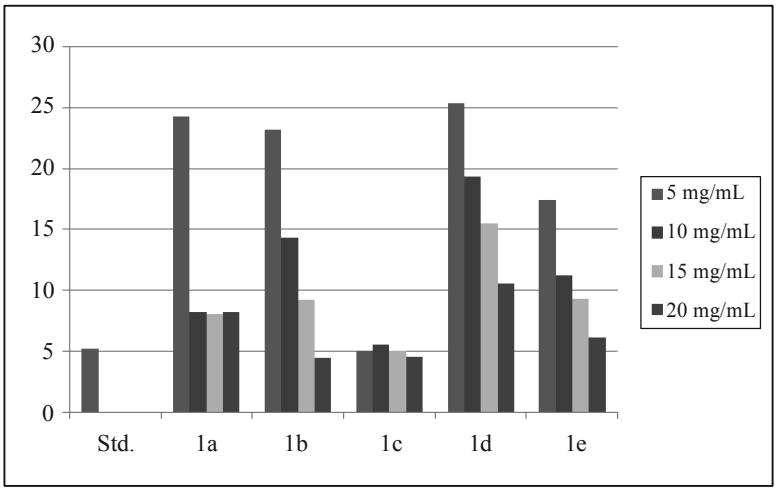


Fig. 1: Comparison of paralysis time at different conc. of compound

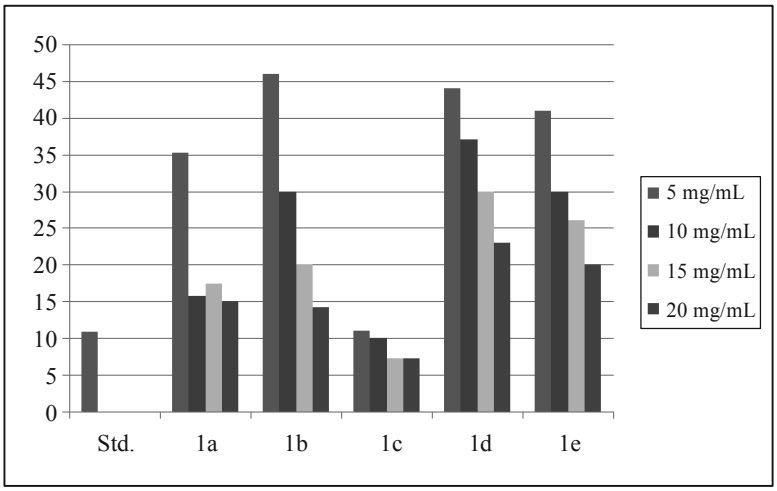


Fig. 2: Comparison of death time at different conc. of compound

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