Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2015, 7(5):64-71
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Synthesis, antihelmintic and insilico evaluation of 5-(substituted styryl)-5-(benzylideneamino)-1, 2, 4-triazolidine-3-ones

K. Sudha Rani[1], D. Rajesh[2], Kandula Priyanka[1] and K. N. V. Chenchu Lakshmi[1]*

[1]Department of Pharmaceutical Chemistry, KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada, Andhra Pradesh, India
[2]Department of Pharmacology, Siddhartha Medical College, NTR Health University, Vijayawada, Andhra Pradesh, India

---

ABSTRACT

A series of 5-(substitutedstyryl)-5-(benzylideneamino) - 1, 2, 4-triazolidine-3-one derivatives were synthesized by condensation of oxazol-5-ones by reaction of hippuric acid and different aldehydes with semicarbazide. Structures of the compounds were characterized on the basis of IR, ^{13}CNMR and ^{1}H NMR. Compounds 1b-12b were screened for antihelmintic activity .Test results revealed that compound 7b and 11b showed paralysis time of 3.3 and 3.1 min and death time of 4.1 and 4.5 min while the standard drug albendazole showed paralysis time of 11 min and death time of 21min, respectively, at the same concentration of 50mg/ml. All compounds were found to posses both vermifuge and vermicide properties.

Keywords: 1, 2, 4 Triazole, Antihelmintic, Albendazole, Earthworms

---

INTRODUCTION

Helminth infections were among the most widespread infections in humans especially in Poverty-stricken and developing countries with warm moist environments and poor sanitary conditions [1] helminthes are increasingly becoming resistant to classical drugs [2], Therefore it has become the need of hour to synthesize some novel antihelmintic agents to overcome resistance and side effects for safe and effective treatment of helmintic infections [3-5] Antihelmintic drugs target the helminth parasitic worms (helminths) and expel them from the body, either by stunning or by killing them. Ideally an antihelmintic agent should have a broad spectrum of action, high percentage of cure, free from toxicity to the host & should be cost effective, but none of the synthetic drugs are available in the market [6] .The antihelmintic drugs are contraindicated for some patients like pregnant and lactating woman because of low safety profile.

Literature survey revealed that triazole heterocyclic ring has proved to be versatile nuclei having a myriad spectrum of pharmacological activities like antihelmintic, antibacterial, antifungal, antioxidant, anti-inflammatory, anticancer and antiviral activities [7-9]. Keeping in view of these valid observations, it was found significant to produce effective drugs with reduced dosing frequency, side effects and improving meets these requirements for the development of new anti-helmintic agent.

The aim of the present work is to investigate the antihelmintic activity of newly synthesized 5-(substitutedstyryl)-5-(benzylideneamino) - 1, 2, 4-triazolidine-3-one derivatives. Triazolidine-3-ones are very effective against various helminthes in decades. Moreover there are certain helminthes, which are found to be resistant to major classes of antihelmintics such as benzimidazoles, imidazothiazoles and macrocyclic lactones. Therefore a search for these 5-

(substitutedstyryl)-5-(benzylideneamino) - 1, 2, 4-triazolidine-3-one and its derivatives leads to the evaluation of prototype compound with antihelmintic activity.

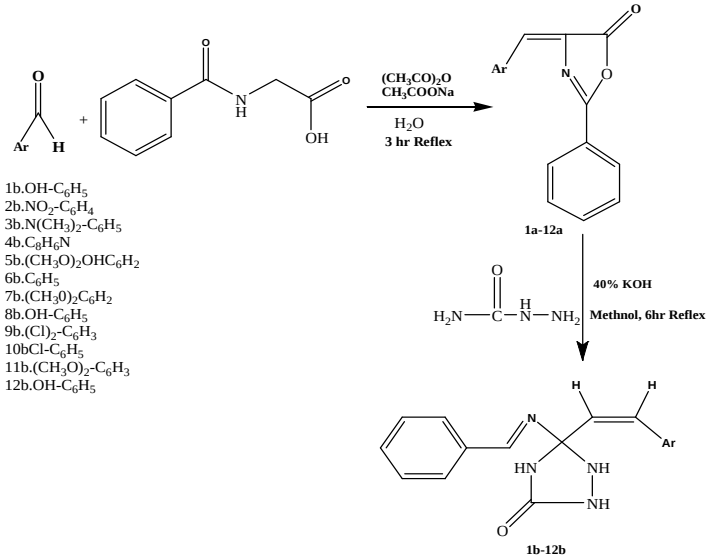
MATERIALS AND METHODS

Melting points were determined in open glass capillaries using GallenKamp (MFB-600) melting point apparatus and were uncorrected. IR spectra (KBr discs) Bruker analyzers were confirmed by Shimadzu FT-IR Spectrophotometer using KBr pellets technique, Model No.8400S (Japan). ^{1}H and ^{13}C NMR spectra were recorded on Bruker 400 MHz NMR spectrometer (Switzerland) using DMSO as solvent. T.L.C. was run on silica gel G plates using ethyl acetate: n-hexane (7:3) as developing solvent to assess the progress of reaction and purity of the compounds. All other chemicals used in the present study were of analytical grade .

Drugs and chemicals

Hippuric acid – (LOBA-B.NO-G228507), Acetic anhydride – (FISHER'S SCIENTIFIC-B.NO-92757004-2),Sodium Acetate – (FINAR-B.NO-19095780), semicarbazide –(LOBA-B.NO-S057310) ,Methanol (SD FINE-CHEMLIMITED- B.NO-IOZA-0502-0409-13),Charcoal – (QUALINGENS-BNO-17335406-S) ,Ethanol – (CSS-B.NO-110605), N,N-Dimethyl formamide (DMF) – (LOBAB.NO-LIO1571306). Albendazole-(ABL-400Mg, MALAR HEALTHCARE) ,sodium chloride(SD FINE CHEMICALS-B.NO-IOZA-SDFCL-DO9Y/0308/607/21),gum acacia (LOBA-V-0324/1).Albendazole and vehicle(1%V/V gum acacia in normal saline were used. All the prototypes were dissolved in minimum quantity of 1%V/V gum acacia and then volume was adjusted to 10ml with normal saline for making the concentration of 50mg/ml with DMF)

General procedure for the Synthesis of 5-(substitutedstyryl)-5-(benzylideneamino) - 1, 2, 4-triazolidine-3-one (1b-12b) involves synthesis of 4-benzylidene-2-phenyloxazol-5(4H)-ones (1a-12a) by condensation of 0.01 moles of hippuric acid with 0.02 moles of different types of aromatic aldehydes in presence of 0.075 moles of acetic anhydride and 0.025 moles of sodium acetate with 2ml of water refluxed for 3hr. The reaction mixture was cooled; precipitate was filtered, dried, recrystallized from methanol. The product from step1 condensed with equimoles (0.001 moles) of semicarbazide in presence of methanol and a few drops of 40% KOH refluxed for 6hrs, cooled; the product formed was filtered, dried and recrystallized from methanol. The progress and the purity of the reaction were confirmed by thin layer chromatography and melting point. The procedure was illustrated under **Scheme 1** and the physical data were tabulated in **Table 1**.



Scheme.1

Compound 1b: (5E)-5-(htdroxystyryl)-5-(benzylideneamino)-1,2,4-triazolidine-3-one: FTIR (γ max, cm^{-1})1600 (-***C*=*C*** stretch), 3006 (=***C*-*H*** stretch), 912(=***C*-*H*** bend), 1702(⁻***C*=*0***) 1529 (-**C=N**), 3393(NH 2^{0}amine stretch), 3288(-***OH*** stretch)***;*** **^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ***5.89,5.94 (s,2H, -C**H**=C), ***δ*** 7.972,7.991 (d**, 1H, *J*** 1.99 Ar-**H**), ***δ*** 7.375-7.839 (m ,5H, J 9.48 Ar-H) ***δ*** 7.51, 7.50(d, 1H, ***J*** 0.51, **H**C=N), ***δ*** 6.953 (s,1H, O-**H**), *δ* 8.624 ***(--C=O),*** 2.51 **(NH*)* ^{13}CNMR:** (400MHZ,$CDCl_3$) ***δ***134. 79, 133. 44, 132.26, 130.89, 130.25, 128.64, 128.30, 128.13, 127.59, 127.06, 127.02 (Ar-**C**), ***δ*** 125.05,124.16 (C=**C**), ***δ*** 171.31 (O= **C**-), ***δ*** 161.17 (**C**=N), ***δ*** 157.81 (Ar-OH-**C**).

Compound 2b:(5E)-5-(4-nitrostyryl)-5-(benzylideneamino)-1,2,4-triazolidine-3-one; FTIR (γ max, cm^{-1})1642 (-***C*=*C*** stretch), 2887 (=***C*-*H*** stretch), 928(=***C*-*H*** bend), 1518 (-**C=N**), 1548(Asymmetric stretch-**NO_2**),

1345(Symmetric stretch- **NO_2**),1718 (**-C=O),** 3421 (**NH** 2^0 amine stretch);**; ^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ***6.06,6.69 (-C**H**=C), ***δ*** 7.29-8.14 (m,5H,J 1.02 Ar-H) , ***δ*** 6.0 (d,1H, J 2.03,**H**C=N), *δ* 8.11 ***(-C=O);*** **^{13}CNMR :**(400MHZ, CD Cl_3) ***δ*** 129.2 ,128.9, 131.1, 128.9, 129.2, 139.9, 141.3,127.3, 123.8, 123.8, 127.3 (Ar-**C**), ***δ*** 123.3,129.5 (C=**C**), ***δ*** 159.8 (O= **C**-), ***δ*** 160.9 (**C**=N), ***δ*** 147.2 (NO_2-**C**).

Table.1-Physical Data

Compound	MF	MW	Physical state		MP(^{O}C)	% yield
			Colour	State		
1b	$C_{17}H_{16}N_4O_2$	308	Yellow	Solid	243^{0}C	63%
2b	$C_{17}H_{15}N_5O_3$	337	Yellow	Solid	228^{0}C	64%
3b	$C_{18}H_{18}N_4O_2$	322	Yellow	Solid	204^{0}C	62%
4b	$C_{17}H_{14}Cl_2N_4O$	360	White	Solid	230^{0}C	60%
5b	$C_{17}H_{15}ClN_40$	326	White	Solid	231^{0}C	61%
6b	$C_{19}H_{17}N_5O$	331	Brown	Solid	229^{0}C	62%
7b	$C_{19}H_{20}N_4O_4$	368	Red	Solid	232^{0}C	64%
8b	$C_{19}H_{20}N_4O_3$	352	Yellow	Solid	211^{0}C	66%
9b	$C_{17}H_{16}N_4O_2$	308	Yellow	Solid	244^{0}C	65%
10b	$C_{20}H_{22}N_4O_4$	382	White	Solid	216^{0}C	63%
11b	$C_{17}H_{16}N_4O$	292	Yellow	Solid	216^{0}C	67%
12b	$C_{19}H_{21}N_50$	335	Yellow	Solid	212^{0}C	65%

Compound 3b:(5E)-5-(4-methoxystyryl)-5-(benzylideneamino)-1,2,4-triazolidine-3-one;
FTIR (γ max, cm^{-1})1640 (***-C=C*** stretch), 3087 (***=C-H*** stretch),1020 (***=C-H*** bend), 1698(***-C=O***), 1520 (**-C=N**), 1244(-**CO**),3449(**NH**2^0aminestretch);**^{1}HNMR**(400MHZ,$CDCl_3$) ***δ***6.5.76,6.55 (-C**H**=C), ***δ*** 6.72 , 7.62 (m, 5H, J9.4 ArH) , ***δ*** 6.0 (d, 1H, J2.05 **H**C=N)*δ* 8.11 ***(C=O);****δ3.73*(OCH_3): **^{13}CNMR:**(400MHZ,$CDCl_3$) ***δ***129.2,128.9,131.1,128.9,129.2,139.9,127.4,114.2,114.2,127.4,127.5 (Ar-**C**), ***δ***123.3,129.5 (C=**C**), ***δ*** 159.8 (O= **C**-NH), ***δ*** 160.9 (**C**=N), ***δ*** 159.8 (-O-**C**),***δ***55.9(-0-CH_3)

Compound4b:(5E)-5-(2,3-dichlorostyryl)-5-(benzylideneamino)-1,2,4-triazolidine-3-one; FTIR (γ max, cm^{-1})1617 (***-C=C*** stretch), 2918 (***=C-H*** stretch),1093 (***=C-H*** bend), 1722(***-C=O***), 1517 (**-C=N**), 3362 (**-NH** 2^0 amine stretch),779 (**-C-Cl); ^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ***5.902 (s, 1H,-C**H**=C), ***δ*** 7.423-7.596 (m,3H,***J*** 4.4 Ar-H) ,7.711-7.819(d**, 2H, *J*** 2.80 Ar-**H**), ***δ*** 7.225(**H**C=N),*δ*7.936,7.918***(***d,1H,J2.16-**C=O*).*^{13}**CNMR:** (400MHZ,$CDCl_3$) ***δ***133.89, 133.52, 131.37, 131.08,127.82,127.77(Ar-**C**), ***δ***159.57 (C=**C**), ***δ*** 174.28 (O= **C**-NH), ***δ*** 166.37 (**C**=N).

Compound5b:(5E)-5-(4-chlorosryryl)5-(benzylideneamino)-1,2,4-triazolidine-3-one; FTIR (γ max, cm^{-1})1614 (***-C=C*** stretch), 3012 (***=C-H*** stretch),922 (***=C-H*** bend), 1701(***-C=O***), 1541 (**-C=N**), 3434 (**-NH** 2^0 amine stretch), 641 (-C-Cl); **^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ*** 6.5.76,6.55 (-C**H**=C), ***δ***7.22,7.62(m5H,J8.54ArH),***δ***6.0(d,1H,J1.99**H**C=N),*δ*8.11***(NHC=O);*****^{13}CNMR:**(400MHZ,$CDCl_3$)***δ***139.9,129.2,128.9,131.1,128.9,129.2,127.8,128.8,127.8,133.3(Ar-**C**), ***δ***123.3,129.5 (C=**C**), ***δ*** 159.8 (O= **C**-NH), ***δ*** 160.9 (**C**=N), ***δ*** 133.5 **(-C-Cl)**

Compound6b:(5E)-5-(Z)-2-(1H-indol-3-yl)vinyl)-5-(benzylideneamino)-1,2,4triazolidine-3-one;
FTIR(γmax,cm^{-1})1651(***-C=C***stretch),3032 (***=C-H*** stretch),1071 (***=C-H*** bend), 1711(***-C=O***), 1541 (**-C=N**), 3412 (-**NH** 2^0 amine stretch) **^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ*** 5.76,6.55 (-C**H**=C),***δ***7.07.62(m,5H,J9.83ArH),***δ***6.0(d,1H,J1.98**H**C=N),*δ*8.11***(NHC=O);*****^{13}CNMR:**(400MHZ,$CDCl_3$)***δ***129.2,128.9,131.1,128.9,129.2,139.9,126.1,119.0,122.2,120.1,111.1,135.5,130.8,110.1 (Ar-**C**), ***δ***129.3,129.5 (C=**C**), ***δ*** 159.8 (O= **C**-NH), ***δ*** 160.9 (**C**=N).

Compound7b:(5E)-5-(4-hydroxy-**3,5-dimethoxystyryl)-5-(benzylideneamino)-1,2,4 triazolidine-3-one;** FTIR (γ max, cm^{-1})1657 (***-C=C*** stretch), 3008 (***=C-H*** stretch),1014 (***=C-H*** bend), 1709(***-C=O***), 1542 (**-C=N**), 3417 (**-NH** 2^0 amine stretch), 3239 (-OH stretch), 1298 (-C-O); **^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ*** 5.76,6.55 (-C**H**=C), δ3.73(O-CH_3),***δ*** 6.20-7.62 (m,5H,J 8.92ArH),***δ***6.0(d,1H,J1.63**H**C=N),*δ*8.11***(NHC=O),***δ5.0(s,1HOH)**^{13}CNMR:**(400MHZ,$CDCl_3$)***δ***129.2,128.9,131.1,128.9,129.2,139.9,126.1,119.0,122.2,120.1,111.1,135.5,130.8,110.1(Ar-**C**), ***δ***129.3,129.5 (C=**C**), ***δ*** 159.8 (O= **C**-NH), ***δ*** 160.9 (**C**=N), δ132.0(-C-OH), ***δ*** 56.2(O-CH_3), δ152.3(-O-C).

Compound 8b: (5E)-5-(2,4-dimethoxystyryl)-5-(benzylideneamino)-1,2,4-triazolidine-3-one ; FTIR (γ max, cm^{-1})1648 (***-C=C*** stretch), 3082 (***=C-H*** stretch),731 (***=C-H*** bend), 1712(***-C=O***), 1512 (**-C=N**), 3429 (**-NH** 2^0 amine stretch), 1236 (-C-O-); **^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ*** 5.92,6.82 (d,1H,J 1.05 -C**H**=C), δ3.73(O-CH_3),***δ*** 6.23-7.62 (m,5H,J 8.06 Ar-H) , ***δ*** 6.0 (d,1H,J 0.62 **H**C=N),

*δ*8.11***(*NHC=O*);*** **^{13}CNMR:**(400MHZ,$CDCl_3$)***δ***129.2,128.9,131.1,128.9,129.2,139.9,100.3,106.5,128.4,107.3 (Ar-**C**), ***δ***129.3,129.5 (C=**C**), ***δ*** 159.8 (O= **C**-NH), ***δ*** 160.9 (**C**=N), ***δ*** 56.3,55.9(O-CH_3), δ158.7,160.9(-O-C);

compound 9b: (5E)-5-(4-hydroxystyryl)-5-(benzylideneamino)-1,2,4-triazolidine-3-one; IR Data: FTIR (γ max, cm^{-1})1636 (-***C*=*C*** stretch), 2988 (=***C*-*H*** stretch),923 (=***C*-*H*** bend), 1709(-***C*=*O***), 1536 (-**C=N**), 3429 (-**NH** 2^0 amine stretch),3208 (-OH stretch), 1090 (-C-O-); **^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ*** 5.76,6.55 (-C**H**=C), δ5.0(C-OH),***δ***6.68-7.62 (m,5H,J 9.45 Ar-H),***δ***6.0(d,1H,J1.8**H**C=N),**^{13}CNMR:**(400MHZ,$CDCl_3$)***δ***129.2,128.9,131.1,128.9,129.2,139.9,127.8,115.8,157.7,115.8,127.8,127.8(Ar-**C**), ***δ***129.3,129.5 (C=**C**), ***δ*** 159.8 (O= **C**-NH), ***δ*** 160.9 (**C**=N), ***δ***56.3,55.9(O-CH_3), ***δ*** 157.7(C-OH);

Compound10b:(5E)-5-(3,4,5-trimethoxystyryl)-5-(benzylideneamino)-1,2,4-triazole-3-one ; **IR Data:** FTIR (γ max, cm^{-1})1623 (-***C*=*C*** stretch), 2932 (=***C*-*H*** stretch), 986(=***C*-*H*** bend), 1697(-***C*=*O***), 1541 (-**C=N**), 3377 (-**NH** 2^0 amine stretch), 1112 (-C-O); **^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ***7.756-7.019 (m,5H,J 9.05 Ar-H) , ***δ*** 6.549 (d,1H,J 0.67 **H**C=N), ***δ*** 3.825,3.680,3.326 (O-**CH_3**), *δ* 10.238***(*-NH-C=O*);*** **^{13}CNMR:**(400MHZ,$CDCl_3$)***δ***139.18,139.06,138.34,130.34(Ar-**C**), ***δ***104.16,103.92 (C=**C**), ***δ*** 153.78 (O= **C**-NH), ***δ*** 156.78 (**C**=N), ***δ*** 56.04,55.91,55.68 (O-**CH_3**).

Compound 11b: (5E)-5-(benzylideneamino)-5-styryl-1,2,4-triazole-3-one; FTIR (γ max, cm^{-1})1650 (-***C*=*C*** stretch), 2919 (=***C*-*H*** stretch),1016 (=***C*-*H*** bend), 1698(-***C*=*O***), 1550 (-**C=N**), 3397 (-**NH** 2^0 amine stretch), 1404 (-C-N); **^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ*** 5.76,6.55 (-C**H**=C), ***δ***7.14-7.62(m,5H,J9.64ArH),***δ***6.0(d,1H,J1.56**H**C=N),*δ*8.11***(*NHC=O*);*** **^{13}CNMR:**(400MHZ,$CDCl_3$)***δ***139.9,129.2,128.9,131.1,128.9,129.2,135.2,126.4,128.7,128.0,128.7126.4(Ar-**C**), ***δ***123.3,129.5 (C=**C**), ***δ*** 159.8 (O= **C**-NH),

Compound12b:(5E)-5-(4-(dimethylamino)styryl)-5-(benzylideneamino)-1,2,4-triazolidine-3-one ; FTIR (γ max, cm^{-1})1642 (-***C*=*C*** stretch), 3085 (=***C*-*H*** stretch),1070 (=***C*-*H*** bend), 1708(-***C*=*O***), 1543 (-**C=N**), 3390 (-**NH** 2^0 amine stretch), 1346 (-C-N); **^{1}H NMR:** (400MHZ,$CDCl_3$) ***δ*** 5.76,6.55(-C**H**=C),***δ*** 6.54-7.62 (m,5H,J8.12Ar-H)***δ***6.0(d,1H,J1.66**H**C=N),*δ*8.11***(*-NH-C=O*),*** ***δ*** 160.9(**C**=N);**^{13}CNMR:**(400MHZ,$CDCl_3$)*δ*129.2,128.9,131.1,128.9,129.2,139.9,124.7,127.3,114.2,127.3 (Ar-C), *δ*123.3,129.5 (C=C), *δ* 159.8 (O= C-NH), *δ* 160.9 (C=N), δ148.8(-C-N), δ40.3(N-CH_3)

Antihelmintic Activity [10]

Indian adult earthworms of the genus and species, *Pheritima posthuma* (family: Megascolecidae), were used to study the antihelmintic activity. The earthworms were collected from the water logged areas of soils in Vijayawada, Andhra Pradesh, India were washed with normal saline to remove all the fecal matter and waste surrounding their body. The earth worms (*Pheritima posthuma*) were 5-8 cm in length and 0.2- 0.3 cm width weighing 0.8–3.04 g were used for all experiment protocols. The earthworms resembled the intestinal roundworm parasites of human beings both anatomically and physiologically and hence were used to study the antihelmintic activity

Table 2: Antihelmintic Activity

Compounds	Dose	Paralysis time in minutes	Death time in minutes
		MEAN±S.E.M	MEAN±S.E.M
1b	50mg/ml	4 ± 0.5	5.13±0.416
2b	50mg/ml	3.6±0.529	5.1±0.36
3b	50mg/ml	3.83±0.763	4.66±0.611
4b	50mg/ml	3.16±0.76	4.8±0.8
5b	50mg/ml	4.1±0.36	5.2±0.72
6b	50mg/ml	3.4±1.2	5.4±0.781
7b	50mg/ml	3.13±0.76	4.53±1.01
8b	50mg/ml	3.7±0.435	5.16±0.472
9b	50mg/ml	3.26±0.823	5.23±0.873
10b	50mg/ml	3.8±0.721	5.73±0.64
11b	50mg/ml	3.93±0.80	5.33±0.35
12b	50mg/ml	3.36±0.984	4.13±0.611
Control	Normal saline	-------	------
Albendazole	50mg/ml	11±1	21.5±2.1

Procedure:

1% Gum acacia solution prepared in normal saline, different concentrations was prepared by using this solution. Samples were taken in petriplates and adult healthy earth warms (n=6) were introduced in to them. Paralysis was said to occur when the worms do not review even in normal saline. Death was concluded when worms lost their

motility followed by fading away of the body colour. The time taken for the earthworms to get paralysed and resulting in death was tabulated in table 2 and fig 1.

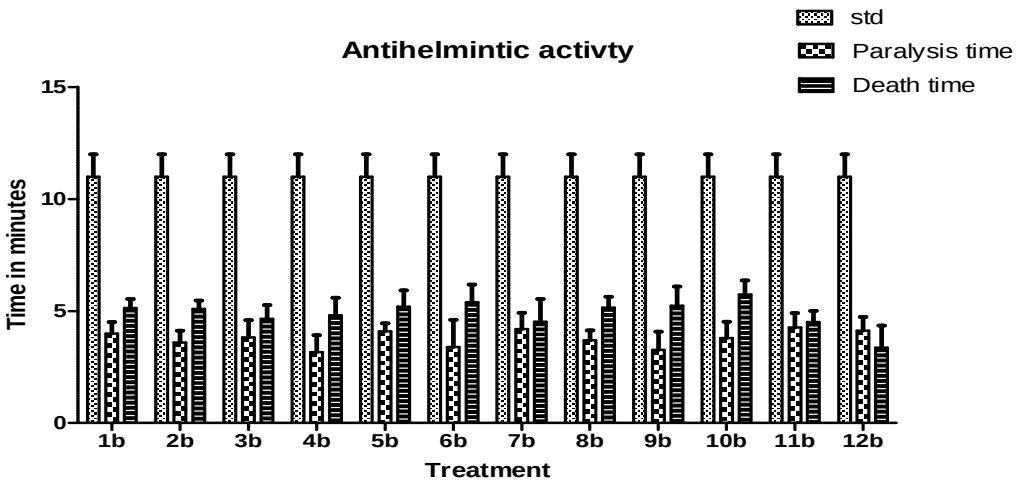


Fig. 1

Statistical Analysis

Results were expressed as mean±s.e.m in table 3. Statistical significance was determined by one-way analysis of variance (ANOVA) followed by Dunnett's test, with the level of significance at $P < 0.0001$.

Table-3 -Anova table

	SS	Df	MS	F	R^2
Treatment	361.9	2	180.9	1074	0.9849
Residual	5.561	33	0.1685		
Total	367.5	35			

SS=sum of square,DF=degree of freedom,MS=mean square,F=factors of the total deviationEach value is represented as mean ±standard error mean (n = 6).Data are found to be significant by testing through one way ANOVA at 99.9% level of significance (p < 0.0001).

In silico evaluation for drug-likeness and toxicity predictions [11-12]

Currently, in this work three cheminformatics programmes were used to evaluate the drug likeness of compounds, toxicity predictions, to assess the inhibition of the derivatives against 5 subtypes of cytochrome P450. Open source program OSIRIS Property Explorer was used to predict the fragment-based drug-likeness of title compounds and comparing them with Fluconazole and tetracycline , to assess the occurrence frequency of each fragment in the individual structure. The program estimated the risks of side effects, such as mutagenic, tumorogenic, irritant and reproductive effects, as well as drug-relevant properties including cLogP, LogS (solubility), MW and drug-likeness.

Molinspiration cheminformatics used for calculation of important molecular properties like logP, Polar surface area, Number of hydrogen bond donors, Number of hydrogen bond acceptors, Number of rotatable bonds, Volume, Number of violations from rule of five. It was also used to predict bioactive scores for the most important drug targets like GPCR ligand, Kinase inhibitors, Ion channel modulators, nuclear receptors, Protease inhibitors, Enzyme inhibitors.

Table .4

Compound	Toxicity Risks				Molecular Properties Calculation				
	MUT	TUMO	IRRI	REP	M.W	CLP	logS	DL	DS
1b					308	2.4	-4.08	2.68	0.76
2b					339	2.43	-5.02	2.36	0.65
3b					322	2.59	-4.4	2.74	0.72
4b					360	3.92	-5.85	3.68	0.52
5b					326	3.31	-5.12	3.38	0.5
6b					331	2.76	-4.91	3.64	0.67
7b					368	2.19	-4.12	3.88	0.77
8b					352	2.49	-4.42	-6.43	0.22
9b					308	2.4	-4.08	2.72	0.37
10b					382	2.38	-4.42	5.94	0.71
11b					292	2.7	-4.38	1.26	0.67
12b					335	2.69	-4.42	-1.84	0.15
Tetracycline					444.4	-1.33	-1.83	5.43	0.81
Fluconazole					323	-0.11	-2.17	1.99	0.87

MUT: *Mutagenic;* ***TUMO:*** *Tumorogenic;* ***IRRI:*** *Irritant;* ***REP:*** *Reproductive Effective;* ***CLP:*** *ClogP;* ***Log s:*** *Solubility mol/lit;* ***DL:*** *Drug-Likeness;* ***DS:*** *Drug-Score.* ***MW:*** *Molecular weigh*

Table.5 Molinspiration: Physical properties

Compound code	Log P	Polar Surface Area	H-Bond Acceptors	H-Bond Donor	Volume
1b	2.974	85.744	6	4	276.0
2b	3.172	111.34	8	3	291.316
3b	3.27	74.75	6	3	293.528
4b	4.293	65.516	5	3	295.053
5b	3.891	65.516	5	3	281.518
6b	3.184	81.307	6	4	296.959
7b	2.568	104.212	8	4	327.091
8b	3.075	83.984	7	3	319.073
9b	2.734	85.744	6	4	276.0
10b	2.844	93.218	8	4	344.619
11b	3.213	65.516	5	3	267.982
12b	3.315	68.754	6	3	313.888

Table.6 Molinspiration: BIOACTIVE SCORES

Compound	GPCR Ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1b	-0.16	-0.13	-0.12	-0.15	-0.28	-0.02
2b	-0.34	-0.22	-0.30	-0.37	-0.39	-0.19
3b	-0.24	-0.25	-0.20	-0.29	-0.32	-0.13
4b	-0.20	-0.17	-0.33	-0.28	-0.32	-0.16
5b	-0.21	-0.18	-0.19	-0.32	-0.34	-0.11
6b	-0.01	-0.15	-0.05	-0.34	-0.23	-0.02
7b	-0.21	-0.20	-0.14	-0.25	-0.29	-0.05
8b	-0.23	-0.27	-0.20	-0.26	-0.32	-0.14
9b	-0.21	-0.19	-0.16	-0.21	-0.29	-0.05
10b	-0.23	-0.24	-0.17	-0.34	-0.32	-0.12
11b	-0.23	-0.18	-0.19	-0.33	-0.33	-0.08
12b	-0.19	-0.19	-0.12	-026	-0.28	-0.09
Tetracycline	-0.15	-0.24	-0.53	-0.09	-0.04	0.52
Fluconazole	0.04	0.01	-0.09	-0.23	-0.09	0.03

The Online Chemical Modelling Environment (OCHEM) a unique and a web-based platform which supports all the steps required to create a predictive model: one such model developed was cytochrome p 450 with 5 subtypes .the compounds were evaluated to assess their inhibition on the subtypes of cytochrome P450.

Table.7 Online Chemical Modelling:

Compound	Aqueous solubility	Log IGC50	AMES	CYP3A 4	CYP2D 6	CYP2CI 9	CYP2C 9	CYP1A 2
1b	2.88	1.22	Active	_	_	_	+	+
2b	3.93	0.57	Active	_	_	_	+	+
3b	3.41	0.78	Active	_	_	+	+	+
4b	4.53	1.22	Active	_	_	+	_	+
5b	3.86	1	Active	_	_	+	_	+
6b	4.44	0.55	Active	_	_	+	+	+
7b	3.92	0.79	Active	+	_	_	_	+
8b	3.84	0.86	Active	_	_	_	_	+
9b	3.03	0.83	Active	_	_	+	+	_
10b	4.42	0.65	Active	+	_	_	_	+
11b	3.15	0.62	Active	_	_	_	+	+
12b	3.54	0.53	Active	_	_	_	_	+
Tetracycline	3.11	0.23	Inactive	_	_	_	_	_
Fluconazole	1.8	0.15	Inactive	_	_	_	_	_

+ Inhibitor, - Non inhibitor, AQ-aqueous, IGC 50-Environmental toxicity

RESULTS AND DISCUSSION

Physicochemical and analytical data were tabulated for synthesized compounds1b-12b as shown in Table 1. The structures of the compounds were characterised through IR and ^{1}H and ^{13}C NMR spectral data, whereas results of antihelmintic studies tabulated in Table 2 reveals that compounds 7b and 11b were found to be the most potent compounds in the series which when compared to the standard , compounds 3b and 4b showed high activity ,other compounds,1b,2b,5b and 8b showed significant antihelmintic activity. The structure-activity relationship studies based on the above results clearly indicate that compounds with electron donating groups on the aromatic ring showed increased potency .the intense activity of the compounds is also greatly influenced by the amount of activation or deactivation and position of the groups on the ring. The amine substituted, methoxy groups in the para position has higher significant activity which clearly indicates that position and the number of substituents is responsible for increased activity.

The derivatives synthesised were evaluated by three online softwares-OSIRIS, MOLINSPIRATION, OCHEM.OSIRIS results predicts that the compounds 1b, 3b, 7b, 10b had drug scores 0.7-0.78 nearer to that of standard drugs i.e. 0.8. compounds 2b,6b,11b had drug scores in the range 0.6-0.68.the other derivatives had less drug score with values ranging between 0.10-0.50.toxicity predictions inferred that compounds 5b-mutagenic,9b-mutagenic ,reproductive ,12b-reproductive and tumorogenic effects whereas the others are safe. From the OCHEM results, all the synthesised compounds were found to inhibit the subtype CYP1A2 of cytochromeP450.Molinspiration results inferred that all the derivatives satisfy Lipinski rule of five so as to behave as a drug and found to have kinase and enzyme inhibition properties.

CONCLUSION

A series of 5-(substitutedstyryl)-5-(benzylideneamino) - 1, 2, 4-triazolidine-3-one derivatives prepared by a novel method and their ability to paralyze and cause death of Indian earthworms. Though the mechanisms underlying this process remain to be fully elucidated detailed mechanistic studies and lead optimization of these 5-(substitutedstyryl)-5-(benzylideneamino) - 1, 2, 4-triazolidine-3-one derivatives are under investigation. It is intended that the results from these studies will assist in elucidating their precise mechanism of action and provide an approach to develop new potent antihelmintic prototypes for further optimization and development to get new leads in the treatment of helminth infestations

Acknowledgement
The authors are thankful to the Siddhartha Academy for General and Technical Education for providing necessary facilities to carry out this research work.

REFERENCES

[1]Nisha Pv, Shruti ***Swamy*** Ks, Kumari M, Vedamurthy Ab, Krishna V and Hoskeri Jh, *international journal of pharmaceutical sciences and drug research*, **2012**, 4, 205-208.
[2]Semwal A and Farswan MS, *Journal of Pharmacognosy and Phytochemistry*, **2012**, 1,85-88.
[3]Kharb, Rajeev, et al, *Der Pharmacia Lettre*, **2012**, 4, 2, 652-657.
[4]Lingala, Srikanth, Raghunandan Nerella, and K. R. S. S. Rao, *International Journal of Pharmaceutical Sciences Review and Research*, **2011**, 10,2 , 100-105.
[5]Patel, Kalpesh, et al, *Int. J. Pharm. Bio. Sci*, **2010**, 1, 3, 1-13.
[6]Ravindra GM, Shailaja GM and Anita AM, *Journal of Pharmaceutical Biology*, **2007**, 10,766-768.
[7]Kharb, Rajeev, et al, *Der Pharmacia Lettre*, **2012**, 4, 2, 652-657.
[8]Kharb, R., M. Shahar Yar, and P. C Sharma, *Current medicinal chemistry*, **2011**, 18.21, 3265-3297
[9]Kharb, Rajeev, Mohammad Shahar Yar, and Probodh Chander Sharma, *reviews in medicinal chemistry*, **2011**,11,1, 84-96.
[10]KNV Chenchu Lakshmi, Deepika Koti, B. Anupama, A. Chakravarthy and M. Priyanka,. *J. of Pharm. Life Sci*, **2014**; 5, 8, 765-3773.
[11]Tetko IV. Computing chemistry on the web. *Drug Discov Today* **2005**; 10:1497-1500.
[12]Organic Chemistry Portal, http://www.organicchemistry. Org/prog/peo/ 22 May, **2012**.