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Microwave assisted synthesis of some new 3-(4-substituted anilino)-5-(3', 4'-disubstituted aryl)-2-isoxazoles as potential Anthelmintic agents.

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ABSTRACT

56 new 3-(4-substituted anilino)-5-(3', 4'-disubstituted aryl)-2-isoxazoles were synthesized by microwave irradiation (560 w) of 3-phenyl or substituted phenyl -1- anilino or substituted anilino -2- propene -1- ones with hydroxylamine hydrochloride and sodium acetate. The structures of the compounds were proved by means of their I R, ^{1}H NMR, mass spectroscope and elemental analysis data.

Key words:- 3- phenyl or substituted phenyl -1- anilino or substituted anilino -2- propene -1- ones, hydroxylamine hydrochloride, sodium acetate, Anthelmintic activity.

INTRODUCTION:

Microwave dielectric heating is widely exploited for acceleration of organic reactions during last one decade[1-16].there is an increasing interest in the utility of environmentally benign synthesis under microwave irradiation. Considerable interest has been focused on the isoxazole structure[17-29], which as been known to

possess a broad spectrum of biological activities such as psychotropic effects[30], potential analgesics[31-32], antimicrobial activity[33-34], herbicidal activity[35], antineoplastic activity[36], , anti inflammatory activity[37], CNS activity[38] and chemotherapy[39].

The discovery of this class of drugs provides an outstanding case history of modern drugs development and also points out the unpredictability of biological activity from structural modification of a prototype drug molecule.

In view of the wide range of therapeutic value of isoxazole ring system promoted us to plan the synthesis of a series of some new isoxazole derivatives by microwave irradiation the traditional synthesis of compounds suffered from the disadvantages such as long reaction time, low yield and inconvenience of handling where as the use of microwave irradiation technology in organic synthesis lead to increase the purity of products, enhance the chemical yield and shorten the reaction time.

EXPERMENTAL SECTION:

Melting point of synthesized compounds was determined by an open-end capillary tube method by electrically heated melting point apparatus expressed in ^{0}C and was uncorrected. The purity of the compounds was checked by TLC. In all the cases the distances traveled by the sample was found to be different from that of the parent compound spotted along with it. Thus confirming the fact that the compounds formed were entirely different from that of the parent compound. R_f and R_m values of title compounds were shown in Table No.-III-3.

The characterization data of the synthesized compounds were given in the Table No.-III-3. The structures of the synthesized compounds were elucidated by Perkin Elmer 1600 series Fourier Transformer-Infrared Spectrophotometer in KBr-Pellet method. IR values are measured in cm^{-1} and the results are shown below. The structures of synthesized compounds were elucidated by ^{1}H FT-NMR (BRUCKER AMX 400 MHz) analyzer using TMS as internal standard. The samples are dissolved in $CdCl_3$, DMSO and the values are measured in chemical shift in delta (δ) ppm. The values of the assigned structures were interpreted as follows. The mass spectrum of the compound was recorded on MDS spiex AP12000 LC-MS mass spectrometer. Mass spectrum of the compound showed molecular ion at m/z and the results are

shown below. The elements of the synthesized compounds were calculated by chem... office software and the data obtained from Carlo Erba- 1108 elemental analyzer are presented in Table No.-III-4 has been found to be in agreement with the molecular formula of the assigned structures.

IR spectra of the compounds showed N-H stretching band at 3240. 52^{cm-1} in the ^{1}H NMR spectra 3.393(NH) and the protons belonging to the aromatic ring and substituent groups were observed within the expected chemical shift values (table No.III-5)

The synthesized compounds (56) were screened for anthelmintic activity by using *Peritima posthuma* (earthworm) obtained from agriculture department using standard drug. This method is effective in predicting the anthelmentic activity of a wide variety of new molecules. .

General procedure for the synthesis of isoxazoles:

Method A (Conventional) Step – 1: Synthesis of 3-phenyl or 3-substituted phenyl-1-anilino or 1-substituted anilino-2-propene-1-ones:

To a solution of acetanilide or its derivative compounds (0.01 mole) in ethanol (25 ml), aldehyde (or) substituted aldehyde (0.01 mole) was added in presence of 2% NaOH solution. The reaction mixture was refluxed for 12 hours. The reaction was monitored by TLC for the completion of reaction. Then hot reaction mixture was poured into crushed ice, and the separated product was filtered and purified by column chromatography

.

Step – 2: Synthesis of 3-[4-substituted anilino]-5-[3`4`-disubstituted aryl]-2-isoxazole.

Isoxazoles were synthesized by refluxing Chalcones (0.01 mole) with hydroxylamine hydrochloride (0.00014 mole) and sodium acetate (0.08 mole) in ethanol, for 6 hours and the reaction was closely monitored by TLC for the completion of reaction. Then hot reaction mixture was poured into crushed ice, and the separated product was filtered and purified by column chromatography

.

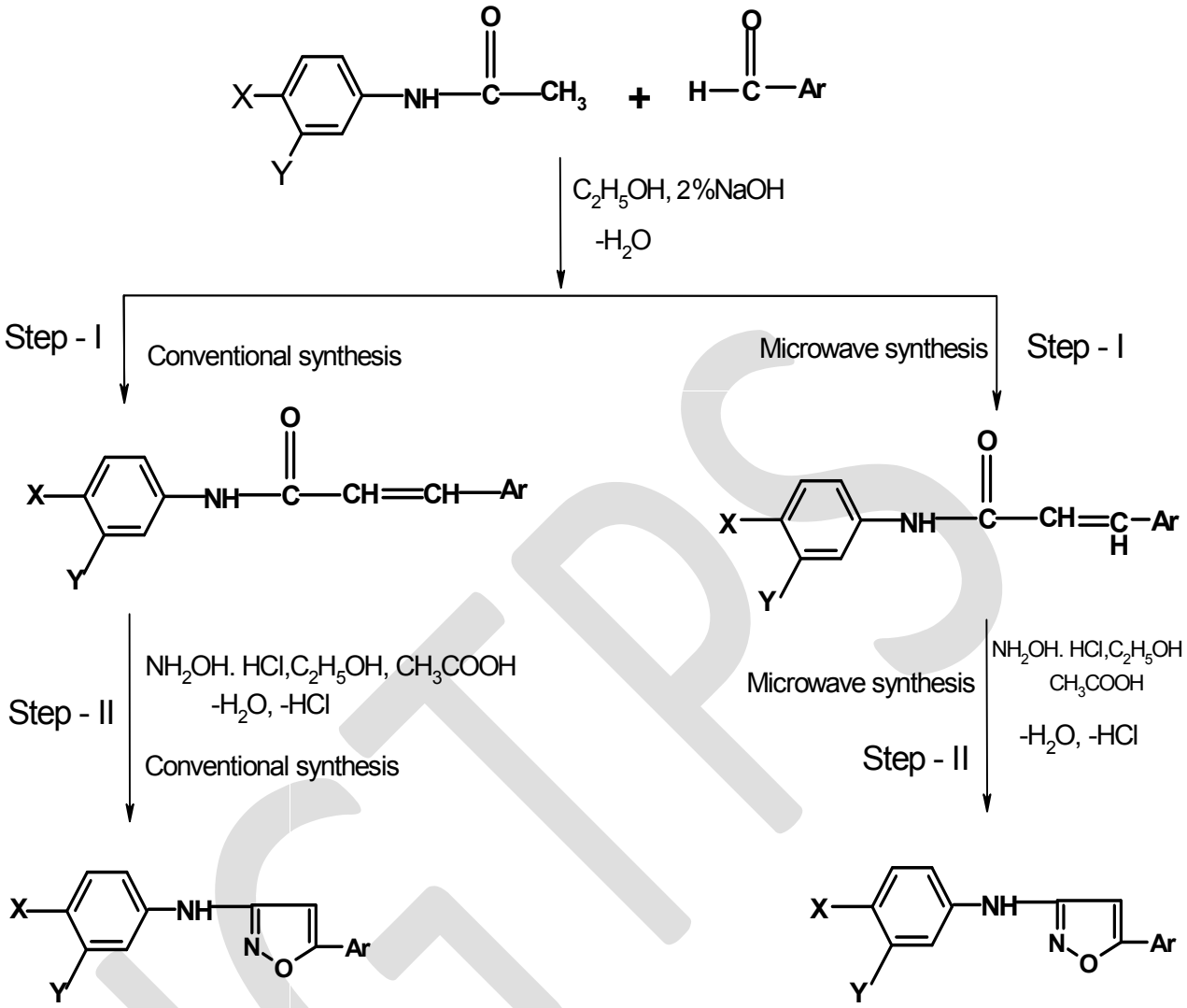
Method B (MORE) Microwave Induced Organic Reaction Enhancement Step – 1: Synthesis of 3-phenyl or substituted phenyl-1-anilino or substituted anilino-2-propene-1-ones:

To a solution of acetanilide and its derivative compounds (0.01 mole) in ethanol (25 ml), aldehyde (or) substituted aldehyde (0.01 mole) was added in the presence of 2% NaOH solution. The reaction mixture was subjected for Microwave irradiation (560W) for specified period (as ment ioned in the Table No.-III-2). The hot reaction mixture was poured into crushed ice and the separated product was filtered and purified by column chromatography.

Step – 2: Synthesis of 3-[4-substituted anilino]-5-[3`4`-disubstituted aryl]-2-isoxazole.

Isoxazoles were synthesized by Microwave irradiation (560W) of chalcone (0.01 mole) with hydroxylamine hydrochloride (0.00014 mole) and sodium acetate (0.08 mole) in ethanol, for specified period (as mentioned in the Table No.-III-2). The hot reaction mixture was poured into crushed ice, filtered and purified by column chromatograph.

By adopting the above synthetic procedure the compounds 1-56(IIIa-IIIz, IIIaa-IIIaz, IIIba-IIIbd) were synthesized by conventional and microwave methods. The physical and spectral characteristics of these isoxazoles 1-56 (IIIa-IIIz, IIIaa-IIIaz, IIIba-IIIbd) were presented.



The various substituents' present in the prepared isoxazoles are listed below: Table No.-III.1

S.No.	Comp. Code	X	Y	Ar
01.	III a	H	H	C_6H_5
02.	III b	H	H	$C_6H_3(OH)(OCH_3)$
03.	III c	H	H	$C_6H_4N(CH_3)_2$
04.	III d	H	H	$C_6H_4(NO_2)$
05.	III e	H	H	$C_6H_4(NO_2)$
06.	III f	H	H	$C_6H_4(OCH_3)$
07.	III g	H	H	$C_5H_4O_2$
08.	III h	OH	H	C_6H_5
09.	III i	OH	H	$C_6H_3(OH)(OCH_3)$
10.	III j	OH	H	$C_6H_4N(CH_3)_2$
11.	III k	OH	H	$C_6H_4(NO_2)$
12.	III l	OH	H	$C_6H_4(NO_2)$
13.	III m	OH	H	$C_6H_4(OCH_3)$
14.	III n	OH	H	$C_5H_4O_2$
15.	III o	Br	H	C_6H_5
16.	III p	Br	H	$C_6H_3(OH)(OCH_3)$
17.	III q	Br	H	$C_6H_4N(CH_3)_2$
18.	III r	Br	H	$C_6H_4(NO_2)$

19.	III s	Br	H	C_6H_4 (NO_2)
20.	III t	Br	H	C_6H_4 (OCH_3)
21.	III u	Br	H	$C_5H_4O_2$
22.	III v	NO_2	H	C_6H_5
23.	III w	NO_2	H	C_6H_3(OH) (OCH_3)
24.	III x	NO_2	H	C_6H_4N (CH_3)$_2$
25.	III y	NO_2	H	C_6H_4 (NO_2)
26.	III z	NO_2	H	C_6H_4 (NO_2)
27.	III aa	NO_2	H	C_6H_4(OCH_3)
28.	IIIab	NO_2	H	$C_5H_4O_2$
29.	III ac	CH_3	H	C_6H_5
30.	III ad	CH_3	H	C_6H_3(OH) (OCH_3)
31.	III ae	CH_3	H	C_6H_4N (CH_3)$_2$
32.	III af	CH_3	H	C_6H_4(NO_2)
33.	III ag	CH_3	H	C_6H_4 (NO_2)
34.	III ah	CH_3	H	C_6H_4(OCH_3)
35.	III ai	CH_3	H	C_4H_3O
36.	III aj	F	H	C_6H_5
37.	III ak	F	H	C_6H_3(OH) (OCH_3)
38.	III al	F	H	C_6H_4N (CH_3)$_2$
39.	III am	F	H	C_6H_4(NO_2)
40.	III an	F	H	C_6H_4 (NO_2)
41.	III ao	F	H	C_6H_4 (OCH_3)
42.	III ap	F	H	$C_5H_4O_2$
43.	III aq	Cl	H	C_6H_5
44.	III ar	Cl	H	C_6H_3(OH) (OCH_3)
45.	III as	Cl	H	C_6H_4N (CH_3)$_2$
46.	III at	Cl	H	C_6H_4 (NO_2)
47.	III au	Cl	H	C_6H_4(NO_2)
48.	III av	Cl	H	C_6H_4 (OCH_3)
49.	III aw	Cl	H	$C_5H_4O_2$
50.	III ax	Cl	F	C_6H_5
51.	III ay	Cl	F	C_6H_3(OH) (OCH_3)
52.	III az	Cl	F	C_6H_4N (CH_3)$_2$
53.	III ba	Cl	F	C_6H_4(NO_2)
54.	III bb	Cl	F	C_6H_4 (NO_2)
55.	III bc	Cl	F	C_6H_4(OCH_3)
56.	III bd	Cl	F	C_4H_3O

Comparison of microwave and conventional reactions of the title compounds Table No-III-2

S.No	Comp. code							
		Reaction time	%Yield	Appearance		Reaction	%Yield	Ap
01.	III a	360	52.6	Solid(crystal),white	1.5	60.11	Solid(crystal),white	
02.	III b	360	60.1	Solid(crystal),broen	2.0	65.5	Solid(crystal),broen	
03.	III c	360	70.5	Solid(crystal),blackish-	2.5	85.2	Solid(crystal),blackish-brown	
04.	III d	360	61.4	Solid(crystal), light-brown	2.0	67.4	Solid(crystal),light-brown	
05.	III e	360	62.6	Solid(crystal), light-orange	2.0	68.1	Solid(crystal),light-orange	
06.	III f	360	64.6	Solid(crystal), light-yellow	2.5	72.1	Solid(crystal),light-yellow	
07.	III g	360	59.5	Solid(crystal), light-	2.0	66.4	Solid(crystal),light-brown	
08.	III h	360	13.43	Solid(amorphous), black	1.5	32.6	Solid(amorphous), black	
09.	III i	360	15.0	Solid(amorphous), light-	1.5	48.4	Solid(amorphous),light-	
10.	III j	360	33.9	Solid(crystal), dark-black	1.0	51.34	Solid(crystal), dark-black	
11.	III k	360	35.8	Solid(amorphous),white	1.5	91.4	Solid(amorphous),white	
12.	III l	360	31.44	Solid(amorphous),light	1.5	90.0	Solid(amorphous),light white	
13.	III m	360	21.00	Solid(crystal),black	1.5	49.6	Solid(crystal),black	
14.	III n	360	18.4	Solid(crystal),black	1.5	30.7	Solid(crystal),black	
15.	III o	360	69.6	Solid(crystal),white	3.0	86.6	Solid(crystal),white	
16.	III p	360	59.2	Solid(amorphous),white	1.5	76.7	Solid(amorphous),white	
17.	III q	360	72	Solid(amorphous),white	2.5	94	Solid(amorphous),white	
18.	III r	360	56.2	Solid(amorphous), black	3.0	76	Solid(amorphous), black	
19.	III s	360	58.4	Solid(crystal), light-yellow	3.0	72	Solid(crystal), light-yellow	
20.	III t	360	56.2	Solid(crystal),white	3.0	82	Solid(crystal),white	
21.	III u	360	49.3	Solid(amorphous),white	3.0	60	Solid(amorphous),white	

22.	III v	360	37.5	Solid(amorphous),light	1.5	58.11	Solid(amorphous), light
23.	III w	360	46.2	Solid(crystal), light-white	1.5	63.2	Solid(crystal), light-white
24.	III x	360	60.6	Solid(amorphous), yellow	2.5	83.96	Solid(amorphous), yellow
25.	III y	360	44.2	Solid(crystal), yellow	12.0	66.2	Solid(crystal), yellow
26.	III z	360	49.1	Solid(amorphous),light	2.0	67.7	Solid(amorphous), light
27.	III aa	360	57.2	Solid(amorphous), yellow	2.0	62.2	Solid(amorphous), yellow
28.	IIIab	360	52.6	Solid(amorphous), yellow	1.5	68.4	Solid(amorphous), yellow
29.	III ac	360	46.2	Solid(amorphous),pure	1.5	56.6	Solid(amorphous), pure white
30.	III ad	360	49.2	Solid(amorphous),light-	1.5	61.	Solid(amorphous), light-
31.	III ae	360	47.9	Solid(amorphous), yellow	2.5	69.3	Solid(amorphous), yellow
32.	III af	360	50.1	Solid(amorphous),white	2.0	66.8	Solid(amorphous),white
33.	III ag	360	52.2	Solid(amorphous),white	2.5	70.1	Solid(amorphous),white
34.	III ah	360	53.9	Solid(crystal), pure-white	2.5	66.1	Solid(crystal), pure-white
35.	III ai	360	48.7	Solid(amorphous),brown	2.5	59.2	Solid(amorphous),brown
36.	III aj	360	26.7	Solid(amorphous),white	2.5	49	Solid(amorphous),white
37.	III ak	360	49.8	Solid(amorphous),light	2.5	61	Solid(amorphous), light black
38.	III al	360	57.7	Solid(amorphous),light	2.0	78	Solid(amorphous), light
39.	III am	360	73.5	Solid(crystal),black	2.0	95.6	Solid(crystal),black
40.	III an	360	41.6	Solid(amorphous)light	2.0	58.6	Solid(amorphous) light
41.	III ao	360	39.7	Solid(crystal),white	2.0	50.6	Solid(crystal),white
42.	III ap	360	29.8	Solid(crystal), light black	1.5	44	Solid(crystal), light black
43.	III aq	360	62.0	Solid(amorphous),white	2.5	80	Solid(amorphous),white
44.	III ar	360	53.7	Solid(amorphous),pure	2.0	64	Solid(amorphous), pure white
45.	III as	360	71.5	Solid(amorphous),white	3.0	91	Solid(amorphous),white
46.	III at	360	21.4	Solid(amorphous),white	2.5	34	Solid(amorphous),white
47.	III au	360	49.8	Solid(amorphous),pure	2.5	68	Solid(amorphous), pure white
48.	III av	360	74.9	Solid(crystal), pure white	2.5	98	Solid(crystal), pure white
49.	III aw	360	55.6	Solid(amorphous), brown	2.5	76	Solid(amorphous), brown
50.	III ax	360	40.8	Solid(crystal),pure white	2.5	60	Solid(crystal),pure white
51.	III ay	360	46.5	Solid(amorphous), white	2.5	69.5	Solid(amorphous), white
52.	III az	360	60.4	Solid(amorphous),light	2.5	81	Solid(amorphous), light
53.	III ba	360	21.4	Solid(crystal), brown	2.5	37	Solid(crystal), brown
54.	III bb	360	63.6	Solid(amorphous),pure	2.0	83.7	Solid(amorphous), pure white
55.	III bc	360	39.2	Solid(amorphous),white	2.0	52	Solid(amorphous),white
56.	III bd	360	56.4	Solid,(amorphous)	2.0	70	Solid,(amorphous)

Physical characterization of 3-(4-Substituted Anilino)-5-(3',4'-Disubstituted Aryl)-2Isoxazoles Table No-III-3

S. No.	Comp.	Mol. Formula and Mol.Wt.	Mp^{0}C	Rf Value	Rm Value
01.	III a	$C_{15}H_{12}N_2O$ (236)	198	0.680	-0.130
02.	III b	$C_{16}H_{14}N_2O_3$ (282)	201	0.672	-0.311
03.	III c	$C_{17}H_{17}N_3O$ (279)	128	0.580	-0.140
04.	III d	$C_{15}H_{11}N_3O_3$ (282)	170	0.499	-0.001
05.	III e	$C_{15}H_{11}N_3O_3$ (282)	172	0.501	0.001
06.	III f	$C_{16}H_{14}N_2O_2$ (266)	175	0.702	-0.372
07.	III g	$C_{14}H_{13}N_2O_3$(255)	192	0.696	-0.360
08.	III h	$C_{15}H_{12}N_2O_2$ (252.616)	82.0	0.590	-0.158
09.	III i	$C_{161}H_{14}N_2O_4$ (282.292)	>220	0.499	0.017
10.	III j	$C_{17}H_{14}N_3O_2$ (295.336)	133.0	0.692	-0.351
11.	III k	$C_{15}H_{11}N_3O_4$ (297.298)	87.0	0.689	-0.345
12.	III l	$C_{15}H_{11}N_3O_4$ (297.298)	111.0	0.699	-0.366
13.	III m	$C_{16}H_{14}N_2O_3$ (271.248)	155.0	0.598	-0.172
14.	III n	$C_{14}H_{11}N_2O_4$ (271.248)	174	0.594	-0.165
15.	III o	$C_{15}H_{11}N_2OBr$(315.162)	79	0.612	-0.198
16.	III p	$C_{16}H_{13}N_2O_3Br$(361.18)	226	0.596	-0.169
17.	III q	$C_{17}H_{16}N_3OBr$(358.22)	129	0.482	-0.031
18.	III r	$C_{15}H_{10}N_3O_3Br$(360.16)	91	0.613	-0.199
19.	III s	$C_{15}H_{10}N_3O_3Br$ (362)	117	0.624	-0.220

20.	III t	$C_{16}H_{13}N_2O_2Br$ (345.18)	149	0.724	-0.376
21.	III u	$C_{14}H_{10}N_2O_3Br$(334.14)	162	0.698	-0.364
22.	III v	$C_{15}H_{11}N_3O_3$ (281.268)	203.0	0.676	-0.319
23.	III w	$C_{16}H_{13}N_3O_5$ (327.294)	203.0	0.668	-0.303
24.	III x	$C_{17}H_{16}N_4O_3$ (324.338)	123.0	0.693	-0.353
25.	III y	$C_{15}H_{10}N_4O_5$ (326.27)	173	0.654	-0.276
26.	III z	$C_{15}H_{10}N_4O_5$ (326.27)	177.0	0.649	-0.267
27.	III aa	$C_{16}H_{13}N_3O_4$ (311.294)	179	0.602	-0.179
28.	IIIab	$C_{14}H_{10}N_3O_5$ (300.25)	191.0	0.594	-0.165
29.	III ac	$C_{16}H_{14}N_2O$(250.29)	199	0.599	-0.174
30.	III ad	$C_{17}H_{16}N_2O_3$(296.31)	201	0.583	-0.145
31.	III ae	$C_{18}H_{19}N_3O$(293.36)	128	0.642	-0.254
32.	III af	$C_{16}H_{13}N_3O_3$ (295.294)	176	0.656	-0.280
33.	III ag	$C_{16}H_{13}N_3O_3$ (297)	171	0.659	-0.286
34.	III ah	$C_{17}H_{16}N_2O_2$ (280.31)	169	0.712	-0.393
35.	III ai	$C_{15}H_{13}N_2O_3$(269.274)	186	0.791	-0.578
36.	III aj	$C_{14}H_{10}N_2O_3F$ (273.24)	140	0.689	-0.345
37.	III ak	$C_{15}H_{11}N_2OF$(254.25)	142	0.678	-0.324
38.	III al	$C_{16}H_{13}N_2O_3F$ (300.28)	143	0.596	-0.169
39.	III am	$C_{17}H_{16}N_3OF$ (297.32)	90	0.693	-0.353
40.	III an	$C_{15}H_{10}N_3O_3F$ (299.26)	138	0.695	-0.358
41.	III ao	$C_{15}H_{10}N_3O_3F$ N (299.26)	140	0.697	-0.362
42.	III ap	$C_{16}H_{13}N_2O_2F$ (284.28)	141	0.704	-0.376
43.	III aq	$C_{15}H_{11}N_2OCl$ (270.7)	162	0.669	-0.158
44.	III ar	$C_{16}H_{13}N_2O_3Cl$ (316.73)	180	0.599	-0.174
45.	III as	$C_{17}H_{16}N_3OCl$ (314.33)	120	0.641	-0.251
46.	III at	$C_{15}H_{10}N_3O_3Cl$ (315.71)	170	0.587	-0.153
47.	III au	$C_{15}H_{10}N_3O_3Cl$ (315.71)	176	0.601	-0.178
48.	III av	$C_{16}H_{13}N_2O_2Cl$(300.73)	152	0.718	-0.406
49.	III aw	$C_{14}H_{10}N_2O_3Cl$ (289.69)	166	0.701	-0.370
50.	III ax	$C_{15}H_{10}N_2OClF$ (288.7)	112	0.699	-0.366
51.	III ay	$C_{16}H_{12}N_2O_4ClF$ (350.72)	116	0.604	-0.183
52.	III az	$C_{17}H_{15}N_3OClF$ (331.17)	93	0.687	-0.341
53.	III ba	$C_{15}H_9N_3O_3ClF$ (333.7)	108	0.598	-0.172
54.	III bb	$C_{15}H_9N_3O_3ClF$ (333.7)	106	0.601	-0.178
55.	III bc	$C_{16}H_{12}N_2O_2ClF$(318.73)	112	0.712	-0.393
56.	III bd	$C_{13}H_8N_2O_2ClF$(288.74)	101	0.713	-0.395

Elemental analysis of 3-(4-Substituted anilino)-5-(3',4'-disubstituted aryl)-2-isoxazoles Table No-III-4

S.No	Comp. Code	X	Y	Ar	Found C	H	N	O	C	H	N
01.	III a	H	H	C_6H_5	76.2	5.08	11.86	6.77	73.96	4.978	10.276
02.	III b	H	H	$C_6H_3(OH)(OCH_3)$	68.0	4.96	9.92	17.02	66.27	4.795	9.864
03.	III c	H	H	$C_6H_4N(CH_3)_2$	64.5	6.09	15.05	5.73	63.51	5.972	14.22
04.	III d	H	H	$C_6H_4(NO_2)$	64.0	3.91	14.94	17.08	62.192	3.713	12.948
05.	III e	H	H	$C_6H_4(NO_2)$	64.0	3.91	14.94	17.08	63.299	3.821	12.898
06.	III f	H	H	$C_6H_4(OCH_3)$	72.1	5.26	10.52	12.03	70.810	5.106	10.256
07.	III g	H	H	$C_5H_4O_2$	65.8	4.31	10.98	18.82	63.277	3.445	10.872
08.	III h	OH	H	C_6H_5	71.3	4.78	11.07	12.6	68.386	4.855	10.701
09.	III i	OH	H	$C_6H_3(OH)(OCH_3)$	68.0	4.99	9.92	17.0	66.72	4.353	9.392
10.	III j	OH	H	$C_6H_4N(CH_3)_2$	69.1	5.80	14.23	10.83	68.168	5.638	12.423
11.	III k	OH	H	$C_6H_4(NO_2)$	60.5	3.72	14.14	21.5	60.050	3.643	13.014
12.	III l	OH	H	$C_6H_4(NO_2)$	60.5	3.72	14.14	21.5	60.001	3.647	13.401
13.	III m	OH	H	$C_6H_4(OCH_3)$	68.0	4.99	9.9	17.0	67.806	3.982	9.892
14.	III n	OH	H	$C_5H_4O_2$	61.9	4.05	10.33	23.5	60.95	3.746	9.203
15.	III o	Br	H	C_6H_5	57.1	3.51	8.89	5.07	56.89	3.421	8.398
16.	III p	Br	H	$C_6H_3(OH)(OCH_3)$	53.2	3.62	7.75	13.28	51.48	2.963	6.577

17.	III q	Br	H	$C_6H_4N(CH_3)_2$	56.9	4.5	11.33	4.46	55.95	3.954	10.631
18.	III r	Br	H	$C_6H_4(NO_2)$	50.0	2.79	11.66	13.32	49.8	2.197	10.967
19.	III s	Br	H	$C_6H_4(NO_2)$	40.0	2.79	11.66	13.32	40.705	2.192	10.897
20.	III t	Br	H	$C_6H_4(OCH_3)$	55.1	3.79	8.11	9.27	56.1	3.297	8.016
21.	III u	Br	H	$C_5H_4O_2$	50.3	3.01	8.36	14.36	49.25	3.003	7.630
22.	III v	NO_2	H	C_6H_5	64.0	3.94	14.94	17.16	63.29	3.496	12.977
23.	III w	NO_2	H	$C_6H_3(OH)(OCH_3)$	58.7	4.03	12.84	24.44	57.4	4.001	10.984
24.	III x	NO_2	H	$C_6H_4N(CH_3)_2$	62.1	4.9	17.2	14.79	60.155	3.966	14.212
25.	III y	NO_2	H	$C_6H_4(NO_2)$	55.2	3.08	17.17	24.5	53.194	3.072	15.715
26.	III z	NO_2	H	$C_6H_4(NO_2)$	55.2	3.08	17.17	24.5	54.933	3.001	16.808
27.	III aa	NO_2	H	$C_6H_4(OCH_3)$	61.7	4.209	13.5	20.	59.716	4.109	12.541
28.	IIIab	NO_2	H	$C_5H_4O_2$	56.0	3.35	13.99	26.6	55.62	3.297	11.93
29.	III ac	CH_3	H	C_6H_5	76.7	5.63	11.19	6.39	74.619	5.436	10.190
30.	III ad	CH_3	H	$C_6H_3(OH)(OCH_3)$	68.9	5.44	9.45	16.9	67.94	4.596	8.939
31.	III ae	CH_3	H	$C_6H_4N(CH_3)_2$	73.6	6.52	14.32	5.45	72.96	6.357	13.32
32.	III af	CH_3	H	$C_6H_4(NO_2)$	65.0	4.43	14.23	16.25	65.6	4.031	12.423
33.	III ag	CH_3	H	$C_6H_4(NO_2)$	65.1	4.43	14.23	16.25	64.79	4.013	13.58
34.	III ah	CH_3	H	$C_6H_4(OCH_3)$	72.8	5.75	9.99	11.41	72.8	5.368	8.972
35.	III ai	CH_3	H	C_4H_3O	66.9	4.86	10.4	17.82	65.2	4.253	10.01
36.	III aj	F	H	C_6H_5	61.5	3.68	10.25	17.	61.5	3.148	9.814
37.	III ak	F	H	$C_6H_3(OH)(OCH_3)$	70.8	5.35	11.0	6.29	68.708	4.187	11.001
38.	III al	F	H	$C_6H_4N(CH_3)_2$	67.0	4.36	9.33	15.98	66.01	4.634	8.798
39.	III am	F	H	$C_6H_4(NO_2)$	68.6	5.42	14.13	5.38	67.952	5.064	12.892
40.	III an	F	H	$C_6H_4(NO_2)$	60.2	3.36	14.0	16.04	58.216	3.164	13.010
41.	III ao	F	H	$C_6H_4(OCH_3)$	60.2	3.36	14.0	16.04	58.618	3.046	13.176
42.	III ap	F	H	$C_5H_4O_2$	67.5	4.61	9.85	11.25	66.95	4.052	8.996
43.	III aq	Cl	H	C_6H_5	66.4	4.09	10.35	5.91	65.40	4.027	10.105
44.	III ar	Cl	H	$C_6H_3(OH)(OCH_3)$	60.6	4.13	8.84	15.15	60.50	3.974	9.884
45.	III as	Cl	H	$C_6H_4N(CH_3)_2$	64.9	5.12	13.37	5.09	64.80	5.075	11.753
46.	III at	Cl	H	$C_6H_4(NO_2)$	157.	3.19	13.31	15.20	55.76	3.094	13.426
47.	III au	Cl	H	$C_6H_4(NO_2)$	157.	3.19	13.31	15.20	56.75	3.010	13.132
48.	III av	Cl	H	$C_6H_4(OCH_3)$	63.9	10.01	13.96	10.64	62.93	9.8	11.973
49.	III aw	Cl	H	$C_5H_4O_2$	59.9	3.98	9.67	16.57	58.35	3.283	10.076
50.	III ax	Cl	F	C_6H_5	62.4	3.49	9.70	5.55	61.8	3.312	9.662
51.	III ay	Cl	F	$C_6H_3(OH)(OCH_3)$	54.7	3.44	7.98	18.24	53.76	3.174	7.884
52.	III az	Cl	F	$C_6H_4N(CH_3)_2$	61.6	4.56	12.69	4.83	60.3	4.156	11.961
53.	III ba	Cl	F	$C_6H_4(NO_2)$	53.9	2.71	12.59	14.38	52.853	2.673	11.952
54.	III bb	Cl	F	$C_6H_4(NO_2)$	53.9	2.71	12.59	14.38	52.853	2.670	11.895
55.	III bc	Cl	F	$C_6H_4(OCH_3)$	60.2	3.79	8.79	10.04	60.018	3.197	8.612
56.	III bd	Cl	F	C_4H_3O	54.0	6.28	9.70	11.08	52.501	5.968	9.694

IR AND H^1 NMR SPECTRAL DATA Table No-III-5

COMPOUND	IBr(KBr,cm^{-1})	^{1}HNMR $CDCl_3$(ppm)[9]
1.IIIa	3240.52(N-H str); 1650.0(CH=CH str); 1361.79(C-NO2 str); 732.97(Ar-CH str);	3.397 (N-H); 7.953(Ar-CH);6.709(CH=CH);
2.IIIb	3286.81(N-H str); 1660.55(CH=CH str); 1365.65(C-NO2 str); 748.41(Ar-CH str); 3259.81(OH);	3.140(N-H); 6.705(CH=CH);10.062(OH); 7.953(ArH)3.462(N-CH3);
3.IIIc	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C=H str); 732.97(Ar-CH str);	3.397(NH); 6.705(CH-CH); 7.953(ArH);2.943(N-CH3);
4.IIId	3286.81(N-H str); 1650.0(CH=CH str); 1346.36(C-NO2 str); 732.97(Ar-CH str);	3.397(NH);7.953(ArH);6.709CH=CH);
5.IIIe	3286.81(N-H str); 1650.0(CH=CH str); 1346.36(C-NO2 str); 732.97(Ar-CH str);	3.397(NH);7.953(ArH);6.709CH=CH);
6.IIIf	3286.81(N-H str); 1650.0 (CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); .953(ArH);3.462(OCH3);
7.IIIg	3286.81(N-H str); 1650.0 (CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
8.IIIh	3286.81(N-H str); 1660.55(CH=CH str); 1365.65(C-NO2 str); 748.41(Ar-CH str);3259.81(OH);	3.140(NH); 6.705(CH=CH); 7.953(ArH);10.062(OH);

9.IIIi	3286.81(N-H str); 1660.55(CH=CH str); 1365.65(C-NO2 str); 748.41(Ar-CH str);3259.81(OH);	3.140(NH); 6.705(CH=CH); 7.953(ArH);10.062(OH);3.462(N-CH3);
10.IIIj	3286.81(N-H str); 1656.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 3259.81(OH);	3.397(NH); 6.705(CH=CH); 7.953(ArH);2.943(N-CH3); 10.062(OH);
11.IIIk	3286.81(N-H str); 1656.0(CH=CH str); 1346.36(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.705(CH=CH); 7.953(ArH);10.062(OH);
12.IIIl	3286.81(N-H str); 1656.0(CH=CH str); 1346.36(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.705(CH=CH); 7.953(ArH);10.062(OH);
13.IIIm	3286.81(N-H str); 1660.55(CH=CH str); 1365.65(C-NO2 str); 748.41(Ar-CH str); 3259.81(N-H str);	3.140(NH); 6.705(CH=CH); 7.953(ArH); 3.462(N-CH3);
14.IIIn	3286.81(N-H str); 1660.55(CH=CH str); 1365.65(C-NO2 str); 748.41(Ar-CH str); 3259.81(N-H str);	3.140(NH); 6.705(CH-ArOH); 7.953(ArH); 10.062(OH);
15.IIIo	3286.81(N-H str); 1660.55(CH=CH str); 1365.65(C-NO2 str); 748.41(Ar-CH str);	3.140(NH); 6.705(CH=CH); 7.953(ArH);
16.IIIp	3286.89(N-H str); 1660.59(CH=CH str); 1365.65(C-NO2 str); 748.41(Ar-CH str); 3259.81(OH);	3.140(NH); 6.705(CH=C); 7.953(ArH); 3.462(N-CH3); 10.062(OH);
17.IIIq	3286.89(N-H str); 1656.81(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.705(CH=CH); 7.953(ArH); 2.943(N-CH3)
18.IIIr	3286.81(N-H str); 1656.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 1346.36(NO2);	3.397(NH); 6.705(CH=CH); 7.953(ArH);
19.IIIs	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 1346.36(NO2);	3.397(NH); 6.705(CH=CH); 7.953(ArH);
20.IIIt	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH); 3.462(OCH3);
21.IIIu	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH); 3.462(OCH3);
22.IIIv	3286.81(N-H str); 1656.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 1346.36(NO2);	3.397(NH); 6.705(CH=CH); 7.953(ArH);
23.IIIw	3286.81(N-H str); 1656.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 1346.36(NO2); 3259.81(OH);	3.397(NH); 6.705(CH=CH); 7.953(ArH); 10.062(OH); 3.462(OCH3);
24.IIIx	3286.81(N-H str); 1656.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 1346.36(NO2); 3259.81(OH);	3.397 (NH); 6.705(CH-ArOH); 7.953(ArH);2.943(N-CH3);
25.IIIy	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 1346.36(NO2);	3.397(NH); 6.705(CH=CH); 7.953(ArH);
26.IIIz	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 1346.36(NO2);	3.397(NH); 6.705(CH=CH); 7.953(ArH);
27.IIIaa	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 1346.36(NO2);	3.397(NH); 6.709(CH=CH); 7.953(ArH); 3.462(OCH3);
28.IIIab	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 1346.36(NO2);	3.397 (NH); 7.9533(Ar-H) ;6.709(C=C);
29.IIIac	3240.52(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(N-H); 6.709(CH=CH); 7.953 (Ar-H); 2.002(N-CH_3)10.062;
30.IIIad	3240.52(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 3259.81(-OH);	3.397(NH); 6.709(CH=CH); 7.953(ArH);2.002(N-CH3); 10.062(-OH);
31.IIIae	3240.52(N-H);1650.0(CH=CH); 361.79(C=N);732.97(Ar-CH);1346.36(C-NO_2)	3.397(NH); 6.709(CH=CH); 7.953(ArH); 2.002(CCH_3); 2.943(-N-CH3);
32.IIIaf	3240.52(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str); 3259.81(-OH);	3.397(NH); 6.709(C=C); 7.953(ArH);2.002(N-CH3);
33.IIIag	3240.52(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.709(C=C); 7.953(ArH);2.002(N-CH3);

	3259.81(-OH);	
34.IIIah	3240.52(N-H str); 1650.0(CH=CH str); 1361.79(C=N); 732.97(Ar-CH str);	3.397(NH); 6.709(C=C); 7.953(ArH);2.002(CH3); 3.462(OCH_3);
35.IIIai	3240.52(N-H str); 1650.0(CH=CH str); 1361.79(C=N); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH);2.002(CH3);
36.IIIaj	3240.52(N-H str); 1650.0(CH=CH str); 1365.65(C=Nstr); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
37.IIIak	3286.81(N-H str); 1660.55(CH=CH str); 1365.65(C=Nstr); 748.41(Ar-CH str); 3259.81(-OH);	3.140(NH); 6.705(CH=CH); 7.953(ArH);3.462(O-CH3); 10.062(-OH);
38.IIIal	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C=N str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH);2.002(N-CH3);
39.IIIam	3240.52(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH-ArOH); 7.953(ArH);
40.IIIan	3240.52(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
41.IIIao	3240.52(N-H str); 1650.0(CH=CH str); 1361.79(C=N); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH); 3.462(-OCH3);
42.IIIap	3286.81(N-H str); 1660.55(CH=CH str); 1365.65(C=N); 748.48(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
43.IIIaq	3286.81 (N-H str); 1650.0(CH=CH str); 1365.65(C=N); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH); 3.462(-OCH3);
44.IIIar	3240.52(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH); 3.462(-OCH3); 10.062(-OH);
45.IIIas	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C=N str); 732.97(Ar-CH str);3259.81(OH)	3.397(NH); 6.709(CH=CH); 7.953(ArH); 3.462(OCH3);
46.IIIat	3286.81 (N-H str); 1650.0(CH=CH str); 1365.65(C=N); 732.97(Ar-CH str); 1346.97(C-NO2);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
47.IIIau	3286.81 (N-H str); 1650.0(CH=CH str); 1365.65(C=N); 732.97(Ar-CH str); 1346.97(C-NO2);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
48.IIIav	3286.81 (N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH); 3.462(OCH3);
49.IIIaw	3286.81(N-H str); 1650.0(CH=CH str); 1365.65(C=N str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
50.IIIax	3240.52(N-H str); 1650.0(CH=CH str); 1361.79(C=N str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
51.IIIay	3240.52(N-H str); 1650.0(CH=CH str); 1361.79(C=N str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
52.IIIaz	3240.52(N-H str); 1650.0(CH=CH str); 136179(C=N str); 732.97(Ar-CH str);	3.397(NH); 6.709(CH=CH); 7.953(ArH); 2.943(N-CH3);
53.IIIba	3286.81(N-H str); 1660.55(CH=CH str); 1365.65(C-NO2 str); 748.41(Ar-CH str); 1346.36(NO2);	3.140(NH); 6.709(CH=CH); 7.953(ArH);
54.IIIbb	3240.52(N-H str); 1650.0(CH=CH str); 1365.65(C-NO2 str); 748.41(Ar-CH str); 1346.36(NO2);	3.397(NH); 6.709(CH=CH); 7.953(ArH);
55.IIIbc	3286.89(NH);1660.59(CH=CH); 1365.65(C=N)748.41(Ar-CH);	3.140(NH); 6.705(CH=CH); 7.953(ArH); 3.462(OCH3);
56..IIIbd	3240.52(NH); 1650.0(CH=CH); 1361.79(C=N); 732.97(Ar-H)	3.397(NH); 6.709(CH=CH); 7.953(ArH);

Anthelmintic Activity of Isoxazoles:

Helminthic infections are now being recognized as cause of much chronic ill health and sluggishness amongst the tropical people. More than half of population in the world suffers from worm infection of one or the other.

All the newly synthesized compounds 57-112 (IIIa-IIIz, IIIaa-IIIaz, IIIba-IIIbd) have tested for anthelmintic activity due to its anatomical and physiological resemblance with the intestine roundworm parasites of human being according to method described in detail by kailashraj and kurupa[40-42].

Experimental / Methodology:

Peritima posthuma(earthworm) obtained from agriculture department, Guntur of nearly equal size (9±1.5cm)was selected for present study. The synthesized compounds were prepared in 3% tween-80 in normal saline or 1% DMF in normal saline to obtain 1mg/ml concentration which was taken in each Petri dish (4inches).The movement of earthworms were observed for the time taken to paralysis and death of individual worms lost up to the 1hr of the test period. Paralysis was said to occur when the worms didn't revive even in normal saline. Death was concluded or ascertained when worms lost their motility even by external stimuli which stimulates and induce movement in the earthworm if alive and followed by fading away of their body colour. The activity was compared with the standard anthelminitic substances i.e. mebendazole, and albendazole under the same condition. The time taken for complete paralysis and death are reported in Table No-III-6

Anthelmintic Activity of Isoxazoles

S.No	Compound code	Paralytic (sec)	Lethal (sec)	S.NO	Compound	Paralytic (sec)	Lethal (sec)
1	III h	23±0.42	66±0.33	20	III ao	16±1.98	54±1.236
2	III i	18±0.52	75±0.691	21	III ap	13±1.36	45±1.200
3	III j	25±0.35	69±0.632	22	III aq	18±0.29	69±0.632
4	III l	17±0.25	73±0.891	23	III ar	19±0.75	49±0.43
5	III n	13±0.50	80±0.121	24	III as	10±0.62	98±0.44
6	III p	13±0.014	90±1.32	25	III at	16±0.36	66±0.51
7	III q	20±1.05	76+0.53	26	III av	15±0.45	34±0.62
8	III r	13±0.014	60±1.0	27	III aw	12±0.39	35±0.32
9	III t	20±1.05	90±1.32	28	III ax	27±0.98	70±1.23
10	III v	23±0.36	66±0.321	29	III ay	17±0.56	73±1.400

11	III w	18±0.33	75±1.631		30	III az	15±1.25	42±1.00
12	III x	25±0..22	69±1.22		31	III ba	14±1.95	50±1.6321
13	III z	17±0.144	73±1.20		32	III bb	14±0.95	48±1.023
14	IIIab	13±0.014	80±1.22		33	III bc	15±0.16	48±1.023
15	III ae	20±1.05	51+0.65		34	III bd	18±0.99	40±0.23
16	III aj	14±0.25	64±0.66			Albendazole	13±0.014	34±0.233
17	III ak	16±0.19	40±0.21			Mebendazole	9±0.1	28±0.11
18	III al	13±1.56	51±0.05			Controle (3%Tween -80 in Norma Saline)	–	–
19	III an	20±1.25	60±0.821					

RESULTS AND DISCUSSION:

In the present investigation 56 newer isoxazole compounds were synthesized by conventional and microwave techniques. The products produced by both methods were characterized by IR, ^{1}HNMR, elemental analysis and Mass spectral analysis and compared. The experimental results of present investigation indicated that all newer isoxazole compounds were synthesized by microwave irradiation method in 1.5 – 6 min, while conventional method required 5-12 hrs. reflux. The results (Table) also indicated that in conventional method the yield was lower as compared to microwave irradiation, demonstrating the effect of microwave irradiation is not purely thermal irradiation but facilitates the polarization of the molecule under irradiation causing rapid reaction to occur.

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