Biomedical & Pharmacology Journal Vol. **2**(2), 201-212 (2009)

Synthesis and pharmacological study of some mannich bases of benzimidazolyl quinazolinones against *Tribolium confusum*

PRAMILLA SAH* and VANITA KACHHAWAHA

Department of Chemistry, J.N.V. University, Jodhpur - 342 005 (India).

(Received: July 12, 2009; Accepted: September 03, 2009)

ABSTRACT

The Mannich bases 2–phenyl–3–(1'H–morpholino/piperidino/ diphenylamino–methyl–2'–alkyl benzimidazolo–6/6,8–disubstituted quinazolin–4(3H)–ones were synthesized by treating 2–phenyl–2'–methyl/ethyl benzimidazolo–6/6,8–disubstituted quinazolin–4(3H)–ones with formaldehyde and appropriate secondary amines. The synthesized compounds were then evaluated for their insecticidal activity against *Tribolium confusum*, the host being jawar seeds. The survival percentage of the beetle reduced significantly and the development period of the insect was also prolonged between 10–14 days on an average by using 1.0, 2.5 and 5.0 ml/100 gm of the host seed by these Mannich bases.

Key words: Mannich bases, *Tribolium confusum*, benzimidazolyl quinazolinones.

INTRODUCTION

Quinazoline nucleus is endowed with various pharmaceutical applications e.g. used in the treatment of leprosy and mental disorders, as anticonvulsants, analgesic and antimicrobial agents[1–5]. Methaquolone. Pyrazosin and Quinethazone are drugs that possess antihypertensive, antidiuretic and anticoagulant activities[6]. A number of Mannich bases have also been associated with a broad spectrum of biological activities i.e. antimicrobial, anti–inflammatory, antifilarial, antifungal etc[7–10]. Recent reports have shown substituted benzimidazoles to be effective in the treatment of cancer, HIV–I (*in–vitro*) infections, as antihelmintic and therapeutic agents[8–15].

Insects cover more than ¾ of the entire world fauna. It is roughly estimated that the animal loss due to the various pests affecting our crops is about 1500 crores per year, consequently their effect as carrier of disease is in no way less than their attack on crops. *Tribolium confusum* is considered as pest of gram flour, milled cereal products and stored commodities. For an efficient control the life cycle, host complex, mode of feeding and breeding play an important role[16–18].

Large number of organic insecticides are available like DDT, BHC etc. The present study hence includes the synthesis and insecticidal activity of some Mannich bases incorporated with the two bioactive nuclei against the jawar seeds infected with this pest.

EXPERIMENTAL

Melting points were taken in open capillaries in an electrical 'Neolab' apparatus and are uncorrected. IR spectra were recorded on Schimadzu 8101 A spectrophotometer. ^{1}HPMR in DMSO and $CDCl_3$ on a Brucker DPX 300 MHz spectrophotometer. Mass was recorded on a JEOL SX 102/DA–6000 mass spectrometer.

Synthesis of monobromo and dibromo anthranilic acids (1)

There were prepared by known procedure.[19]

Synthesis of N–Benzoyl–4–substituted–4/6–disubstituted anthranilic acids (2)

The method of Dash *et. al.*[20] and Reddy *et. al.*[21] was followed.

2–phenyl–6/6,8–disubstituted benzoxazinones (3)

0.015 mol of N–benzoyl–4–substituted/4,6–disubstituted anthranilic acids were refluxed for 30 min. in presence of acetic anhydride (10 ml). The solid mass which separated on cooling was recrystallized by repeated washing with petroleum ether (60–80°).

3_a $R_1 = R_2 = H$, Yield 75%, M.P. °C 120°
3_b $R_1 = Br$, $R_2 = H$, Yield 75%, M.P. °C 150°
3_c $R_1 = Br$, $R_2 = Br$, Yield 75%, M.P. °C 160°

2–Amino methyl/ethyl benzimidazoles (4)

These were synthesized by the process of Cescon and Day.[22]

2–phenyl–(2'–methyl/ethyl benzimidazolo)–6/6,8–disubstituted quinazolin–4(3H)–ones–(5_a–5_f)

Equimolar ratio of 2–aminomethyl benzimidazole (4_a) and 2–phenyl benzoxazinone (3_a) were refluxed in pyridine (10 ml) for 6 hrs. The solution was cooled, poured into ice water and neutralized with con. HCl (11.5 N). The solid which separated out was filtered, dried and recrystallized with ethanol. Similarly the other derivatives (5_b–5_f) were synthesized. Their physical and analytical data are given in Table I.

2–phenyl–3–(1'H–morpholino/piperidino/diphenylamino–methyl–2'–alkyl benzimidazolo)–6/6,8–dibromo substituted quinazolin–4 (3H)–ones (6_a–6_l)

1 ml of 37% formaldehyde and 0.01% mole of morpholine was added to 0.01 mole of 5a in 5 ml ethanol with constant stirring. A turbid solution so obtained soon became clear on warming on a water bath for 2 minutes. It was left overnight at room temperature. The Mannich base so obtained was recrystallised from chloroform petroleum ether (60–80%) (1:1) ratio. Other Mannich bases were prepared similarly. The physical and analytical data is given in Table 2.

Evaluation of insecticidal activity

Tribolium confusum was reared on whole wheat flour supplemented with brewer's yeast at 30 ± 2 °C and 70 ± 5% relative humidity in the laboratory by following the known procedure.[23]

The insecticidal activity against *Tribolium confusum* was evaluated in terms of percentage adult mortality and percentage adult emergence on the host jawar grains.

Table 1: Physical and analytical data of 2–phenyl–(2'–methyl/ethyl benzimidazolo)–6/6,8–disubstituted quinazolin–4(3h)–ones

Compd.	Yield (%)	M.P. °	Molecular Formula	Analysis Found (Calcd.) %		
				C	H	N
5_a	65	90	$C_{22}H_{16}N_4O$ (352)	74.77 (74.99)	4.52 (4.54)	15.88 (15.90)
5_b	60	100	$C_{23}H_{18}N_4O$ (366)	75.42 (75.40)	5.10 (4.91)	15.40 (15.31)
5_c	60	100	$C_{22}H_{15}N_4OBr$ (431)	61.35 (61.25)	3.47 (3.48)	13.05 (12.99)
5_d	55	110	$C_{23}H_{17}N_4OBr$ (445)	62.05 (62.02)	3.78 (3.82)	12.54 (12.58)
5_e	65	120	$C_{22}H_{14}N_4OBr_2$ (510)	51.78 (51.76)	2.76 (2.74)	10.79 (10.98)
5_f	65	130	$C_{23}H_{16}N_4OBr_2$ (524)	52.75 (52.67)	3.04 (3.05)	10.71 (10.68)

Adult Mortality

To study the effect of the different synthesized Mannich bases on the adult mortality of *Tribolium confusum*, ten newly emerged adults were introduced in the culture tubes containing ten grams of chemically treated jawar grains. The stock solution was made by mixing 5 gms of the synthesized compound with 95 ml of benzene. This

Table 2 : Characteristic data of 2–phenyl–3–(1'–h–Morpholino/piperidino/ diphenylamino-methyl–2'–alkyl benzimidazolo)–6/6,8–disubstituted Quinazolin–4(3h)–ones

Compd.	R	R_1	R_2	R_3	M.P.°	Molecular Formula	Analysis of Nitrogen Found (Calcd.) %
6_a	H	H	H	Morpholino	110	$C_{27}H_{25}N_5O_2$ (451)	15.56(15.52)
6_b	H	H	H	Piperidino	110	$C_{28}H_{27}N_5O$ (449)	15.61(15.59)
6_c	H	H	H	Diphenylamino	120	$C_{35}H_{27}N_5O$ (533)	13.25(13.13)
6_d	CH_3	H	H	Morpholino	115	$C_{28}H_{27}N_5O_2$ (465)	15.08(15.05)
6_e	CH_3	H	H	Piperidino	120	$C_{29}H_{29}N_5O$ (463)	15.21(15.11)
6_f	CH_3	H	H	Diphenylamino	125	$C_{36}H_{29}N_5O$ (547)	12.78(12.79)
6_g	H	Br	H	Piperidino	180	$C_{28}H_{26}N_5OBr$ (558)	12.57(12.54)
6_h	CH_3	Br	H	Diphenylamino	130	$C_{36}H_{28}N_5OBr$ (626)	11.27(11.18)
6_i	H	Br	Br	Morpholino	130	$C_{27}H_{23}N_5O_2Br_2$ (609)	11.51(11.49)
6_j	H	Br	Br	Piperidino	190	$C_{28}H_{25}N_5OBr_2$ (607)	11.47(11.53)
6_k	CH_3	Br	Br	Diphenylamino	140	$C_{36}H_{27}N_5OBr_2$ (705)	10.13(9.92)
6_l	CH_3	Br	Br	Morpholino	135	$C_{28}H_{25}N_5O_2Br_2$ (623)	11.32(11.23)

Yield between 45 – 65%

Table 3 : Spectral data of the newly synthesized compounds

IR (KBr, cm^{-1})	5_a 1670 (C=O), 1625 (C=N), 1315 (C–N), 2895, 3030 (–CH, Stretching), 3300 (–NH) 5_g 1665 (C=O), 1620 (C=N), 1327 (C–N), 2890, 3035 (–CH, Stretching), 3310 (–NH), 740 (C–Br) 6_a 1665 (C=O), 1620 (C=N), 1318 (C–N), 2895, 3030 (–CH, Stretching) 6_e 1670 (C=O), 1625 (C=N), 1315 (C–N), 2885, 3030 (–CH, Stretching) 6_k 1660 (C=O), 1620 (C=N), 1320 (C–N), 2890, 3035 (–CH, Stretching), 750 (C–Br)
^{1}HPMR (DMSO + $CDCl_3$, δ ppm)	5_a : 4.34 (2H, s, N–CH_2–C), 6.87 (1H, s, NH), 7.52 – 8.11 (13H, m, ArH) 6_a : 4.32 (2H, s, N–CH_2–C), 4.75 (2H, s, N–CH_2–N), 2.91 (4H, t, CH_2–N–CH_2), 3.33 (4H, t, CH_2–O–CH_2), 7.56 – 8.01 (13H, m, ArH) 6_b : 4.35 (2H, s, N–CH_2–C), 4.70 (2H, s, N–CH_2–N), 2.75 (4H, t, CH_2–N–CH_2), 1.70 (6H, s, CH_2– CH_2–CH_2), 7.48 – 7.96 (13H, m, ArH) 6_c : 4.35 (2H, s, N–CH_2–C), 4.82 (2H, s, N–CH_2–N), 7.38 – 8.25 (23H, m, ArH)
Mass Spectra	6_c MS^+ 533, m/z, 351, 235, 221 (100%), 193, 182, 180, 130, 118, 116, 103

Table 4 : Adult mortality of *Tribolium confusum* on jawar seeds treated with mannich bases of benzimidazolyl quinazolinones

Compd.	% Adult Mortality											
	1.0 ml/100g				2.5 ml/100g				5.0 ml/100g			
	R_1	R_2	R_3	Mean	R_1	R_2	R_3	Mean	R_1	R_2	R_3	Mean
6_a	10	10	0	6.67	10	10	20	13.33	20	20	10	16.67
6_b	10	10	10	10	10	20	20	15.67	30	30	40	33.33
6_c	10	0	10	6.67	10	20	30	20	30	40	50	40
6_d	20	20	10	16.7	30	40	30	33.33	50	40	40	43.33
6_e	20	20	20	20	30	30	40	33.33	50	50	50	50
6_f	20	10	20	16.7	30	20	20	23.33	40	40	50	43.33
6_g	10	10	0	6.67	20	20	20	20	30	40	40	36.67
6_h	10	10	20	13.3	20	20	20	20	30	30	40	33.33
6_i	20	30	30	26.7	30	30	30	30	40	50	50	46.67
6_j	20	20	20	20	30	30	30	30	50	50	60	53.33
6_k	10	10	20	13.3	30	30	40	33.33	50	50	50	50
6_l	20	10	10	13.3	40	30	30	33.33	60	60	60	60
Control	0	0	0	0	0	0	0	0	0	0	0	0

4A : Anova : Two–Factor with Replication

6_a Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	20	40	50	110
Average	6.67	13.33	16. 67	12.22
Variance	33.33	33.33	33.33	44.44

6_b

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	39	50	100	180
Average	10	16.67	33.33	20
Variance	0	33.33	33.33	125

6_c

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	20	60	120	200
Average	6.67	20	40	22.22
Variance	33.33	100	100	269.44

6_d

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	50	100	130	280
Average	16.67	33.33	43.33	31.11
Variance	33.33	33.33	33.33	161.11

6_e

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	60	100	150	310
Average	20	33.33	50	34.44
Variance	0	33.33	0	177.78

6_f

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	50	70	130	250
Average	16.67	23.33	43.33	27.78
Variance	33.33	33.33	33.33	169.44

6_g

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	20	60	110	190
Average	6.67	20.00	36.67	21.11
Variance	33.33	0.00	33.33	186.11

6_h

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	40	60	100	200
Average	13.33	20.00	33.33	22.22
Variance	33.33	0.00	33.33	94.44

6_i

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	80	90	140	310
Average	26.67	30.00	46.67	34.44
Variance	33.33	0.00	33.33	102.78

6_j

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	60	90	160	310
Average	20	30	53.33	34.44
Variance	0	0	33.33	227.78

6_k

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	40	100	150	290
Average	13.33	33.33	50.00	32.22
Variance	33.33	33.33	0.00	269.44

6_l

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	40	100	180	320
Average	13.33	33.33	60.00	35.56
Variance	33.33	33.33	0.00	427.78

Total

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g
Count	36	36	36
Sum	510	920	1520
Average	14.17	25.56	42.22
Variance	53.57	71.11	143.49

ANOVA

Source of variation	df	MS	F
Chemical	11	516.08	18.58
Concentration	2	7167.59	258.03
Chemical* Conc.	22	77.69	2.80
Error	72	27.78	
Total	107		
SEM	=	3.04	
CD AT 5%	=	5.96	

Table 4 : Adult mortality of *Tribolium confusum* on jawar seeds treated with mannich bases of benzimidazolyl quinazolinones

Compd.	% Adult Mortality											
	1.0 ml/100g				2.5 ml/100g				5.0 ml/100g			
	R_1	R_2	R_3	Mean	R_1	R_2	R_3	Mean	R_1	R_2	R_3	Mean
6_a	10	10	20	13.33	20	20	10	16.67	30	30	20	26.67
6_b	10	20	20	16.7	30	30	20	26.67	40	40	50	43.33
6_c	20	20	30	23.3	30	30	30	30	40	50	50	46.67
6_d	30	20	30	26.7	40	40	50	43.33	50	50	50	50
6_e	30	30	30	30	50	50	40	46.67	50	50	60	53.33
6_f	30	30	20	26.7	40	40	40	40	50	50	50	60
6_g	20	20	20	20	30	30	30	30	40	40	40	40
6_h	30	30	40	33.3	40	30	40	36.67	50	40	50	46.67
6_i	10	10	10	10	10	10	20	13.33	20	20	10	16.67
6_j	10	10	10	10	20	20	20	20	30	30	30	30
6_k	10	10	10	10	10	10	20	13.33	20	20	30	23.33
6_l	10	10	10	10	20	20	10	16.67	30	20	30	26.67
Control	90	90	90	90	90	90	90	90	90	90	90	90

4A : Anova : Two–Factor with Replication

6_a Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	40	50	80	170
Average	13.33	16.67	26. 67	18.89
Variance	33.33	33.33	33.33	61.11

6_b

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	50	80	130	260
Average	16.67	26.67	43.33	28.89
Variance	33.33	33.33	33.33	161.11

6_c

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	70	90	140	300
Average	23.33	30.00	46.67	33.33
Variance	33.33	0.00	33.33	125.00

6_d

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	80	130	150	360
Average	26.67	43.33	50	40
Variance	33.33	33.33	0	125

6_e

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	90	140	160	390
Average	30	46.67	53.33	43.33
Variance	0	33.33	33.33	125

6_f

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	80	120	150	350
Average	26.67	40.00	50.00	38.89
Variance	33.33	0.00	0.00	111.11

6_g

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	60	90	120	270
Average	20	30	40	30
Variance	0	0	0	75

6_h

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	100	110	140	350
Average	33.33	36.67	46.67	38.89
Variance	33.33	33.33	33.33	61.11

6_i

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	30	40	50	120
Average	10	13.33	16.67	13.33
Variance	0	33.33	33.33	25.00

6_j

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	30	60	90	180
Average	10	20	30	20
Variance	0	0	0	75

6_k

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	30	40	70	140
Average	10	13.33	23.33	15.56
Variance	0	33.33	33.33	52.78

6_I

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g	Total
Count	3	3	3	9
Sum	30	50	80	160
Average	10	16.67	26.67	17.78
Variance	0	33.33	33.33	69.44

Total

Summary	1.0 ml/100 g	2.5 ml/100 g	5.0 ml/100 g
Count	36	36	36
Sum	690	1000	1360
Average	19.17	27.78	37.78
Variance	82.14	149.21	160.63

ANOVA

Source of variation	df	MS	F
Chemical	11	1039.31	51.02
Concentration	2	3123.15	153.32
Chemical* Conc.	22	37.29	1.83
Error	72	20.37	
Total	107		
SEM	=	2.61	
CD AT 5%	=	5.11	

solution was applied on jawar grains at three different doses (levels) i.e. 1.0, 2.5 and 5.0 ml/100 gms of jawar grains respectively. It was kept for sometime till a homogeneous mass was formed. Culture tubes containing the adults (ten in number) of *Tribolium confusum* were covered with a muslin cloth and then tied with a rubber band. The tubes were placed in an incubator at 28 ± 2°C and 75 ± 5% R.H. The mortality percentage of adults in their number was observed after ten days.

Each experiment was performed in triplicate. The percentage of adult mortality at the three concentration levels are given in Table 4.

Adult Emergence

Twenty newly hatched larvae were collected from the stock culture of *Tribolium confusum* maintained in wheat flour were carefully transferred to culture tubes containing jawar grains treated with different Mannich bases to study the development period. The required amount of the compound was mixed with jawar grains at concentration levels of 1.0, 2.5 and 5 ml/100 gm, respectively. The culture tubes were covered with a muslin cloth and tied with a rubber band. The tubes were placed in an incubator at 28 ± 2°C and 75 ± 5% R.H. The observations were made on period required for adult emergence till the emergence of last adult from 5^{th} to 14^{th} day and the emerged beetles were removed to prevent further breeding. Each experiment was performed in triplicate, and the percentage of adult emergence has been given in Table 5.

Statistical Analysis

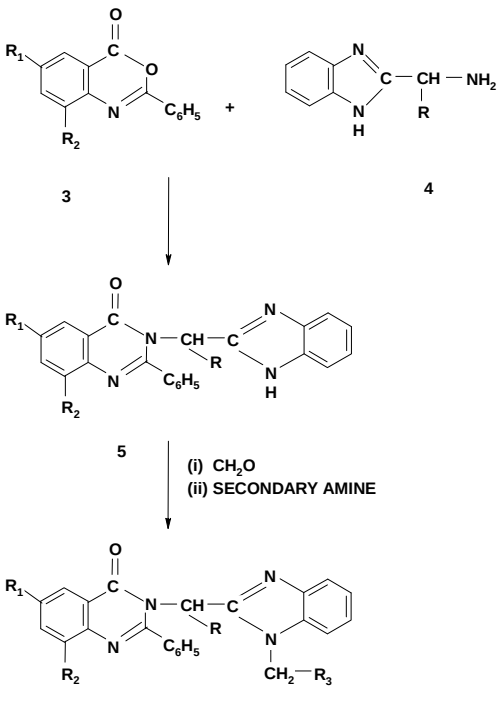
Analysis of variance (ANOVA) was also performed to see the significance of treatment given. [4A, 5A]

Insecticidal Activity

The percentage of adult mortality (Table IV) at 1 ml/100 gm seeds in seeds treated with 2–phenyl–3–(1'H–morpholinomethyl–2'–methyl benzimidazolo)–6,8 dibromo quinazolin–4(3H)–one was maximum in 6_i (26.7%) while three derivatives 6_a, 6_c, 6_g showed the minimum value of 6.67%.

At the concentration of 2.5 ml/100 gm the adult mortality percentage increased upto 33.33% in case of 6_d, 6_e, 6_k and 6_i in the seeds treated with the compounds as compared to the control (0%). With the further increase in the concentration @ 5 ml/100 gm the percentage of adult mortality was much higher i.e. 60% (6_l).

The highest mortality percentage was observed when morpholine was one of the substituent in the synthesis of the Mannich bases. Furthermore presence of a bromo group also effectively increased the mortality rate of the insect at all the concentrations.



Scheme 1

It is also apparent that the percentage of mortality showed a random increase with an increase in the concentration, while ANOVA data show CD at 5% to be 5.96.

Adult Emergence

The adult emergence of *Tribolium confusum* on jawar seeds treated with Mannich bases (Table V) in percentage @ 1 ml/100 gm was 10% (6_i, 6_j, 6_k and 6_l) and ranged upto 33.3% for 2–phenyl–3–(1'H–diphenylamino– methyl–2'–ethyl benzimidazolo)–6–bromo–quinazolin–4(3H) –one (6_h).

At a concentration of 2.5 ml/100 gm the adult emergence percentage increased and ranged between 13.33% (6_i and 6_k) to 46.67% in case of 2–phenyl–3–(1'H–piperidino methyl–2'–ethyl benzimidazolo)–quinazolin–4 (3H)–one (6_e).

With further increase in concentration at the rate of 5 ml/100 gm, the highest adult emergence percentage was recorded as 53.33% (6_e) and lowest was 16.67% (6_i).

All the treatments caused lower adult emergence in comparison to the control (90%) with all the three doses. The ANOVA analysis showed the CD at 5% to be 5.11. Therefore the test chemicals greatly effected the life cycle of *T. confusum*.

Various methods have been published to minimize the problem.[24–25]

Some synthetic compounds like the benzimidazole derivatives have been found to be effective against *Tribolium confusum* infesting house hold grain sorghum.[26] The above data further highlight the importance of heterocyclic compounds and hence these Mannich bases could be useful as possible insecticidal agents.

ACKNOWLEDGEMENT

The authors are thankful to the Director SAIF, CDRI, Lucknow for the spectral analysis, the Head Department of Zoology, J.N.V. University, Jodhpur for the biological screening of the compound and the Statistical Division of Central Arid Zone Research Institute, Jodhpur.

REFERENCES

1. El–Helpy, A.G., *J. Pharm. Sci.,* **14**: 193 (1994).
2. Kanna, R., Saxena, A.K., Srivastava, V.K. and Shankar, K., *Indian J. Chem.,* **29**B: 1056 (1990).
3. Kant, P. and Saxena, R.K., *Indian J. Hetero. Chem.,* **12**: 315 (2003).
4. Alagarswamy, V., Muthu Kumar, V., Pavalaram, N., Vasanthanathan, P. and Revathi, P., *Biol. Pharm. Bull.,* **26**(4): 557 (2003).
5. Sharma, B.P., Lakhan, R. and Singh, B., *J. Indian Chem. Soc.,* **82**: 651 (2005).
6. Swift, J.G., Dickens, E.A. and Beacker, B.A., *Arch. Int. Pharmacodyn.,* **128**: 112 (1960).
7. Varma, R.S., Shukla, A., Fatma, N. and Chatterjee, R.K., *Indian J. Chem.,* **32**B: 347 (1993).
8. Ghantwal, S.R. and Samant, S.D., *J. Indian Chem. Soc.,* **77**: 100 (2000).
9. Gaikwad, N.J. and Gautam, P., *Indian J. Hetero. Chem.,* **12**(2): 181 (2002).
10. Satayanarayana, D., Prakash Reddy, R.K., Ramana, M.V., Subrahmanyam, E.V.S., Himaja, M. and Kalluraya, B., *Indian J. Hetero. Chem.,* **10**(1): 45 (2000).
11. Walmaley, D.L., Drysdale, M.J., Northfield, C.J. and Fromont, C., *PCT Int. Appl.* WO **134**: 318 (2006) *Chem. Abs.* **146**: 81861q.
12. Rida, S.M., Cet Hawash, S.A.M., Fahmy, H.T.Y., Hazza, A.A. and El–Meligy, M.M.M., *Archives Pharmacol. Research,* **29**(10): 826 (2006).
13. Mavrova, A.Ts., Anichina, K.K., Vuchev, D.I., Tsenov, J.A., Denkova, P.S., Kondeva, M.S. and Micheva, M.K., *Eur. J. Med. Chem.,* **41**(12): 1412 (2006).
14. Reuton, P. Maddaford, S., Rakhit, S. and Andrews, J., *PCT. Int. Appl.* WO **17**: 764 (2007) Chem. Abs., **146** : 229352x.
15. Parmar, S. and Sah, P., *Indian J. Hetero. Chem.,* **16**: 367 (2007).
16. Krishnamurti, B. Mysore Agric, J. **22**: 40-45 (1943).
17. Prakash, A., Pasalu, I.C. and Rao, J., *Trop. Stored Prod. Inf.,* **47**: 15 (1984).
18. Sokoloff, A., The Biology of Tribolium, Oxford Univ. Press, London, **1**: 300 (1972).
19. Wheeler, A.S. and Oats, W.M., *J. Am. Chem. Soc.,* **32**: 770 (1910).
20. Dash, B., Dova, E.K. and Panda, C.S., *J. Indian Chem. Soc.,* **LV11**: 835 (1980).
21. Reddy, G.S. and Reddy, K.K., *Indian J. Chem.,* **16**B: 1109 (1978).
22. Cescon, L.A. and Day, A.R., *J. Org. Chem.,* **27**: 581 (1962).
23. Uehara, M., Watanabe, M., Kimura, M., Morimoto, M. and Yoshida, *M., Eur. Pat. Appl.,* **97**: 932 (2001).
24. Anonymous, Annual Tech. Report Central Rice Research Institute, Cuttack (India), 167–169 (1969).