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Synthesis of some biologically important 2-thiobarbituric acid derivatives incorporating benzothiazole moiety

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ABSTRACT

*Some N-(4/6-substituted-1,3-benzothiazol-2-yl)–N'-phenyl thiourea derivatives **(3)** have been synthesized by the reaction of substituted benzothiazoles with phenyl isothiocyanate in absolute ethanol. These **(3)** were condensed with malonic acid in acetyl chloride to get 1-(4/6-substituted-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituric acid derivatives **(5)**. All the synthesized compounds were characterized by elemental analysis, IR, ^{1}H NMR and Mass spectral studies. Compounds **3** and **5** were screened for their entomological and antibacterial activities.*

Keywords: benzothiazole; thiobarbituric acid; entomological activity; antibacterial activity; thiourea

INTRODUCTION

The survey of literature related to benzothiazoles and thiobarbiturates show that compounds with these nuclei are very important in the field of pharmaceutical industries. Benzothiazole derivatives play a vital role in biological field such as antimicrobial (*1, 2*) anti-inflammatory (*3*) antiallergic (*4*) antitubercular (*5*) anticancer (*6*) fungicidal (*7*) anti-histamines (*8*) schistosomicidal (*9*) etc.. Thiobarbituric acid derivatives have vast medicinal importance showing a number of activities e.g. antifungal (10) antidepressant (*11*) antimicrobial (*12, 13*) antitubercular (*14*) herbicides (*15*) antioxidant (*16*) membrane protector (*16*) radio protector (*16*) anticonvulsant (*17*) etc.. Looking at the importance of these moieties, it was thought that the derivatives containing both the nuclei in the same compound are expected to show improved biological activities. In continuation to our research work on benzothiazole derivatives we are reporting the synthesis of 1-(4/6-substituted-1,3-benzothiazol-2-yl)-3-Phenyl-2-thiobarbituric acid derivatives (**5**) by the reaction of substituted 2-aminobenzothiazoles (**1**) with phenyl isothiocyanate (**2**) followed by the condensation with malonic acid (**4**) (Scheme 1). The

synthesized compounds have been screened for their antibacterial activity and entomological activities (antifeedant activity, acaricidal activity, contact toxicity and stomach toxicity).

MATERIAL AND METHODS

Reagent grade chemicals were used without further purification. All the melting points were taken in open capillaries and are uncorrected. The purity of synthesized compounds was checked by Thin Layer Chromatographic studies. IR spectra were measured on FT IR Perkin Elmer (Spectrum RX1) spectrophotometer (υ in cm^{-1}) using KBr disc. ^1H NMR was recorded in $CDCl_3$ and DMSO with tetramethylsilane (TMS) as the internal standard at 300 MHz on a Bruker DRTX-300 spectrophotometer. The chemical shifts are reported as parts per million (ppm). Fast atom bombardment mass spectra (FABMS) were recorded at room temperature on a Jeol SX-102/DA-6000 mass spectrophotometer/data system using Argon/Xenon (6 kV, 10 mA) as the FAB gas. The accelerating potential was 10 kV. The elemental analysis of compounds was performed on Elementar Vario EL III Carlo Erba-1108 elemental analyzer.

Preparation of N-(4/6-substituted-1,3-benzothiazol-2-yl)–N'-phenyl thiourea derivatives (3a-3i)

A mixture of 2- amino-4/6-substituted benzothiazole (0.01 mole) and phenyl isothiocyanate (0.01 mole) was refluxed in ethanol (40 mL) for 8 hr. The separated solid was filtered, dried and crystallized from ethanol.

N-(6-Chloro-1,3-benzothiazol-2-yl)–N'-phenyl thiourea ***(3a)***

Yield (70%); m.p. 50-52 ^{o} C; IR (KBr) cm^{-1}: 3380 (NH), 1333 (C=S), 1108 (C-N), 810 (C-Cl); ^1H NMR (300 MHz) 7.01- 7.39 (m, 8H, Ar-H), 8.42 (s, 2H, 2X NH); MS 320 (M+). Anal. Calcd. For $C_{14}H_{10}N_3S_2Cl$: C, 52.57; H, 3.15; N, 13.14; S, 20.05%. Found C, 52.65; H, 3.10; N, 13.11; S, 20.10%.

N-(6-Nitro-1,3-benzothiazol-2-yl)–N'-phenyl thiourea ***(3b)***

Yield (65%); m.p. 55-58 ^{o} C; IR (KBr) cm^{-1}: 3458(NH), 1330 (C=S), 1105 (C-N), 1544 (NO_2); ^1H NMR (300 MHz) 6.90- 7.14 (m, 8H, Ar-H), 8.40 (s, 2H, 2X NH); MS 330 (M+). Anal. Calcd. For $C_{14}H_{10}N_4O_2S_2$ C, 50.90; H, 3.05; N, 16.96; S, 19.41%. Found C, 50.96; H, 3.02; N, 16.95; S, 19.40%.

N-(6-Bromo-1,3-benzothiazol-2-yl)–N'-phenyl thiourea ***(3c)***

Yield (68%); m.p. 67-70 ^{o} C; IR (KBr) cm^{-1}: 3433 (NH), 1328 (C=S), 1100 (C-N), 560 (C-Br); ^1H NMR (300 MHz) 7.10- 7.42 (m, 8H, Ar-H), 8.43 (s, 2H, 2X NH); MS 364 (M+). Anal. Calcd. For $C_{14}H_{10}N_3S_2Br$ C, 46.16; H, 2.77; N, 11.54; S, 17.60%. Found: C, 46.20; H, 2.70; N, 11.55; S, 17.58%.

N-(6-Methyl-1,3-benzothiazol-2-yl)–N'-phenyl thiourea ***(3d)***

Yield (58%); m.p. 49-53 ^{o} C; IR (KBr) cm^{-1}: 3390(NH), 1330 (C=S), 1107 (C-N), 2988 (C-H); ^1H NMR (300 MHz) 2.49 (s,3H,Ar-CH_3), 6.90- 7.21 (m, 8H, Ar-H), 8.55 (s, 2H, 2X NH); MS 299 (M+). Anal. Calcd. For $C_{15}H_{13}N_2S_2$: C, 60.17; H, 4.38; N, 14.03; S, 21.42%. Found: C, 60.21; H, 4.30; N, 14.05; S, 21.40%.

N-(4-Methyl-1,3-benzothiazol-2-yl)–N'-phenyl thiourea ***(3e)***

Yield (65%); m.p. 50-52 ^{o} C; IR (KBr) cm^{-1}: 3404 (NH), 1334 (C=S), 1104 (C-N), 1290 (C-H); ^1H NMR (300 MHz) 2.53 (s, 3H, Ar-CH_3), 6.99- 7.30 (m, 8H, Ar-H), 8.65 (s, 2H, 2X NH); MS

299 (M+). Anal. Calcd. For $C_{15}H_{13}N_2S_2$: C, 60.17; H, 4.38; N, 14.03; S, 21.42%. Found: C, 60.20; H, 4.36; N, 14.00; S, 21.44%.

N-(6-Ethoxy-1,3-benzothiazol-2-yl)–N'-phenyl thiourea ***(3f)***
Yield (70%); m.p. 53-55 ^{o} C; IR (KBr) cm^{-1}: 3375 (NH), 1330 (C=S), 1102 (C-N), 1038 (C-O-C); ^{1}H NMR (300 MHz) 1.41 (t, 3H, CH_3), 4.04 (q, 2H, Ar-OCH_2) 8.60 (s, 2H, 2X NH) 6.91-7.39 (m, 8H, Ar-H); MS 329 (M+). Anal. Calcd. For $C_{16}H_{15}N_3OS$ C, 58.33; H, 4.59.15; N, 12.76; S, 19.47%. Found C, 58.33; H, 4.55; N, 12.75; S, 19.46%.

N-(6-Methoxy-1,3-benzothiazol-2-yl)–N'-phenyl thiourea ***(3g)***
Yield (67%); m.p. 60-64 ^{o} C; IR (KBr) cm^{-1}: 3351 (NH), 1316 (C=S), 1104 (C-N), 1045 (C-O-C); ^{1}H NMR (300 MHz) 3.89 (s, 3H, Ar-OCH_3) 7.01- 7.48 (m, 8H, Ar-H), 8.45 (s, 2H, 2X NH); MS 315 (M+). Anal. Calcd. For $C_{15}H_{13}N_3OS_2$: C, 57.12; H, 4.15; N, 13.32; S, 20.33%. Found: C, 57.13; H, 4.13; N, 13.33; S, 20.32%.

N-(6-Fluoro-1,3-benzothiazol-2-yl)–N'-phenyl thiourea ***(3h)***
Yield (70%); m.p. 50-52 ^{o} C; IR (KBr) cm^{-1}: 3416 (NH), 1311 (C=S), 1107 (C-N), 1075 (C-F); ^{1}H NMR (300 MHz) 7.15- 7.47 (m, 8H, Ar-H), 8.39 (s, 2H, 2X NH); MS 303 (M+). Anal. Calcd. For $C_{14}H_{10}N_3S_2F$: C, 52.57; H, ; N, . Found: C, 52.57; H, ; N, .

N-(6-Carboxylic-1,3-benzothiazol-2-yl)–N'-phenyl thiourea ***(3i)***
Yield (65%); m.p. 57-60 ^{o} C; IR (KBr) cm^{-1}: 3413 (NH), 1335 (C=S), 1110 (C-N), 1690 (C=O), 3451 (O-H); ^{1}H NMR (300 MHz) 7.06- 7.39 (m, 8H, Ar-H), 8.36 (s, 2H, 2X NH), 10.98 (s, 1H,COOH); MS 329 (M+). Anal. Calcd. For $C_{15}H_{11}N_3O_2S_2$: C, 55.43; H, 3.22; N, 13.85; S, 21.14%. Found: C, 55.45; H, 3.20; N, 13.83; S, 21.14%.

Preparation of 1-(4/6-substituted-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid derivatives (5a-5i)
A mixture of compound (**3a-3i**) (0.01 mole) and malonic acid (0.015 mole) in acetyl chloride (10 mL) was heated on water bath for 10 hr at 40^{0} C. The solution was poured onto crushed ice and the resulting solid was filtered, washed with cold water and recrystallized from ethanol and chloroform to give compounds (**5a-5i**).
1-(6-Chloro-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid ***(5a)***
Yield (60%); m.p. 122-124 ^{o} C; IR (KBr) cm^{-1}: 3021 (Ar-H), 2980 (aliphatic CH), 1690 (C=O) 1108 (C-N), 1630 (C=N), 1438 (C=S), 823 (C-Cl); ^{1}H NMR (300 MHz) 2.73 (s, 2H, CH_2), 6.92-7.41 (m, 8H, Ar-H); MS 388 (M+). Anal. Calcd. For $C_{17}H_{10}N_3O_2S_2Cl$: C, 52.64; H, 2.60; N, 10.83; S, 16.53%. Found C, 52.65; H, 2.59; N, 10.82; S, 16.50%.

1-(6-Nitro-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid ***(5b)***
Yield (55%); m.p. 101-105 ^{o} C; IR (KBr) cm^{-1}: 3021 (Ar-H), 2980 (aliphatic CH), 1690 (C=O), 1108 (C-N), 1438 (C=N); ^{1}H NMR (300 MHz) 2.74 (s, 2H, CH_2), 7.14- 7.51 (m, 8H, Ar-H); MS 398 (M+). Anal. Calcd. For $C_{17}H_{10}N_4O_4S_2$: C, 51.25; H, 2.53; N, 14.06; S, 16.10%. Found C, 51.26; H, 2.50; N, 14.05; S, 16.11%.

1-(6-Bromo-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid ***(5c)***
Yield (52%); m.p. 89-92 ^{o} C; IR (KBr) cm^{-1}: 3021 (Ar-H), 2960 (aliphatic CH), 1698 (C=O), 1653 (C=N), 1442 (C=S), 580 (C-Br); ^{1}H NMR (300 MHz) 2.78 (s, 2H, CH_2), 7.10- 7.48 (m, 8H, Ar-H); MS 432 (M+). Anal. Calcd. For $C_{17}H_{10}N_3S_2O_2Br$: C, 47.23; H, 2.31; N, 9.72; S, 14.83%. Found C, 47.30; H, 2.31; N, 9.72; S, 14.82%.

1-(6-Methyl-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid ***(5d)***
Yield (50%); m.p. 85-89 ^{o} C; IR (KBr) cm^{-1}: 3035 (Ar-H), 2948 (aliphatic CH), 1702 (C=O), 1645 (C=N), 1414 (C=S); ^{1}H NMR (300 MHz) 2.76 (s, 2H, CH_2), 7.16- 7.79 (m, 8H, Ar-H), 2.35 (s, 3H, Ar-CH_3); MS 367 (M+). Anal. Calcd. For $C_{18}H_{13}N_3S_2O_2$: C, 58.84; H, 3.57; N, 11.44; S, 17.45%. Found C, 58.85; H, 3.53; N, 11.42; S, 17.44%.

1-(4-Methyl-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid ***(5e)***
Yield (55%); m.p. 81-84 ^{o} C; IR (KBr) cm^{-1}: 3010 (Ar-H), 2983 (aliphatic CH), 1690 (C=O), 1647 (C=N), 1440 (C=S); ^{1}H NMR (300 MHz) 2.73 (s, 2H, CH_2); 7.14- 7.53 (m, 8H, Ar-H), 2.33 (s,3H, Ar-CH_3); MS 367 (M+). Anal. Calcd. For $C_{18}H_{13}N_3S_2O_2$: C, 58.84; H, 3.57; N, 11.44; S, 17.45%. Found C, 58.86; H, 3.55; N, 11.43; S, 17.46%.

1-(6-Ethoxy-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid ***(5f)***
Yield (62%); m.p. 160-163 ^{o} C; IR (KBr) cm^{-1}: 3021 (Ar-H), 2985 (aliphatic CH), 1700 (C=O), 1660 (C=N), 1436 (C=S), 1030 (C-O-C); ^{1}H NMR (300 MHz) 1.43 (t, 3H, CH_3), 2.73 (s, 2H, CH_2), 4.05 (q, 2H, Ar-OCH_2), 7.02- 7.51 (m, 8H, Ar-H); MS 397 (M+). Anal. Calcd. For $C_{19}H_{15}N_3S_2O_3$: C, 57.41; H, 3.80; N, 10.57; S, 16.13%. Found C, 57.44; H, 3.76; N, 10.56; S, 16.15%.

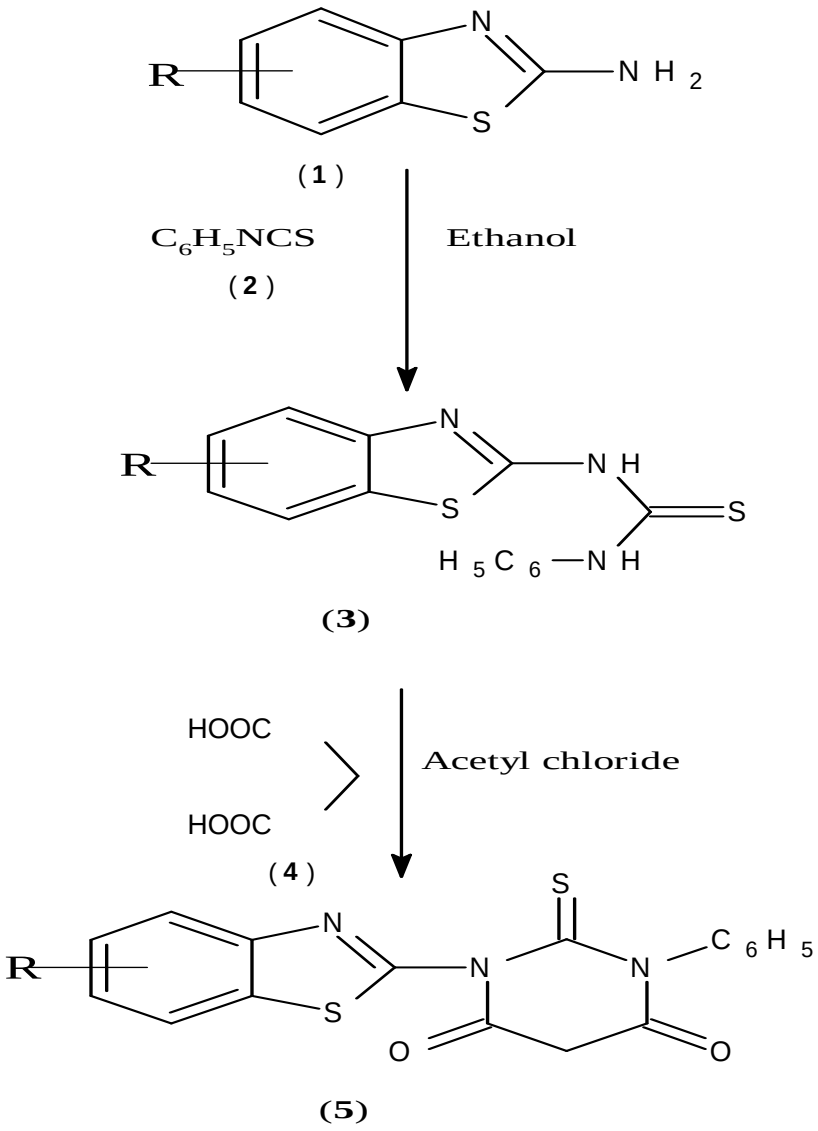
1-(6-Methoxy-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid ***(5g)***
Yield (56%); m.p. 110-115 ^{o} C; IR (KBr) cm^{-1}: 3022 (Ar-H), 2990 (aliphatic CH), 1694 (C=O), 1658 (C=N), 1430 (C=S), 1044 (C-O-C); ^{1}H NMR (300 MHz) 3.75 (s, 3H, OCH_3), 2.75 (s, 2H,CH_2), 7.18- 7.58 (m, 8H, Ar-H); MS 383 (M+). Anal. Calcd. For $C_{18}H_{13}N_3S_2O_3$: C, 56.38; H, 3.42; N, 10.96; S, 16.72%. Found C, 56.40; H, 3.38; N, 10.94; S, 16.71%.

1-(6-Fluoro-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid ***(5h)***
Yield (55%); m.p. 90-93 ^{o} C; IR (KBr) cm^{-1}: 3016 (Ar-H), 2897 (aliphatic CH), 1690 (C=O) 1644 (C=N), 1432 (C=S), 1085 (C-F); ^{1}H NMR (300 MHz) 2.67 (s, 2H, CH_2), 7.11- 7.40 (m, 8H, Ar-H); MS 371 (M+). Anal. Calcd. For $C_{17}H_{10}N_3S_2O_2F$: C, 54.98; H, 2.71; N, 11.31; S, 17.27%. Found C, 55.05; H, 2.68; N, 11.29; S, 17.28%.

1-(6-carboxylic-1,3-benzothiazol-2-yl)-3-phenyl-2-thiobarbituricacid ***(5i)***
Yield (48%); m.p. 101-103 ^{o} C; IR (KBr) cm^{-1}: 3027 (Ar-H), 2891 (aliphatic CH), 1699 (C=O), 1649 (C=N), 1430 (C=S), 3310 (O-H); ^{1}H NMR (300 MHz) 2.70 (s, 2H, CH_2), 7.16- 7.54 (m, 8H, Ar-H),11.12 (s, 1H,COOH); MS 397 (M+). Anal. Calcd. For $C_{18}H_{11}N_3S_2O_4$: C, 54.40; H, 2.97; N, 10.57; S, 16.14%. Found: C, 54.45; H, 2.95; N, 10.55; S, 16.15%.

RESULTS AND DISCUSSION

The structures of all the synthesized compounds were established on the basis of their spectroscopic and analytical data. The elemental analysis (C, H and N) found for all the compounds were in close agreement with the calculated values. The infrared (IR) spectra of compounds (**3**) exhibit signal peak in the range 3458-3351 cm^{-1} due to NH- stretching and 1335-1311 cm^{-1} for C=S. Compounds (**5**) display two characteristic bands at 1705-1690 cm^{-1} and 2990- 2860 cm^{-1} due to C=O and CH_2 stretching, respectively.



Where R = 6-Cl ; 6-NO_2 ; 6-Br; 6-CH_3; 4-CH_3 ; 6-OC_2H_5 ; 6-OCH_3; 6-F; 6-COOH
Scheme – 1

Pharmacology

Antibacterial activity

All the synthesized compounds were tested against gram positive bacteria *S. aureus* and *M. lutius and* gram negative bacteria *E. coli*, and *K. species* using paper disc method (*18*). Muller Hinton Agar (Hi-Media Pvt. Ltd. Mumbai, India) was used to culture the test bacteria. The microbial culture were grown at 37 ^{0}C for 8 hours and then appropriately diluted with sterile 0.8% saline solution. The concentration of test drugs was kept 200 µg/mL in DMF. Standard drugs streptomycin and ceftazidime were used for comparison. In case of *E. coli* at 200 ppm compounds (**5a-5i**) show moderate activity. In case of *K. species* compounds **5g** show good activity and rest of the compounds show moderate activity. The inhibition of compounds **5a, 5c,5f, 5g** show good activity while other compound **3f, 3g, 5b, 5d ,5e** and **5h** are moderate in case of *S. aureus* while rest of the compounds were less active. Compounds (**5a-5i**) show better activity than the remaining compounds against *M. lutius* (Table I).

Antifeedant activity

The antifeedant activity of these compounds was carried out by leaf dip method (*19, 20*) using fourth instars larvae of *Spodoptera litura*. The test compounds were dissolved in acetone. The leaf discs of about 25 cm^2 were prepared and dipped for thirty seconds in various concentrations of the test compounds. Now air-dried the leaf discs to evaporate the excess acetone and offered for feeding. The insects were allowed to feed for 24 h. After 24 h leaf area uneaten was measured by using leaf area meter. The difference between leaf area provided and the leaf area uneaten is taken as amount of leaf area consumed. The feeding inhibition was calculated and used for calculation of effective concentration (EC_{50}/ LD_{50}) using Maximum likelihood programmer MLP 3.01. The results clearly indicate that the compounds show higher, moderate and less antifeedant activity against the larvae of the insect. Compounds **5b, 5h** and **5i** showed higher activity and compounds **5a, 5d** and **5f** showed moderate activity against mites (Table II).

Acaricidal activity

The acaricidal activity of these compounds was carried out by leaf dip method (*19, 20*). The test compounds were dissolved in acetone. Leaf discs of Mulberry (5 cm^2 diameter) were dipped in different compounds for 30 seconds. Now air dried the leaf discs to remove the excess of acetone and placed over wet cotton in Petri plate. The adult female mites were released on treated leaf discs and mortality data were recorded after 48 hours. Mites released on leaf treated only with acetone and tween 20 emulsifier served as control. The mortality data were used for calculation of LC_{50}/ LD_{50} using Maximum Likelihood Programmer MLP 3.01. *Tetranychus urticae*, a species of mite using acetone as a standard. The results obtained clearly show that compound **5a, 5b, 5h, 5i** and **5g** shows the highest acaricidal activity with respect to the other compounds. Rest of the compounds shows moderate activity against the mites (Table III).

Contact toxicity

The contact toxicity of these compounds was carried out by topical application method (*21, 22*) against larvae of *Spodoptera litura,* which is harmful for Indian crops. First the given compounds were dissolved in acetone. Now each compound was applied on the dorsal surface of the larvae. About 10 µl of each sample solution was applied on each larva. Some of the larvae of insect were treated by acetone alone, works as control. Now the mortality data was recorded after 24 hrs, and the treated mortality was corrected with control morality. These corrected mortality data was used for calculation of LC_{50}/ LD_{50} using Maximum Likelihood programmer MLP 3.01. The results clearly indicate that the compounds show moderate and less contact toxicity against the larvae of the insect .Compounds **5a, 5h** and **5i** show good activity and compound **5d** and **5g** show moderate activity and the rest of the compounds show lower to moderate activity against the mites (Table IV).

Stomach toxicity

The stomach toxicity of these compounds was carried out by leaf dip method [19, 20]. In this method we used fourth instar larvae of *Spodoptera litura* of an insect which is responsible for the damage of Indian agricultural crops. Ten larvae were used for each replication and three replications were maintained for each compound .The given compounds were dissolved in acetone. The leaf disc were prepared out of caster leaf and dipped in various compounds of the test compounds for thirty seconds. Now air dried the leaf discs to evaporate the excess acetone. (The leaf discs dipped only in acetone served as control). The mortality data were recorded after 24 hrs, and the treatment mortality was corrected with control mortality. These mortality data were used for calculation of LC_{50}/LD_{50} using maximum likelihood programmer, MLP 3.01. The results clearly indicate that the compounds **5a** and **2i** show good stomach toxicity and

compounds **5g** and **5h** moderate activity and the rest of the compounds show lower to moderate activity against the mites (Table V).

Table I: The zone of inhibition of the compound as well as standard drugs tested for antibacterial activity.

Solutions are in µg/mL; Data represent zones of inhibition (mm) as follows:- 0 mm; + 6-8 mm; ++9-12mm; +++ 13-19 mm; ++++ 20-26 mm

Compound	R	*E. coli*		*K. Species*		*S. aureus*		*M. lutius*	
		200	100	200	100	200	100	200	100
3a	Cl	++	+	++	+	++	+	++	+
3b	NO_2	++	+	+	+	++	+	++	+
3c	Br	+	+	+	+	++	+	++	+
3d	CH_3	+	+	++	+	++	+	++	+
3e	4-CH_3	++	+	++	+	+	+	+	+
3f	OC_2H_5	++	++	++	+	+++	++	++	+
3g	OCH_3	++	+	++	+	+++	++	++	+
3h	F	++	+	++	+	++	+	++	+
3i	COOH	++	+	+	+	++	+	++	+
5a	Cl	+++	+++	+++	++	+++	++	+++	++
5b	NO_2	+++	++	++	++	+++	++	+++	++
5c	Br	+++	++	+++	++	+++	++	+++	++
5d	CH_3	+++	++	+++	++	+++	++	+++	++
5e	4-CH_3	+++	++	+++	++	+++	++	+++	++
5f	OC_2H_5	+++	++	+++	++	+++	+++	+++	++
5g	OCH_3	+++	+++	++++	+++	+++	+++	++	++
5h	F	+++	++	++	++	+++	++	+++	++
5i	COOH	++	+	++	++	+++	++	+++	++
DMF	----	-	-	-	-	-	-	-	-
Streptomycin	----	++++		++++		++++		++++	
Ceftazidime	-----	++++		++++		++++		++++	

Table II: Antifeedant activity

Compound	Fiducial Limits	Slop ±	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
5a	0.62–1.46	1.05±0.14	1.09 (3)	0.87
5b	0.30–0.48	1.25±0.15	3.48 (3)	0.37
5c	0.71–2.21	0.89±0.14	0.20 (3)	1.08
5d	0.49–1.25	0.87±0.13	0.89 (3)	0.71
5e	0.82–3.41	0.81±0.14	0.43 (3)	1.35
5f	0.68–1.72	1.03±0.14	0.66 (3)	0.98
5g	0.84–2.34	1.06±0.15	0.70 (3)	1.24
5h	0.43–0.87	1.03±0.14	0.34 (3)	0.58
5i	0.43–0.87	1.03±0.14	0.34 (3)	0.58

Table III: Acaricidal activity

Compound	Fiducial Limits	Slop ±	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
5a	0.05–0.09	1.16±0.09	12.67 (3)	0.07
5b	0.05–0.10	0.97±0.8	13.22 (3)	0.07
5c	0.12–0.26	0.89±0.8	8.52 (3)	0.17
5d	0.08–0.20	0.75±0.7	5.53 (3)	0.12
5e	0.12–0.30	0.78±0.08	1.70 (3)	0.18
5f	0.14–0.31	0.96±0.09	7.52 (3)	0.20
5g	0.05–0.10	0.87±0.7	20.01 (3)	0.07
5h	0.04–0.09	0.70±0.06	4.61 (3)	0.05
5i	0.05–0.10	0.93±0.08	13.22 (3)	0.06

Table IV: Contact toxicity

Compound	Fiducial Limits	Slop ±	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
5a	0.29–0.39	1.97±0.16	4.39 (3)	0.34
5b	1.87–12.08	1.09±0.19	1.60 (3)	3.53
5c	1.33–3.99	1.42±0.20	2.38 (3)	2.01
5d	0.74–1.32	1.62±0.18	3.24 (3)	0.94
5e	1.87–12.07	1.09±0.19	1.62 (3)	3.53
5f	1.57–9.32	1.07±0.17	0.72 (3)	2.83
5g	0.48–0.75	1.61±0.16	2.94 (3)	0.59
5h	0.40–0.59	1.66±0.15	5.66 (3)	0.48
5i	0.28–0.40	1.96±0.16	4.39 (3)	0.33

Table V: Stomach toxicity

Compound	Fiducial Limits	Slop ±	Chi. Sq. (3)	LC_{50}/LD_{50} At 24 hrs.
5a	0.49–0.77	1.57±0.16	2.79 (3)	0.60
5b	0.86–1.99	1.28±0.16	0.80 (3)	1.20
5c	1.61–9.55	1.01±0.17	0.68 (3)	2.97
5d	0.82–1.67	1.45±0.17	0.65 (3)	1.10
5e	1.61–9.55	1.45±0.17	0.68 (3)	2.97
5f	0.86–1.99	1.28±0.16	0.80 (3)	1.20
5g	0.54–0.90	1.49±0.16	3.39 (3)	0.68
5h	0.57–1.05	1.32±0.15	0.63 (3)	0.74
5i	0.49–0.76	1.57±0.16	2.78 (3)	0.60

CONCLUSION

All the newly synthesized compounds were screened for antibacterial activity at a concentration of 200 µg/mL and 100 µg/mL using DMF as a control streptomycin and ceftazidime used as standard against gram positive and gram negative bacteria. The data in the Table I indicate that among the synthesized compounds **5a, 5f, 5g** compounds were found to posses a broad spectrum activity. However, the activities of the tested compounds are much less than those of standard antibacterial agents used. The compounds also show potent antiulcer activity, anti-inflammatory activity and antitumor activity. Antifeedant activity, acaricidal activity against *Spodoptera litura* and *Tetranychus urticae*, respectively. From the results, it is clear that these compounds would be better used in drug development to combat bacterial infections, and would be better used as antifeedant and acaricidal activity in the future as well.

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