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SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME NOVEL 2-CYCLIC AMINE BENZOTHIAZOLE DERIVATIVES

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Abstract:

The synthesis of a new series of 2-(cyclic amine)-1, 3-benzothiazole derivatives were synthesized in satisfactory yield and evaluated for their anti-microbial activities. 2-(cyclic amine)-1, 3-benzothiazoles were synthesized by treating 2-chloro benzothiazole with various cyclic amines. Purity of all the compounds has been checked on thin layer chromatographic plate technique. The structures of these newly synthesized compounds were characterized by elemental analysis and spectral data like IR, ^{1}HNMR, ^{13}CNMR and mass spectroscopy. All the synthesized compounds have been screened for their anti-microbial activity (MIC) in vitro by broth dilution method with two Gram-positive bacteria, two Gram-negative bacteria and two fungal stains. The compounds exhibit significant antibacterial activity, when compared with that of standard drug Streptomycin. Also show moderate degree of antifungal activity when compared with a standard drug Amphotericin-B.

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INTRODUCTION:

A heterocyclic compound is one which possesses a cyclic structure with at least two different kinds of hetero atoms in the ring. Nitrogen, oxygen, and sulphur are the most common heteroatoms. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways.The heterocyclic derivatives containing nitrogen and sulphur atom serve as a unique and having varied biological activities. Benzothiazole is a privilaged bicyclic ring system. Due to its potent and significant biological activities it has great pharmaceutical importance. Since most of the benzothiazole derivatives were reported for their diversified activity viz, Antitumor [16,17], Antitubercular [15], Antidiabetic activity [11,12], Antimalarial[7], Anticonvulsant [16,19], Anthelmintic [6,16], Analgesic [24], Anti-Depressant [24], Anti-inflamatory [13,16], Anti-psychotic [16] and an Antihypoxic [21]. The pharmacological potency of cyclic amines e.g., piperazines, morpholine and piperadine as well as the biological activity of benzothiazole analogues has drawn our attention to synthesize the compounds containing both these moieties in a single molecular frame work. The small and simple benzothiazole nucleus if present in compounds involved in research aimed at evaluating new products that possess interesting biological activities. 2-substituted benzothiazole has emerged in its usage as a core structure in the diversified therapeutically applications. The substitution of cyclic amines at second position in benzothiazole skeleton is influential for the biological activity of the molecule. Based on the above observation it is worthwhile to prepare new 2-cyclic amine benzothiazole derivatives for their antimicrobial activities.

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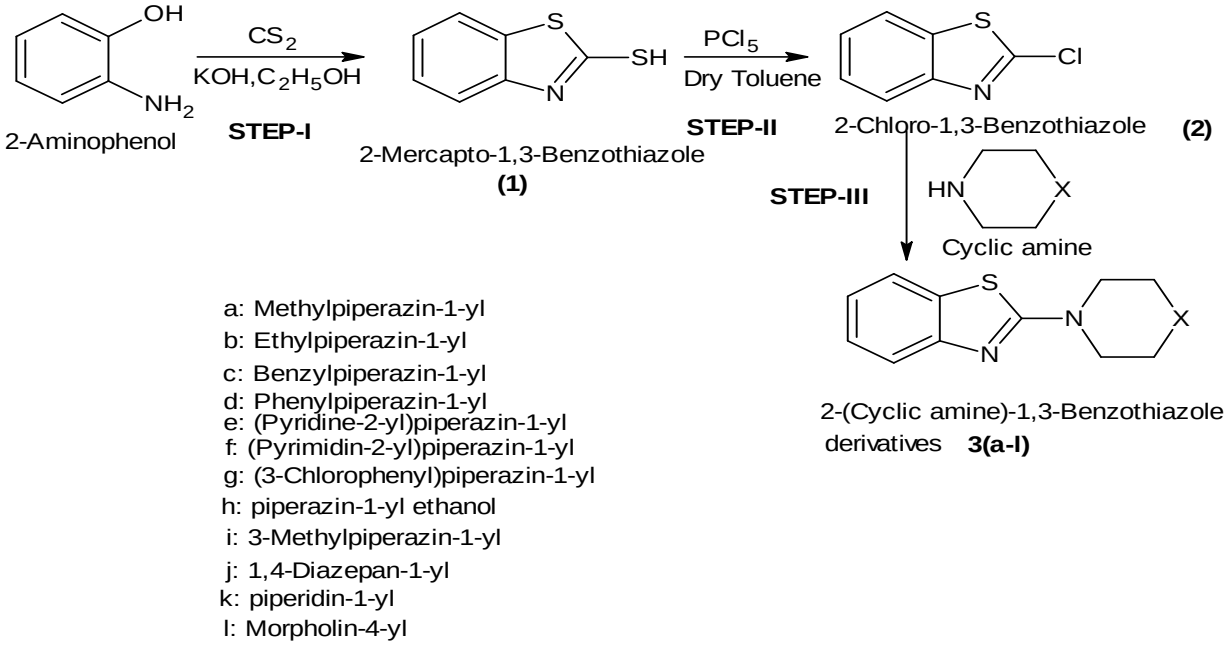
MATERIALS AND METHODS:

All the chemicals and solvents used were of synthetic grade obtained from U .V Pharmaceuticals. Completion of the reactions was monitored time to time by analytical thin layer chromatography (TLC) using E-Merck 0.25mm silica gel plates. Visualization was accomplished with UV light (256nm) and iodine chamber. The purity of compounds was checked by a single spot in TLC and solvent system for TLC was determined on trial & error basis. All the melting points were determined in open capillaries, using Boitus melting point apparatus, expressed in ^{o}C and are uncorrected. All the IR spectra were recorded on Shimadzu FT-IR Spectrophotometer using 1 % potassium bromide pellet method. The mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. The ^{1}H NMR and ^{13}CNMR spectra of the compounds were determined in $CDCl_3$ solution on a Bruker AMX 400 MHz NMR spectrophotometer using TMS as an internal standard and the values are expressed in δ ppm. The results are in agreements with the structures assigned

EXPERIMENTAL SECTION



Scheme-1: Synthesis of 2-Cyclic amine-1,3-Benzothiazolederivatives 3(a-l)

Procedure for the preparation of 2-mercapto-1,3-benzothiazole (1): 2-Aminophenol (9.9 g, 0.09 mole) was refluxed for 8 h with potassium hydroxide (6.6 g, 0.14 mole) and carbon disulfide (100 mL) in ethanol (150 mL). The reaction mixture was concentrated under vacuum; 1 N aqueous hydrochloric acid (100 mL) and ethyl acetate (200 mL) were added to the residue. The organic layer was washed with water (2 X 50 mL), dried over Na_2SO_4, and concentrated under vaccum. 2-Mercapto-1,3-benzothiazole (1) was obtained as a yellow powder and was crystallized from ethanol (11.2 g, 82 %).White solid. M.P 189-192°C.

Procedure for the preparation of 2-chlorobenzothiazole (2): Phosphorus pentachloride (18.5 g, 0.09 mole) was added slowly to the solution of 5-chloro-2-mercapto-1,3-benzothiazole (1) (11.2 g, 0.074 m.mol) in dry toluene (300 mL) at 20°C. The reaction mixture was stirred at 120°C for 3 h. The reaction mixture was subjected to fractional distillation under vacuum to obtain pure 2-chlorobenzothiazole (2) (95-95°C/20 mm) (8.7 g, 76 %).

General procedure for the preparation of 2-(cyclic amine)-1,3-benzothiazole derivatives [3(a-l)]: The 2-chlorobenzothiazole **(2)** (2.6 m.mol, 400 mg) was added to a solution of cyclic amine (2.6 m.mol, 260 mg) in dry acetonitrile (30 mL) at 0°C. The mixture was stirred at 0°C – room temperature for 30 minutes, quenched in ice water (30 mL), extracted with ethyl acetate (3 X 20 mL) and dried over Na_2SO_4. After concentration, the residue was purified by flash chromatography to obtain the pure product and was crystallized from methanol.

2-(4-methylpiperazin-1-yl)-1,3-benzothiazole (3a): White solid. M.P 37-38°C, ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.22 (t, J= 7.3 Hz, 2H, 2XAr-H); 7.09 (t, J= 7.3 Hz, 1H, Ar-H); 6.95 (t, J= 7.3 Hz, 1H, Ar-H); 3.67 (t, J= 5.1 Hz, 4H, 2XN-CH_2); 2.48 (t, J= 5.1 Hz, 4H, 2XNCH_2); 2.30 (s, 3H, N-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.0, 148.7, 142.8, 124.0, 120.8, 116.3, 108.7, 54.0, 45.9, 45.2. IR (KBr, cm-1): 3057 (=C-H), 2933, 2854 (-C-H), 1639, 1578 (-C=C), 1456 (-C-H ben), 1363 (- C-N), 1285, 1002 (-C-S), 746 (=C-H ben).

EI-MS (m/z): 233 $(M+1)^+$.

Anal. calcd for $C_{12}H_{15}N_3S$ (233): C, 66.34; H, 6.96; N, 19.34. Found: C, 66.36; H, 6.94; N, 19.37.

2-(4-ethylpiperazin-1-yl)-1,3-benzothiazole (3b): White solid. M.P 78-80°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.30 (d, J= 7.7 Hz, 1H, Ar-H); 7.20 (d, J= 7.7 Hz, 1H, Ar-H); 7.11 (t, J= 7.7 Hz, 1H, Ar-H); 6.96 (t, J= 7.7 Hz, 1H, Ar-H); 3.70 (t, J= 4.9 Hz, 4H, 2XN-CH_2); 2.54 (t, J= 4.9 Hz, 4H, 2XN-CH_2); 2.45 (q, J= 7.2 Hz, 2H, CH_3CH_2); 1.11 (t, J= 7.2 Hz, 3H, CH_3CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.0, 148.6, 142.9, 123.9, 120.6, 116.1, 108.6, 52.2, 51.9, 45.4, 11.7. IR (KBr, cm-1): 3052 (=C-H), 2970 (-C-H), 1638, 1578, 1525 (-C=C), 1459 (-C-H ben), 1399 (- C-N), 1243 (-C-S), 746 (=C-H ben).

EI-MS (m/z): 247 (M^+).

Anal. calcd for $C_{13}H_{17}N_3S$ (247): C, 67.51; H, 7.41; N, 18.17. Found: C, 67.54; H, 7.39; N, 18.15.

2-(4-benzylpiperazin-1-yl)-1,3-benzothiazole (3c): White solid. M.P 230-231°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.34-7.25 (m, 6H, 6XAr-H); 7.19 (d, J= 7.8 Hz, 1H, Ar-H); 7.11 (t, J= 7.8 Hz, 1H, Ar-H); 6.96 (t, J= 7.8 Hz, 1H, Ar-H); 3.70 (t, J= 4.7 Hz, 4H, 2XN-CH_2); 3.54 (s, 2H, Ph-CH_2); 2.56 (t, J= 4.7 Hz, 4H, 2XN-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 162.1, 148.7, 143.0, 136.9, 129.2, 128.4, 127.4, 123.9, 120.6, 116.2, 108.7, 62.9, 52.1, 45.4. IR (KBr, cm-1): 3028 (=C-H), 2917, 2860 (-C-H), 1640, 1578, 1494 (-C=C), 1455 (-C-H ben), 1395 (-C-N), 1245 (-C-S), 739 (=C-H ben).
EI-MS (m/z): 309 (M^+).
Anal. calcd for $C_{18}H_{19}N_3S$ (309): C, 73.70; H, 6.53; N, 14.32. Found: C, 73.74; H, 6.52; N, 14.33.

2-(4-phenylpiperazin-1-yl)-1,3-benzothiazole (3d): White solid. M.P 150-151°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.33 (d, J= 7.6 Hz, 1H, Ar-H); 7.26 (d, J= 7.6 Hz, 1H, Ar-H); 7.23 (d, J= 6.8 Hz, 2H, 2Ar-H); 7.14 (t, J= 6.8 Hz, 1H, Ar-H); 6.99 (t, J= 7.6 Hz, 1H, Ar-H); 6.92 (d, J= 6.8 Hz, 2H, 2XAr-H); 6.88 (t, J= 7.6 Hz, 1H, Ar-H); 3.85 (t, J= 5.3 Hz, 4H, 2XNCH_2); 3.29 (t, J= 5.3 Hz, 4H, 2XN-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.8, 150.8, 148.6, 142.6, 129.2, 124.1, 120.9, 120.8, 116.9, 116.3, 108.8, 49.2, 45.5. IR (KBr, cm-1): 2980, 2914, 2822 (-C-H), 1629, 1575, 1497(-C=C), 1455 (-C-H ben), 1237 (-C-S), 735 (=C-H ben).
EI-MS (m/z): 295 $(M+1)^+$.
Anal. calcd for $C_{17}H_{17}N_3S$ (295): C, 73.10; H, 6.13; N, 15.04. Found: C, 73.08; H, 6.12; N, 15.05.

2-[4-(pyridin-2-yl)piperazin-1-yl]-1,3-benzothiazole (3e): White solid. M.P 186-188°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.19-8.15 (m, 1H, Ar-H); 7.51-7.44 (m, 1H, Ar-H); 7.33 (d, J= 7.7 Hz, 1H, Ar-H); 7.23 (d, J= 7.7 Hz, 1H, Ar-H); 7.13 (dt, J= 6.6, 1.1 Hz, 1H, Ar-H); 6.99 (dt, J= 6.6, 1.3 Hz, 1H, Ar-H); 6.68-6.61 (m, 2H, 2XAr-H); 3.88-3.77 (m, 4H, 2XN-CH_2); 3.74-3.67 (m, 4H, 2XN-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.9, 158.2, 148.7, 146.8, 142.8, 138.4, 124.0, 120.9, 116.4, 113.8, 108.8, 107.8, 45.2, 44.9. IR (KBr, cm-1): 3053 (=C-H), 2993, 2917 (-C-H), 1635, 1576, 1480 (-C=C), 1459 (-C-H ben), 1435 (-C-N), 1242 (-C-S), 744 (=C-H ben).
EI-MS (m/z): 296 (M^+).
Anal. calcd for $C_{16}H_{16}N_4S$ (296): C, 68.55; H, 5.75; N, 19.99. Found: C, 68.59; H, 5.78; N, 19.96.

2-[4-(pyrimidin-2-yl)piperazin-1-yl]-1,3-benzothiazole (3f): White solid. M.P 183-185°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.30 (d, J= 5.0 Hz, 2H, 2XArH); 7.33 (d, J= 7.6 Hz, 1H, Ar-H); 7.23 (d, J= 7.6 Hz, 1H, Ar-H); 7.13 (t, J= 7.6 Hz, 1H, Ar-H); 6.99 (t, J= 7.6 Hz, 1H, Ar-H); 6.51 (t, J= 5.0 Hz, 1H, Ar-H); 4.04-3.94 (m, 4H, 2XN-CH_2); 3.81-3.72 (m, 4H, 2XN-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.6, 161.4, 157.8, 148.6, 144.4, 124.3, 121.1, 116.3, 110.6, 108.9, 45.5, 43.2. IR (KBr, cm-1): 2911, 2860 (-C-H), 1651, 1581, 1490 (-C=C), 1451 (-C-H ben), 1393 (-C-N), 1251 (-C-S), 733 (=C-H ben).
EI-MS (m/z): 297 (M^+).
Anal. calcd for $C_{15}H_{15}N_5S$ (297): C, 64.04; H, 5.37; N, 24.89. Found: C, 64.08; H, 5.41; N, 24.94.

2-[4-(3-chlorophenyl)piperazin-1-yl]-1,3-benzothiazole (3g): White solid. M.P 134-136°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.33 (d, J= 6.8 Hz, 1H, Ar-H); 7.23 (d, J= 7.6 Hz, 1H, Ar-H); 7.17 (d, J= 7.6 Hz, 1H, Ar-H); 7.13 (t, J= 7.6 Hz, 1H, Ar-H); 7.00 (t, J= 7.6 Hz, 1H, Ar-H); 6.90 (t, J= 2.3 Hz, 1H, Ar-H); 6.85 (d, J= 7.6 Hz, 1H, Ar-H); 6.79 (d, J= 7.6 Hz, 1H, Ar-H); 3.84 (t, J= 5.3 Hz, 4H, 2XN-CH_2); 3.31 (t, J= 5.3 Hz, 4H, 2XN-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.9, 151.9, 150.9, 142.8, 135.0, 130.1, 124.1, 120.9, 120.3, 116.6, 116.4, 114.7, 108.8, 48.6, 45.3. IR (KBr, cm-1): 3015 (=C-H), 2913 (-C-H), 1625, 1593, 1478 (-C=C), 1397 (-C-N), 1253 (-C-S), 695 (=C-H ben).
EI-MS (m/z): 329 $(M+1)^+$.
Anal. calcd for $C_{17}H_{16}ClN_3S$(329): C, 65.07; H, 5.14; N, 13.39. Found: C, 65.09; H, 5.14; N, 13.36.

2-[4-(1,3-benzothiazol-2-yl)piperazino]-1-ethanol (3h): Brown solid. M.P 35-36°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.42 (d, J= 7.6 Hz, 1H, Ar-H); 7.30 (d, J= 7.6 Hz, 1H, Ar-H); 7.19 (t, J= 7.6 Hz, 1H, Ar-H); 7.11 (t, J= 7.6 Hz, 1H, Ar-H); 4.64 (t, J= 6.0 Hz, 2H, O-CH_2); 2.82 (t, J= 6.0 Hz, 2H, N-CH_2); 2.52 (t, J= 5.2 Hz, 4H, 2XN-CH_2); 1.60 (t, J= 5.2 Hz, 4H, 2XN-CH_2); 1.49-1.38 (m, 1H, OH). IR (KBr, cm-1): 3423 (-O-H), 2936, 2855 (-C-H), 1631, 1578, 1483 (-C=C), 1458 (-C-H ben).
EI-MS (m/z): 263 (M^+).
Anal. calcd for $C_{13}H_{17}N_3OS$(263): C, 63.14; H, 6.93; N, 16.99. Found: C, 63.19; H, 6.88; N, 17.05.

2-(3-methylpiperazin-1-yl)-1,3-benzothiazole (3i): Brown solid. M.P 51-52°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.30 (d, J= 7.6 Hz, 1H, Ar-H); 7.19 (d, J= 7.6 Hz, 1H, Ar-H); 7.11 (t, J= 7.6 Hz, 1H, Ar-H); 6.95 (t, J= 7.6 Hz, 1H, Ar-H); 4.11 (d, J= 11.3 Hz, 2H, N-CH_2); 3.07 (m, 2H, N-CH_2); 2.91 (m, 2H, N-CH_2); 2.71 (m, 1H, N-CH); 1.80 (s, 1H, NH); 1.11 (d, J= 8.3 Hz, 3H, CH-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.5, 148.5, 142.8, 123.6, 120.3, 116.0, 108.3, 51.7, 50.0, 44.9, 44.5, 18.5. IR (KBr, cm-1): 3322 (-N-H), 3057 (=C-H), 2958, 2856 (-C-H), 1639, 1578 (-C=C), 1459 (-C-H ben), 1401, 1357 (-C-N), 1283, 1246 (-C-S), 805, 745 (=C-H ben).
EI-MS (m/z): 233 (M^+).
Anal. calcd for $C_{12}H_{15}N_3S$ (233): C, 66.34; H, 6.96; N, 19.34. Found: C, 66.36; H, 6.99; N, 19.29.

2-(1,4-Diazepan-1-yl)-1,3-benzothiazole (3j): Brown solid. M.P 195-198°C. ^{1}H NMR (200 MHz,

$CDCl_3$) δ: 7.31 (d, J= 7.6 Hz, 1H, Ar-H); 7.23 (d, J= 7.6 Hz, 1H, Ar-H); 7.13 (t, J= 7.6 Hz, 1H, Ar-H); 6.98 (t, J= 7.6 Hz, 1H, Ar-H); 3.96 (s, 2H, N-CH_2); 3.76 (t, J= 6.0 Hz, 4H, 2XN-CH_2); 3.07 (t, J= 5.2 Hz, 1H, N-CH); 2.91 (t, J= 5.2 Hz, 1H, N-CH); 2.27 (quintet, J= 6.0 Hz, 1H, CH_2CHCH_2); 1.97 (quintet, J= 6.0 Hz, 1H, CH_2CHCH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.6, 148.9, 143.1, 124.0, 120.6, 116.2, 108.7, 49.5, 49.1, 48.4, 47.4, 26.7. IR (KBr, cm-1): 3399 (-N-H), 3050 (=C-H), 2934 (-C-H), 1639, 1578 (-C=C), 1459 (-C-H ben), 1402 (-C-N), 1244 (-C-S), 744 (=C-H ben).

EI-MS (m/z): 233 (M^+).

Anal. calcd for $C_{12}H_{15}N_3S$ (233): C, 66.34; H, 6.96; N, 19.34. Found: C, 66.31; H, 6.97; N, 19.32.

2-(piperidin-1-yl)-1,3-benzothiazole (3k): Brown solid. M.P 71-72°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.33 (d, J= 7.9 Hz, 1H, Ar-H); 7.23 (d, J= 7.9 Hz, 1H, Ar-H); 7.14 (t, J= 7.9 Hz, 1H, Ar-H); 6.99 (t, J= 7.9 Hz, 1H, Ar-H); 3.70 (s, 4H, 2XN-CH_2); 1.74 (s, 6H, 3XCH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.9, 148.4, 142.2, 124.1, 120.7, 115.8, 108.7, 46.8, 25.2, 23.9. IR (KBr, cm-1): 3057 (=C-H), 2936, 2854 (-C-H), 1638, 1577, 1525 (-C=C), 1455 (-C-H ben), 1394 (-C-N), 1221 (-C-S), 744 (=C-H ben).

EI-MS (m/z): 218 (M^+).

Anal. calcd for $C_{12}H_{14}N_2S$ (218): C, 71.26; H, 6.98; N, 13.85. Found: C, 71.29; H, 7.00; N, 13.82.

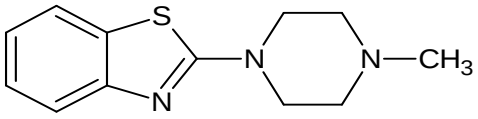
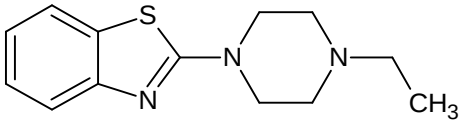
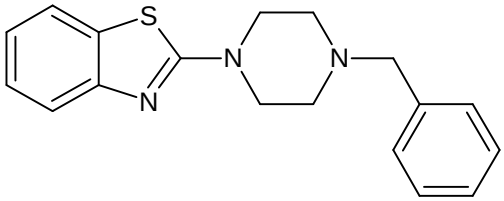
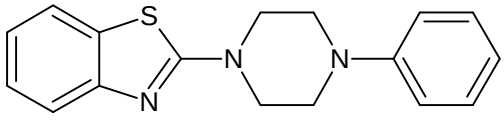
2-(morpholin-4-yl)-1,3-benzothiazole (3l): Brown solid. M.P 205-206°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.32 (d, J= 7.9 Hz, 1H, Ar-H); 7.21 (d, J= 7.9 Hz, 1H, Ar-H); 7.13 (t, J= 7.9 Hz, 1H, Ar-H); 6.98 (t, J= 7.9 Hz, 1H, Ar-H); 3.77 (t, J= 4.5 Hz, 4H, 2XO-CH_2); 3.64 (t, J= 4.5 Hz, 4H, 2XN-CH_2). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 161.2, 148.2, 141.1, 124.3, 121.3, 116.0, 108.9, 66.0, 45.8. IR (KBr, cm-1): 3057 (=C-H), 2966, 2863 (-C-H), 1637, 1578, 1525 (-C=C), 1454 (-C-H ben), 1398 (-C-N), 1242, 1105 (-C-S), 745 (=C-H ben).

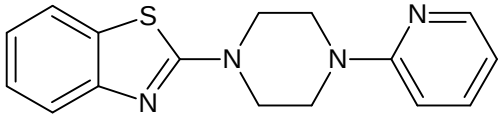
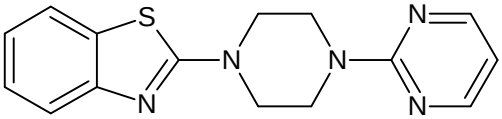
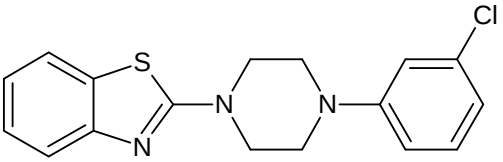
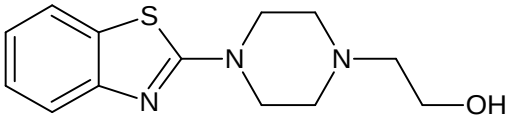
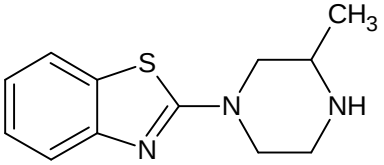
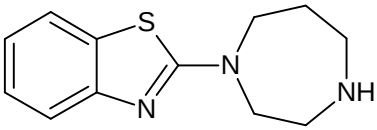
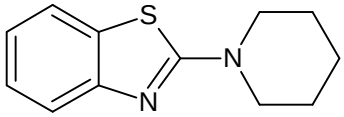
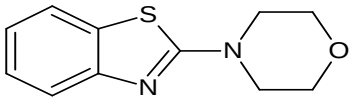
EI-MS (m/z): 220 (M^+).

Anal. calcd for $C_{11}H_{12}N_2OS$ (220): C, 64.69; H, 5.92; N, 13.72. Found: C, 64.65; H, 5.94; N, 13.69.

RESULT AND DISCUSSION:

Table 1: Physical data of 2-(cyclic amine)-1,3-benzothiazole derivatives [3(a-l)]

Compound	2-(Cyclicamine)-1,3-Benzothiazole derivatives	M.W	M.P(°C)	Yield (%)	Time(min)
3a	 2-(4-methylpiperazin-1-yl)-1,3-benzothiazole	233.3	37-38	70	30
3b	 2-(4-ethylpiperazin-1-yl)-1,3-benzothiazole	247.3	78-80	65	45
3c	 2-(4-benzylpiperazin-1-yl)-1,3-benzothiazole	309.4	230-231	75	35
3d	 2-(4-phenylpiperazin-1-yl)-1,3-benzothiazole	295.4	150-151	80	40

3e	 2-[4-(pyridin-2-yl)piperazin-1-yl]-1,3-benzothiazole	296.3	186-188	78	30
3f	 2-[4-(pyrimidin-2-yl)piperazin-1-yl]-1,3-benzothiazole	297.3	183-185	85	35
3g	 2-[4-(3-chlorophenyl)piperazin-1-yl]-1,3-benzothiazole	329.8	134-136	82	35
3h	 2-[4-(1,3-benzothiazol-2-yl)piperazin-1-yl]ethanol	263.3	35-36	70	55
3i	 2-(3-methylpiperazin-1-yl)-1,3-benzothiazole	233.3	51-52	69	50
3j	 2-(1,4-diazepan-1-yl)-1,3-benzothiazole	233.3	195-198	74	45
3k	 2-(piperidin-1-yl)-1,3-benzothiazole	218.3	71-72	78	50
3l	 2-(morpholin-4-yl)-1,3-benzothiazole	220.2	205-206	68	50

BIOLOGICAL EVALUATION

Preparation of Culture Media: Nutrient broth was used as growth medium for bacteria and Saubouraud dextrose broth for fungi. Nutrient broth was prepared by dissolving 13gm of dehydrated powder (HI-media) in 100ml of distilled water. Saubouraud

dextrose broth was prepared by dissolving 4gm of dextrose and 1gm of peptone in 100ml of distilled water. The media were sterilized by autoclaving at 15lbs pressure for 20 minutes.

Preparation of Stock Culture: Stock cultures were obtained by aseptically transferring a loopful of test organisms to 100ml of sterile broth and incubated for 24 hours at 37^0C.

Standardization of Stock Culture: Stock cultures were placed in the incubator (37^0C for bacteria and 24^0C for fungi) and shaken well. One ml of stock cultures was aseptically transferred to 9 ml of sterile water containing 0.05% tween 80. This was mixed with using a cyclomixer and serially diluted from 10-1 to 10-10. From each dilution, 0.2ml was taken and spread on sterile nutrient agar plates for bacteria and Sabouraud dextrose agar plates for fungi, which were incubated for 18 hours. After incubation, the numbers of colonies in the plate were counted. The number of colonies for a plate that was formed from the maximum dilute tube was noted. The number of microorganisms in stock were then calculated and expressed as colony forming units per ml (cfu/ml). By back calculation the stock culture was found to contain 15×10^8 cfu/ml.

Preparation of Working Stock Culture: Stock culture (0.1ml) was diluted with nutrient broth (100ml) and Sabouraud dextrose broth (100ml) respectively to obtain 10^5 cfu/ml. This was then used for further *in vitro* screening.

Preparation of Drug Dilutions: Solutions of the title compounds in DMSO (1mg/ml) were prepared and used for screening their antimicrobial activity[28].

Antimicrobial Screening

In the search of new antimicrobial agents, all the twelve synthesized compounds were subjected to antimicrobial screening by estimating the minimum inhibitory concentration (MIC) by adopting serial dilution technique. Test was carried out on four bacterial strains, namely *Bacillus subtilis* (MTCC 441), *Staphylococcus aureus* (MTCC 96), Klebsiella pneumoniae (MTCC 618), *Escherichia coli* (MTCC 443) and two fungal strains, namely *Candida albicans* (MTCC 227) and *Aspergilla niger* (MTCC 282).

Determination of MIC: The study involved a series of six assay tubes for each title compound against each microorganism. The entire test was done in duplicate. To the first assay tube, 1.8ml of seeded broth and 0.2ml of title compound (1mg/ml) was added and mixed thoroughly and the two fold serial dilution was done up to the sixth tube containing 1 ml of seeded broth. The additions of the drug solution and serial dilution were done under strict aseptic conditions. Solvent control, negative control (growth control) and drug control were maintained during the experiment. The assay tubes were incubated at 37^0C and 25^0C respectively for 24 hours for bacteria and fungi. The lowest concentration, which apparently caused complete inhibition of growth of microorganisms, was considered as the minimum inhibitory concentration (MIC).The MIC values of the test compounds are recorded in Table 2.

Table 2: Anti microbial activity of 2-(cyclic amine)-1,3-benzothiazole derivatives [3(a-l)] (Expressed as MIC in µg/mL)

Compound	Antibacterial activity				Antifungal activity	
	Gram (+ve)		Gram (-ve)			
	B. subtilis	*S. aureus*	*E. coli*	*K. pneumoniae*	*C. Albicans*	*A. niger*
3a	150	150	150	150	-	-
3b	150	150	150	75	8	9
3c	150	150	150	150	-	-
3d	150	150	75	150	-	-
3e	150	150	150	150	8	-
3f	150	150	150	75	-	-
3g	150	75	150	150	-	-
3h	150	75	150	75	-	-
3i	150	150	75	150	-	-
3j	150	150	75	75	-	-
3k	150	150	150	150	9	8
3l	150	75	150	37.5	7	-
Streptomycin	6.25	6.25	6.25	3.125	-	-
Amphotericin-B(50µg)	-	-	-	-	23.5	25

CONCLUSION:

In the present study, 12 new 2-(Cyclic amine)-1,3-benzothiazole derivatives were synthesized and characterized by spectral analysis. Few of those derivatives were screened for antimicrobial activity. Among the synthesized compounds 3a-l, only 3h, 3j and 3l showed moderate antibacterial activity while other compounds were inactive. Among these three compounds, 3h contains N-(2- hydroxyethyl) group while 3j and 3l contains NH and O respectively at the 4th position of cyclic amine. These results indicate that larger groups at 4th position of cyclic amine have no significant contribution to the antibacterial activity of these compounds. 3b with N-ethyl group and 3c with N-benzyl group at the 4th position of cyclic amine and 3k with piperidine as cyclic amine showed moderate antifungal activity while other compounds were inactive. the results evidence that larger groups at 4th position of cyclic amine have no significant contribution to the antifungal activity of these compounds.

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