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Research Article

# Synthesis, Characterization and Evaluation of Novel 2-Aryl Benzothiazole Derivatives as Potential Antibacterial Agents

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**ABSTRACT**

Bacterial resistance to antibacterial agents is of grave concern in the medical community, as many species of bacteria have evolved as resistant strains. In the present study a series of novel 2-aryl substituted benzothiazoles were synthesized. The synthesized benzothiazole derivatives were characterized physicochemically, by elemental analysis and spectral (IR and $^1$H-NMR) analysis. All the synthesized compounds were screened for their in-vitro antibacterial activity against Gram-positive and Gram-negative bacteria. The results revealed that most of the compounds have better activity against Staphylococcus aureus, Bacillus subtilis, Escherichia coli, and Pseudomonas aeruginosa as compared with the standard Gentamicin and Amoxycillin and less active than the standard Ciprofloxacin. Further research can warrant more consideration on benzothiazoles as prospective antimicrobials.

**Keywords:** Antibacterial, benzothiazoles, aminothiophenol, polyphosphoric acid.

## INTRODUCTION

Antimicrobial resistance has been called one of the world's most pressing public health problems. Addressing the issue of antimicrobial resistance is one of atmost priority in the fields of public health today. World Health Organization defines antimicrobial resistance as "a microorganism's resistance to an antimicrobial drug that was once able to treat an infection by that microorganism". Resistance can appear spontaneously because of random mutations; or more commonly following gradual buildup over time and because of misuse of antibiotics or antimicrobials[1]. Resistant microbes are increasingly difficult to treat, requiring alternative medications or higher doses, both of which may be more expensive or more toxic. Alarmingly, the development of resistance such as multi-drug resistance towards a number of antibiotics poses a challenge to the scientific community in the discovery of new therapies. Thus, there is a need to develop newer and effective molecules with high safety profile.

Among all benzoheterocycles, benzothiazole has considerable place in research especially in synthetic field of pharmaceutical chemistry because of its potent and significant pharmacological activities. Benzothiazoles serve as unique and versatile scaffolds for experimental drug design. Benzothiazoles (BTA) are fused membered rings, which contain heterocycles bearing thiazole. Sulphur and nitrogen atoms constitute the core structure of thiazole and many pharmacologically and biologically active compounds[2]. BTA shows a variety of pharmacological properties, and its analogs offer a high degree of structural diversity that has proven useful for the search of new therapeutic agents. BTA derivatives have been intensively studied, as the pharmacophore it is one of the privileged structures in medicinal chemistry. BTA have emerged as a core structure for diversified therapeutic applications which include, antimicrobial[3,4], anticancer[5], antidiabetic[6,7,8], anticonvulsant[9,10], antioxidant[11], anti-inflammatory[12], and antipsychotic[13] activities. They are also used in industry as vulcanisation accelerators. Various benzothiazoles such as 2-aryl benzothiazoles received much attention due to unique structure and its uses as radioactive amyloid imagining agents.

Benzothiazole ring is present in various marine or terrestrial natural compounds, which have useful biological properties[14]. It is reported that the isosteres and derivatives of benzothiazoles have antimicrobial activities against gram negative, gram positive bacterias (e.g., E.coli, Pseudomonas aeruginosa, Enterobacter, Staphylococcus epidermis, etc) and the yeast (e.g. candida albicans).

As benzothiazoles serve as unique and versatile scaffolds for experimental drug design, in the present study various benzothiazole derivatives were synthesized, characterized by 1HNMR and ATR IR techniques and were evaluated for their Antibacterial activity.

## MATERIALS AND METHODS

Experimental

All chemicals and solvents were supplied by Sigma Aldrich, Merck, and CDH under certificate of purity. The melting range of the synthesized compounds was measured by Scientech-2211 digital auto melting/boiling point apparatus. Proton magnetic resonance ($^1$HNMR) spectra were recorded on Bruker 400 MHz NMR

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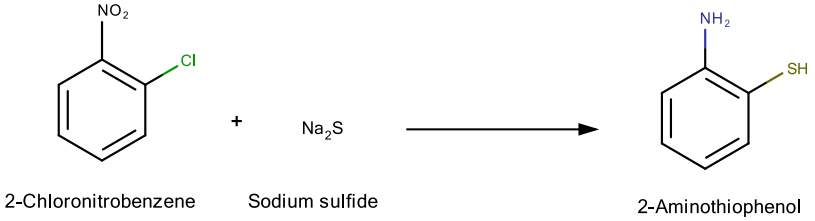
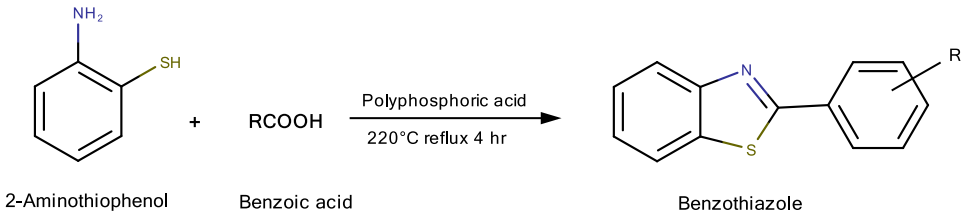
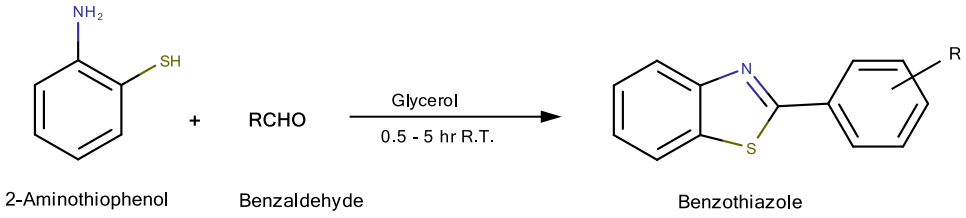


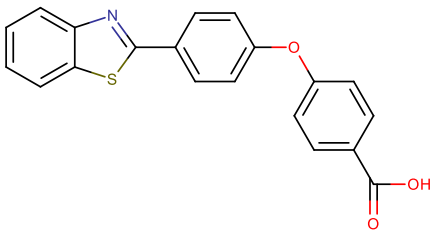
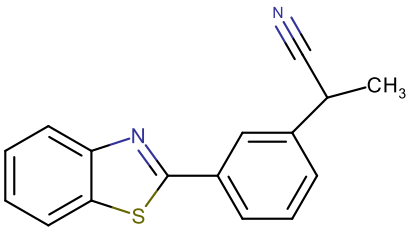
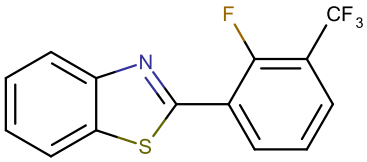



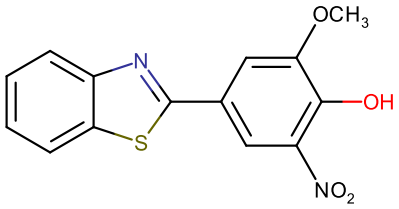
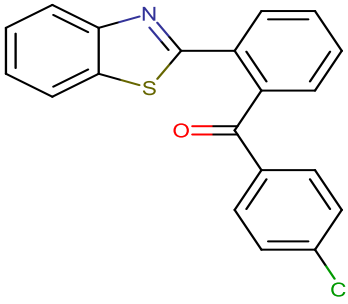
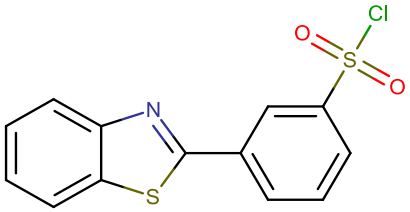
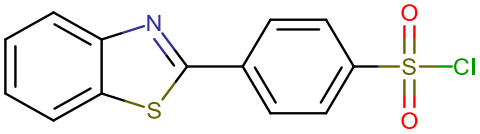
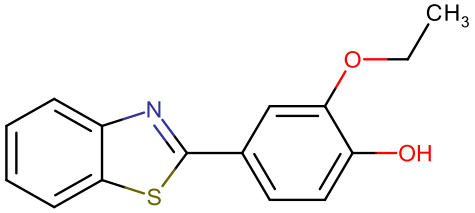
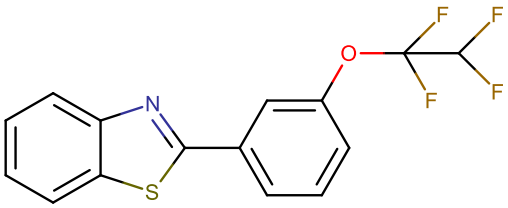
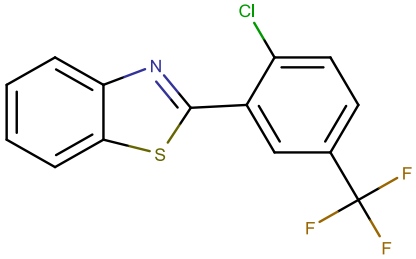

**Scheme I**




**Scheme II**

Table 1: List of synthesized compounds.

| Name | Structure | IUPAC name |
|---|---|---|
| BTA-1 |  | 4-[4-(1,3-benzothiazol-2-yl) phenoxy] benzoic acid |
| BTA-2 |  | 2-[3-(1,3-benzothiazol-2-yl) phenyl] propanenitrile |
| BTA-3 |  | 2-[2-fluoro-3-(trifluoromethyl) phenyl]-1,3-benzothiazole |

| | | |
|---|---|---|
| BTA-4 |  | 4-(benzothiazol-2-yl)-2-methoxy-6-nitrophenol |
| BTA-5 |  | 2-[2-(4-chlorobenzoyl) phenyl]-1,3-benzothiazole |
| BTA-6 |  | 3-(1,3-benzothiazol-2-yl)benzene-1-sulfonyl chloride |
| BTA-7 |  | 4-(1,3-benzothiazol-2-yl)benzene-1-sulfonyl chloride |
| BTA-8 |  | 4-(1,3-benzothiazol-2-yl)-2-ethoxyphenol |
| BTA-9 |  | 2-[3-(1,1,2,2-tetrafluoroethoxy) phenyl]-1,3-benzothiazole |
| BTA-10 |  | 2-[2-chloro-5-(trifluoromethyl) phenyl]-1,3-benzothiazole |

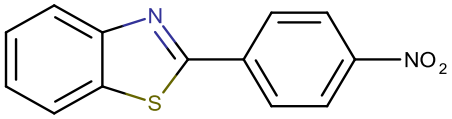
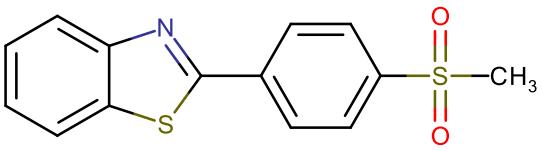
| | | |
|---|---|---|
| BTA-11 |  | ?-(4-nitrophenyl) benzothiazole |
| BTA-12 |  | 2-(4-methanesulfonyl phenyl)-1,3-benzothiazole |

Table 2: Physical data of synthesized compounds.

| Name | Molecular formula | Molecular weight | Melting Point (˚C) | Yield (%) | Solubility |
|---|---|---|---|---|---|
| BTA-1 | $C_{20}H_{13}NO_3S$ | 347.39 | 121-123 | 62 | Chloroform, DMSO, Ethanol, Methanol |
| BTA-2 | $C_{16}H_{12}N_2S$ | 264.34 | 114-120 | 71 | Chloroform, DMSO, Ethanol |
| BTA-3 | $C_{14}H_7F_4NS$ | 298 | 115-120 | 74 | Chloroform, DMSO, Ethanol, Methanol |
| BTA-4 | $C_{14}H_{10}N_2O_4S$ | 303.31 | 118-121 | 56 | Chloroform, DMSO, Ethanol, Methanol |
| BTA-5 | $C_{20}H_{12}ClNOS$ | 349.83 | 115-117 | 82 | Chloroform, DMSO, Ethanol, Methanol |
| BTA-6 | $C_{13}H_{18}ClNO_2S_2$ | 309.79 | 116-121 | 65 | Chloroform, DMSO, Ethanol |
| BTA-7 | $C_{13}H_{18}ClNO_2S_2$ | 309.79 | 117-119 | 83 | Chloroform, DMSO, Ethanol, Methanol |
| BTA-8 | $C_{15}H_{13}NO_2S$ | 271.22 | 125-127 | 70 | Chloroform, DMSO, Ethanol, Methanol |
| BTA-9 | $C_{15}H_8F_4NOS$ | 327.3 | 112-116 | 56 | Chloroform, DMSO, Ethanol, Methanol |
| BTA-10 | $C_{14}H_7ClF_3NS$ | 313.73 | 115-119 | 70 | Chloroform, DMSO, Ethanol, Methanol |
| BTA-11 | $C_{13}H_8N_2O_2S$ | 256.28 | 116-118 | 54 | Chloroform, DMSO, Ethanol, Methanol |
| BTA-12 | $C_{14}H_{11}NO_2S_2$ | 289.37 | 120-125 | 69 | Chloroform, DMSO, Ethanol, Methanol |

spectrometer using $CDCl_3$ as solvent. Chemical shifts were reported in parts per million relative to internal standard tetramethylsilane (TMS). IR spectra were recorded on Bruker- Alpha 1005151/06 ATIR spectrophotometer. Reaction progress was checked by TLC using Merck Silica gel 60 F-254 coated glass plates. The solvent system used was n-Hexane: Ethyl acetate in the ratio of 2:3. The bacterial strains for evaluating the antibacterial activity were obtained from IIIM Chandigarh.

*Synthetic procedure:* [15,16]

*Step I: For synthesis of 2-aminothiophenol*

A clear solution of sodium sulphide nonahydrate (4.8g, 0.02M) in water (20 ml) was prepared. 2-chloronitrobenzene (1.28g, 0.008M) was added to it in one single portion and the mixture was refluxed for 8 hrs. After 4 hrs, small amount of yellow colored oil appeared in the reaction mixture due to the formation of 2-chloroaniline as the by-product. The reaction mixture was cooled after 8 hrs and then extracted with ether to remove 2-chloroaniline. The aqueous layer containing sodium salt of 2-aminothiophenol was saturated with sodium chloride and then acidified with glacial acetic acid. Addition of acetic acid should be done carefully to get the maximum yield of 2-aminothiophenol.

*Step II: For synthesis of benzothiazoles*

Using 2-aminothiophenol and benzoic acid (Scheme I)

Equimolar quantities of 2-aminothiophenol and substituted benzoic acid were added to 15g of polyphosphoric acid and refluxed for 4 hr at 220˚C.The reaction mixture was cooled and poured into a large volume of rapidly stirred ice cold water. The slurry was made alkaline with 50% sodium hydroxide solution. The progress of the reaction was monitored by TLC, using n-Hexane: Ethyl acetate in the ratio of 2:3 as the mobile phase. During the basification, ice was added to prevent an excessive rise in temperature. The crude product was obtained by extracting the reaction mixture with toluene and subsequent evaporation of the solvent in rotary vacuum evaporator followed by recrystallization from ethanol.

Using 2-aminothiophenol and benzaldehyde

Table 3: Spectral study of synthesized compounds.

| Name | IR spectra data | $^1$HNMR spectra data ($CDCl_3$) |
|---|---|---|
| BTA-1 | 1710.98ν (C=O), 1690.08 ν (C=N), 1515.41 ν (C-C), 1411.45ν (C=C), 1058.96 ν (C-O-C), 754.78 ν (Ar C-H), 686.54 ν (C-S) | δ11.0 (s, 1H, COOH), 8.32-8.00 (m, 4H, Ar-H), 7.55 (t, 2H, Ar-H), 7.45 (d, 2H, Ar-H), 7.13 (d, 2H, Ar-H), 6.72 (d, 2H, Ar-H) |
| BTA-2 | 2303.91 ν (C≡N), 1665.11 ν (C=N), 1585.15 ν (C-C), 1431.68 ν (C=C), 759.19 ν (Ar C-H), 645.11 ν (C-S) | δ 8.20-8.05 (d, 2H, Ar-H), 7.52 (t, 2H, Ar-H), 7.33-6.99 (m, 4H, Ar-H), 3.46 (m, 1H, CH), 1.57 (d, 3H, $CH_3$) |
| BTA-3 | 1607.75 ν (C=N), 1515.50 ν (C-C), 1465.28 ν (C=C), 1050.58 ν (C-F), 745.14 ν (Ar C-H), 692.81 ν (C-S) | δ 8.25-8.12 (d, 2H, Ar-H), 7.56 (t, 2H, Ar-H), 7.46 (d, 1H, Ar-H), 7.34 (d, 1H, Ar-H), 7.02 (t, 1H, Ar-H) |
| BTA-4 | 3376.99 ν (OH), 1615.35 ν (C=N), 1549.28 ν (C-C), 1468.13 ν (C=C), 1318.19 ν (C-N), 1041.48 ν (C-O-C), 799.98 ν (Ar C-H), 672.07 ν (C-S) | δ 8.32-8.00 (d, 2H, Ar-H), 7.88 (s, 1H, Ar-H), 7.52 (t, 2H, Ar-H), 7.25 (s, 1H, Ar-H), 5.08 (s, 1H, OH), 3.99 (s, 3H, $CH_3$) |
| BTA-5 | 1801.85 ν (C=O), 1650.31 ν (C=N), 1515.40 ν (C-C), 1435.28 ν (C=C), 756.63 ν (Ar C-H), 722.64 ν (C-Cl), 692.40 ν (C-S) | δ 8.03-8.00 (d, 2H, Ar-H), 7.85 (d, 1H, Ar-H), 7.70 (d, 2H, Ar-H), 7.59-7.32 (m, 7H, Ar-H) |
| BTA-6 | 1610.16 ν (C=N), 1544.62 ν (C-C), 1409.12 ν (C=C), 1199.10 ν ($SO_2Cl$), 796.71 ν (Ar C-H), 679.41 ν (C-S) | δ 8.32-8.05 (m, 3H, Ar-H), 7.72 (d, 1H, Ar-H), 7.69 (d, 1H, Ar-H), 7.55 (m, 3H, Ar-H) |
| BTA-7 | 1605.61ν (C=N), 1506.82 ν (C-C), 1439.52 ν (C=C), 1204.16 ν ($SO_2Cl$), 754.50 ν (Ar C-H), 670.11 ν (C-S) | δ 8.15 (d, 1H, Ar-H), 8.12 (d, 1H, Ar-H), 7.99 (d, 2H, Ar-H), 7.72 (d, 2H, Ar-H), 7.54 (t, 2H, Ar-H) |
| BTA-8 | 3367.45 ν (OH), 1601.01 ν (C=N), 1508.41 ν (C-C), 1437.38 ν (C=C), 1039.98 ν (C-O-C), 750.17 ν (Ar C-H), 655 ν (C-S) | δ 8.59-8.05 (d, 2H, Ar-H), 7.49 (d, 2H, Ar-H), 6.97-6.68 (m, 3H, Ar-H), 4.65 (s, 1H, OH), 3.97 (m, 2H, $CH_2$), 1.53 (t, 3H, $CH_3$) |
| BTA-9 | 1728.86 ν (C=N), 1596.70 ν (C-C), 1439.12 ν (C=C), 1192.42 ν (C-F), 832.32 ν (Ar C-H), 722.53 ν (C-S) | δ 8.25 (d, 1H, Ar-H), 8.12 (d, 1H, Ar-H), 7.56 (t, 2H, Ar-H), 7.21 (t, 1H, Ar-H), 7.04- 6.73 (m, 3H, Ar-H) |
| BTA-10 | 1698.40 ν (C=N), 1515.09 ν (C-C), 1404.36 ν (C=C), 1077.57 ν (C-F), 789.28 ν (C-Cl), 742.04 ν (Ar C-H), 641.72 ν (C-S) | δ 8.32- 8.00 (d, 2H, Ar-H), 7.71 (s, 1H, Ar-H), 7.55 (t, 2H, Ar-H), 7.40 (d, 1H, Ar-H), 6.72 (d, 1H, Ar-H) |
| BTA-11 | 1669.26 ν (C=N), 1586.48 ν ($NO_2$), 1516.91 ν (C-C), 1417.09 ν (C=C), 752.05 ν (Ar C-H), 657.15 ν (C-S) | δ 8.28- 8.04 (m, 4H, Ar-H), 7.73 (d, 2H, Ar-H), 7.51 (t, 2H, Ar-H) |
| BTA-12 | 1647.80 ν (C=N), 1523.76 ν (C-C), 1440.49 ν (C=C), 1022.14 (S=O), 802.37 ν (Ar C-H), 690.53 ν (C-S) | δ 8.31- 8.09 (d, 2H, Ar-H), 7.97 (d, 2H, Ar-H), 7.68(d, 2H, Ar-H) 7.55 (t, 2H, Ar-H), 2.41 (s, 3H, $CH_3$) |

Table 4: Diameter of Zone of Inhibition (mm) of compounds against *Staphylococcus aureus*.

| | Dilutions µg/ml | | |
|---|---|---|---|
| Compound | 60µg/ml | 80µg/ml | 100µg/ml |
| BTA-1 | - | 12 | 14 |
| BTA-2 | - | 8 | 10 |
| BTA-3 | 10 | 14 | 24 |
| BTA-4 | 12 | 18 | 22 |
| BTA-5 | - | 14 | 18 |
| BTA-6 | - | - | 10 |
| BTA-7 | - | 16 | 20 |
| BTA-8 | - | 8 | 16 |
| BTA-9 | 18 | 20 | 22 |
| BTA-10 | 10 | 16 | 22 |
| BTA-11 | 10 | 14 | 20 |
| BTA-12 | - | 10 | 14 |
| Gentamycin | 14 | 18 | 21 |
| Amoxicillin | 16 | 19 | 22 |
| Ciprofloxacin | 20 | 26 | 32 |

Equimolar quantities of 2-aminothiophenol (1.25 g, 10 mmol) and the appropriate aldehyde (10 mmol) in glycerol (10 ml) were heated until a clear solution was obtained and then left at room temperature for 0.5–5 h (TLC control). The reaction mixture was quenched with water and the resulting solid product was collected by filtration, dried and recrystallized from ethanol to afford final compounds.

*Antibacterial Activity*

All the synthesized compounds were evaluated for *in vitro* antibacterial activity against gram positive bacterial strains such as *Staphylococcus aureus*, *Bacillus subtilis* and gram negative bacterial strains such as, *Escherichia coli* and *Pseudomonas aeruginosa* at concentrations of 60µg/ml, 80µg/ml and 100µg/ml by cup plate method using DMSO as solvent control and ciprofloxacin as standard. Nutrient agar was employed as culture media. After 24 h of incubation at 37˚C, the zone of inhibition was measured in mm.

*Procedure*

Table 5: Diameter of Zone of Inhibition (mm) of compounds against *Bacillus subtilis.*

| | Dilutions µg/ml | | |
|---|---|---|---|
| Compound | 60µg/ml | 80µg/ml | 100µg/ml |
| BTA-1 | 10 | 12 | 16 |
| BTA-2 | - | - | 12 |
| BTA-3 | 12 | 18 | 22 |
| BTA-4 | 10 | 14 | 20 |
| BTA-5 | - | 12 | 18 |
| BTA-6 | - | 14 | 16 |
| BTA-7 | 10 | 14 | 16 |
| BTA-8 | - | - | 10 |
| BTA-9 | 12 | 14 | 16 |
| BTA-10 | 16 | 18 | 22 |
| BTA-11 | 8 | 14 | 18 |
| BTA-12 | 10 | 14 | 16 |
| Gentamycin | 14 | 16 | 20 |
| Amoxicillin | 14 | 17 | 21 |
| Ciprofloxacin | 20 | 26 | 30 |

Table 6: Diameter of Zone of Inhibition (mm) of compounds against *E.coli.*

| | Dilutions µg/ml | | |
|---|---|---|---|
| Compound | 60µg/ml | 80µg/ml | 100µg/ml |
| BTA-1 | - | - | 10 |
| BTA-2 | - | 6 | 12 |
| BTA-3 | 16 | 22 | 22 |
| BTA-4 | 14 | 16 | 24 |
| BTA-5 | 10 | 14 | 16 |
| BTA-6 | - | 14 | 16 |
| BTA-7 | 14 | 16 | 22 |
| BTA-8 | - | 14 | 18 |
| BTA-9 | 12 | 16 | 20 |
| BTA-10 | 10 | 16 | 24 |
| BTA-11 | 10 | 14 | 20 |
| BTA-12 | - | 10 | 14 |
| Gentamycin | 14 | 16 | 20 |
| Amoxicillin | 14 | 17 | 21 |
| Ciprofloxacin | 20 | 24 | 28 |

The nutrient agar medium was prepared by dissolving 23 g of nutrient agar in 100 ml distilled water. The nutrient agar so prepared was allowed to boil, after that it was autoclaved at 121℃, 15 Psig for 30 minutes and cooled to 45-50℃. The medium was then inoculated aseptically with 0.5 ml of strains of *S.aureus*, *B.subtilis*, *P.aeruginosa* and *E.coli* at room temperature. The petriplates were sterilized by autoclaving. Into each sterile petridish about 15 ml of inoculated molten agar medium was poured. The plates were left at room temperature for solidification. After solidification, the cups of 6 mm diameter were made by scooping out the medium with the sterlised corn borer and were labelled.

All the synthesised compounds and reference were dissolved in DMSO to get required concentration of 60µg/ml, 80µg/ml and 100µg/ml. The solution of each compound, reference and a control (DMSO) were added separately into each cup. The plates were incubated at 37˚C for 24 hours and the diameter of zone of inhibition was measured with the help of antibiotic zone reader.

## RESULTS AND DISCUSSION

Chemistry

The benzothiazole derivatives were synthesized from cost effective materials like Sodium Sulphide and ortho Chloro Nitro Benzene. All compounds were synthesized in appreciable yield. The structures of the synthesized compounds were established on the basis of ATR IR and $^{1}$HNMR spectrophotometry. The result obtained from spectral analysis was found to be in accordance with the data reported in literature[15]. The major peaks were recorded at 1728-1605 cm-1 for C=N group, at 1365-1305 $cm^{-1}$and 722-640 $cm^{-1}$ for C-S group, Absorption peaks for other functional groups were also observed in the respective derivatives. $^{1}$HNMR: NMR peak for C**H**$_3$ group was found at δ1.53-3.99ppm and for aromatic hydrogens (Ar-**H**) in the range δ6.99-8.32ppm

Antibacterial activity

All the 12 newly synthesized compounds were screened for antibacterial activity at a concentration of 60µg/ml, 80µg/ml and 100µg/ml by cup-plate method against two gram positive bacteria namely *Staphylococcus aureus* and *Bacillus subtilis* and two Gram-negative bacteria namely *Escherichia coli* and *Pseudomonas aeruginosa*. Three standards Gentamycin, Amoxicillin and Ciprofloxacin were used to evaluate the activity of the synthesized compounds. The results are summarized in the Table 4, 5, 6 and 7.

*Staphylococcus aureus*

BTA-3, BTA-4, BTA-7, BTA-9, BTA-10 showed better antibacterial activity than standard Gentamicin and Amoxicillin at 100µg/ml.

BTA-4, BTA-9, BTA-10 showed equal antibacterial activity to the standard Amoxicillin at 100µg/ml.

BTA-3, BTA-4, BTA-5, BTA-7, BTA-9, BTA-10, BTA-11 at 80µg/ml showed better antibacterial activity than standard Gentamicin and Amoxicillin at 60µg/ml.

BTA-3, BTA-4, BTA-5, BTA-7, BTA-9, BTA-10, BTA-11 at 100µg/ml showed better antibacterial activity than standard Gentamicin and Amoxicillin at 80µg/ml.

***Bacillis subtilis***

BTA-3, BTA-4 and BTA-10 at 100µg/ml showed equal antibacterial activity to standard Gentamicin and Amoxicillin at 100µg/ml.

BTA-3, BTA-4, BTA-6, BTA-7, BTA-9, BTA-10, BTA-11, BTA-12 at 80µg/ml showed better antibacterial activity than standard Gentamicin and Amoxicillin at 60µg/ml.

BTA-4, BTA-6, BTA-7, BTA-11 and BTA-12 at 80µg/ml showed equal antibacterial activity to standard Gentamicin and Amoxicillin at 60µg/ml.

BTA-1, BTA-3, BTA-4, BTA-5, BTA-6, BTA-7, BTA-9, BTA-10, BTA-11 and BTA-12 at 100µg/ml showed equal antibacterial activity to standard Gentamicin and Amoxicillin at 80µg/ml.

BTA-1, BTA-6, BTA-7, BTA-9 and BTA-12 at 100µg/ml showed equal antibacterial activity to standard Gentamicin at 80µg/ml.

***E. coli***

Table 7: Diameter of Zone of Inhibition (mm) of compounds against *Pseudomonas aeruginosa.*

| | Dilutions µg/ml | | |
|---|---|---|---|
| Compound | 60µg/ml | 80µg/ml | 100µg/ml |
| BTA-1 | 8 | - | 12 |
| BTA-2 | - | 6 | 10 |
| BTA-3 | 10 | 16 | 22 |
| BTA-4 | 10 | 14 | 20 |
| BTA-5 | - | 10 | 14 |
| BTA-6 | - | 12 | 16 |
| BTA-7 | 12 | 16 | 12 |
| BTA-8 | - | 8 | 22 |
| BTA-9 | - | 14 | 16 |
| BTA-10 | 10 | 16 | 20 |
| BTA-11 | - | 8 | 20 |
| BTA-12 | - | 6 | 8 |
| Gentamycin | 14 | 16 | 20 |
| Amoxicillin | 14 | 17 | 21 |
| Ciprofloxacin | 22 | 26 | 28 |

BTA-3, BTA-4, BTA-7, BTA-9, BTA-10, BTA-11 showed better antibacterial activity against *E.coli* than standard Gentamicin and Amoxicillin at 100µg/ml.

BTA-9 and BTA-11 showed equal antibacterial activity against *E.coli* to standard Amoxicillin and Gentamicin at 100µg/ml.

*Pseudomonas aeruginosa*

BTA-3, BTA-4, BTA-7, BTA-9, BTA-10 at 80µg/ml showed better antibacterial activity than standard Gentamicin and Amoxicillin at 60µg/ml.

BTA-3, BTA-4, BTA-6, BTA-8, BTA-9, BTA-10, BTA-11 at 100µg/ml showed better antibacterial activity to standard Gentamicin and Amoxicillin at 80µg/ml.

BTA-6 and BTA-9 showed better antibacterial activity against *P.aeruginosa* to standard Amoxicillin and Gentamicin at 100µg/ml

In summary, out of 12 compounds synthesized 5 compounds (BTA-3, BTA-4, BTA-7, BTA-9 and BTA-11) exhibited good activity against Staphylococcus aureus, 3 compounds (BTA-3, BTA-4, BTA-10) against Bacillis subtilis, 2 compounds (BTA-9 and BTA-11) against E.coli and 2 compounds (BTA-3 and BTA-8) against Pseudomonas aeruginosa. From the results it was observed that the compounds showed a generalized trend of being more or equal active at higher concentration than the standard amoxicillin and gentamicin at lower concentration. It was also observed that the compounds showed less activity than the standard ciprofloxacin. BTA-3 exhibited good antibacterial activity against three bacterial strains and probably it may be due to the presence of fluoro and trifluoromethyl group at position C-2 and C-3 position on the phenyl ring of 2-Aryl benzothiazole nucleus.

## CONCLUSION

Emergence of resistance often complicate the treatment of various bacterial and fungal infections, thus the need to develop better and newer antimicrobial agents will always be there. In this regard we synthesized 12 newer derivatives of benzothiazoles and subjected them to antibacterial evaluation using conventional cup-plate method against two Gram-positive bacteria *Staphylococcus aureus* ATCC 29737 and *Bacillus subtilis* ATCC 6633 and two Gram-negative bacteria *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 25619. Ciprofloxacin, amoxicillin and gentamycin were used as standard drugs. In general it was observed that most of the synthesized compounds exhibited better/equal antibacterial activities as compared to the reference drugs Gentamicin and Amoxicillin. While no compound showed better activity than the standard drug Ciprofloxacin. Improvement in the antibacterial activity can be further achieved by modifying the substituents in the benzothiazole ring and additional structural activity investigations.

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