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Dihydrobenzofuran clubbed benzimidazole having benzothiazole derivatives as potential anthelmintic and antitubercular agents

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ABSTRACT

In the present communication, a series of novel N-(2-((benzo[d]thiazol-2-ylthio)methyl)-1-benzyl-1H-benzo[d] imidazol-6-yl)aryl benzamides(6a-l) and 4-amino-N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo [d]imidazol-6-yl)-5-substituted-2,3-dihydrobenzofuran-7-carboxamides(7a-b) were efficiently synthesized and evaluated for their in vitro anthelmintic and antitubercular activity against Indian earthworms (Pheretimaposthuma) and M. tuberculosis H37Rv strains. The results of biological study revealed that compounds6b-c, 6g, 6k and 7a-b inhibited excellent anthelmintic activity in the range of 1:45-9:35 and 1:05-8:05 mean paralyzing, while compounds6b-c, 6f-h 6k and 7a-b awarded with inductively electron withdrawing chlorine and electron donating methyl groups afforded maximum MICs ranging from 1.81 to 10.92 µM against Mtb. Compounds 7b and 6k possessed highest inhibition at MIC of 1.81 & 2.1 µM. All the newly synthesized analogues were characterized by IR, ^{1}H NMR, ^{13}CNMR and mass spectroscopic techniques.

Keywords: Anthelmintic activity; Antitubercular activity; Benzimidazole; Benzothiazole; Dihydrobenzofuran

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INTRODUCTION

Tuberculosis (TB) is a lung infection initiated mainly by Mycobacterium tuberculosis (Mtb) and is the greatest single infection cause of high mortality worldwide. According to the latest measurements, around 2 million people globally die annually by tuberculosis, out of which developing countries have significant involvement[1]. Control and anticipation of tuberculosis and helminthes is a major challenge for the development of multidrug resistant tuberculosis[2]. Moreover, Anthelmintic or antihelminthics are drugs that expel parasitic worms (helminthes) and other internal parasites from the body by either stunning or killing them and without causing significant damage to the host. They are used to treat people or animals who are infected by helminthes. Despite the efforts of academic institutions and pharmaceutical companies affianced in the design, synthesis and development of new antitubercular and anthelmintic leads, the current TB and anthelmintic therapeutic armory is poor. To overcome this problem, we have synthesized a series of benzimidazole clubbed benzothiazole and dihydrobenzofuran derivatives and screening them for their antitubercular and anti-anthelmintic property.

The benzimidazole nucleus has been key pharmacophore and privileged structure in medicinal chemistry and is remarkably effective compounds both with respect to their inhibitory activity and their favorable selectivity ratio[3-5]. Benzimidazoles are considered as a promising class of bioactive heterocyclic compounds encompassing a diverse range of biological activities such as antioxidant[6], antiviral[7], antihypertensive[8], analgesic[9], antiallergic[10],

anticoagulant[11], anti-inflammatory[12], antimicrobial[13], antiulcer[14], antihelminthics[15]and antiparasitic[16]. In addition, the azole group of heterocyclic compounds observed significant pharmacokinetic property and lipophilicity that influence the ability of drug to reach the target by transmembrane diffusion and showed promising activity against resistant TB by inhibiting the biosynthesis of lipids[17-18].

Benzothiazole derivatives have exhibited interesting biological activities [19–21]and attracted continuing interest for further molecular exploration as useful anticancer agents [22-23] and also induced HepG2 cell apoptosis in vitro [24]. Moreover, benzofurans have been drawn as promising structural units in the field of medicinal chemistry and drew a lot of attention on various pharmacological activities like anti-microbial [25-27], anti-inflammatory [28], antioxidant [29], antithyroid [30] and antitumor [31-33], cytoprotective agents [34], arrhythmia [35] and Alzheimer diseases [36-37].

Motivated by the above findings, our aim was to obtain more active antitubercular and anthelmintic agents. We also decided to go for antitubercular activity against Mycobacterium tuberculosis H37Rv and anthelmintic activity against Pheretimaposthuma with possible novel mechanisms of action. It was thought worthwhile to synthesize some new dihydrobenzofuran clubbed benzimidazole having benzothiazole derivatives that comprises the above aforementioned moieties in single molecular framework in order to investigate there in vitro anti-anthelmintic and antitubercular activity. In continuation to this, in our present communication, we have synthesized N-(2-((benzo[d]thiazol-2-ylthio)methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)arylbenzamides 6a-l and 4-amino-N-(2-((benzo[d]thiazol-2-ylthio)methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-5-substituted-2,3-dihydrobenzofuran-7-carboxamides 7a-b and characterized by 1H NMR, 13C NMR and Mass spectrometry techniques.

MATERIALS AND METHODS

All reactions except those in aqueous media were carried out by standard techniques for the exclusion of moisture. Melting points were determined on an electro thermal melting point apparatus and were reported uncorrected. TLC on silica gel plates (Merck, 60, F254) was used for purity checking and reaction monitoring. Column chromatography on silica gel (Merck, 70–230 mesh and 230–400 mesh ASTH for flash chromatography) was applied when necessary to isolate and purify the reaction products. Elemental analysis (% C, H, N) was carried out by a Perkin-Elmer 2400 CHN analyzer. IR spectra of all compounds were recorded on a Perkin-Elmer FT-IR spectrophotometer in KBr. 1H NMR spectra were recorded on Varian Gemini 300 MHz and 13C NMR spectra on Varian Mercury-400, 100 MHz in DMSO-d6 as a solvent and tetramethylsilane (TMS) as an internal standard. Mass spectra were scanned on a Shimadzu LC-MS 2010 spectrometer. Anhydrous reactions were carried out in oven-dried glassware in nitrogen atmosphere

Preparation of 4-amino-5-chloro-2, 3-dihydrobenzofuran-7-carboxylic acid (1f)

Methyl 4-acetamido-2-hydroxybenzoate (1a) was chlorinated by sulfuryl chloride in MDC to form methyl 4-acetamido-5-chloro-2-hydroxybenzoate (1b) which further brominated to generate methyl 4-acetamido-3-bromo-5-chloro-2-hydroxybenzoate (1c). It is condensed with 1,2-dibromoethane to obtain methyl 4-acetamido-3-bromo-2-(2-bromoethoxy)-5-chlorobenzoate (1d) which on cyclization by Zinc in dimethyl acetamide to form methyl 4-acetamido-5-chloro-2,3-dihydrobenzofuran-7-carboxylate (1e) followed by hydrolysis using sodium hydroxide to get intermediate 4-amino-5-chloro-2,3-dihydrobenzofuran-7-carboxylic acid (1f). Yield: 82%; IR (KBr, νmax, cm-1): 3522 (O-H), 3430 (NH2), 3062 (C-H, aromatic), 1695 (C=O), 1510 (C=C), 1311 (C-O), 756 (C-Cl); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 2.98 (t, 2H, J = 5.5 Hz, C3-H, Benzofuran ring), 4.60 (s, 2H, -NH2 D2O exch.), 5.97 (t, 2H, J = 6.0 Hz, C2-H, Benzofuran ring), 7.45 (d, 1H, J = 8.2 Hz, C6-H benzofuran ring), 11.12 (s, 1H, -COOH); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 165.24, 160.13, 144.88, 130.05, 111.38, 108.83, 102.49, 71.94, 27.12; LCMS (m/z): 213.0 (M+); Anal. Calcd.for $C_9H_8ClNO_3$: C, 50.60; H, 3.77; N, 6.56; Found: C, 50.76; H, 3.65; N, 6.68%.

Preparation of 4-amino-2,3-dihydrobenzofuran-7-carboxylic acid (1i)

Thionyl chloride (8.35 g, 0.0702 mol) is added to a solution of 1f (10 g, 0.0468 mol) in methanol (70 mL) at 25-30°C. Reaction mixture was refluxed for 5 hrs and then concentrated by evaporate to dryness under reduced pressure. Above crude was dissolved in 200 mL methanol and charge sodium hydroxide (2.8 g, 0.0702 mol) and palladium catalyst (2.0 g) to it. Apply 3.0-3.5 kg/cm2 hydrogen pressure and maintain for 4.0 hrs at 30-35°C and reaction was monitored by TLC. Filter the reaction mass on Hyflow bed and filtrate mL was concentrated under reduced pressure. Above deschloro intermediate (1h) was hydrolyzed by sodium hydroxide (2.8 g, 0.0702 mol) in 40 mL of water in reflux for 10-12 hrs. After completion the reaction, the RM was neutralized to get intermediate (1i).

Yield: 79%; IR (KBr, νmax, cm-1): 3510 (O-H), 3422 (NH2), 3052 (C-H, aromatic), 1688 (C=O), 1518 (C=C), 1312 (C-O); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 2.94 (t, 2H, J = 5.4 Hz, C3-H, Benzofuran ring), 4.37 (t, 2H, J = 6.1 Hz, C2-H, Benzofuran ring), 6.42 (d, 1H, J = 7.8 Hz, C5-H benzofuran ring), 7.14 (s, 2H, -NH2), 7.68 (d, 1H, J = 8.4 Hz, C6-H benzofuran ring), 11.02 (s, 1H, -COOH); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 166.7, 162.9, 150.8, 128.4, 107.4, 105.8, 103.1, 71.8, 28.1; LCMS (m/z): 179.0 (M+); Anal. Calcd.for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82; Found: C, 60.22; H, 5.12; N, 7.91%.

Preparation of 2-(chloromethyl)-6-nitro-1H-benzo[d]imidazole (2)
To a solution of 60 mL 6 N hydrochloric acid, 4-nitro-o-phenylenediamine (10 g, 0.065 mol) and chloro acetic acid (9.45 g, 0.10 mol) were added. The reaction mass was heated at 85-90°C for 16-18 hrs. Reaction was monitored by TLC. RM was cooled to 25-30°C and was diluted with 10 mL water. The reaction mass was then neutralized by ammonia solution and stirred for 60 min for complete crystallization. Solid obtained was filtered and washed with 20 ml of water. The solid material was purified in DMF and water. It was dried at 70-75°C. Yield: 86%; IR (KBr, νmax, cm-1): 3351 (N-H), 3042 (C-H, aromatic), 2844 (C-H, -CH2), 1524 (C=C), 1480 (N=O), 756 (C-Cl); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 4.2 (s, 2H, -CH2), 7.7 (d, 1H, J = 8.1 Hz, Ar-H), 8.12 (d, 1H, J = 7.9 Hz, Ar-H attached to –NO2), 8.72 (s, 1H, Ar-H attached to –NO2), 9.14 (s, 1H, -NH D2O exch.); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 145.8, 144.1, 142.3, 141.7, 118.9, 116.8, 113.4, 38.4; LCMS (m/z): 212.0 (M+); Anal. Calcd.for $C_8H_6ClN_3O_2$: C, 45.41; H, 2.86; N, 19.86; Found: C, 45.30; H, 2.98; N, 19.76%.

Preparation of 2-(((6-nitro-1H-benzo[d]imidazol-2-yl)methyl)thio)benzo[d]thiazole (3)
A mixture of compound (2) (10 g, 0.047 mol), acetone (400 mL), potassium carbonate (13.0 g, 0.094 mol) and mercaptobenzothiazole (15.5 g, 0.092 mol) was stirred for 4 hrs at reflux temperature. Reaction was monitored by TLC to check completion of reaction. The reaction mass was filtered in hot condition. The reaction mixture was then concentrated by evaporate to dryness under reduced pressure and isolated by methanol (60 mL) and water (60 mL). Then the reaction mass was stirred for 2 hrs for complete crystallization. The material was dried at 60-65°C for 12 hrs. Yield: 80%; IR (KBr, νmax, cm-1): 3381 (N-H), 3056 (C-H, aromatic), 2864 (C-H, -CH2), 1521 (C=C), 1481 (N=O); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.2 (s, 2H, -CH2), 7.6 (dd, 2H, J = 7.6, 8.1 Hz, Ar-H benzothiazole ring), 7.8 (d, 1H, J = 7.9 Hz, Ar-H benzimidazole ring), 8.00 (dd, 1H, J = 7.7, 8.2 Hz, Ar-H benzothiazole ring), 8.12 (dd, 1H, Ar-H attached to –NO2), 8.29 (dd, 1H, Ar-H benzothiazole ring), 8.48 (s, 1H, Ar-H attached to –NO2), 9.24 (s, 1H, -NH D2O exch.); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.9, 153.4, 145.6, 144.2, 142.6, 141.7, 135.3, 125.6, 124.7, 121.2, 121.9, 118.3, 116.2, 113.2, 35.9; LCMS (m/z): 342.0(M+); Anal. Calcd.for C15H10N4O2S2: C, 52.62; H, 2.94; N, 16.36; S, 18.73; Found: C, 52.50; H, 2.81; N, 16.48; S, 18.63%.

Preparation of 2-(((1-benzyl-6-nitro-1H-benzo[d]imidazol-2-yl)methyl)thio)benzo[d]thiazol (4)
To a solution of compound (3) (10 g, 0.029 mol) in acetone (300 mL), anhydrous potassium carbonate (5.0 g, 0.036 mol) and benzyl bromide (3.5 g, 0.029 mol) were added. Then reaction mass was refluxed for 4 hrs. Reaction was monitored by TLC and complies then filtered in hot condition and concentrated under vacuum. The material was isolated by methanol 50 ml and filtered to separate out the solid material. It was dried at 60-65°C for 6.0 hrs. Yield: 89%; IR (KBr, νmax, cm-1): 3051 (C-H, aromatic), 2862 (C-H, -CH2-S), 2830 (C-H, -CH2-Ph), 1524 (C=C), 1471 (N=O); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.1 (s, 2H, -CH2-S-), 5.52 (s, 2H, -CH2), 7.21 (dd, 2H, J = 7.4, 7.6 Hz, C2-H & C6-H, Ar-H), 7.31 (t, 1H, J = 7.9 Hz, C4-H, Ar-H), 7.39 (dd, 2H, J = 7.4, 8.1 Hz, C3-H, C5-H, Ar-H), 7.49 (dd, 2H, J = 7.4, 8.0 Hz, C5-H & C6-H benzothiazole ring), 7.4 (d, 1H, J = 7.7 Hz, C7-H benzimidazole ring), 7.84 (dd, 1H, C7-H benzothiazole ring), 8.02 (dd, 1H, C6-H benzimidazole ring), 8.09 (dd, 1H, J = 7.6, 8.1 Hz, C4-H benzothiazole ring), 8.54 (d, 1H, C4-H benzimidazole); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 165.04, 155.95, 146.55, 143.02, 142.92, 139.80, 136.06, 134.89, 128.84, 126.74, 124.67, 121.91, 119.38, 115.23, 111.36, 107.78, 47.11, 28.82; LCMS (m/z): 432.0 (M+); Anal. Calcd.for $C_{22}H_{16}N_4O_2S_2$: C, 61.09; H, 3.73; N, 12.95; S, 14.83; Found: C, 61.22; H, 3.84; N, 12.82; S, 14.71%.

Preparation of 2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-amine (5)
Stannous chloride (25.0 g, 0.13 mol) were added to a solution of compound 4 (10 g, 0.029 mol), isopropyl alcohol (100 mL) and ConcHCl (25 mL). Reaction mass was stirred for 24 hrs at room temperature. Reaction was monitored by TLC and 50% non polar impurity was formed. RM was concentrated using vacuum and then charge 150 ml of RO water and adjust the pH of reaction by liquor ammonia upto 8-9. White color sludge will formed was extracted three times with 150 mL of ethyl acetate, combined organic layer washed with water (250 mL) and the organic layer concentrated by under vaccum. Separate the product and non polar impurity by column chromatography using mobile phase ethyl acetate : n-hexane (1:9). Yield: 48%; IR (KBr, νmax, cm-1): 3389 (N-H, NH2), 3041 (C-H,

aromatic), 2860 (C-H, -CH2-S), 2832 (C-H, -CH2-Ph), 1530 (C=C); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.06 (s, 2H, -CH2-S-), 5.50 (s, 2H, -CH2), 6.21 (s, 2H, -NH2 D2O exch.), 6.52 (dd, 1H, J = 7.8 Hz, C6-H benzimidazole ring), 6.94 (d, 1H, J = 8.1 Hz, C4-H benzimidazole), 7.20 (dd, 2H, J = 7.2, 7.7 Hz, C2-H & C6-H, Ar-H), 7.28 (t, 1H, J = 7.1 Hz, C4-H, Ar-H), 7.36 (dd, 2H, J = 7.4, 7.9 Hz, C3-H, C5-H, Ar-H), 7.42 (d, 1H, J = 7.4 Hz, C7-H benzimidazole ring), 7.59 (dd, 2H, J = 7.4, 8.1 Hz, C5-H & C6-H benzothiazole ring), 7.88 (dd, 1H, J = 7.9 Hz, C7-H benzothiazole ring), 8.12 (dd, 1H, J = 7.4, 8.1 Hz, C4-H benzothiazole ring); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 165.13, 152.66, 149.56, 143.78, 142.44, 135.95, 129.67, 128.89, 127.82, 126.24, 124.50, 121.47, 113.44, 110.42, 104.68, 47.44, 29.21; LCMS (m/z): 402.0 (M+); Anal. Calcd.for $C_{22}H_{18}N_4S_2$: C, 65.64; H, 4.51; N, 13.92; S, 15.93; Found: C, 65.78; H, 4.63; N, 13.81; S, 15.82%.

Preparation of N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl) arylbenzamides (6a-l)
To solution of benzoic acid or substituted benzoic acid derivatives (10 g, 0.081 mol) toluene200 ml, 1-2 drops of Dimethyl foramide and thionyl chloride10 ml were added. Heat to 70-75°C for two hours. Concentrate the reaction mass under vacuum, degas it .Cool to room temperature and add methylene dichloride 150 ml .Triethylamine 10 ml added slowly. Then Compound 5 (20.0 g, 0.046 mol) in methylene dichloride (150 mL) solution was added dropwise at 20-25°C.Stir for 30 min. Reaction was monitored by TLC.Then water 200 ml were added into reaction. Organic layer is separated and washed twice with 100 mL 2% sodium hydroxide solution. Organic phase separated and concentrate by vaccum. Products isolated by methanol (150 mL) and stir for one hour for complete crystallization and filtered to separate out the solid material to get 6a. It was dried at 60-65°C.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)benzamide (6a)
Yield: 68%; IR (KBr, νmax, cm-1): 3289 (N-H), 3032 (C-H, aromatic), 2852 (C-H, -CH2-S), 2822 (C-H, -CH2-Ph), 1688 (C=O), 1524 (C=C); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.08 (s, 2H, -CH2-S-), 5.57 (s, 2H, -CH2), 7.26-8.28 (m, 17H, Ar-H), 9.21 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.9, 164.2, 153.6, 141.5, 137.8, 137.1, 135.2, 134.8, 134.2, 132.9, 132.2, 128.8 (2), 128.2 (2), 127.7 (2), 127.2 (2), 125.7, 125.1, 124.6, 123.8, 121.9, 121.2, 115.4, 109.6, 51.4, 33.2; LCMS (m/z): 506.06 (M+); Anal. Calcd. for $C_{29}H_{22}N_4OS_2$: C, 68.75; H, 4.38; N, 11.06; S, 12.66; Found: C, 68.88; H, 4.49; N, 11.18; S, 12.56%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-3-chloro- benzamide (6b)
Yield: 74%; IR (KBr, νmax, cm-1): 3296 (N-H), 3036 (C-H, aromatic), 2856 (C-H, -CH2-S), 2826 (C-H, -CH2-Ph), 1692 (C=O), 1528 (C=C), 743 (C-Cl); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.06 (s, 2H, -CH2-S-), 5.54 (s, 2H, -CH2), 7.28-8.26 (m, 16H, Ar-H), 9.27 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.7, 164.1, 153.5, 141.7, 137.9, 137.2, 135.7, 135.1, 134.8, 134.1, 132.9, 132.2, 130.3, 128.8, 128.2, 127.8 (2), 127.2, 125.9, 125.5, 125.1, 124.6, 123.7, 121.8, 121.2, 115.4, 109.4, 51.9, 33.5; LCMS (m/z): 540.08 (M+); Anal. Calcd. for $C_{29}H_{21}ClN_4OS_2$: C, 64.37; H, 3.91; N, 10.35; S, 11.85; Found: C, 64.24; H, 3.81; N, 10.48; S, 11.94%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-4-chloro- benzamide (6c)
Yield: 70%; IR (KBr, νmax, cm-1): 3294 (N-H), 3031 (C-H, aromatic), 2861 (C-H, -CH2-S), 2832 (C-H, -CH2-Ph), 1697 (C=O), 1531 (C=C), 746 (C-Cl); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.06 (s, 2H, -CH2-S-), 5.54 (s, 2H, -CH2), 7.28-8.26 (m, 16H, Ar-H), 9.27 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.9, 164.1, 153.7, 141.6, 137.9 (2), 137.1, 135.1, 134.5, 132.9, 132.2, 130.1 (2), 128.9 (2), 128.2 (2), 127.8 (2), 125.8, 125.2, 124.6, 123.8, 121.9, 121.1, 115.6, 109.6, 51.7, 33.3; LCMS (m/z): 540.04 (M+); Anal. Calcd. For C29H21ClN4OS2: C, 64.37; H, 3.91; N, 10.35; S, 11.85; Found: C, 64.22; H, 3.80; N, 10.49; S, 11.95%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-3-methoxy- benzamide (6d)
Yield: 68%; IR (KBr, νmax, cm-1): 3284 (N-H), 3021 (C-H, aromatic), 2848 (C-H, -CH2-S), 2832 (C-H, -CH2-Ph), 2816 (C-H, OCH3), 1688 (C=O), 1528 (C=C); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 3.87 (s, 3H, OCH3), 5.04 (s, 2H, -CH2-S-), 5.51 (s, 2H, -CH2), 7.24-8.24 (m, 16H, Ar-H), 9.23 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.8, 164.2, 160.8, 153.4, 141.4, 137.9, 137.1, 135.7, 135.1, 134.3, 132.7, 132.2, 129.8, 128.8 (2), 127.7 (2), 125.8, 125.1, 124.5, 123.6, 121.7, 121.1, 119.7, 117.8, 115.5, 113.1, 109.4, 55.9, 51.6, 33.2; LCMS (m/z): 536.14 (M+); Anal. Calcd. for $C_{30}H_{24}N_4O_2S_2$: C, 67.14; H, 4.51; N, 10.44; S, 11.95; Found: C, 67.27; H, 4.41; N, 10.57; S, 11.85%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-4-methoxy- benzamide (6e)
Yield: 70%; IR (KBr, νmax, cm-1): 3281 (N-H), 3024 (C-H, aromatic), 2851 (C-H, -CH2-S), 2831 (C-H, -CH2-Ph), 2818 (C-H, OCH3), 1691 (C=O), 1528 (C=C); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 3.81 (s, 3H, OCH3), 5.06

(s, 2H, -CH2-S-), 5.52 (s, 2H, -CH2), 7.21-8.21 (m, 16H, Ar-H), 9.21 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.9, 164.5, 164.0, 153.6, 141.3, 137.8, 137.2, 135.2, 134.5, 132.6, 128.8 (2), 128.2 (2), 127.8 (2), 126.6, 125.9, 125.3, 124.6, 123.4, 121.9, 121.3, 115.7, 114.3 (2), 109.6, 55.7, 51.7, 33.4; LCMS (m/z): 536.13 (M+); Anal. Calcd. for C30H24N4O2S2: C, 67.14; H, 4.51; N, 10.44; S, 11.95; Found: C, 67.29; H, 4.40; N, 10.57; S, 11.84%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-2-methyl- benzamide (6f)
Yield: 64%; IR (KBr, νmax, cm-1): 3284 (N-H), 3024 (C-H, aromatic), 2854 (C-H, -CH2-S), 2828 (C-H, -CH2-Ph), 2821 (C-H, CH3), 1685 (C=O), 1528 (C=C); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 2.51 (s, 3H, CH3), 5.02 (s, 2H, -CH2-S-), 5.50 (s, 2H, -CH2), 7.20-8.20 (m, 16H, Ar-H), 9.21 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.9, 160.4, 153.6, 141.6, 137.8, 137.2, 136.5, 135.1, 134.5, 132.7 (2), 132.1, 131.6, 128.8 (2), 128.3, 127.9 (2), 127.3, 125.8, 125.2, 124.7, 123.8, 121.9, 121.3, 115.6, 109.6, 51.7, 33.2, 18.2; LCMS (m/z): 520.13 (M+); Anal. Calcd. for $C_{30}H_{24}N_4OS_2$: C, 69.20; H, 4.65; N, 10.76; S, 12.32; Found: C, 69.35; H, 4.75; N, 10.65; S, 12.21%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-3-methyl- benzamide (6g)
Yield: 67%; IR (KBr, νmax, cm-1): 3282 (N-H), 3027 (C-H, aromatic), 2849 (C-H, -CH2-S), 2829 (C-H, -CH2-Ph), 2814 (C-H, CH3), 1689 (C=O), 1532 (C=C); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 2.32 (s, 3H, CH3), 4.97 (s, 2H, -CH2-S-), 5.46 (s, 2H, -CH2), 7.24-8.18 (m, 16H, Ar-H), 9.26 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.8, 164.2, 153.6, 141.7, 138.6, 137.9, 137.1, 135.1, 134.5, 134.0, 132.7, 132.1, 131.3, 128.9 (2), 128.2, 127.8 (2), 125.6, 125.1, 124.8, 124.1, 123.8, 121.8, 121.2, 115.3, 109.4, 51.8, 33.4, 20.8; LCMS (m/z): 520.14 (M+); Anal. Calcd. for C30H24N4OS2: C, 69.20; H, 4.65; N, 10.76; S, 12.32; Found: C, 69.36; H, 4.75; N, 10.67; S, 12.22%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-4-methyl- benzamide (6h)
Yield: 69%; IR (KBr, νmax, cm-1): 3284 (N-H), 3026 (C-H, aromatic), 2847 (C-H, -CH2-S), 2827 (C-H, -CH2-Ph), 2817 (C-H, CH3), 1691 (C=O), 1534 (C=C); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 2.35 (s, 3H, CH3), 4.99 (s, 2H, -CH2-S-), 5.49 (s, 2H, -CH2), 7.24-8.19 (m, 16H, Ar-H), 9.27 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.9, 164.1, 153.7, 141.8, 141.2, 137.8, 137.2, 135.2, 134.6, 134.0, 132.5, 131.1, 129.2 (2), 128.9 (2), 127.9 (2), 127.2 (2), 125.8, 125.1, 124.6, 123.6, 121.6, 121.1, 115.3, 109.4, 51.8, 33.3, 21.4; LCMS (m/z): 520.12 (M+); Anal. Calcd. for $C_{30}H_{24}N_4OS_2$: C, 69.20; H, 4.65; N, 10.76; S, 12.32; Found: C, 69.35; H, 4.74; N, 10.66; S, 12.21%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-2-nitro- benzamide (6i)
Yield: 69%; IR (KBr, νmax, cm-1): 3281 (N-H), 3036 (C-H, aromatic), 2856 (C-H, -CH2-S), 2834 (C-H, -CH2-Ph), 1698 (C=O), 1540 (C=C), 1492 (NO2); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.09 (s, 2H, -CH2-S-), 5.59 (s, 2H, -CH2), 7.24-8.39 (m, 16H, Ar-H), 9.31 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.8, 164.1, 153.3, 146.2, 141.5, 137.7, 137.1, 135.0, 134.7, 134.1, 133.2, 132.7, 128.8 (2), 127.7 (2), 126.4, 125.9, 125.2, 124.6, 124.0, 123.8, 122.5, 121.9, 121.0, 115.3, 109.2, 51.6, 33.3; LCMS (m/z): 551.12 (M+); Anal. Calcd. for $C_{29}H_{21}N_5O_3S_2$: C, 63.14; H, 3.84; N, 12.70; O, 8.70; S, 11.63; Found: C, 63.28; H, 3.75; N, 12.83; S, 11.53%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-4-nitro- benzamide (6j)
Yield: 75%; IR (KBr, νmax, cm-1): 3290 (N-H), 3034 (C-H, aromatic), 2854 (C-H, -CH2-S), 2833 (C-H, -CH2-Ph), 1701 (C=O), 1538 (C=C), 1488 (NO2); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.11 (s, 2H, -CH2-S-), 5.57 (s, 2H, -CH2), 7.27-8.41 (m, 16H, Ar-H), 9.30 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.9, 164.3, 153.7, 151.2, 141.6, 137.9, 137.2, 136.7, 135.2, 134.5, 132.8, 129.7 (2), 128.6 (2), 127.5 (2), 125.8, 125.1, 124.7, 124.1 (2), 123.4, 121.8, 121.2, 115.4, 109.1, 51.7, 33.3; LCMS (m/z): 551.13 (M+); Anal. Calcd. for C29H21N5O3S2: C, 63.14; H, 3.84; N, 12.70; O, 8.70; S, 11.63; Found: C, 63.29; H, 3.76; N, 12.84; S, 11.52%.

N-(2-((benzo[d]thiazol-2-ylthio)methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-2,6-dichloro- benzamide (6k)
Yield: 76%; IR (KBr, νmax, cm-1): 3288 (N-H), 3031 (C-H, aromatic), 2851 (C-H, -CH2-S), 2830 (C-H, -CH2-Ph), 1694 (C=O), 1534 (C=C), 756 (C-Cl); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.07 (s, 2H, -CH2-S-), 5.51 (s, 2H, -CH2), 7.25-8.21 (m, 15H, Ar-H), 9.27 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.8, 164.2, 153.7, 141.4, 137.8, 137.1, 135.1, 134.9, 134.1, 132.8, 132.2 (2), 130.3, 128.8 (2), 128.1 (2), 127.6 (2), 125.8, 125.2, 124.6, 123.8, 121.9, 121.1, 115.5, 109.2, 51.8, 33.1; LCMS (m/z): 574.04 (M+); Anal. Calcd. for $C_{29}H_{20}Cl_2N_4OS_2$: C, 60.52; H, 3.50; N, 9.73; S, 11.14; Found: C, 60.66; H, 3.40; N, 9.84; S, 11.04%.

N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-2-chloro-5-nitrobenzamide (6l)
Yield: 74%; IR (KBr, νmax, cm-1): 3292 (N-H), 3037 (C-H, aromatic), 2857 (C-H, -CH2-S), 2834 (C-H, -CH2-Ph), 1704 (C=O), 1535 (C=C), 1494 (NO2), 761 (C-Cl); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 5.11 (s, 2H, -CH2-S-), 5.61 (s, 2H, -CH2), 7.26-8.51 (m, 15H, Ar-H), 9.34 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.9, 164.1, 153.6, 146.2, 141.3, 140.8, 137.9, 137.2, 135.1, 134.2, 133.3, 132.8, 130.8, 128.9 (2), 128.3, 127.7 (2), 125.9, 125.1, 124.6, 123.7, 122.6, 121.8, 121.3, 115.6, 109.4, 51.7, 33.1; LCMS (m/z): 585.05 (M+); Anal. Calcd. for $C_{29}H_{20}ClN_5O_3S_2$: C, 59.43; H, 3.44; N, 11.95; S, 10.94; Found: C, 59.58; H, 3.55; N, 11.84; S, 10.83%.

Preparation of 4-amino-N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d] imidazol-6-yl)-5-substituted-2,3-dihydrobenzofuran-7-carboxamides (7a-b)
Triethylamine (7.0 mL) and Ethyl chloroformate (5.0 mL) were added to a solution of 4-amino-5-substituted-2,3-dihydrobenzofuran-7-carboxylic acid derivatives (0.046 mol) in Methylene dichloride (150 mL) at 20-25°C and stir for 2.0 hrs .Then Compound 5 (0.046 mol) in methylene dichloride (150 mL) solution was added dropwise at room temperature. Stir RM for 7.0-8.0 hrs at 25-30 °C. Reaction was monitored by TLC and reaction mass is concentrated by vacuum. Material was isolated by water (200 mL). Stir for 60 min and filtered to separate out the solid material. Wet cake products take in acetone (80 mL). and filtered off to get desired product 7a-b.

4-amino-N-(2-((benzo[d]thiazol-2-ylthio) methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-2,3-dihydrobenzofuran-7-carboxamide (7a)
Yield: 79%; IR (KBr, νmax, cm-1): 3356 (NH2), 3272 (N-H), 3038 (C-H, aromatic), 2856 (C-H, -CH2-S), 2829 (C-H, -CH2-Ph), 1696 (C=O), 1524 (C=C), 1224 (C-O-C); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 3.02 (t, 2H, C3-H, Benzofuran ring), 4.42 (t, 2H, C2-H, Benzofuran ring), 5.18 (s, 2H, -CH2-S-), 5.67 (s, 2H, -CH2), 7.12-8.18 (m, 14H, Ar-H), 8.56 (s, 2H, NH2 D2O exch.), 9.27 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.7, 164.1, 159.8, 153.5, 149.2, 141.4, 137.8, 137.1, 135.2, 134.6, 132.8, 128.8 (2), 127.7 (2), 126.2, 125.7, 125.1, 124.6, 123.5, 121.9, 121.2, 115.6, 109.6, 108.3, 107.3, 105.9, 70.8, 52.0, 33.4, 27.4; LCMS (m/z): 563.16 (M+); Anal. Calcd. for C31H25N5O2S2: C, 66.05; H, 4.47; N, 12.42; S, 11.38; Found: C, 66.21; H, 4.38; N, 12.56; S, 11.27%.

4-amino-N-(2-((benzo[d]thiazol-2-ylthio)methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-5-chloro-2,3-dihydrobenzofuran-7-carboxamide (7b)
Yield: 81%; IR (KBr, νmax, cm-1): 3361 (NH2), 3270 (N-H), 3036 (C-H, aromatic), 2856 (C-H, -CH2-S), 2828 (C-H, -CH2-Ph), 1691 (C=O), 1524 (C=C), 1227 (C-O-C), 756 (C-Cl); 1H NMR (400 MHz, DMSO-d6, δ, ppm): 3.07 (t, 2H, C3-H, Benzofuran ring), 4.57 (t, 2H, C2-H, Benzofuran ring), 5.08 (s, 2H, -CH2-S-), 5.61 (s, 2H, -CH2), 7.23-8.18 (m, 13H, Ar-H), 8.52 (s, 2H, NH2 D2O exch.), 9.25 (s, 1H, NH-CO); 13C NMR (100 MHz, DMSO-d6, δ, ppm): 164.8, 164.0, 157.8, 153.7, 144.5, 141.5, 137.8, 137.1, 135.0, 134.4, 132.5, 128.7 (2), 127.6 (2), 126.2, 125.8, 125.2, 124.6, 123.6, 121.8, 121.1, 116.9, 115.5, 109.8, 109.2, 108.5, 70.6, 51.8, 33.2, 26.5; LCMS (m/z): 597.13 (M+); Anal. Calcd. for $C_{31}H_{24}ClN_5O_2S_2$: C, 62.25; H, 4.04; N, 11.71; S, 10.72; Found: C, 62.39; H, 4.13; N, 11.60; S, 10.82%.

Anthelmintic activity
All the compounds were initially screened for their in vitro anthelmintic activity against Indian earthworms (Pheretimaposthuma) strain by Mathew et al method exactly as described previously [38, 39]. The results of the anthelmintic studies are presented in Table 1. The drug in clinical use, Albendazole was used as a reference drug. Compounds 6b-c, 6g, 6k and 7a-b inhibited excellent anthelmintic activity in the range of 1:45-9:35 and 1:05-8:05 mean paralyzing at 0.2% and 0.5% concentration with corresponding 6:20-18:10 and 4:10-17:25 mean death time respectively. Among all the screen compounds, compound 6k having 2,6-(Cl)2 substituent at the phenyl ring was found to be the most potent compound with 1:45 and 1:05 mean paralyzing time as compared to standard Albendazole. Second line active compounds 7b and 6b having chloro group showed activity at 2:40 and 3:45. It is interesting to note that chloro substituent in phenyl ring demonstrated high inhibitory activity against Pheretimaposthuma as compared other substituted derivatives, indicating that the electronic properties of the substituent's have major influence on the anthelmintic activity.

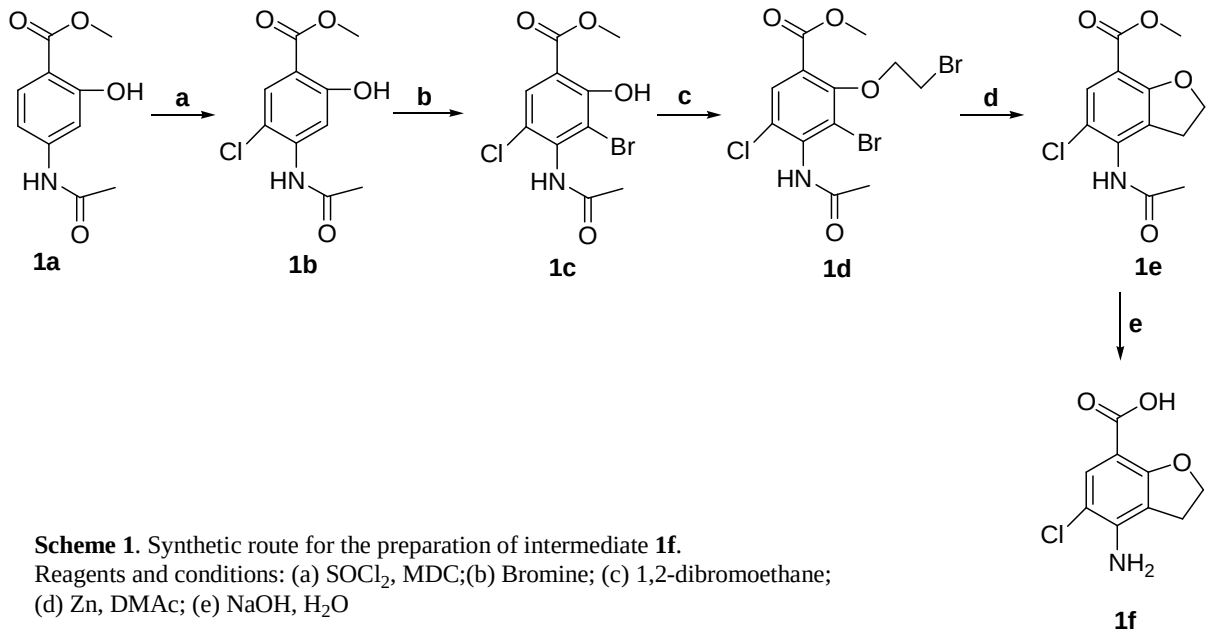
Antimycobacterial activity
The encouraging results from the anthelmintic activity impelled us to go for the screening of title compounds 6a-l and 7a-b for their in vitro antitubercular activity. Intermediates (3, 4 & 5) and all the final compounds along with the standard drug for comparison were firstly evaluated for their activity against the M. tuberculosis H37Rv strain in Middle brook 7H12 medium using MicroplateAlamar Blue Assay (MABA) MIC method [40]. The drug in clinical

use, isoniazid and Rifampicin were used as a reference drugs. The results of actual MICs of tested compounds were reported in Table 2. The results observed that final analogues 6a-l & 7a-b displayed superior anti-tubercular activity compared to all the intermediates (3,4 and 5). Among the fourteen synthesized compounds, compounds 6b-c, 6f-h 6k and 7a-bendowed with inductively electron withdrawing chlorine and electron donating methyl groups afforded maximum MICs ranging from 1.81 to 10.92 µM against Mtb. Compounds 7b (3-Cl in dihydrobenzofuran) and 6k (dichloro) possessed highest inhibition at MIC of 1.81 & 2.1 µM amongst all the tested derivatives as compared to standard INH. For final derivatives, introduction of chlorine substituent in

6b-c&6k was tolerated, 3-chloro in yielding the best activity (3-Cl > 4-Cl). Furthermore, among the second line active compounds, 6f-h brandished MICs in range of 4.56-10.92 µM, in which compound 6g having methyl in meta position showed better result at MIC of 4.56 µM whereas compound 6h displayed inhibition at MICs of 8.42 µM.

RESUTS AND DISCUSSION

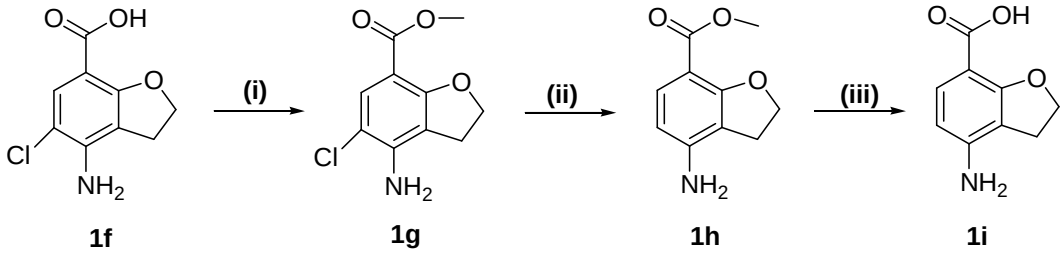
The synthetic route for the preparation of N-(2-((benzo[d]thiazol-2-ylthio)methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)arylbenzamides 6a-land4-amino-N-(2-((benzo[d]thiazol-2-ylthio)- methyl)-1-benzyl-1H-benzo[d]imidazol-6-yl)-5-substituted-2,3-dihydrobenzofuran-7-carboxamides 7a-b is summarized in Scheme 3. The dihydrobenzofuran intermediates 1f and 1i were used as precursors for the synthesis of title compounds 7a-b and their synthesis were achieved according to Scheme 1&2. Intermediate 1a is chlorinated using sulfuryl chloride to get intermediate 1b which is further brominated to get intermediate 1c. Compound 1c is coupled with 1,2-dibromoethane followed by cyclization with Zn in DMAc to form intermediate 1e which is hydrolyzed with sodium hydroxide to generate final intermediate 1f in very good yield(82%). IR spectra of compounds 1f showed the characteristic O-H, N-H and C=O stretching absorption bands at 3522, 3430 and 1695 cm-1, respectively. In addition, C-Cl stretching absorption appeared around at 756 cm-1. While, the 1H NMR spectra of 1f displayed characteristic singlets for amino and carboxylic group proton at around δ4.60 ppm and δ□11.12 ppm respectively, two triplets appeared at around δ□2.98 □ppm and δ5.97 □ppm according to C3 and C2 protons of benzofuran ring. Furthermore, 13C NMR spectra of 1f demonstrated characteristic signals around at δ□165.24, 144.88 and 111.38 ppm corresponding to -C=O, -C-NH2 and -C-Cl carbon, respectively. The mass spectrum of 1f showed molecular ion peak at m/z = 213.02 [M+ 72%], in agreement with its proposed structure.



Scheme 1. Synthetic route for the preparation of intermediate **1f**.
Reagents and conditions: (a) $SOCl_2$, MDC;(b) Bromine; (c) 1,2-dibromoethane;
(d) Zn, DMAc; (e) NaOH, H_2O

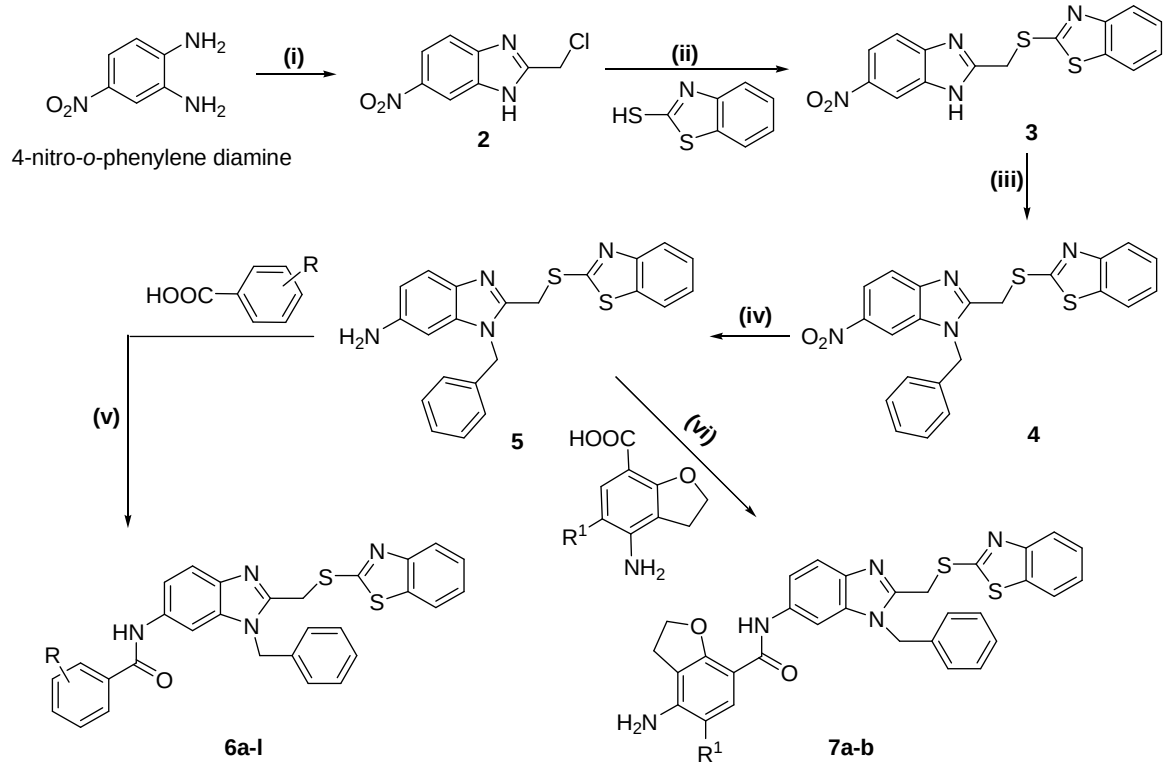
The key intermediate 1i prepared from intermediate 1f in which compound 1f is converted into ester followed by deschlorination using Pd and sodium hydroxide in autoclave at 3.0-3.5 kg/cm2 hydrogen pressure to form intermediate 1h. Compound 1h is hydrolyzed by sodium hydroxide to get desired intermediate 1i. For compounds 1i, IR spectra proved useful in tracing the disappearance of the –C-Cl stretching absorption of the parent compounds 1f.

While, 1H NMR spectra revealed the appearance of singlet peak in the range of δ□6.42 ppm corresponding to C5-H proton of benzofuran ring.13C NMR confirmed the proposed structures 1i with the appearance of a signal at around δ□105.8 ppm due to deschloro carbon. The mass spectrum for the compound 1i was consistent with the proposed structure.



Scheme 2: Synthetic route for the preparation of intermediate **1i.** Reagents and conditions:
(i) $SOCl_2$, MeOH; (ii) Pd catalyst, H_2 gas, NaOH, MeOH; (iii) NaOH, water

The title compounds 6a-l and 7a-b prepared according to Scheme 3. Cyclization of key starting 4-nitro-o-phenylene diamine with monochloro acetic acid followed by condensation with mercaptobenzothiazole compound using acetone and K2CO3 to get intermediate 3. Intermediate 3 converted into 4 by condensation with benzyl bromide which is reduced to form intermediate 5. Acid amine coupling of intermediate 5 with different benzoic acid derivatives and intermediates 1f and 1i to get desired compounds 6a-l and 7a-b respectively.



Scheme 3. Synthetic route for the preparation of title compounds **6a-l** & **7a-b.**
Reagents and conditions: (i) $ClCH_2COOH$, 6 N HCl; (ii) K_2CO_3, CH_3COCH_3; (iii) $PhCH_2Br$, K_2CO_3; (iv) $SnCl_2$, HCl, IPA; (v) $SOCl_2$, TEA, MDC, NaOH; (vi) ECF, TEA, MDC.

Table 1. Results of anthelmintic activity of the tested compounds

Entry	R or R^1	Mean paralyzing time (min)		Mean death time (min)	
		Concentration (In %)		Concentration (In %)	
		0.20%	0.50%	0.20%	0.50%
3	--	>50:00	>50:00	>60:00	>60:00
4	--	48:20	47.10	59:00	57:20
5	--	44:00	43:40	55:25	54:35
6a	-H	38:25	32:58	55:10	41:04
6b	-3-Cl	3:45	3:25	10:05	9:35
6c	-4-Cl	8:40	7:50	16:30	14:20
6d	-3-OCH_3	37:20	36:80	44:25	42:35
6e	-4-OCH_3	44:30	40:20	56:80	54:20
6f	-2-CH_3	34:25	32:25	48:50	46:25
6g	-3-CH_3	9:35	8:05	18:10	17:25
6h	-4-CH_3	28:45	26:95	40:15	38:25
6i	-2-NO_2	46:30	44:35	>60:00	>60:00
6j	-4-NO_2	42:35	40:05	58:55	57:65
6k	-2,6-$(Cl)_2$	1:45	1:05	6:20	4:10
6l	-2-Cl-5-NO_2	15:05	10:15	27:15	18:35
7a	-H	4:25	3:95	8:35	7:55
7b	-5-Cl	2:40	1:38	7:05	4:8
Negative control		--	--	--	--
Standard		0:30	0:20	0.35	0.3

[a]Albendazole

Table 2. Results of antitubercular activity of the tested compounds

Entry	-R or R^1	MIC (µM)[a]
3	--	>128
4	--	>128
5	--	92.20
6a	-H	91.20
6b	-3-Cl	2.81
6c	-4-Cl	6.51
6d	-3-OCH_3	34.2
6e	-4-OCH_3	54.2
6f	-2-CH_3	10.92
6g	-3-CH_3	4.56
6h	-4-CH_3	8.42
6i	-2-NO_2	100.2
6j	-4-NO_2	92.4
6k	-2,6-$(Cl)_2$	2.1
6l	-2-Cl-5-NO_2	28.5
7a	-H	3.92
7b	-5-Cl	1.81
Standard [b]		0.40
Standard [c]		0.81

[a] *Minimum inhibitory concentration against $H_{37}Rv$ strain of M. Tuberculosis (µM)*
[b] *Rifampicin*
[c] *Isoniazid*

CONCLUSION

On the basis of the biological activity results, our main objective of the present study was to synthesized and screening of anthelmintic and antitubercular activities of some new dihydrobenzofuran clubbed benzimidazole having benzothiazole derivatives with the hope of discovering new bioactive motifs that could be useful as potent antitubercular and anthelmintic agents. Our aim has been confirmed by the synthesis of structural hybrids comprising basically 2-chloromethyl benzimidazole moiety attached to 2-mercapto benzothiazole and dihydrobenzofuran. Many of the synthesized motifs (6b-c, 6g, 6k and 7a-b), possessing chloro and methyl groups were identified as most potent anthelmintic and antitubercular agents compared to the standard drugs. Among the screened compounds, compounds 6k and 7b with electron withdrawing group/atoms such as chloro showed the most promising anthelmintic and antitubercular activity. Out of them, compound 6k (1:45 & 1:05 mean paralyzing time) showed highest anthelmintic, while compound 7b (1.81 µM) displayed highest antitubercular activity. The results

described here, merits further investigations in our laboratories using a forward chemical approach for finding lead molecules as antitubercular and anthelmintic agents.

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