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Synthesis, Characterization, Biological evaluation and Computational study for Prediction of Molecular Properties of Some Novel N-{(1,3-benzo[d]thiazol-2-yl)carbamothioyl}-2/4-substituted benzamides

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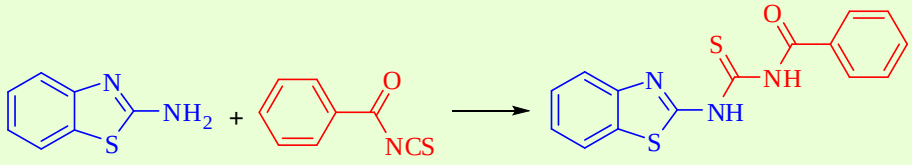
Abstract : As a part of systematic investigations a series of novel N-{(1,3-benzo[d]thiazol-2-yl)carbamothioyl}-2/4-substituted benzamides**3a-g**were synthesized by the reaction of 2-aminobenzothiazole **1**with benzoyl isothiocyanates **2a-g.**The structure elucidation of these compounds was completed by means of chemical tests, elemental (C, H, N and S) and spectral (IR, ^{1}H NMR and mass) analysis. All of them were screened for their antibacterial activity against Gram positive and Gram negative bacteria showing promising results, and have shown moderate to potent antibacterial activity comparable to standard drugs. Physiochemical parameters, toxicity profiles and drug likeness properties were studied using bioinformaticals tools like molinspiration.

Keywords : Benzothiazoles, 2-Aminobenzothiazoles, Benzamides, Benzoylisothiocyanates.



1 **2a-g** **3a-g**

Introduction:

Benzamides are considered as advantaged scaffold which played a noticeable role for increasing the biological activities and so far, they have drawn a huge consideration owing to their expanded applications in the field of pharmaceutical chemistry.They have been reported to play a crucial role in drug development[1]. Benzamides derivatives, e.g. metoclopramide and cisapride are used clinically for the treatment of different medical conditions[2]. Benzamides are important structural unit present in many compounds having potential biological activities, For example, molecules, like proteins which play an essential role in almost all biological processes such as enzymatic catalysis (nearly all known enzymes are proteins), transport/storage (haemoglobin), immune protection (antibodies) and mechanical support (collagen). Benzamides are known for their anti-inflammatory and immunomodulatory[3], anti-tumoral[4], antipsychotic[5], antituberculosis[6], antifungal, antiviral[7], analgesic[8], anticonvulsant[9], antiinflammatory[10], antibacterial[11], antimalarial, anthelmintic[12]and anticancer[13]etc. activities.

Benzothiazole is one of the most important heterocycle that has received overwhelming response owing to its diversified molecular design and remarkable optical, liquid and electronic properties[14]. N-Substituted benzothiazoles are highly reactive and hence extensively utilized as reactant or reaction intermediates. Presece of-NH_2 and endocylic N functions are suitably situated to enable reaction with common electrophillic agents to form a variety of fused heterocyclic compounds[15].Hence synthesis of new compounds containing benzothiazole nucleus involved in research are of considerable interest.

Keeping all these facts in mind, it was thought to study comprehensive account of the synthetic utility of 2-aminobenzothiazoles in building novel benzamides and aimed to evaluate them for biological activities.

Before actual synthesis, our interest is in the study of theoretical molecular properties. Thus molinspiration software program[16]was used to predict different theoretical properties such as toxicity risk, solubility, drug likeness. Recently, many researchers have use these tools successfully and presented the correlations with the experimentally found pharmacological activities[17-20].

The structural elucidation of newly synthesized compounds was done using spectroscopic tools such as IR, ^{1}H NMR, ^{13}C NMR, Mass and elemental analysis technique. The end products were evaluated for their antimicrobial activity using well diffusion method.

Experimental:

General:

All reactions were performed in oven-dried glassware's with magnetic stirring. All the chemicals and solvents are obtained from E-Merck, India (AR grade) and were used without further purification. Melting points of compounds were taken in an open capillary tubes by Toshniwal melting point apparatus in Celsius scale and uncorrected. The purity of the compound was verified by performing thin layer chromatography (TLC) on silica gel G (Merck) coated glass plates and spots were visualized by exposure to iodine vapors using Toluene : ethyl acetate (1:1) as a solvent system. IR spectra were recorded using KBr pellets on FTIR spectrophotometer (Perkin Elmer - Spectrum RX-IFTIR). ^{1}H-NMR spectra were recorded on sophisticated multinuclear FT NMR Spectrometer model Advance-II (Bruker) (CIL, Chandigarh, India); ^{1}H frequency is 400 MHz Chemical shift (δ) are expressed in ppm relative to tetra methyl silane (TMS) as an internal standard. Mass spectra (FAB-MS) were recorded on Waters Micromass Q-T of Microspectrophotometer (SAIF, Chandigarh, India) and elemental analysis were carried out using Elementar Vario EL III CHN analyzer (STIC India, Cochin).

1. General procedure for the synthesis of 2-Aminobenzothiazole 1

The mixture of aniline (0.25 mole), HCl (0.25 mole) and ammonium thiocyanate (0.12 mole) 30g in 60 ml water on refluxing for 3 hours gave phenyl thiourea, which on vigorous stirring with bromine for 10 hours at room temperature produced corresponding hydrobromide which was converted into 2-aminobenzothiazole **1** upon basification. The yields of the respective 2-aminobenzothiazoles were found to be excellent.

2. Synthesis of 2/4-substituted benzoylisothiocyanate 2a-g

Substituted benzoyl chloride (0.1 mole) was added dropwise on to a solution of ammonium thiocyanate (0.1 mole) in dry benzene (25ml) with vigorous stirring. The mixture was boiled for two hours. Cooled and filtered. Substituted benzoyl isothiocyanates **2a-g** were obtained in the form of liquid.

3. Synthesis of N-{[(1,3-benzothiazol-2-yl)amino]carbonothioyl}-2/4-substitutedbenzamide 3a-g

2-aminobenzothiazole (0.01mole) **1** and substituted benzoyl isothiocyanates (0.01mole) **2a-g** were refluxed in a mixture of dry benzene (25ml) and 2-propanol (5ml) for 3 hours. The solid material obtained was filtered, dried and recrystallized from benzene. The spectral data of **3a-g** are given below.

N-(Benzo[d]thiazol-2-ylcarbamothioyl)benzamide5a.

m.p.: 189^{0}C; IR (KBr, ν_{max}, cm^{-1}): 1058.13 (C=S, stretching), 1490.11 (Ar C=C, stretching), 1612.11 (C=N, stretching), 1677.17 (C=O, stretching), 3086.18 (Ar C-H, stretching), 3343.17, 3401.16 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm), 7.52-8.07 (m, 9H, Ar-H), 8.18 (s, 1H, NHC=O, D_2O exchangeble), 12.28 (bs, 1H, NHC=S, D_2O exchangeable), ^{13}C-NMR spectrum displayed signals at δ 187.58 (s, C-1, C=S), 167.16 (s, C-1, -C-NH), 165.18 (s, C-1, C=O), and other singlet's at 113.75, 121.36, 126.94, 128.18, 129.28, 129.71, 131.09 for –CH carbon and 135.09, 136.33, 147.23 for for –C; Mass spectra, (EI) m/z: 313.03 (M^+ peak).

N-(benzo[d]thiazol-2-ylcarbamothioyl)-4-chlorobenzamide 5b.

m.p.: 254^{0}C; IR (KBr, ν_{max}, cm^{-1}): 801.12 (C-Cl, stretching), 1052.13 (C=S, stretching), 1544.15 (Ar C=C, stretching), 1642.71 (C=N, stretching), 1652.31 (C=O, stretching), 3106.24 (Ar C-H, stretching), 3368.34, 3143.54 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.58-8.28 (m, 8H, Ar-H), 8.84 (s, 1H, NHC=O, D_2O exchangeble), 13.05 (bs, 1H, NHC=S, D_2O exchangeable); ^{13}C-NMR spectrum displayed signals at δ 177.52 (s, C-1, C=S), 172.16 (s, C-1, -C-NH), 164.13 (s, C-1, C=O), and other singlet's at 115.6, 122.3, 124.6, 125.5, 128.8, 130.2, 131.3 for –CH and 131.8, 138.7, 154.2for –C; Mass spectra, (EI) m/z: 347 (M^+ peak).

N-(benzo[d]thiazol-2-ylcarbamothioyl)-4-methylbenzamide 5c.

m.p.: 199^{0}C; IR (KBr, ν_{max}, cm^{-1}): 1091.13 (C=S, stretching), 1461 (CH_3, bend), 1591.18 (Ar C=C, stretching), 1598.73 (C=N, stretching), 1677.34 (C=O, stretching), 2923 (C–H, stretching), 3082.19 (Ar C-H, stretching), 3288.31, 3174.49 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.42-8.18 (m, 8H, Ar-H), 9.73 (s, 1H, NHC=O, D_2O exchangeble), 12.82 (bs, 1H, NHC=S, D_2O exchangeable), 2.37 (s, 3H, CH_3); Mass spectra, ^{13}C-NMR spectrum displayed signals at δ 177.52 (s, C-1, C=S), 172.16 (s, C-1, -C-NH), 164.13 (s, C-1, C=O), and other singlet's at 21.6, 117.4, 120.5, 125.4, 126.8, 129.7, 131.3, 132.4 for –CH and 132.6, 139.4, 149.3 for –C; Mass spectra,; (EI) m/z: 327(M^+ peak).

N-(benzo[d]thiazol-2-ylcarbamothioyl)-4-methoxybenzamide 5d.

m.p.: 172^{0}C; IR (KBr, ν_{max}, cm^{-1}): 1123.83 (C=S, stretching), 1583.18 (Ar C=C, stretching), 1568.53 (C=N, stretching), 1681.14 (C=O, stretching), 2768 (O- CH_3, stretching), 2936.74 (C–H Aliph, stretching), 3071.13 (Ar C-H, stretching), 3381.39, 3167.37 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.22-8.12 (m, 8H, Ar-H), 8.20 (s, 1H, NHC=O, D_2O exchangeble), 12.59 (bs, 1H, NHC=S, D_2O exchangeable), 3.82 (s, 1H, OCH_3); ^{13}C-NMR spectrum displayed signals at 178.32 (s, C-1, C=S), 171.18 (s, C-1, -C-NH), 163.14 (s, C-1, C=O), 55.16 (s, C-1, -OCH_3), and other singlet's at 114.6, 119.2, 122.7, 124.2, 124.9, 125.6 for –CH and also singlet at 126.8, 130.8, 155.2, 163.2 for –C;Mass spectra, (EI) m/z: 343 (M^+ peak).

N-(benzo[d]thiazol-2-ylcarbamothioyl)-4-nitrobenzamide 5e.

m.p.: 268^{0}C; IR (KBr, ν_{max}, cm^{-1}): 1113.16 (C=S, stretching), 1326 (C-NO_2,stretching), 1498.03 (Ar C=C, stretching), 1623.91 (C=N, stretching), 1661.80 (C=O, stretching), 3086.47 (Ar C-H, stretching), 3396.41, 3184.76 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.25-8.26 (m, 8H, Ar-H), 9.86 (s, 1H, NHC=O, D_2O exchangeble), 13.02 (bs, 1H, NHC=S, D_2O exchangeable); ^{13}C-NMR spectrum displayed signals at 181.34 (s, C-1, C=S), 176.15 (s, C-1, -C-NH), 163.14 (s, C-1, C=O), singlet for –CH at 116.9, 122.5, 124.1, 124.8, 125.6, 129.6, and also singlet at 130.5, 140.3, 154.2, for –C; Mass spectra (EI) m/z: 358.02 (M^+ peak).

N-(benzo[d]thiazol-2-ylcarbamothioyl)-2-chlorobenzamide 5f.

m.p.: 253^{0}C; IR (KBr, ν_{max}, cm^{-1}): 768.12 (C-Cl, stretching), 1098.26 (C=S, stretching), 1581.46 (Ar C=C, stretching), 1597.23 (C=N, stretching), 1678.31 (C=O, stretching), 3036.74 (Ar C-H stretching), 3407.94, 3118.65 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.47-7.95 (m, 8H, Ar-H), 8.17 (s, 1H, NHC=O, D_2O exchangeble), 12.98 (bs, 1H, NHC=S, D_2O exchangeable); ^{13}C-NMR spectrum displayed signals at 181.34 (s, C-1, C=S), 176.15 (s, C-1, -C-NH), 163.14 (s, C-1, C=O), singlet for –CH at 117.5, 122.8, 124.6, 125.8, 127.9, 128.1, 130.5, 131.6, 133.9 and also singlet at 130.9, 132.5, 134.1, 153.7 for –C; Mass spectra (EI) m/z: 347(M^+ peak).

N-(benzo[d]thiazol-2-ylcarbamothioyl)-2-methylbenzamide 5g.

m.p.: 201^{0}C; IR (KBr, ν_{max}, cm^{-1}): 1068.9 (C=S, stretching), 1470 (CH_3, bend), 1587.13 (Ar C=C, stretching), 1601.62 (C=N, stretching), 1676.42 (C=O, stretching), 2928 (C–H, stretching), 3084.36 (Ar C-H, stretching), 3289.11, 3179.78 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.43-8.21 (m, 8H, Ar-H), 9.76 (s, 1H, NHC=O, D_2O exchangeble), 12.91 (bs, 1H, NHC=S, D_2O exchangeable), 2.46 (s, 3H, CH_3); ^{13}C-NMR spectrum displayed signals at δ ^{13}C-NMR spectrum displayed signals at δ 182.52 (s, C-1, C=S), 175.16 (s, C-1, -C-NH), 166.15 (s, C-1, C=O), 19.1 (s, C-1, -CH_3), singlet for –CH at 116.7, 123.8, 124.5, 125.3, 128.7, 131.5, 132.6, 134.5 and also singlet at 126.2, 130.8, 137.5, 153.6 for –C; Mass spectra, (EI) m/z: 327(M^+ peak).

Biological activity:

The newly synthesized N-{[(1,3-benzo[d]thiazol-2-ylcarbamothioyl)-2/4-substituted benzamides**3a-g** were examined for their anti-bacterial activity by using well diffusion method. The standard cultures of *S. aureus* (Gram positive), *B. subtilis* (Gram positive), *E. coli* (Gram negative) *and P. aeruginosa* (Gram negative) were obtained from Department of Biotechnology, Dr. Ambedkar College, Nagpur. N-substituted benzoxazolyl benzamides and standard drug were dissolved in DMF to prepare stock solutions.

For the growth of bacterial colony Muller Hinton agar was used as the culture medium, that was prepared by using Beef Extract (2.00 gm), Acid Hydrolysate of Casein (17.50 gm), Starch (1.50 gm), Agar (17.00 gm), in 1000 ml of distilled Water. The pH of agar medium was adjusted to 7.3 at 25ºC. Prepared agar medium was mixed well and autoclaved at 15 lbs pressure for at least 20 minutes, to sterilize the media. In the 100ml sterile medium single loop-full of micro-organisms were inoculated and incubated for 24 h at 37°C. This media were poured in petridishes slowly and allowed to solidify. Two well were created in the agar medium with the help of a borer of 6 mm diameter. Test samples/ standards (0.1 ml) was introduced into the well. All the plates were incubated at 37°C for 24 hours. The antibacterial activities of compounds were evaluated by measuring the zone of inhibition in mm. The diameter of the zone of inhibition for samples was measured and recorded **Table 2**.

Table 1. Physical properties and elemental analysis of N-{(1,3-benzo[d]thiazol-2yl)carbamothioyl}-2/4-substituted benzamides 3a-g

Product Code	R	Mol. formula	Mol. weight	Yield (%)	M.P.^{0}C	Elemental composition: found (calculated) %			
						C	H	N	S
3a	H	$C_{15}H_{11}N_3OS_2$	313.40	83	189	56.39 (57.49)	3.49 (3.54)	13.52 (13.41)	20.49 (20.46)
3b	4-Cl	$C_{15}H_{10}ClN_3OS_2$	347.84	80	254	51.82 (51.79)	2.88 (2.90)	11.93 (12.08)	18.56 (18.44)
3c	4-CH_3	$C_{16}H_{13}N_3OS_2$	327.42	78	199	58.81 (58.69)	3.96 (4.00)	12.68 (12.83)	19.48 (19.59)
3d	4-OCH_3	$C_{16}H_{13}N_3O_2S_2$	343.42	79	172	56.12 (55.96)	3.78 (3.82)	12.46 (12.24)	17.98 (18.67)
3e	4-NO_2	$C_{15}H_{10}N_4O_3S_2$	358.39	88	268	51.05 (50.27)	3.07 (2.81)	15.23 (15.63)	16.71 (17.89)
3f	2-Cl	$C_{15}H_{10}ClN_3OS_2$	347.84	92	253	50.98 (51.79)	3.02 (2.90)	12.98 (12.08)	17.96 (18.44)
3g	2-CH_3	$C_{16}H_{13}N_3OS_2$	327.42	77	214	57.89 (58.69)	4.13 (4.00)	13.15 (12.83)	18.46 (19.59)

Table 2: Antibacterial activity of N-(benzo[d]thiazol-2-ylcarbamothioyl)-2/4-substituted Benzamides 3a-g

Compound	(Zone of inhibition in mm at 100 µg/mL)			
	Gram-positive		Gram-negative	
	S. aureus	B. subtilis	E. coli	P. aeruginosa
3a	14	9	16	13
3b	10	11	17	-
3c	12	14	19	15
3d	5	-	13	8
3e	11	13	18	7
3f	-	12	8	9
3g	4	-	6	8
Standard Drug	18	12	17	19

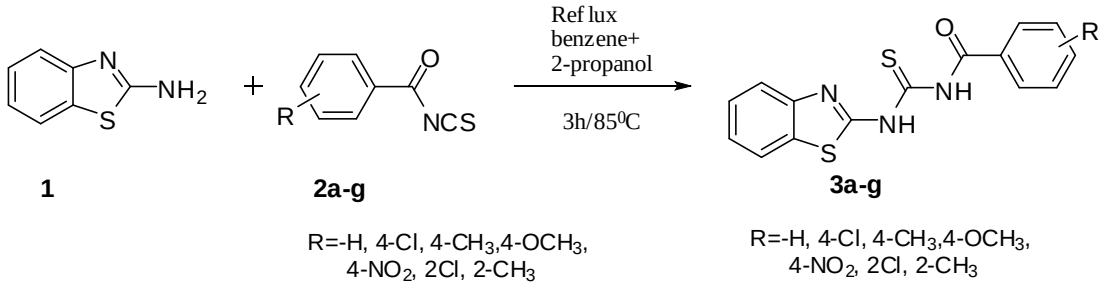
Results and discussion:

Chemistry:

In the present work, we have reported synthesis ofN-{(1,3-benzo[d]thiazol-2-yl)carbamothioyl}-2/4-substituted benzamides**3a-g**from 2-aminobenzothiazole**1**and benzoyl isothiocyanates **2a-g** as presented in **scheme 1.**

2-Aminobenzothiazole**1**was synthesized by treatment of ammonium thiocyanate on aryl amine followed by bromination and then after basification with ammonium hydroxide by a known preparation method[21].The yields of the respective 2-aminobenzothiazoles were found to be excellent. The 2-aminobenzothiazole showed characteristic peaks at 1257-1294 cm^{-1} for (C-S) , 1310-1434 cm^{-1} for (C-N), 1567-1625 cm^{-1} for (C=N), 3341 - 3410 cm^{-1} for (NH) in FTIR spectral data. The ^{1}H NMR spectra shows a broad singlet at 5.21 - 6.28 ppm due to ($–NH_2$)protons (D_2O exchangeable) besides those for aromatic protons in the region 6.93 - 8.24ppm. 2/4-Substituted benzoylisothiocyanates **2a-g**were obtained by reactingsubstituted benzoyl chlorides with ammonium thiocyanates[22]**.** The FTIR bands showed band for (C=O) at 1682-1728 cm^{-1} and (N-C-S) at 2125-2245 cm^{-1}. The ^{1}H-NMR sprectum showed multiplet at δ 7.19-8.39 for aromatic protons.

The target compounds N-{(1,3-benzothiazol-2-yl)amino]carbonothioyl}-2/4-substituted benzamides were synthesized by modified (less time and high yield) procedure[23], the reaction was carried out in benzene-2-propanol (5:1) mixture.Thus, interaction of 2-aminobenzothiazoles **1** with benzoyl isothiocyanates **2a-g** gaveN-{(1,3-benzo[d]thiazol-2-yl)carbamothioyl}-2/4-substituted benzamides**3a-g** in excellent yield (**scheme I**).



Scheme I. Synthesis of N-{(1,3-benzo[d]thiazol-2-yl)carbamothioyl}-2/4-substituted benzamides 3a-g

The structural elucidation of compounds was done through chemical tests, elemental (C, H, N and S) analysis and spectroscopic tools such as, FTIR, ^{1}H NMR and mass spectroscopy. IR (KBr) spectra of the compound **3a-g**had strong absorptions at 3106.24-3036.74(aromatic C-H). It displayed absorptionband near 3407.94-3288.31cm^{-1} corresponds to presence of free N-H and 3401.16-3118.65cm^{-1} for associated N-H.Absorptions at 1681.14-1652.31cm^{-1} and 1123.83-1052.13cm^{-1} that were assigned to C=O and C=S functions, respectively. In the IR spectrum of the**3a-g**peaks of C=O stretching, -NH_2bending and stretching indicated the presence of amide linkage.

The ^{1}H-NMR data of **3a-g** obtained in DMSO solution are given in the experimental section and are consistent with the structural results. The aromatic protons produced well-defined signals at δ 7.22-8.28, ^{1}H-

NMR data confirmed presence of (NHC=O) and (NHC=S) by showing singlet at 8.17-9.86 and broad singlet at 12.28-13.05, respectively, exchangeable with D_2O. The disappearance of the -NH_2signal from the ^{1}H NMR spectrum and the presence of singlet in the region of δ 12.28-13.05indicate that the -NH_2group has been converted to amide linkage. Physical properties and elemental analysis of data for newly synthesized compounds are presented in **Table 1.**

In *vitro* biological activity: All the newly synthesized compounds **3a-g** were tested for their antibacterial activity. It was determined well disk diffusion method at a concentration of 100mg/ml using DMF as a solvent against the different bacterial strains such as *S. aureus, B. subtilis, E. coli and P. aeruginosa.* The zone of inhibition of each strain was recorded shown in **Table 2**. The activity has been compared with known standard drug ampicillin and erythromycin. It can be observed that some of the newly synthesized compounds possess good to moderate antimicrobial activity as compared with standard drug.

Computational Studies:

Molinspiration calculations:

Molinspiration is a web based software use to check the bioavailability of compounds. Physicochemical parameters of compounds play a vital role in generation and determination of bioactivity of any compound**.** It is use to evaluate the different parameters such as MiLogP, TPSA, Molecular weight, Molecular volume, Number of Hydrogen Bond Acceptors, Number of Hydrogen Bond Donors and Computed drug-likeness score.

MiLogP (octanal/water partition coefficient) has been calculated by the methodology develop by molispiration and calculated as sum of fragment-based contributions and corrections factors and used to predict the permeability of molecule across the cell membrane[24]**(Table 3).** Lipophilicity (log p value) is an important parameter which determines solubility, reactivity and degradation of drugs, prior reaching to a pharmacological target. PSA is another helpful parameter for the prediction of molecular transport properties. It may be defined as a sum of surface contributions of polar atoms (usually oxygens, nitrogens and attached hydrogens) in a molecule, Polar surface area (PSA) has been shown to be very good descriptor characterizing drug absorption, including intenstinal absorption, bioavailability, Caco-2 monolayers permeability and blood brain barrier penetration[25-26]. A methodology to calculate molecular polar surface area (TPSA) has been described by Ertl et al. as a sum of fragment contributions[27]. Therefore, log P and PSA values for compounds using molinspiration software programs were calculated and compared them with values obtained for standard drugs ampicillin.

Oral bioavailability is an important property under investigation in the drug discovery process. The molecular properties were calculated on the basis of molecular descriptor i.e. Lipinski's rule of five (rule of thumb)[28]. In the rule-of-five model, compounds are considered likely to be well absorbed and orally active when they possess the following attributes- number of H-bond donars <5 (nitrogen or oxygen atoms with one or more hydrogen atoms), number of H-bond acceptors< 10 (nitrogen or oxygen atoms), molecular weight <500, cLogP <5, and number of rotatable bonds <10.

Lipinski's rule of five identifies the molecular properties are important for a drug's pharmacokinetics in the human body: absorption, intenstinal permeability, distribution, metabolism, and excretion. Obtained results of various parameters (Milog P (partition coefficient), molecular weight, number of heavy atoms, number of hydrogen donor, number of hydrogen acceptor and number of violation, number of rotatable bonds, volume) for the isolated compounds **3a-g** have been reported in **Table 3** and compared with the standard drugs.

For all the compounds **3a-g**, the calculated clogP values were around 3.54-4.25 (<5), which is the upper limit for the drugs to be able to penetrate through biomembranes according to Lipinski's rules[29]. All of these compounds present good oral bioavailability. Compounds with optimal range lipophilicity might have increased chances of success in development. PSA is a common measure for the optimization of a drug's ability to permeate cells. Molecules with PSA values greater than 140 A^0 or more are expected to exhibit poor intenstinal absorption[30]. **Table 3** shows that all the compounds are well below this limit. It has to be kept in mind that log P and PSA values are only two important, but not sufficient criteria for prediction of oral absorption of a drug. Number of rotatable bonds measures molecular flexibility and is considered to be a very good descriptor of absorption and bioavailbility of drugs. All the compounds can easily bind to the receptor as *n* violatios = 0 for the given set of compounds. Two or more violations of the rule of five suggest the probability of problems in bioavailability. It is interesting to see that, all the synthesized compounds follows Lipinski's rule of five. The

positive results recorded confirm that more or less most of these compounds could be used as potential antibacterial agent after some modifications.

Table 3: Molinspiration calculations[a] of synthesized compounds.

Compounds	MW	Milog P	TPSA	OH-NH	Bond rot.	$n\text{-}_{violations}$	Vol	O-N
a	313.41	3.58	54.02	2	4	0	257.65	4
b	347.85	4.25	54.02	2	4	0	271.19	4
c	327.43	4.03	54.02	2	4	0	274.21	4
d	343.43	3.63	63.25	2	5	0	283.19	5
e	358.40	3.54	99.84	2	5	0	280.98	7
f	347.85	4.21	54.02	2	4	0	271.19	4
g	327.43	3.98	54.02	2	4	0	274.21	4
Ampicillin	349.41	-0.87	112.73	4	4	0	298.86	7

[a]MW, molecular weight; TPSA, total polar surface area; OH-NH, OH-NH interactions; $n_{violations}$, number of violations; Vol, Volume; O-N, O-N interactions

Table 4: Drug likeness[a] of newly synthesized compounds

Compounds	GPCRL	ICM	KI	NRL	PI	EI
a	-0.63	-0.63	-0.30	-0.94	-0.64	-0.22
b	-0.58	-0.61	-0.29	-0.90	-0.62	-0.25
c	-0.63	-0.68	-0.32	-0.91	-0.64	-0.28
d	-0.59	-0.66	-0.29	-0.83	-0.59	-0.26
e	-0.67	-0.61	-0.38	-0.89	-0.64	-0.32
f	-0.59	-0.62	-0.31	-0.87	-0.68	-0.29
g	-0.61	-0.70	-0.31	-0.87	-0.63	-0.27
Ampicillin	0.04	-0.47	-0.71	-0.61	0.87	0.25

[a]GPCRL, GPCR ligand; ICM**,** Ion channel modulator; KI, Kinase inhibitor; NRL, Nuclear receptor ligand; PI; Protease inhibitor and EI, Enzyme inhibitor

A material is considered bioactive if it has interaction with or effect on any cell tissue in the human body, pharmacological activity is usually taken to describe beneficial effects, i.e. the effects of drug candidates as well as a substance's toxicity. The bioactivity scores synthesized compounds **3a-g** were assessed on the basis of (GPCR ligands, kinase inhibitors KI, ion channel modulators ICM, enzymes inhibitor EI, Protease inhibitor PI and nuclear receptors NRL) and are valued in **Table 4**. The bioactivity score for GPCR ligand is found to be -0.58 to -0.67, for ion channel modulator activity is -0.61 to-0.70. Similar results are obtained for kinase inhibition **s**howed score -0.29 to -0.38. Bioactivity scores for nuclear receptor ligand, protease inhibitor and enzyme inhibition was found to be in the range. It indicated the probability of good to moderate activity towards GPCR ligands, ion channel modulators, kinase inhibitors, nuclear receptor ligands, protease inhibitors and other enzyme targets.These scores for organic molecules can be interpreted as active (bioactivity score > 0), moderately active (bioactivity score: -5.0-0.0) and inactive (bioactivity score <-5.0)[31].All compounds have consistent negative values in all categories and numerical are even more negative than of standard drugs used for comparison. Therefore, it is readily seen that all the compounds are expected to have similar activity to standard drugs used based upon these six criteria. The compounds showed similar bioactivity scores on comparison with standards taken for the study. It indicates the molecules were active towards drug target.

Conclusion

We have efficiently synthesized series of novel N-{(1,3-benzo[d]thiazol-2-ylcarbamothioyl)-2/4-substituted benzamides**3a-g** from 2-aminobenzothiazole in good to excellent yields. All the compounds were characterized using spectroscopic and analytical tools. Some of final products were screened for their antibacterial activity and it was observed that some of the compounds are having moderate to potent anti bacterial activity which is compared with standard drug.

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