IJPSR (2018), Volume 9, Issue 3 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 31 May, 2017; received in revised form, 15 August, 2017; accepted, 17 August, 2017; published 01 March, 2018

SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME METHYL 4-(1*H*-BENZO[*d*] IMIDAZOL-2-YL) PHENYL CARBAMODITHIOATE AMINE DERIVATIVES

L. P. Singh[*1], O. P. Tiwari [2] and Brijyog[1]

Institute of Pharmacy [1], Harish Chandra P.G. College Varanasi - 221002, Uttar Pradesh, India.
Varanasi College of Pharmacy [2], Varanasi - 221105, Uttar Pradesh, India.

Keywords:

Synthesis, Heterocyclic, Benzimidazole, Thiourea, Antimicrobial Activity

Correspondence to Author:
Laliteshwar Pratap Singh

Assistant Professor,
Institute of Pharmacy,
Harish Chandra P.G. College,
Varanasi - 221002, Uttar Pradesh, India.

E. mail: lalitpharma@gmail.com

ABSTRACT: Benzimidazole is a heterocyclic aromatic organic compound which has been an important pharmacophore and privileged structure in medicinal chemistry. Substituted benzimidazoles have considerable interest as compounds with a wide spectrum of biological activity and low toxicity. In the present study, a new series of benzimidazole thiourea derivatives are synthesize and screened for antibacterial and antifungal activity. The Methyl 4-(1*H*-benzo[*d*]imidazol-2-yl) phenyl carbamodithioate amine derived from Methyl 4-(1*H*-benzo[*d*]imidazol-2-yl) phenyl carbamodithioate (TD1-TD6) have been synthesized by reacting the thio methyl group with different amines in presence of ethanol. The synthesized compounds were characterized by FT-IR, 1H NMR, Mass spectra and elemental analysis. The synthesized compounds were screened for their *in vitro* growth inhibiting activity against four bacterial strains *Bacillus subtilis, Staphylococcus aureus* (Gram positive bacteria*); Escherichia coli, Pseudomonas aureginosa* (Gram negative bacteria) and two fungal strains namely *Candida albicans and Asperginous niger*. The synthesize compounds were compared with standard agents norfloxacin for antibacterial and fluconazole for antifungal activity using well plate method. Compounds exhibit good activity in bacteria *Bacillus subtilis* and fungous *Candida albicans*. Synthetic compounds show moderate to high antibacterial and antifungal activity. Some compounds show appreciable antimicrobial activity.

INTRODUCTION: The chemistry of thioureas and their derivatives has attracted a lot of attention due to their interesting physicochemical properties. The synthetic ease of thioureas, and use of inexpensive chemicals and reagents in synthesis and their wide range of pharmaceutical application has made them potential moiety for designing of new compounds.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.9(3).1194-00

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.9(3).1194-00

The modification that may be done on either nitrogen atoms of thiourea enhances the physical and chemical properties and their biological activities. Benzimidazole derivatives widely used in medicinal chemistry and drug development. Derivatives of benzimidazole have numerous biological activities, such as antibacterial [1 - 4], antifungal [5], analgesic [6], anti-inflammatory [7] antitumor [8 - 13] antiviral [14 - 17], anticonvulsant [18] antidiabetic [19] and antidepressant [20] properties.

Nitrogen-containing heterocyclic systems have a diverse spectrum of pharmacological properties. Different heterocyclic motifs can be incorporated to produce molecules with enhanced biological properties. A review of the literature suggests that

there is the scope for the design of additional benzimidazole derivatives with antimicrobial activity, by examining the effect of a number of different functional groups. Thiocarbamide, thiourea derivatives have biological activity such as antibacterial [21, 22] antimicrobial [23] antioxidant [24] anti HIV [25, 26] anti malarial [27] and anticancer [28]. The review of benzimidazole and thiourea motivate to synthesize such derivatives.

MATERIALS AND METHODS: The identification and purity of the products was checked by TLC with different combination and strength of mobile phases, *i.e.* hexane: ethyl acetate (2:6) or methanol: chloroform (1:8) using iodine vapour and UV light as detecting agents. Melting points were taken in open capillaries in an electric melting point apparatus and are uncorrected. The ^{1}H NMR spectra were recorded on a Bruker Avance II 400 NMR spectrometer with DMSO and $CDCl_3$ as solvents and TMS as internal standard. The chemical shifts were expressed in δ (ppm) values. The IR spectra were recorded on a Bruker alpha FT-IR spectrophotometer. The Mass spectra were recorded in terms of mass to charge ratio (m/z) on Waters LCMS-MS. All the chemicals used were of synthetic grade and were procured from S.D. Fine Chem. Ltd. and Merck, Mumbai, India.

Synthesis of Benzimidazole Thiourea Derivatives:

Synthesis of 4 - (1*H*-benzo[*d*] imidazol – 2 - yl) benzenamine: Equimolar quantities of of benzene -1, 2 - diamine (0.002mol, 218 mg) and *p*-amino benzoic acid (0.002 mol, 274 mg) were mixed with polyphosphoric acid (10 ml) in a FBF and a stirrable paste was prepared and refluxed on dimmer-stat. The reaction mixture was heated slowly to 180 °C. Heating was continued for 4 hours at 180 °C. At the end of the reaction, the resulting solution was cooled to 100 °C and then poured on crushed ice with constant stirring. The product was extracted using ethyl acetate and then washed with dilute solution of 10% sodium bicarbonate, then with brine and citric acid solution. Ethyl acetate portion was concentrated and the residue was decolourized and purified to get the 4-(1*H*-benzo[*d*]imidazol-2-yl)benzenamine.

Synthesis of (4-(1*H*-benzo[*d*]imidazol-2yl) phenyl) carbamodithioic acid: To a solution of 0.15 moles of KOH in ethanol and 0.15 moles of 4-(1*H*-benzo[*d*]imidazol-2-yl)benzenamine was added 0.15 moles of CS_2. The mixture was diluted with ethanol and stirred at room temperature for 12-16 h. the mixture was then neutralized with conc. HCl and the resulting precipitate was filtered off, washed with water and recrystallized form ethanol.

Synthesis of Methyl 4-(1*H*-benzo[*d*]imidazol-2-yl) phenyl carbamodithioate: In a 100 mL round bottom flask, 0.0275 moles of (4-(1*H*-benzo[*d*] imidazol-2yl) phenyl)carbamodithioic acid, 0.038 moles of sodium carbonate and 0.042 moles of dimethyl sulfate were placed. The mixture was heated substantially until the temperature reached 75°C and the mixture started to liquefy. Heating was continued for 30 min at this temperature and then the temperature was slowly increased to 85-87°C. At this temperature the mixture started to thicken; 30 mL of water was added and continued heating for another 1.5 h. On completion of the reaction as monitored by TLC, 250 mL of hot water was added to the mixture with stirring. The mixture was allowed to cool and the solid obtained was filtered at pump and washed with water to obtain the product.

Synthesis of amine derivative of Methyl 4-(1*H*-benzo[*d*]imidazol-2-yl)phenyl carbamodithioate (TD 1- TD 6): To 0.1 Methyl 4-(1*H*-benzo[*d*] imidazol-2-yl)phenyl carbamodithioate was added 0.15 mole of appropriate amine (N-methyl benzamine, p-toiuidine, phenyl methanamine, 4-nitrobenzamine, naphthalene-1-amine, pyridine-2-amine) in ethanol and the mixture was refluxed for 2-3 h with continuous stirring. The product obtained was filtered, washed with ethanol, dried and characterized.

3-(4-(1H-benzo[d]imidazol-2-yl)-1-methyl -1-phenyl thiourea, TD1: Yield: 72%; Melting Point: 249-251°C; IR (KBr, cm-1): 1393.03 (C-N str), 3554.0 (N-H str), 1653 (Aromatic C=N str), 1614.34 (C-C Aromatic) 3107.64 (C-H str), 1288.54 (C=S str); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.45 (s, 3H), 4.03 (s, 1H, NH), 4.92 (s, 1H, NH), 6.60 – 6.79 (m, 5H), 7.20 – 7.22 (m, 4H), 7.59 (d, *J* = 9 Hz, 2H), 7.93 (d, *J* = 9 Hz, 2H); MS (FAB) m/z : 358.13 (M+), 359.13 (100%); Anal. Calcd (found) C 70.36 (70.41); H 5.06 (5.03); N 15.63 (15.35).

1-(4-(1*H*-benzo[*d*]imidazol-2-yl) phenyl) - 3 -*p*-tolylthiourea, TD2: Yield: 78%; Melting Point: 255-258°C; IR (KBr, cm^{-1}): 1428.04 (C-N_{str}), 3397 (N-H $_{str}$), 1676 (Aromatic C=N $_{str}$), 1610 (C-C Aromatic) 3042 (C-H $_{str}$), 1267.37 (C=S $_{str}$); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.40 (s, 3H), 4.02 (bs, 2H, 2NH), 4.94 (bs, 1H, NH), 6.37 (d, *J* = 9 Hz, 2H), 6.69 (d, *J* = 9 Hz, 2H), 6.99 (d, *J* = 8.2 Hz, 2H), 7.21 (t, *J* = 6.5 Hz, 2H), 7.57 (d, *J* = 7.4 Hz, 2H), 7.91 (d, *J* = 5.2 Hz, 2H); MS (FAB) m/z **:** 358.13(100%) 359.13(22.9%); Anal. Calcd (found) C, 70.36 (70.39); H, 5.06 (5.02); N, 15.63 (15.52).

1-(4-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)-3-benzyl thiourea, TD3: Yield: 68%; Melting Point: 261-263°C; IR (KBr, cm^{-1}): 1396.28 (C-N_{str}), 3112 (N-H $_{str}$), 1652 (Aromatic C=N $_{str}$), 1613.27 (C-C Aromatic) 3045.31 (C-H $_{str}$), 1287.91 (C=S $_{str}$); ^{1}H NMR (400 MHz, DMSO-d_6): δ 2.01 (bs, 1H, NH), 4.01 (bs, 1H, 1NH), 4.73 (s, 2H), 4.92 (bs, 1H, NH), 6.67 (d, *J* = 8.8 Hz, 2H), 7.22 – 7.32 (m, 7H), 7.58 (d, *J* = 9.2 Hz, 2H), 7.92 (d, *J* = 8.8 Hz, 2H). MS (FAB) m/z **:** 358.13(100%) 359.13(22.92%); Anal. Calcd (found) C, 70.36 (70.45); H, 5.06 (5.05); N, 15.63 (15.26).

1-(4-(1*H*-benzo[*d*]imidazol-2-yl) phenyl) - 3 - (4-nitrophenyl)thiourea, TD4: Yield: 81 %; Melting Point: 254-257°C; IR (KBr, cm^{-1}): 1392.25 (C-N_{str}), 3232.34 (N-H $_{str}$), 1651.34 (Aromatic C=N $_{str}$), 1613.94 (C-C Aromatic) 3112.47 (C-H $_{str}$), 1284.08 (C=S $_{str}$), 1585.45 (N=O), 855.86 (C-NO_2); ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.02 (bs, 2H, 2NH), 4.92 (bs, 1H, 1NH), 6.62 – 6.72 (m, 4H), 7.24 (t, *J* = 9.6 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.91 (d, *J* = 6.0 Hz, 2H), 8.01 (d, *J* = 7.3 Hz, 2H). MS (FAB) m/z: 389.09(100%) 390.10(21.9%); Anal. Calcd (found) C, 61.68 (62.01); H, 3.88 (3.93); N, 17.98 (17.85).

1-(4-(1*H*-benzo[*d*] imidazol - 2-yl) phenyl) – 3 - (naphthalen-1yl) thiourea, TD5: Yield: 74 %; Melting Point: 268-271°C; IR (KBr, cm^{-1}): 1377.97 (C-N_{str}), 3667.83 (N-H_{str}), 1687.76 (Aromatic C=N_{str}), 1613.80 (C-C Aromatic) 3099.37 (C-H_{str}), 1299.77 (C=S_{str}); ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.02 (bs, 2H, 2NH), 4.91 (bs, 1H, 1NH), 6.68 (d, *J* = 9.2 Hz, 2H), 6.97 (d, *J* = 6.8 Hz, 1H), 7.21 – 7.39 (m, 3H), 7.55 – 7.60 (m, 5H), 7.91 – 8.09 (m, 4H). MS (FAB) m/z: 394.13(100%) 395.13(26.2%); Anal. Calcd (found) C, 73.07 (72.98); H, 4.60 (4.59); N, 14.20 (14.05).

1-(4-(1*H*-benzo[*d*] imidazol - 2 - yl) phenyl) - 3-(pyridin-2-yl)thiourea, TD6: Yield: 69 %; Melting Point: 256-259°C; IR (KBr, cm^{-1}): 1349.64 (C-N_{str}), 3230.63 (N-H $_{str}$), 1648.30 (Aromatic C=N $_{str}$), 1519.35 (C-C Aromatic) 3108.54 (C-H $_{str}$), 1264.15 (C=S $_{str}$); ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.02 (bs, 2H, 2NH), 4.92 (bs, 1H, 1NH), 6.61 - 6.69 (m, 3H), 7.20 - 7.34 (m, 3H), 7.52 - 7.58 (m, 3H), 7.90 - 8.06 (m, 3H). MS (FAB) m/z : 345.10 (100%), 346.10(20.7%); Anal. Calcd (found) C, 66.07 (66.0); H, 4.38 (4.35); N, 20.27 (19.96).

Synthetic Scheme:

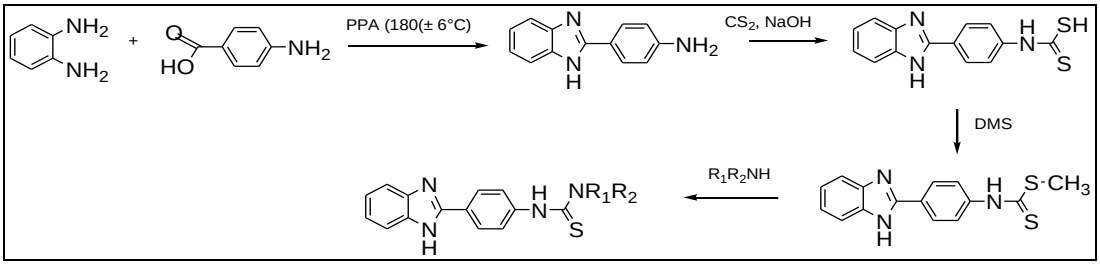
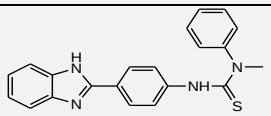
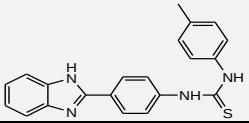
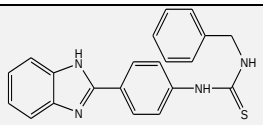
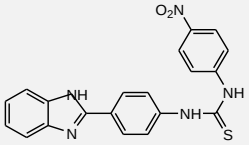
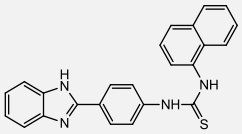
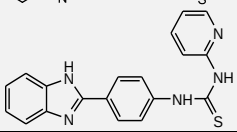


TABLE 1: SUMMARY OF THE SYNTHESIZED COMPOUNDS

Compound	Structure	Molecular Formulae	Molecular Mass	% Yield
3-(4-(1*H*-benzo[*d*]imidazol-2-yl)-1-methyl-1-phenylthiourea, TD1		$C_{21}H_{18}N_4S$	358.10	72
1-(4-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)-3-*p*-tolylthiourea, TD2		$C_{21}H_{18}N_4S$	358.10	78

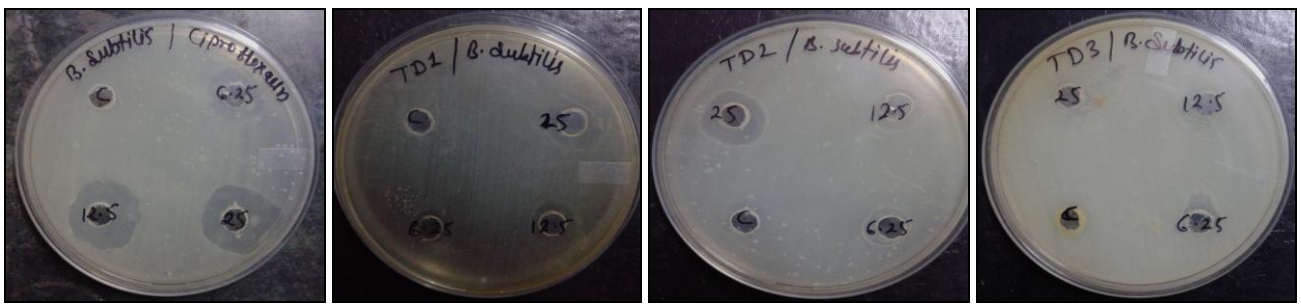
1-(4-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)-3-benzylthiourea, TD3:		$C_{21}H_{18}N_4S$	358.10	68
1-(4-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)-3-(4-nitrophenyl)thiourea, TD4		$C_{20}H_{15}N_5O_2S$	389.10	81
1-(4-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)-3-(naphthalen-1-yl)thiourea, TD5		$C_{24}H_{18}N_4S$	394.13	74
1-(4-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)-3-(pyridin-2-yl) thiourea, TD6		$C_{19}H_{15}N_5S$	345.00	69

Screening for Antimicrobial Activity: The well diffusion method was used to determine the antimicrobial activity of the synthesized compound using standard procedure [29]. The microbial cultures used in the study were obtained in lyophilized form. With the help aseptic techniques the lyophilized cultures are inoculated in sterile nutrient and potato dextrose broth than incubated for 24 hours at 37 ^{o}C. After incubation the growth is observed in the form of turbidity. These broth cultures were further inoculated on to the agar plates with loop full of microbes and further incubated for next 24 hours at 37 ^{o}C to obtain the pure culture and stored as stocks that are to be used in further research work. There were 3 concentration used which are 25 and 12.5, 6.25 µg/ml for each synthesized compound in antimicrobial studies.

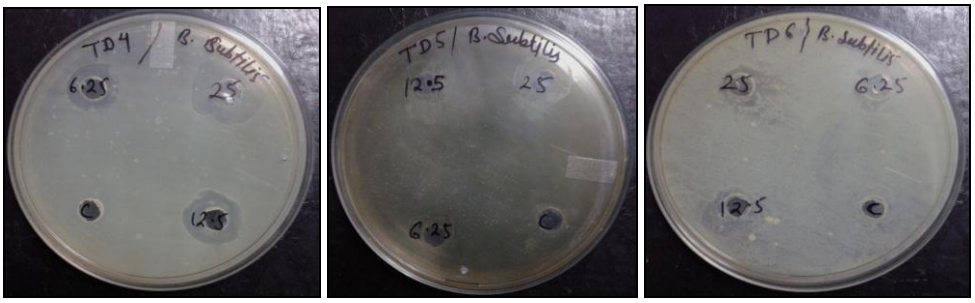
The placing of wells with the antibiotics on the surfaces of agar immediately after inoculation with the organism tested. Undiluted over night broth cultures should never be used as an inoculums. The plates were incubated at 37 ^{o}C for 24 hr. and then examined for clear zones of inhibition around the wells impregnated with particular concentration of drug. The zone of inhibition for bacterial and fungal are represented in **Fig. 1** and **Fig. 2** respectively. The antimicrobial screening results are presented in **Table 2** and **3**.

TABLE 2: ANTIBACTERIAL ACTIVITY OF SYNTHETIC COMPOUNDS ON *BACILLUS SUBTILIS*

S.no.	Compounds	Zone of inhibition in mm Mean for *Bacillus subtilis* at different concentration (µg/ml)		
		25 µg/ml	12.5 µg/ml	6.25 µg/ml
1	TD1	16±0.05	12±0.08	10±0.09
2	TD2	17±0.06	15±0.08	13±0.09
3	TD3	22±0.07	21±0.06	15±0.08
4	TD4	21±0.08	17±0.12	15±0.06
5	TD5	16±0.08	11±0.12	09±0.06
6	TD6	16±0.05	14±0.08	12±0.06
7	Standard	25±0.04	21±0.09	13±0.11



CIPROFLOXACIN **TD1** **TD2** **TD3**



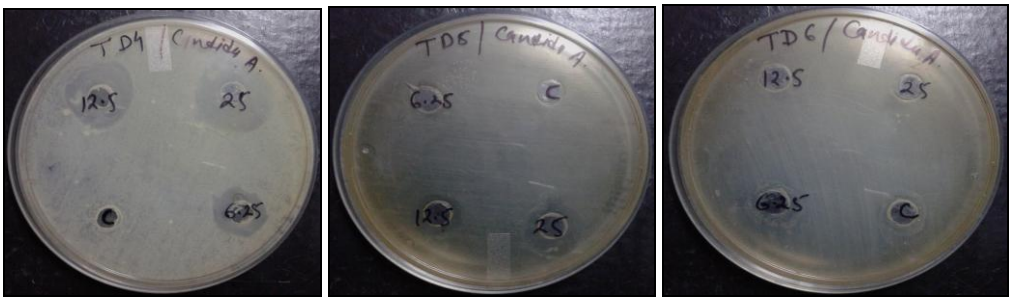
TD4 **TD5** **TD6**

FIG. 1: PHOTO PLATES OF ANTIBACTERIAL STUDY OF SYNTHETIC COMPOUNDS ON *BACILLUS SUBTILIS*

TABLE 3: ANTIFUNGAL ACTIVITY OF SYNTHETIC COMPOUNDS ON *CANDIDA ALBICANS*

S.no.	Compounds	Zone of inhibition in mm Mean for *Candida albicans* at different concentration (µg/ml)		
		25 µg/ml	12.5 µg/ml	6.25 µg/ml
1	TD1	24±0.05	20±0.08	12±0.09
2	TD2	20±0.06	13±0.08	11±0.09
3	TD3	10±0.07	08±0.06	07±0.08
4	TD4	24±0.08	21±0.12	16±0.06
5	TD5	11±0.08	08±0.12	07±0.06
6	TD6	17±0.05	10±0.08	08±0.06
7	Standard	28±0.11	20±0.09	16±0.04

FLUCONAZOLE **TD1** **TD2** **TD3**



TD4 **TD5** **TD6**

FIG. 2: PHOTO PLATES OF ANTIFUNGAL STUDY OF SYNTHETIC COMPOUNDS ON *CANDIDA ALBICANCE*

RESULTS AND DISCUSSION : In the present study, a new series of Methyl 4-(1*H*-benzo [*d*]imidazol-2-yl)phenyl carbamodithioate amine derived from methyl Methyl 4-(1*H*-benzo[*d*] imidazol-2-yl) phenyl carbamodithioate (TD1-TD6) have been synthesized by reacting the thio methyl group with different amines in presence of ethanol. The starting material 4-(1*H*-benzo[*d*] imidazol-2-yl) benzenamine was synthesized by condensation of benzene -1, 2-diamine and p-amino benzoic acid, catalyzed by polyphosphoric acid. The structural assessment of the compounds was made on the basis of spectral data.

The synthesized compounds were screened for their *in vitro* growth inhibiting activity against different strains of bacteria and fungi *viz*., *Bacillus subtilis* and *Candida albicans*; were compared with known antibiotics ciprofloxacin and fluconazole zone of inhibition against bacterial and fungal strains.

Compounds exhibit moderate to high antibacterial and antifungal activity. Compounds TD3 and TD4 exhibit highest antibacterial activity other are moderate antibacterial activity. The compounds TD1, TD2, TD4 and TD6 having antifungal activity among them TD1 and TD4 shows highest antifungal activity.

CONCLUSION: The biological evaluation of synthesized compounds of benzimidazole thiourea derivatives show moderate to high degree of antimicrobial as well as antifungal activity, but no one is better than standard drug norfloxacin and fluconazole. The synthesized compounds 1-(4-(1*H*-benzo[*d*]imidazol-2-yl) phenyl) - 3 - benzylthiourea and 1-(4-(1*H*-benzo[*d*]imidazol-2-yl) phenyl)-3-(4-nitrophenyl) thiourea shows highest antibacterial activity. 3-(4-(1*H*-benzo[*d*]imidazol-2-yl)-1-methyl -1-phenylthiourea and 1-(4-(1*H*-benzo[*d*]imidazol-2-yl) phenyl)-3-(4-nitrophenyl) thiourea shows highest antifungal activity. These studies provide researchers to synthesize more derivatives and evaluate biological activity including antimicrobial activity.

ACKNOWLEDGEMENT: The authors are thankful to Sagar Institute of Research and Technology - Pharmacy, Panjab University, Chandigarh and Central Analytical Facility, MFP-PARC, Bhopal for providing data.

CONFLICT OF INTEREST: No conflict of interest.

REFERENCES:

1. Alasmary FAS, Snelling AM, Zain ME, Alafeefy AM, Awaad AS and Karodia N: Synthesis and evaluation of selected benzimidazole derivatives as potential antimicrobial agents. Molecules 2015, 20, 15206-15223.
2. Kumar K, Awasthi D, Lee SY, Cummings JE, Knudson SE, Slayden RA and Ojima I: Benzimidazole-based antibacterial agents against *Francisella tularensis*. Bioorganic Medicinal Chemistry 2013; 21: 3318–3326.
3. Yoon YK, Ali MA, Wei AC, Choon TS and Ismail R: Synthesis and evaluation of antimycobacterial activity of new benzimidazole aminoesters. European Journal of Medicinal Chemistry. 2015; 93: 614-624.
4. Ramprasad J, Nayak N, Dalimba U, Yogeeswari P, Sriram D, Peethambar SK, Achur R and Kumar S, Synthesis and biological evaluation of new imidazo[2,1-b][1,3,4] thiadiazole-benzimidazole derivatives, European Journal of Medicinal Chemistry. 2015; 95: 49-63.
5. Ke Y, Zhi X, Yu X, Ding G, Yang C and Xu H: Combinatorial synthesis of benzimidazole-azo-phenol derivatives as antifungal agents. Combinatorial Chemistry & High Throughput Screening. 2014; 17(1):89-95.
6. Datar PA and Limaye S: Design and synthesis of Mannich bases as benzimidazole derivatives as analgesic agents. Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry 2015, 14, 35–46. 20.
7. Achar KCS, Hosamani KM and Seetharamareddy HR: In vivo analgesic and anti-inflammatory activities of newly synthesized benzimidazole derivatives. European Journal of Medicinal Chemistry 2010; 45, 2048–2054.
8. Soderlind KJ, Gorodetsky B, Singh AK, Bachur NR, Miller GG and Lown JW: Bis-benzimidazole anticancer agents: targeting human tumour helicases. Anti-Cancer Drug Design. 1999; 14(1):19-36.
9. Reddy TS, Kulhari H, Reddy VG, Bansal V, Kamal A and Shukla R: Design, synthesis and biological evaluation of 1, 3 - diphenyl - 1Hpyrazole derivatives containing benzimidazole skeleton as potential anticancer and apoptosis inducing agents, European Journal of Medicinal Chemistry. 2015; 101:790-805.
10. Guan Q, Han C, Zuo D, Zhai M, Li Z, Zhang Q, Zhai Y, Jiang X, Bao K, Wu Y and Zhang W: Synthesis and evaluation of benzimidazole carbamates bearing indole moieties for antiproliferative and antitubulin activities, European Journal of Medicinal Chemistry. 2014; 87: 306-315.
11. Sharma A, Luxami V and Paul K: Purine-benzimidazole hybrids: Synthesis, single crystal determination and *in vitro* evaluation of antitumor activities, European Journal of Medicinal Chemistry. 2015; 93: 414-422.
12. Kaushik K, Ashok G, Swati D, Mustafa K and Hiral T: Benzimidazole: A Promising Lead For Anticancer Drug Design, Universal Journal of Pharmacy, 2013; 2(3): 57-62.
13. Wang YT, Qin YJ, Yang N, Zhang YL, Liu CH and Zhu HL: Synthesis, biological evaluation, and molecular docking studies of novel 1-benzene acyl-2-(1-methylindol-3-yl)- benzimidazole derivatives as potential tubulin polymerization inhibitors, European Journal of Medicinal Chemistry. 2015; 99: 125-137.
14. Tonelli M, Simone M, Tasso B, Novelli F, Boido V, Sparatore F, Paglietti G, Pricl S, Giliberti G and Blois S: Antiviral activity of benzimidazole derivatives. Antiviral activity of 2-phenylbenzimidazole derivatives. Bioorganic Medicinal Chemistry. 2010; 18: 2937–2953.
15. Vitale G, Corona P, Loriga M, Carta A, Paglietti G, Giliberti G, Sanna G, Farci P, Marongiu, ME and Colla P: 5-Acetyl-2-arylbenzimidazoles as antiviral agents. European Journal of Medicinal Chemistry. 2012; 53: 83–97.
16. Pan T, He X, Chen B, Chen H, Geng G, Luo H, Zhang H and Bai C: Development of benzimidazole derivatives to inhibit HIV-1 replication through protecting APOBEC3G protein, European Journal of Medicinal Chemistry. 2015; 95: 500-513.
17. Tonelli M, Novelli F, Tasso B, Vazzana I, Sparatore A, Boido V, Sparatore F, la Colla P, Sanna G and Giliberti G : Antiviral activity of benzimidazole derivatives. III. Novel anti-CVB-5, anti-RSV and anti-Sb-1 agents. Bioorganic Medicinal Chemistry. 2014; 22: 4893–4909.
18. Shingalapur RV, Hosamani KM, Keri RS and Hugar MH: Derivatives of benzimidazole pharmacophore: Synthesis, anticonvulsant, antidiabetic and DNA cleavage studies. European Journal of Medicinal Chemistry. 2010; 45: 1753–1759.
19. Bansal Y and Silakari O: The therapeutic Journey of benzimidazoles: A review. Bioorganic Medicinal Chemistry. 2012; 20: 6208-6236.

20. Siddiqui N, Andalip, Bawa S, Ali R, Afzal O, Akhtar MJ, Azad B and Kumar R: Antidepressant potential of nitrogen-containing heterocyclic moieties: An updated review. Journal of Pharmacy and Bioallied Sciences. 2011; 3: 194–212.
21. Halim NIM, Kassim K, Fadzil AH and Yamin BM: Synthesis, characterization and antibacterial studies of benzoylthiourea derivatives. International Proceedings of Chemical, Biological and Environmental Engineering 2011: 14: 53-59.
22. Ahmad I, Mehmood Z and Mohammad F: Screening of some Indian medicinal plants for their antimicrobial properties. Jou of Ethnopharmacology. 1998; 62:183-93.
23. Adekunle AS and Adekunle OC: Preliminary assessment of antimicrobial properties of aqueous extract of plants against infectious diseases. Biology and Medicine 2009; 1(3): 20-24.
24. Aqil F, Ahmad I: Antibacterial properties of traditionally used Indian medicinal plants. Methods and Findings in Experimental Clinical Pharmacology. 2007; 29(2): 79-92.
25. Atindehou KK, Kone M, Tenneaux C, Traore D, Hosterrman K and Doss M: Evaluation of the antimicrobial potential of medicinal plants from the Ivory coast. Phytotherapy Research 2002; 16: 497-502.
26. Chakraborty A and Brantner AH: Antibacterial steroid alkaloids from the stem bark of *Holarrhena pubescens*. Journal of Ethnopharmacology. 1999; 68: 339-344.
27. Saeed S, Rashid N, Jones PG, Ali M and Hussain R: Synthesis, characterization and biological evaluation of some thiourea derivatives bearing benzothiazole moiety as potential antimicrobial and anticancer agents. European Journal of Medicinal Chemistry 2010; 45(4):1323-1331.
28. Schreiner PR: Metal-free organocatalysis through explicit hydrogen bonding interactions. Chemical Society Reviews 2003; 32(5): 289-96.
29. Bauer AW, Kirby WM, Sherris JC and Turck M: Antibiotic susceptibility testing by a standardized single disk method. Am J Clin Pathol.1966; 45(4):493-6.

How to cite this article:
Singh LP, Tiwari OP and Brijyog: Synthesis and antimicrobial activity of some methyl 4-(1*h*-benzo[*d*] imidazol-2-yl) phenyl carbamodithioate amine derivatives. Int J Pharm Sci & Res 2018; 9(3): 1194-00. doi: 10.13040/IJPSR.0975-8232.9(3).1194-00.