RESEARCH ARTICLE

Synthesis, Characterization and Docking Studies of New Benzimidazole Derivatives Containing 1,3,4 thiadiazole Ring and Study of their Antibacterial Activity

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ABSTRACT

A new series of benzimidazole derivatives containing 1,3,4-thiadiazole ring moiety were synthesized by nucleophilic substitution of 2-(bromomethyl)-1H-benzimidazole with some derivatives of 1,3,4-thiadiazol-2-amine compounds. The resulting compounds were characterized by various techniques like fourier-transform infrared spectroscopy (FTIR), Proton nuclear magnetic resonance (^{1}H-NMR) and Carbon-13 nuclear magnetic resonance ^{13}C-NMR and evaluated their antibacterial activity *in vitro* against four types of bacteria isolates two gram negative (*Staphylococcus aureus* and *Staphylococcus epidermidis*) and two gram positive (*Escherichia coli* and *Pseudomonas aeruginosa*). Indeed, the synthesized compounds showed moderate to good activity against these types of bacteria. Docking studies of compounds (6c and 7c) on eubacterial ribosomal decoding A site (*E. coli* 16S rRNA A. site) (pdb:1j7t) have been conducted to find the possible mode of action of the molecules.

Keywords: 1,3,4-thiadiazole, Antibacterial, Benzimidazole, Molecular docking.

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INTRODUCTION

The development of new reaction routes would be advantageous for opening new avenues for the synthesis of novel, more potent, and selective antibacterial compounds to deal with resistant bacteria since harmful bacteria's resistance to commonly used antibiotics has become a big challenge around the world for medicinal chemists.[1,2] Among of the available several heterocyclic compounds, benzimidazoles still one of the importance antimicrobial agents. The benzimidazole derivatives play a significant function in biological chemistry, they are important intermediates in the synthesis routes of many biologically active compounds.[3] Benzimidazoles are a promising class of bioactive heterocyclic chemicals with a wide range of biological effects.[4] This nucleus, in particular, is a component of vitamin B_{12}.[5] Therefore, benzimidazole has an important and wide range of biological activity in the pharmaceutical industry[6] such as antibacterial,[7] anti-inflammatory,[8] antiviral activity,[9] antidiabetic,[10] anti-trichinellosis,[11] etc. In the last years, several kinds of research have been reported to synthesize novel benzimidazole derivatives to investigate their activity as antimicrobial agents.[12-17] Because of its enormous importance and wide range of bioactivities, benzimidazoles and 1,3,4-Thidiazoles, efforts have been made to construct libraries of these compounds and screen them for potential biological activities from time to time Few studies have focused on the synthesis of benzimidazole derivatives bearing 1,3,4-thiadiazole ring[18,19] and reported the synthesis of novel benzimidazole derivatives containing oxazole ring[20] oxadiazole ring,[12,21] 12,4-triazole,[22] and azole ring.[15]Looking at the importance and relevance of the benzimidazole and 1,3,4-thiadiazol nucleus, we thought that we designed and synthesized some novel benzimidazole derivatives containing the 1,3,4-thiadiazole moiety and screening them for possible antibacterial activity would be useful.

EXPERIMENTAL

Material and Methods

Pure starting materials from BDH and sigma were used for the preparation of synthesized compounds. All chemicals, solvents, and reagents were of synthetic grade and were buy it commercially, Stuart-SMP3 electronic system was used to measure melting points, the FTIR spectrum was recorded by SHIMADZU (FTIR 8400S), while Bruker (400MHz) used for recorded ^{1}H and ^{13}C-NMR spectrums, dimethylsulfoxide (DMSO)-d_6 as a solvent and TMS as a reference, thin-layer chromatography (TLC) technique was used to ensure of completion of the reaction, the spots were visualized by using UV Cabinet for TLC.

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Synthesis of 2-(bromomethyl)-1*H*-benzimidazole (a)

A mixture of (2.16 g, 20 mmol) of *O*-phenylenediamine and (4.16 g, 30 mmol) of bromoacetic acid was dissolved in 30 to 40 mL of 4N HCl by heating, the reaction mixture was refluxed for 5 hours. The mixture cooled down and neutralized with 32% ammonia solution and the obtained precipitate was filtered, washed with distilled water several times, and dried. The product was recrystallized from ethanol. The completion of the reaction and purity of the obtained product was tested by TLC mobile phase (hexane: ethyl acetate) (6:4) percentage (V: V).

Beige to dark yellow, yield 80%, mp 148–150°C, FT-IR (cm^{-1}) 3425 (N-H), 3024 (C-H, aromatic), 2943–2848 (C-H, aliphatic), 1621 (C=N), 1593-1440 (C=C, aromatic); ^{1}H-NMR(DMSO- d6, 400MHz) 4.95 (s, 2H, CH_2), 7.22–7.57 (m, 4H, Ar), 10.54 (s, 1H, N-H); ^{13}C-NMR (DMSO-d6, 125MHz) 37.97, 114.96, 122.04, 138.15, 149.28.

Synthesis of Compounds (1-7) b

(10 mmol, 5 mL) of $POCl_3$ was added thoroughly and carefully to a mixture of (10 mmol) from benzoic acid derivatives and (0.91 g, 10 mmol) from thio-semicarbazide, refluxed for 3 hours. After cooling down of the reaction mixture (25 mL) of distill water was added drop-wise and carefully with stirring and refluxed for 4 hours. The mixture cooled down and then neutralized with potassium hydroxide solution, and the obtained precipitate was filtered and washed with distilled water several times and dried. The product was recrystallized from ethanol. The completion of the reaction and purity of the obtained product was tested by TLC mobile phase (hexane: ethyl acetate) (7:3) percentage (V: V).

5-phenyl-1,3,4-thiadiazol-2-amine (1b):

Pale yellow, yield 86%, mp 223–225°C, FTIR (cm^{-1}) 3391 and 3270 (NH_2), 3098(C-H, aromatic), 1630(C=N), 1586 and 1455 (C=C, aromatic).

5-(2-fluorophenyl)-1,3,4-thiadiazol-2-amine(2b)

Pale beige, yield 89%, mp 215–217°C, FTIR (cm^{-1}) 3272 and 3197 (NH_2), 3089(C-H, aromatic), 1633(C=N), 1581 and 1475 (C=C, aromatic).

5-(2-iodophenyl)-1,3,4-thiadiazol-2-amine (3b)

Beige, yield 77%, mp 212–214°C, FTIR (cm^{-1}) 3340 and 3232 (NH_2), 3084(C-H, aromatic), 1616(C=N), 1585 and 1494 (C=C, aromatic).

5-(2-chlorophenyl)-1,3,4-thiadiazol-2-amine (4b)

Pale yellow, yield 80%, mp 213–215, FTIR (cm^{-1}) 3290 and 3203 (NH_2), 3086 (C-H, aromatic), 1639 (C=N), 1596 and 1458 (C=C, aromatic).

5-(3- chlorophenyl)-1,3,4-thiadiazol-2-amine (5b)

Pale yellow, yield 85%, mp 204–206°C, FTIR (cm^{-1}) 3296 and 3170 (NH_2), 3084 (C-H, aromatic), 1614(C=N), 1566 and 1415 (C=C, aromatic).

5-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine (6b)

Yellow, yield 82%, mp 244–246°C, FTIR (cm^{-1}) 3377 and 3294 (NH_2), 3069(C-H, aromatic), 1620(C=N), 1604 and 1440, 1508 and 1342 (NO_2), (C=C, aromatic).

5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-amine (7b)

Dark yellow, yield 85%, mp 265–267°C, FTIR (cm^{-1}) 3360 and 3251 (NH_2), 3097 (C-H, aromatic), 1627(C=N), 1535 and 1350 (NO_2), 1593 and 1435 (C=C, aromatic).

Synthesis of Compounds (1-7) c

A mixture of (1.05 g, 5 mmol) of compound (A), (5mmol) of 1,3,4-thiadiazol-2-amine derivatives (B_1-B_{11}) and (0.83 g, 5mmol) potassium iodide was dissolved in 25 mL of ethanol. After 6 hrs of refluxing a solution of potassium hydroxide (5 mmol, 0.28 g in 2.5mL of H_2O) was added to the mixture, and refluxing continued for 2 hrs. The mixture cooled down and poured onto crushed ice, and the obtained precipitate was filtered, washed with distil water several times, and dried. The product was recrystallized from ethanol. The completion of the reaction and purity of obtained product was tested by TLC mobile phase (hexane: ethyl acetate) (9:1) percentage (V: V).

N-((1H-benzo[d]imidazol-2-yl)methyl)-5-phenyl-1,3,4-thiadiazol-2-amine (1c):

Yellow, yield 55%, mp 253–255°C, FTIR (cm^{-1}) 3350 (Ar, N-H), 3178 (alph-NH), 3061(Ar-CH), 2962 and 2852 (aliph-CH), 1620(C=N), 1589 and 1480 (Ar, C=C); ^{1}H-NMR (DMSO- d6, 400MHz) 3.36 (s, 2H, CH_2), 6.75 (s, 1H, amine N-H), 7.13 –7.74 (m, 9H, Ar), 10.48 (s, 1H, benzimidazol N-H); ^{13}C-NMR (DMSO-d6, 125MHz) 45.04 (CH_2), 114.91-130.08(Ar-rings), 149.82(benzimidazole,C=N), 165.69 and 168.39 (1,3,4-thiadiazole, C=N).

N-((1H-benzo[d]imidazol-2-yl)methyl)-5-(2-fluorophenyl)-1,3,4-thiadiazol-2-amine (2c)

Dark yellow, yield 57%, mp 195–197°C, FTIR (cm^{-1}) 3421 (Ar, N-H), 3259 (alph-NH), 3057(Ar-CH), 2987 and 2889 (aliph-CH), 1629(C=N), 1597 and 1463 (Ar, C=C); ^{1}H-NMR (DMSO- d6, 400MHz) 3.42 (s, 2H, CH_2), 6.52(s, 1H, amine N-H), 7.13 –7.81 (m, 8H, Ar), 10.47 (s, 1H, benzimidazol N-H); ^{13}C-NMR (DMSO-d6, 125MHz) 42.06 (CH_2), 110.27-136.12(Ar-rings), 153.58(benzimidazole,C=N), 158.96 and 169.84 (1,3,4-thiadiazole, C=N).

N-((1H-benzo[d]imidazol-2-yl)methyl)-5-(2-iodophenyl)-1,3,4-thiadiazol-2-amine (3c)

Yellow, yield 64%, mp 222–224°C, FTIR (cm^{-1}) 3323 (Ar, N-H), 3178 (alph-NH), 3055(Ar-CH), 2964 and 2873(aliph-CH), 1616(C=N), 1579 and 1469 (Ar, C=C); ^{1}H-NMR (DMSO-d6, 400MHz) 3.44 (s, 2H, CH_2), 6.79 (s, 1H, amine N-H), 7.13 –7.77 (m, 4H, Ar), 10.46 (s, 1H, benzimidazol N-H); ^{13}C-NMR (DMSO- d6, 125MHz) 42.04 (CH_2), 98.23-130.12(Ar-rings), 153.63(benzimidazole,C=N), 166.46 and 167.41 (1,3,4-thiadiazole, C=N).

N-((1H-benzo[d]imidazol-2-yl)methyl)-5-(2-chlorophenyl)-1,3,4-thiadiazol-2-amine (4c)

Dark yellow, yield 85%, mp 175–177°C, FTIR (cm^{-1}) 3427 (Ar, N-H), 3174 (alph-NH), 3064(Ar-CH), 2976 and 2873(aliph-CH), 1635(C=N), 1595 and 1477 (Ar, C=C); ^{1}H-NMR (DMSO-d6, 400MHz) 3.44 (s, 2H, CH_2), 6.33 (s, 1H, amine N-H), 7.17 –7.98 (m, 4H, Ar), 10.15 (s, 1H,

benzimidazol N-H); ^{13}C-NMR (DMSO- d6, 125MHz) 44.79 (CH_2), 114.97-138.46(Ar-rings), 151.50(benzimidazole,C=N), 166.08 and 169.99 (1,3,4-thiadiazole, C=N).

N-((1H-benzo[d]imidazol-2-yl)methyl)-5-(3-chlorophenyl)-1,3,4-thiadiazol-2-amine (5c)

Dark yellow, yield 65%, mp 245–247 ºC, FTIR (cm^{-1}) 3417 (Ar, N-H), 3230 (alph-NH), 3068(Ar-CH), 2968 and 2881(aliph-CH), 1631(C=N), 1591 and 1479 (Ar, C=C); ^{1}H-NMR (DMSO-d6, 400MHz) 3.43 (s, 2H, CH_2), 6.62 (s, 1H, amine N-H), 7.13 –7.87 (m, 4H, Ar), 10.47 (s, 1H, benzimidazol N-H); ^{13}C-NMR (DMSO- d6, 125MHz) 41.64 (CH_2), 114.64-133.67(Ar-rings), 151.96(benzimidazole,C=N), 163.13 and 168.94 (1,3,4-thiadiazole, C=N).

N-((1H-benzo[d]imidazol-2-yl)methyl)-5-(4-nitrophenyl)-1,3,4-thiadiazol-2-amine (6c)

Dark yellow, yield 71%, mp <250 ºC, FTIR (cm^{-1}) 3410 (Ar, N-H), 3201 (alph-NH), 3033(Ar-CH), 2931 and 2860(aliph-CH), 1635(C=N), 1525 and1346 (NO_2), 1590 and 1463 (C=C, aromatic); ^{1}H-NMR (DMSO- d6, 400MHz) 3.38 (s, 2H, CH_2), 6.47 (s, 1H, amine N-H), 7.08 –8.25 (m, 4H, Ar), 10.46 (s, 1H, benzimidazol N-H); ^{13}C-NMR (DMSO-d6, 125MHz) 41.96 (CH_2), 115.56-147.18(Ar-rings), 153.92(benzimidazole,C=N), 165.86 and 169.86 (1,3,4-thiadiazole, C=N).

N-((1H-benzo[d]imidazol-2-yl)methyl)-5-(3,5-dinitrophenyl)-1,3,4-thiadiazol-2-amine (7c)

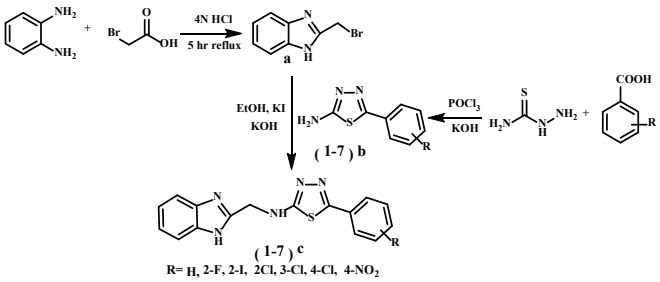
Yellow, yield 61%, mp 207–209ºC, FTIR (cm^{-1}) 3417 (Ar, N-H), 3251 (alph-NH), 3074(Ar-CH), 2945 and 2837(aliph-CH), 1629(C=N), 1530 and1340 (NO_2), 1598 and 1456 (Ar, C=C); ^{1}H-NMR (DMSO- d6, 400MHz) 3.44 (s, 2H, CH_2), 6.52 (s, 1H, amine N-H), 7.15 –7.92 (m, 4H, Ar), 10.48 (s, 1H, benzimidazol N-H); ^{13}C-NMR (DMSO-d6, 125MHz) 41.84 (CH_2), 114.55-133.81(Ar-rings), 153.62 (benzimidazole, C=N), 166.32 and 168.70 (1,3,4-thiadiazole, C=N).

RESULTS AND DISCUSSION

Experimental

The reaction steps for various title compounds were shown in Scheme 1, and physical characteristics of synthesized compounds listed in Table 1, the starting material (a) 2-(bromomethyl)-1*H*-benzimidazole (a) according to a published procedure by the reaction of *O*-phenylenediamine with bromoacetic acid in 4N HCl,[23,24] FT-IR for compound (a) was showed the stretching of N-H at (3425) cm^{-1} and the stretching of C=N in (1620) cm^{-1}.

Some derivatives compounds of 2-amino-5-(substitute-dphenyl)-1,3,4-thiadiazole (1-7) b were prepared from the reaction of benzoic acid derivatives with thiosemicarbazide in presence of $POCl_3$.[23-27] FT-IR for these compounds was showed two bands of the stretching of NH_2 between (3391–3170) cm^{-1} and the stretching of C=N in (1614-1643) cm^{-1}. Nucleophilic substitution of compound (a) with compounds (1-7) b resulting compounds (1-7) c according to reported procedure.[28-30] The structure of compounds (1-7) c was identified by FTIR, ^{1}H and ^{13}C-NMR, FTIR spectrum for (1-7) c was showed strong sharp band related to N-H of benzimidazole in range (3444–3323) cm^{-1} and next band referred to N-H of 1,3,4-thiadiazole in range (3259-3174) and band of C=N in range (1635–1616). In addition of ^{1}H-NMR was showed singlet peak between



Scheme 1: Synthesis of benzimidazole derivatives

Table 1: Physical characteristics of synthesized compounds.

No.	*R*	*Formula*	*M.wt*	*Color*	*M.P (ºC)*	*Yield %*	R_f
A	H	$C_8H_7BrN_2$	211.06	Beige to dark yellow	148–150	80	0.36
1B	H	$C_8H_7N_3S$	177.23	Pale yellow	223–225	86	0.46
2B	2-F	$C_8H_6FN_3S$	195.22	Pale beige	215–217	89	0.52
3B	2-I	$C_8H_6IN_3S$	303.12	beige	212–214	77	0.60
4B	2-Cl	$C_8H_6ClN_3S$	211.68	Pale yellow	213–215	80	0.46
5B	3-Cl	$C_8H_6ClN_3S$	211.68	Pale yellow	204–206	85	0.48
6B	4-NO_2	$C_8H_6N_4O_2S$	222.23	Yellow	244–246	82	0.45
7B	3,5-di NO_2	$C_8H_5N_5O_4S$	267.23	Dark yellow	265–267	85	0.62
1C	H	C16H13N5S	307.38	yellow	253–255	55	0.66
2C	2-F	C16H12FN5S	325.37	Dark yellow	195–197	57	0.42
3C	2-I	C16H12IN5S	433.27	Yellow	222–224	64	0.50
4C	2-Cl	C16H12ClN5S	341.83	Dark yellow	175–177	85	0.40
5C	3- Cl	C16H12ClN5S	341.83	Dark yellow	245–247	65	0.43
6C	4-NO_2	C16H12N6O2S	352.38	Dark yellow	<250	71	0.39
7C	3,5-di NO_2	C16H11N7O4S	397.38	Yellow	207–209	61	0.55

δ (3.38 -3.44) accounted to CH_2 and singlet peak between δ (6.33-6.75) related to NH of 1,3,4-thaidaizole and number of peaks between δ (7.13-8.25) referred to aromatic protons showed singlet peak between δ (10.15-10.48) accounted to NH of benzimidazole.

Antibacterial Activity

The treatment of infectious diseases is a major challenge, owing to several variables, including bacterial resistance to antibiotics. The plant's biological impact the produced chemical was tested against Ge^{-ve} and Ge^{+ve} bacteria isolates. The listed results in Table 2 showed the study of the antibacterial activity of some synthesized compounds in four concentrations (100, 50, 25, 12.5) mg/mL. They showed moderate to good activity as the antibacterial agents compared with standard antibiotic ceftazidime, ceftriaxone, clarithromycin, amikacin, chloramphenicol, azetronam. The antibacterial activity of the synthesized compounds was tested against two types of Ge^{+ve} bacteria isolates (*S. aureus* and *S. epidermidis*) and against two types of Ge^{-ve} bacteria isolates (*P. aeruginosa* and *E. coli*).

Table 2: Antibacterial activity of synthesized compounds.

		Zone of inhibition (in mm)			
		Gram-positive		*Gram-negative*	
Comp. No.	*Concentration mg/mL*	*S. aureus*	*S. epidermidis*	*P. aeruginosa*	*E. coli*
1C	100	20	18	11	17
	50	18	18	-	22
	25	18	19	11	22
	12.5	18	17	12	21
2C	100	22	18	11	16
	50	20	19	-	19
	25	20	19	11	18
	12.5	15	15	-	-
3C	100	21	16	12	14
	50	19	16	11	11
	25	16	15	13	-
	12.5	14	14	13	-
4C	100	22	18	-	24
	50	20	19	13	-
	25	20	19	-	-
	12.5	15	15	-	-
5C	100	21	16	-	22
	50	19	16	-	20
	25	16	15	-	15
	12.5	14	14	-	-
6C	100	22	20	-	19
	50	20	20	12	-
	25	20	18	-	17
	12.5	15	16	-	-
7C	100	17	20	-	22
	50	24	22	-	20
	25	24	23	-	15
	12.5	24	20	-	-
Clarithromycin	15	12	13	-	-
Ceftazidime	30	-	-	17	-
Ceftriaxone	30	-	-	-	12
Amikacin	30	18	21	-	-
Azetronam	30	-	-	30	-
Chloramphenicol	30	-	-	-	21
DMSO	-	-	-	-	-

According to Table 2 all analogs showed good activity against (*S. aureus* and *S. epidermidis*), and the most active compounds were 5c, 6c, and 7c. While all analogs showed poor activity and, in some concentrations, didn't show any activity against *P. aeruginosa* due to position and type of substituted group. All analogs especially 1c, 5c and 7c showed good activity and in some concentrations, didn't show any activity against *E. coli* due to position and type of substituted group.

Molecular Docking Study

Molecular docking studies have been performed on eubacterial ribosomal decoding A site (*E. coli* 16S rRNA A. site) (pdb:1j7t) to rationalize the probable mode of action binding affinity, and orientation of the molecules at the active site of receptor, and the Molecular docking data of (6c and 7c) listed in Table 3.[31] The compound (6c) formed (5) close interatomic hydrogen bonds (O·····H). The first, second and third resulted hydrogen bonds from interaction oxygen atoms of nitro group connected to benzene ring of compound (6c) with hydrogen respectively, H_{42}, H_{41}, H_{41} atoms of nitrogen bases (Cyt-11), (Gau-33) and (Gau-32) with distance of bond respectively (2.2), (2.4) and (2.4) A°. The fourth hydrogen bond resulted from the interaction between nitrogen atom of 1,3,4-thidiazole ring with hydrogen H_7 atom of nitrogen base (Ade-29) with distance of bond (2.6) A°. The fifth hydrogen bond resulted from the interaction between nitrogen atom of benzimidazole ring with hydrogen H_{42} atom of nitrogen base (Cyt-28) with distance of bond (2.1) A° as shown as in Figure 1.

The most active compound (7c) was formed (7) close interatomic hydrogen bonds. The first and second hydrogen bonds resulted from the interaction between hydrogen respectively, H_7 and H_{62} of nitrogen base (Ade) with oxygen atoms of nitro groups connected to the benzene ring of compound (7c) with a distance of bond, respectively (1.9), (2.2) A°. The third hydrogen bond resulted from the interaction between hydrogen H_{33} of nitrogen base (Cyt-33) with nitrogen atom of benzimidazole ring with a distance of bond (2.6) A°. The fourth and fifth hydrogen bonds resulted from the interaction between oxygen O_6 atoms of both nitrogen bases (Gau-12) and (Gau-13) with hydrogen of the secondary amine

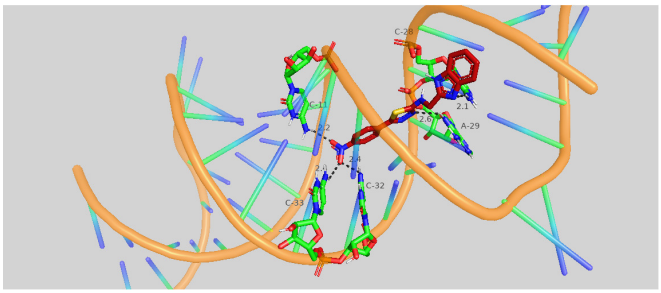


Figure 1: Docked conformation of compound 6c (red color) in the binding site of eubacterial ribosomal decoding A site (pdb:1j7t). Hydrogen bonds are shown by black dashed line.

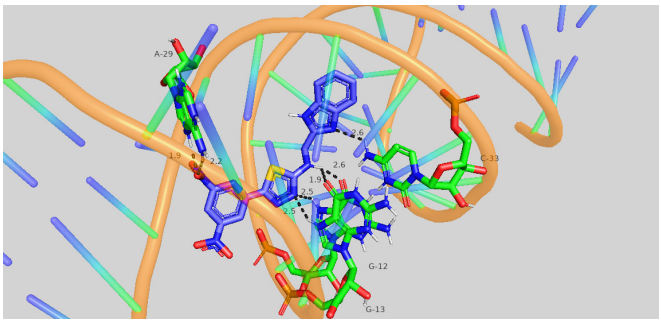


Figure 2: Docked conformation of compound 7c (blue color) in the binding site of eubacterial ribosomal decoding A site (pdb:1j7t). Hydrogen bonds are shown by black dashed line.

Table 3: Molecular docking data of (6c and7c)

Comp. No.	*Position of H.B*	*Distance of bond (A°)*	*π-π interactions*
6c	C_9: O (NO_2) -:B(Cyt-11): H_{42}	2.2	C_9-(A-29) ((B)
	C_9: O (NO_2): -:B(Gau-33) H_{41}	2.4	C_9-(C-30) (B)
	C_9: O (NO_2): -:B(Gau-32) H_{41}	2.4	C_9-(G-26)(B)
	C_9: N (1,3,4-thiadiazole) -:B(Ade-29) H_7	2.6	C_9-(G-13) (A)
	C_9: N (benzimidazole): -:B(Cyt-28) H_{42}	2.1	C_9-(A-31) (B) C-(U-27) (B)
7c	C_{10}: O (NO_2): -:B(Ade-29) H_7	1.9	C_{10}-C11 (A)
	C_{10}: O (NO_2): -:B(Ade-29) H_{62}	2.2	C_{10}-C32 (B)
	C_{10}: N (benzimidazole): -:B(Cyt-33) H_{33}	2.6	C_{10}-C28 (B)
	C_{10}: H (amine): -:B(Gau-12): O_6	1.9	C_{10}-C31 (B)
	C_{10}: H (amine): -B(Gau-13): O_6	2.6	-
	C_{10}: N (1,3,4-thiadiazole): -B(Gau-12) H_7:	1.9	-
	C_{10}: N (1,3,4-thiadiazole): -B(Gau-13): H_7	2.6	-
ref (paromo-mycin)	ref: O10 - A: Gua 13: OP2	3.1	-
	B: Cyt 25 - OP2 - ref: O40	2.9	-
	ref: N42 - B: Gua 26: O6	2.8	-
	ref: O28 - B: Urd 27: OP2	2.7	-

group of compound (7c) with a distance of bond respectively (1.9), (2.6) A°. The sixth and seventh hydrogen bonds resulted from the interaction between hydrogen H_7 of both nitrogen bases (Gau-12) and (Gau-13) with nitrogen atom of 1,3,4-thidiazole ring with a distance of bond respectively (2.6) and(1.9) A° as shown in Figure 2.

CONCLUSION

In the present work seven target derivatives of benzimidazole have been synthesized. All analogs were characterized through spectroscopic techniques like FT-IR, ^{1}H and ^{13}C NMR. All analogs have been evaluated for antibacterial activity against four types of bacteria and showed moderate to good activity against (*S. aureus* and *S. epidermidis*) and (*P. aeruginosa* and *E. coli*). Molecular docking study has been established for some compounds keeping in view the role of different substituents on phenyl ring in the biological evaluation.

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