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Synthesis and Antimicrobial Activity of 5-Bromo-7-Methoxybenzofuranyl-2-Carbonylazide Derivatives

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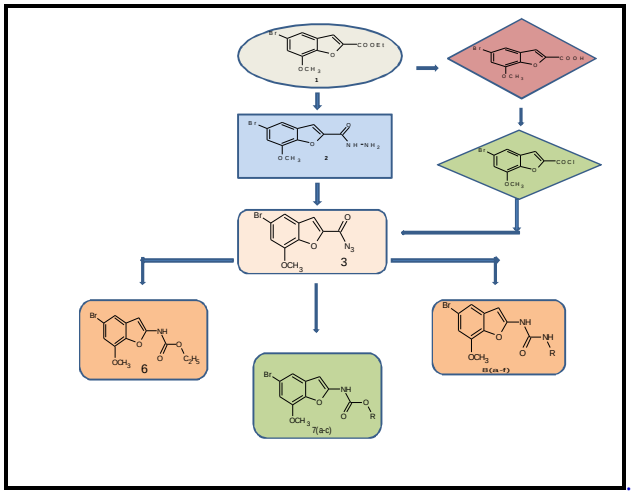
ABSTRACT

In continuation to find pharmaceutically potent benzofuran derivates, we under took the synthesis of carbamates and carbamides involving 5-bromo-7-methoxybenzofuran nucleus. From the key intermediate 5-bromo-7-methoxy-1-benzofuran-2-carbonyl azide ***(1)****, we have synthesized a series of carbamates* ***6, 7a-c*** *and carbamides/aryl ureas 8****(a-f)*** *by treating with ethanol, phenols and aromatic primary amines respectively. The structures of all the compounds were confirmed by their spectral data. All the newly synthesized compounds were screened for antibacterial and antifungal activity using various organisms and are compared to standard drugs. Some of them exhibited encouragive results.*

Graphical Abstract:



Scheme for the synthesis of 5-bromo-7-methoxy-1-benzofuran-2--carbamates **6, 7a-c** and carbamides/aryl ureas 8**(a-f).**

Keywords: Benzofuran, Carbonyl azide, Carbamates, Carbamides, Antibacterial, Antifungal activity.

INTRODUCTION

Carbamates were prepared from carbamic acid by using the moieties like amino acids and carboxyl of various aryl or alkyl groups and these stable carbamates are identified by the linkage -NH-CO-O-. If cyclic compounds contain carbamates then this type of compounds are called as cyclic carbamates [**1**]. Because of the reported pharmaceutical properties of someof organic carbamates and aryl ureas [**2, 3**]. These are the major group of compounds with biological activity [**4**], fungicides [**5-8**]. Carbamates and their derivatives have shown a major role in the pharmaceutical field due to the amine group in the carbamates structure [**9-11**]. Some of the intermediates of carbamates are used in the Synthesis of biologically active compounds [**12-16**]. The research work on in this field is continued in the synthesis of more effective biologically active compounds. Some of the carbamates were used in the pharma industry as drugs and prodrugs [**17**] for various diseases. Some of the compounds which contain carbamate linkage have shown excellent biological activity [**18-20**]. Carbamtes were also used in the study of various diseases, such as antibacterial, anticonvulsant, anticancer, anthelmintic, antimalarial, antiviral, anti-inflammatory, antifilarial, anti-HIV, antiestrogenic, CNS and CVS active agents, antiprogestational, antifungal, antitubercular, antidaiabetic, antiosteoporosis anti-obesity and anti-alzheimer drugs [Figure 1 and 2] [**21, 22**].

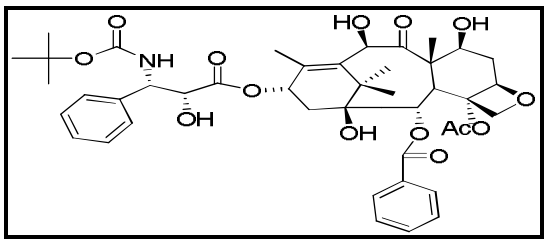


Figure 1. Taxol analogues: anticancer

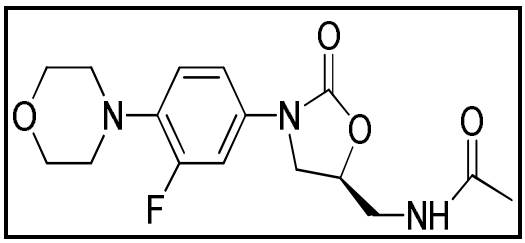


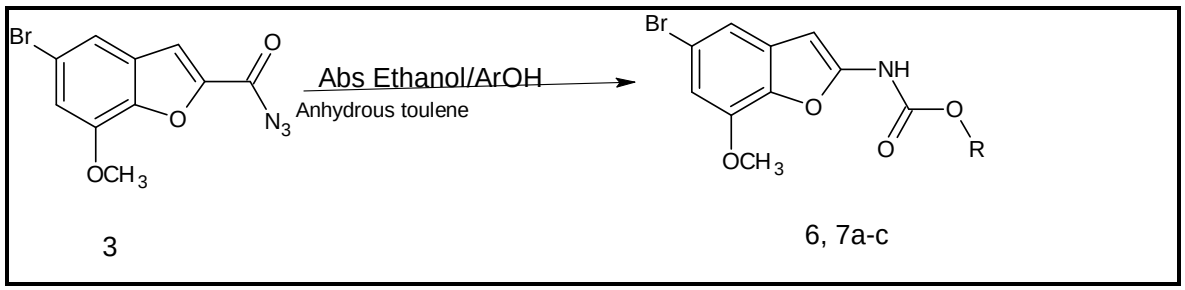
Figure 2. Linezolid: antibacterial

Chemistry: Owing to the pharmacological properties of benzofuran derivatives and in the continuation of our search for pharmaceutically potent benzofuran derivates, we undertook the synthesis of carbamates and carbamides involving 5-bromo-7-methoxybenzofuran nucleus. The key intermediate for those compounds was5-bromo-7-methoxy-1-benzofuran-2-carbonyl azide **(3)** which was synthesized by 5-bromo-7-methoxy-1-benzofuran-2-ethyl carboxylate **(1)** by treating with hydrazinehydrate (99% in ethanol) [**19-21**]. The resulting carbohydrazide **(2)** was when reacted with NaNO2and acetic acid in the presence of dioxane yielded the compound 5-bromo-7-methoxy-1-benzofuran-2-carbonyl azide **(3)**. Compound **3** was also obtained by another route. The alternative method consisted of hydrolyzing the ethyl carboxylate ester **1** to corresponding acid **4** by controlled hydrolysis using ethanolic KOH, which was then converted in to its acid chloride **5**by treating with thionyl chloride**.** The crude acid chloride was then converted to carbonyl azide **3** by treating with sodium azide in ice cold condition. The crude compound **3** was converted in to a series of carbamates **6, 7a-c** and aryl ureas **8a-c** via Curtius rearrangement of the azide when treated with ethanol, phenols and aromatic amines respectively.

The compound ethyl (5-bromo-7-methoxy-1-benzofuran-2-yl) carbamate (**6**) was obtained by refluxing the carbonyl azide **3** with absolute ethanol. The other carbamates (5-bromo-7-methoxy-benzofuran-2-yl)-carbamic acid aryl esters **7a-c**were obtained by refluxing the compound **3** with phenols.

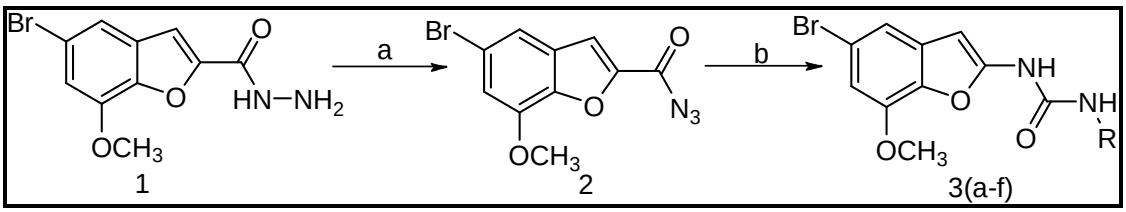
The Curtius rearrangement of caebonyl azide **3** in presence of various aromatic amines in dry tolune produced the respective carbamides/aryl ureas **8a-f.**

Carbamides/aryl ureas **(8)** by treating with substituted various amines in the presence of dry toluene **8(a-f)** are outlined in the scheme 1.



6, R= C_2H_5, 7, R= a- $C_6H_4Br(4)$, b-$C_6H_4F(4)$, c-$C_6H_4Cl(4)$

Scheme 1. for the preperation of ethyl(5-bromo-7-methoxy-1-benzofuran-2-yl)carbamate (**6**) and (5-bromo-7-methoxy-benzofuran-2-yl)-carbamic acid aryl esters **7a-c**



Reaction conditions: a) $NaNO_2$, Dioxane, Acetic acid, **b)** R-NH_2, Anhydrous toluene **R:** a= -$C_6H_4NO_2$ (4), b=- $C_6H_4Cl(3)$, c =- $C_6H_4NO_2(2)$, d =- $C_6H_4Cl(2)$, e = - C_6H_5,f = -$C_6H_4CH_3(4)$

Scheme 2. Synthesis of carbonyazide and 1-(5-bromo-7-Methoxy-benzofuran-2-yl)-3-aryl-ureas.

MATERIALS AND METHODS

All reagents and solvents were used as of analytical grade. IR spectra were taken on FTIR-Perkin Elmer Spectrum-Two spectrophotometers (range: (IR) 4000-400 cm_{-1}) m (KBr disc method). ^{1}HNMR spectra were recorded on BRUKER 400 MHz and ECX-JEOL 400(S), AVIII400 (L) using $CDCl_3$ and $MSOD_6$ as TMS as an internal reference. Mass Spectra were recorded in water model-synapt G2, APCI source Positive mode, desolvation 200 L h^{-1}. Melting points were determined in open capillary tubes and were uncorrected.

Method-A: The 5-bromo-7-methoxy-benzofuran-2-carboxylic acid hydrazide**(2)**(10 g, 0.048 mol) was suspended in a mixture of dioxan (60 mL) and glacial acetic acid (60 mL) cooled to 0^{o}C in a freezing mixture. An ice cold solution of sodium nitrite (5.2 g in 20 mL water) was introduced in small portion with vigorous stirring. The temperature of the reaction mixture was maintained below 2^{o}C. After the complete addition, the reaction was allowed to stand at room temperature for 30 min and the pale yellow solid thus separated was collected, washed with cold water. The product was dried over phosphorus pentoxide in a vacuum. (The crude product was used for the next step without recrystallisation).

5-Bromo-7-methoxy-1-benzofuran-2-carbonylazide(3): Yield 85%, melting point 110^{o}C(d), Molecular formula $C_{10}H_6BrN_3O_3$, IR (cm^{-1}): 2146 cm^{-1} (N_3-azide), 1710 cm^{-1} (C=O), MS: *m/z* 299 (Mol. Weight: 295), ^{1}HNMR (500 MHz, $CDCl_3$): δppm 3.354 (s, 3H, OCH_3), 7.15-7.5 (m, 3H, Ar-H).

Method-B: To a solution of 5-bromo-7-methoxy-1-benzofuran-2-ethyl carboxylate **(1)** (0.02 mol) in absolute ethanol (30 mL), potassium hydroxide (2 g in 20 mL) in absolute ethanol, was added and the reaction mixture was heated under reflux for 2h on a water bath. The excess of ethanol was

distilled off under reduced pressure and the residual solution was diluted with cold water. The clear solution thus obtained was cooled and acidified with dilute hydrochloric acid carefully to precipitate the carboxylic acid **4**. It was collected, washed with water and crystallized from a mixture of benzene and petroleum ether as colourless needles. (Yield 82%, mp. 194^{o}C, Molecular formula $C_{10}H_7BrO_4$).

The IR spectrum of the carboxylic acid **4** exhibited absorption peak at 1650 cm^{-1} confirms-COOH group, *m/z* was found to be 270 is concurrent with the calculated mass value.

5-bromo-7-Methoxy-benzofuran-2-carbonyl chloride (5): A mixture of carboxylic acid **4** (5g) and thionyl chloride (10ml) was refluxed on a water bath for 2h. The excess of thionyl chloride was removed under reduced pressure. The residual solid was washed with petroleum ether. The crude acid chloride **5**thus obtained was used in the next step without further purification. (Yield 78%, mp. 154^{o}C, Molecular formula $C_{10}H_6BrClO_3$)

5-Bromo-7-methoxy-1-benzofuran-2-carbonyl azide (3): To a stirred solution of the acid chloride **5** (2 g) in acetone (50 mL), a solution of sodium azide (0.6 g in 2 mL water) was added drop wise at 0^{o}C. After the complete addition of sodium azide solution, the temperature of the reaction mixture was raised to 25^{o}C and this temperature was maintained for 30 min to ensure the completeness of the reaction. The reaction mixture was diluted with cold water (100 mL) and the pale yellow azide **3** which separated was collected after washing with cold water. It was dried over phosphorus pentoxide in vacuum. The crude compound was used for next reactions. (Yield 78 %, mp. 110^{o}C(d), Molecular formula $C_{10}H_6BrN_3O_3$).

Carbonyl azide prepared by method A and B, have melting point 110°C, and their mixed melting point has not depressed. IR, 1HNMR and mass spectra were identical.

Ethyl (5-bromo-7-methoxy-1-benzofuran-2-yl) carbamic acid ester/Carbamate (6): A suspension of carbonyl azide **3** (0.01 mol) in absolute ethanol (10 mL) was refluxed on steam bath for 3h. The reaction mixture was concentrated under reduced pressure and then diluted with water. The product that separated was collected and crystallized from mixture of benzene and petroleum ether as colourless needles yield 73%, mp. 207^{o}C, Molecular formula $C_{12}H_{12}BrNO_4$. In the IR there is the absence of azide absorption peak at 2146 cm^{-1} (N_3-azide) and presence of ester absorption peak at 3300-3450 cm^{-1}, merged with –NH merged with CH stretching frequency 1750 cm^{-1} (-CO-O-) confirms the conversion of azide to amino ester. MS: *m/z* 299 (Mol. Weight: 295), ^{1}HNMR (500 MHz, $CDCl_3$): δ 8.23 (s, 1H, NH); 3.354 (s, 3H, OCH3); 7.15-7.5 (m, 3H, Ar-H).

General procedure for the synthesis of (5-bromo-7-Methoxy-benzofuran-2-yl)-carbamic acid aryl ester/Carbamates (7a-c): A mixture of azide **3** (0.001 mol) was suspended in anhydrous toluene (30 mL) and heated in an oil bath at 70- 80^{o}C till the evolution of nitrogen gas stopped (nearly 1h). Then the appropriate phenol (0.001 mol) in dry toluene (10 mL) was added and the reaction mixture was heated at 110-120°C for 3 h. After the removal of toluene under reduced pressure, the residue was dissolved in ether, the ethereal solution was washed with 10% aqueous solution of sodium hydroxide to remove any unreacted phenol and finally with water. The organic layer was dried over anhydrous calcium chloride. The removal of solvent furnished resinous mass which solidified on cooling. Further purification was achieved by crystallisation from suitable solvent. Melting point, % yield solvent for the crystallisation and IR data are given in the table 1.

^{1}HNMR and Mass spectra of representative compound **7b** exhibited the following data to confirm the structures of compounds **7a-c** PMR**:** δppm 3.254(s, 3H, OCH_3); 6.42-7.181(m, 7H, Ar-H); 8.23(s, 1H, NH);*m/e*= 379.

Table 1. Analytical data of the carbamates**7a-c**

Compounds	"R"	Yield %	MP °C	Solvent	Molecular Formula	IR data (cm^{-1})	
						NH	C=O
7a	C_6H_5Br (p)	79	222	Ethanol	$C_{16}H_{11}Br_2NO_4$	343	1655
7b	C_6H_5F (p)	70	216	Ethanol	$C_{16}H_{11}BrFNO_4$	344	1616
7c	C_6H_5Cl(m)	69	200	Methanol	$C_{16}H_{11}BrClNO_4$	328	1622

General procedure for the synthesis of 1-(5-bromo-7-Methoxy-benzofuran-2-yl)-3-aryl-ureas/ Carbamides (8a-f): A mixture of azide **3** (0.001 mol) and an appropriate amine (0.001 mol) in anhydrous toluene (15 mL) was heated under reflux (120°C) in an oil bath for 5hrs. The crystalline products **8a-f**, separated out from the reaction mixture was collected, washed with toluene and petroleum ether. The analytical sample was obtained by crystallisation from a suitable solvent.The analytical data are recorded in table 2.

Table 2. Analytical data of the compounds 8a-f

Compound	Substituent "R"	Yield %	Melting Point °C	Solvent	Molecular formula
8a	$C_6H_5NO_2$ (p)	82	197	Aq.ethanol	$C_{16}H_{12}BrN_3O_5$
8b	C_6H_5Cl (m)	80	214	Ethanol	$C_{16}H_{12}BrClN_{23}$
8c	$C_6H_5NO_2$ (o)	78	183	Methanol	$C_{16}H_{12}BrN_3O_5$
8d	C_6H_5Cl (o)	81	191	Ethanol	$C_{16}H_{12}BrClN_{23}$
8e	C_6H_5	75	175	Ethanol	$C_{16}H_{13}BrN_2O_3$
8f	$C_6H_5CH_3$	73	187	Aq.ethanol	$C_{17}H_{15}BrN_2O_3$

RESULTS AND DISCUSSION

1-(5-bromo-7-methoxy-1-benzofuran-2-yl)-3-(4-nitrophenyl) urea (8a): Yield 82%, melting point 197°C, Molecular formula $C_{16}H_{12}BrN_3O_5$, IR (cm^{-1}): 3341 cm^{-1} (NH), 1634 cm^{-1} (C=O), MS: *m/z* 406 and 408 (Mol. Weight: 406), ^{1}HNMR (500 MHz, DMSO-d_6): δppm 3.90 (s, 3H, OCH_3), 6.00(s, 2H, NH), 6.88-8.31(m 7H, Ar-H).

1-(5-bromo-7-methoxy-1-benzofuran-2-yl)-3-(4-chlorophenyl)urea (8b): Yield 80%, melting point 214°C, Molecular formula $C_{16}H_{12}BrClN_2O_3$,IR (cm^{-1}): 3234cm^{-1} (NH), 1646 cm^{-1} (C=O),MS: *m/z 395*and 393 (Mol. Weight: 395), ^{1}HNMR (500 MHz, DMSO-d_6): δppm 3.90 (s, 3H, OCH_3), 6.1 (s, 2H, NH), 6.89-7.81(m,7H, Ar-H).

1-(5-bromo-7-methoxy-1-benzofuran-2-yl)-3-(2-nitrophenyl)urea (8c): Yield 78%, melting point 183°C, Molecular formula $C_{16}H_{12}BrN_3O_5$, IR (cm^{-1}): 3451cm^{-1} (NH), 1649cm^{-1} (C=O), MS: *m/z* 404and 406 (Mol. Weight: 406), ^{1}HNMR (500 MHz, DMSO-d_6): δppm 3.89 (s, 3H, OCH_3), 6.05(s, 2H, NH), 7.00-7.90(m,7H, Ar-H).

1-(5-bromo-7-methoxy-1-benzofuran-2-yl)-3-(2-chlorophenyl)urea (8d): Yield 81%, melting point 191°C, Molecular formula $C_{16}H_{12}BrClN_2O_3$, IR (cm^{-1}): 3470cm^{-1} (NH), 1655 cm^{-1} (C=O),MS: *m/z 395*and 393 (Mol. Weight: 395), ^{1}HNMR (500 MHz, DMSO-d_6): δppm 3.89 (s, 3H, OCH_3), 6.12 (s, 2H, NH), 7.10-8.00(m,7H, Ar-H).

1-(5-bromo-7-methoxy-1-benzofuran-2-yl)-3-phenylurea (8e): Yield 75%, melting point 175°C, Molecular formula $C_{16}H_{13}BrN_2O_3$, IR (cm^{-1}): 3432 cm^{-1} (NH), 1650 cm^{-1} (C=O),MS: *m/z 359* and 361 (Mol. Weight: 361), ^{1}HNMR (500 MHz, DMSO-d_6): δppm 3.85 (s, 3H, OCH_3), 6.03 (s, 2H, NH), 7.00-7.88(m,8H, Ar-H).

1-(5-bromo-7-methoxy-1-benzofuran-2-yl)-3-(4-methylphenyl) urea (8f): Yield 73%, melting point 187°C, Molecular formula $C_{17}H_{15}BrN_2O_3$, IR (cm^{-1}): 3469 cm^{-1} (NH), 1653 cm^{-1} (C=O), MS: *m/z* 372 and 374 (Mol. Weight: 374), ^{1}HNMR (500 MHz, DMSO-d_6): 3.923 (s, 3H, OCH_3), 2.231(s, 3H, CH_3), 7.80 (s, 1H, NH), 6.391 (s, 1H, NH), 7.149- 7.78 (m 3H, Ar-H).

APPLICATION

Biological properties

Anti-bacterial activity: The antibacterial activity of the newly synthesized compounds were screened for the concentrations **50** µg mL^{-1} and **100** µg mL^{-1} using the organisms *S. aureus*, *E. coli*, and *P. aureginosa* by Cup-Plate Method which are compared with standard drugs penicillin and streptomycin. The zone of inhibition was calculated by measuring the minimum dimensions of the zone of inhibition of bacterial growth. The results are recorded in table 1.

All the compounds**6, 7a-c, 8a-f** of the series have shown good to moderate activity against all organisms (*S. aureus*, *E. coli* and *P. aureginosa*) compared standard drug penicillin and while comparing the standard drug Streptomycin all compounds exhibits considerable zone of inhibition for the concentrations **50 µg mL^{-1}** against the organism *E. coli*, all the compounds have exhibited less activity compared to the other organisms.

For the concentration **100 µg mL^{-1}** the compounds 8**c**, 8**d** have shown prominent activity against all the organisms, remaining compounds have shown considerable zone of inhibition which are compared to the standard drug penicillin. While comparing to standard drug streptomycin, all the compounds exhibit less activity. Antibacterial activity of the compounds 8**a-f** is shown in table 3.

Table 3. Antibacterial activity

Compounds	Zone of inhibition (in mm)					
	S. aureus		*E. coli*		*P. aureginosa*	
	50 µg mL^{-1}	100 µg mL^{-1}	50 µg mL^{-1}	100 µg mL^{-1}	50 µg mL^{-1}	100 µg mL^{-1}
3	14	16	13	17	14	18
6	13	17	12	16	15	19
7a	14	17	11	15	13	19
7b	12	17	13	17	14	17
7c	11	14	12	15	14	19
8a	13	17	10	15	11	16
8b	12	16	11	16	12	15
8c	14	19	11	17	13	16
8d	11	15	12	17	14	18
8e	12	14	11	14	12	16
8f	13	16	12	15	13	17
Standard						
Penicillin	15	21	16	20	17	23
Streptomycin	24	28	22	27	21	26
Control						
D.M.F.	Nil	Nil	Nil	Nil	Nil	Nil

Anti-fungal activity: The antifungal activities of the synthesized compoundswere performed against standard fungal strains *Aspergillus niger* and *Candida albicans* in DMF by the broth micro-dilution method. The MIC determination of the tested compounds was investigated in comparison with Griseofulvin by broth micro-dilution method.

Antifungal activity of these compounds for concentration **50 µg mL^{-1}** are shown in table 2. Here all the compounds exhibit considerable zone of inhibition against the organism *Aspergillus niger* than the organism *Candida albicans* which are compared with standard drug Griseofulvin.

For the concentration **100 µg mL^{-1}**, all the compounds exhibited good moderate zone of inhibition against the organism *Aspergillus niger* than the organism *Candida albicans* which are compared with standard drug Griseofulvin which is incorporated in table 2.

Table 2. Antifungal activity

Compounds	Zone of Inhibition (in mm)			
	Aspergillus niger		*Candida albicans*	
	50 µg mL^{-1}	100 µg mL^{-1}	50 µg mL^{-1}	100 µg mL^{-1}
3	13	18	12	18
6	14	17	13	16
7a	12	16	11	14
7b	13	17	10	16
7c	11	16	13	18
8a	16	19	15	20
8b	15	19	14	19
8c	13	18	12	17
8d	14	18	13	19
8e	13	17	12	16
8f	14	19	11	16
Standard				
Griseofulvin	21	26	22	27
Control				
D.M.F.	Nil	Nil	Nil	Nil

Antifungal activity of all the compounds exhibits good moderate zone of inhibition to the organisms *Aspergillus niger* and *Candida albicans* for the Concentration **50 µg mL^{-1}** which are compared to the standard drug Griseofulvin. And all most all compounds have shown excellent activity against the organism *Aspergillus niger* compared to other organism *Candida albicans.* Antifungal activity of all above said compounds for the concentration **100 µg mL^{-1}** have shown prominent activity against the organism *Aspergillus niger*, but for the organism *Candida albicans* these compounds exhibits less activity and these compounds were compared to standard drug Griseofulvin.

Antibacterial activity: Allthe compounds have exhibited considerable activity against the below said bacteria. The **3e** against *Staphylococcus aureus*, **3a** against *Staphylococcus albums*, exhibited very good antibacterial activity this is due to the effect of attachment of chloro and bromo substituted triazolothiadiazole on benzofuran moiety, but all **3**series compounds displayed less activity against *Klebsiella pneumoniae*. The compound **3c** exhibited minimum antibacterial activity this might be due to the attachment of electron donating methoxy group on substituted triazolo thiadiazole terminus. The results are shown in table 4.

Table 4. Antibacterial activity of synthetic compounds in MIC

Compound No.	Diameter of Zone of inhibition (mm)		
	Staphylococcus aureus	*Staphylococcus albus*	*Klebsiella pneumoniae*
DMSO	-	-	-
3a	12	16	12
3b	10	06	10
3c	09	06	10
3d	12	12	12
3e	15	08	12
Azithromycin	20	25	30

The compounds **4a** and **4e** exhibited potentive activity against the *Escherichia coli*, in 50 µg mL^{-1} and **4b** in 100 µg mL^{-1} have shown good zone of inhibition against *Staphylococcus aureus* due to

electron withdrawing hydroxyl and nitro group present on p- position of substituted phenyl ring. The compounds **6c** and **6e** have accounted very good activity in 50 µg $mL^{-1}$and 100 µg mL^{-1} respectively against *Pseudomonas aureginosa*. The compounds **4b, 4d** and **4c, 4e** have performed their antibacterial activity in higher zone in50 µg mL^{-1} and 100 µg mL^{-1} respectively against *Escherichia coli*, this enhanced antibacterial activity is due to again substituent effect of electron withdrawing group and among all bromo substituted analogs were shown significant results (Table 5).

Antifungal activity: he compound **2** and **3** series compounds displayed moderate antifungal activity in MIC, hence these compounds were found to have good zone of inhibition in higher concentration rather in MIC. The compound **4c** have exhibited good activity against above said fungi compared to other derivatives may be due to methoxy group substitution effect on triazolo thiadiazole analogue. The antifungal activities of test compounds were comparatively similar in both the concentration against *Candida albicans* and *Aspergillus niger*. The activity are given in table 6 and 7.

Table 5. Antibacterial activities of test compounds in (µg mL^{-1})

Test Compounds	Substituent 'R'	Zone of inhibition (in mm)					
		Gram positive		Gram-negative			
		Staphylococcus aureus		*Pseudomonas aureginosa*		*Escherichia coli*	
		50 µg mL^{-1}	100 µg mL^{-1}	50 µg mL^{-1}	100 µg mL^{-1}	50 µg mL^{-1}	100 µg mL^{-1}
2	--	13	17	14	19	13	18
4a	C_6H_5	14	18	13	17	15	19
4b	$C_6H_4NO_2$(p)	12	21	13	17	17	20
4c	$C_6H_4OCH_3$(p)	13	17	15	17	16	21
4d	C_6H_4Cl(m)	15	16	14	18	17	18
4e	C_6H_4OH(p)	15	20	13	20	16	21
Penicillin		15	22	--	--	--	--
Streptomycin		--	--	21	28	22	27

Table 6. Antifungal activities of test compounds 5(a-e) by MIC Method

Test Compounds	Fungal strain	
	Aspergillus niger	*Candida albicans*
3a	5.00	5.10
3b	5.50	5.50
3c	5.25	5.10
3d	5.00	5.50
3e	5.50	5.25
Fluconazole	13.25	13.50

Table 7. Antifungal activities of test compounds in (50 and 100 µg mL^{-1})

Compound No.	Zone of inhibition (in mm)			
	Candida albiacans		*Aspergillus niger*	
	50 µg mL^{-1}	100 µg mL^{-1}	50 µg mL^{-1}	100 µg mL^{-1}
2	12	17	14	20
4a	13	16	13	19
4b	15	19	14	18
4c	13	20	15	20
4d	14	17	14	16
4e	15	18	13	16
Griseofulvin	22	28	21	26

CONCLUSION

All the compounds of the compounds **6, 7a-c** and **8a-f** have shown good moderate anti-bacterial activity against all organisms *S. aureus, E. coli,* and *P.aureginosa* compared standard penicillin, while comparing the standard drug Streptomycin all compounds exhibits Considerable zone of inhibition for the concentrations **50 µg mL^{-1}** against the organism *E.coli* all most all the compounds have exhibit less activity compared to the other organisms. For the concentration **100 µg mL^{-1}** the compounds **8c, 8d**have shown prominent activity against all the organisms, remaining compounds have shown considerable zone of inhibition which are compared to the standard drugs penicillin.

Antifungal activity of the all the compounds **6,7a-c** and **8a-f** for Concentration **50 µg mL^{-1}** haveshown considerable zone of inhibition against the organism *Aspergillus niger* than the organism *Candida albicans* and For the concentration **100 µg mL^{-1}**, all the compounds exhibits good to moderate zone of inhibition against the all the organisms which are compared with standard drug Griseofulvin.

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