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SYNTHESIS, ANTIMICROBIAL AND ANTIOXIDANT ACTIVITIES OF 3-SUBSTITUTEDMETHYLENEAMINO-2-BENZOYLBENZOFURANS AND INDOLE DERIVATIVES

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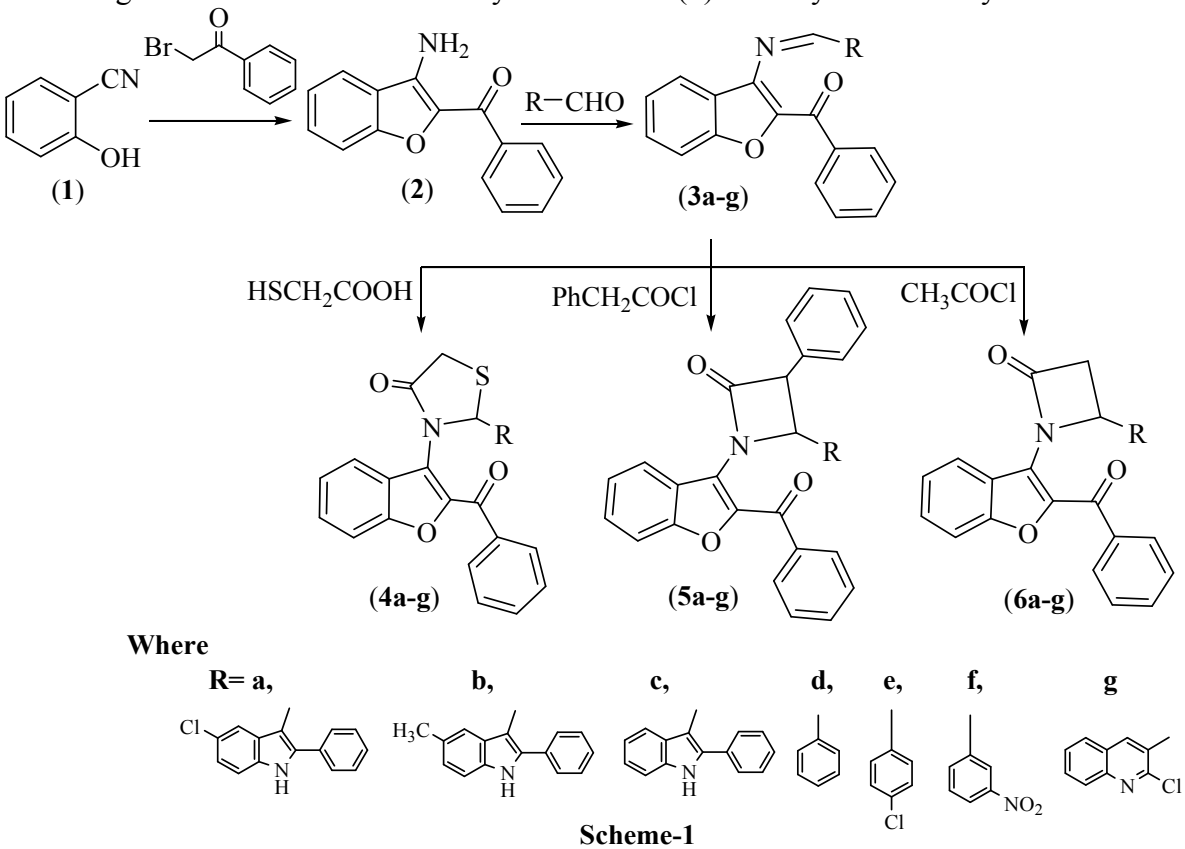
Abstract
The main aim of the present study was to develop antimicrobial and antioxidant compounds. As a part of systematic investigation of synthesis and biological activities of indole analogues linked to biological active pharmacophores, we report herein the antimicrobial and antioxidant activities of some novel indole derivatives viz., 3-substitutedmethyleneamino- 2-benzoylbenzofurans (**3a-g**), 3-(2-benzoylbenzofuran-3-yl)-2-substitutedthiazolidin-4-ones (**4a-g**), 1-(2-benzoylbenzofuran-3-yl)-4-substituted-3-phenylazetidin-2-ones (**5a-g**) and 1-(2-benzoylbenzofuran-3-yl)-4-substitutedazetidin-2-ones (**6a-g**). Antibacterial activity results revealed that, compound **3a** showed good zone of inhibition versus *E. Coli, K. Penumonia* and *P. Aeruginosa*, whereas the compound **3a** showed good antifungal activity versus *A. Niger* and *A. Terrus*. In case of antioxidant activity, compounds **3b** and **3f** showed promising radical scavenging activity, ferric ions (Fe^{+3}) reducing antioxidant power (FRAP) and metal chelating activity.

Keywords: Benzofuran, indole, thiazolidinone, azetidinone, antimicrobial, antioxidant activity.

Introduction
Infectious diseases caused by micro and myco organisms, viz., bacteria, fungi, viruses and parasites are still a major threat to human health, despite tremendous inventions in drug chemistry. Antimicrobial resistance refers to micro-organism that has developed the ability to inactivate, exclude or block the inhibitory or lethal mechanism of the antimicrobial agents[i].
The number of heterocyclic derivatives containing oxygen and nitrogen atom possess broad spectrum of biological activities[ii]. In addition, antioxidant compounds in food play important roles as health-protein factor. Scientific evidence suggests that antioxidant reduces the risk for chronic diseases including cancer and heart diseases. Benzofuran derivatives possess a wide range of biological activities. They have been reported to possess antimicrobial[iii-vi], antitumour[vii,viii], anti-inflammatory[ix], etc activities. Numerous methods for the synthesis of indole derivatives and their various reactions offer enormous scope in the field of medicinal chemistry to prepare compounds exhibiting promising biological activities such as antitumor[x-xiii], anti-inflammatory[xiv-xvi], antioxidant[xxii], etc. Also 4-thiazolidinones[xxiii-xx] and 2-azetidinones[xxi-xxiii] have been reported to play an important role in medicinal chemistry.

Result and discussion

The starting material 3-amino-2-benzoylbenzofuran (**2**) was synthesized by the reaction of



Scheme-1

salicylonitrile (**1**) with phenacyl bromide in anhydrous acetone containing potassium carbonate at refluxed temperature[xxiv]. Compound (**2**) on condensation with aryl or heteroaryl aldehydes in 1,4-dioxane at reflux temperature yielded 3-(substituted methyleneamino)-2-benzoylbenzofurans (**3a-g**). Compounds (**3a-g**) on cyclocondensation with thioglycolic acid, phenyl acetyl chloride and acetyl chloride afforded 3-(2-benzoylbenzofuran-3-yl)-2-substitutedthiazolidin-4-ones (**4a-g**), 1-(2-benzoylbenzofuran-3-yl)-4-substituted-3-phenylazetidin-2-ones (**5a-g**) and 1-(2-benzoylbenzofuran-3-yl)-4-substitutedazetidin-2-ones (**6a-g**) (**Scheme-1**).

Antimicrobial activity

All the synthesized compounds (**3-6**) were evaluated for their antibacterial activity against *Escherichia coli* (MTCC-723)*, Staphylococcus Aureus* (ATCC-29513)*, Klebsiella penumoniae* (NCTC-13368) and *Pseudomonas aeruginosa* (MTCC-1688) and for antifungal activity against *Aspergillus nizer* (MTCC-281)*, Aspergillus oryzae* (MTCC-3567^T)*, Aspergillus terrus* (MTCC-1782) and *Aspergillus flavus* (MTCC-1973) by cup-plate method at concentration 1000, 750 and 500 µg/ml following reported procedure[xxv]. The zones of inhibition (in mm) were compared with the standards streptomycin and flucanazole for antibacterial and antifungal activity, respectively. The results are reported in **Table-1** and **2**.

The investigation of antibacterial screening revealed that, compounds **3a**, **3b**, **4a**, **4d**, **4e**, **5a** and **5b** exhibited maximum zone of inhibition against *E. Coli,* whereas compounds **4f**, **5e**, **6b** and **6c** showed maximum zone of inhibition against *S. Aureus*. Compounds **3a**, **3e**, **3f**, **4f**, **4g** and **5b**

exhibited the maximum zone of inhibitory against *K. Penumoniae.* Compounds **3a** and **3g** exhibited the good zone of inhibition against *P. Aeruginosa.*

In case of antifungal screening, compounds **3a**, **3c**, **3f**, **5g**, **6a** and **6e** exhibited promising activity against *A. Niger,* whereas compounds **4a** and **6a** exhibited maximum zone of inhibition against *A. Oryzae.* Compounds **3a, 4a, 4f, 5e** and **6b** exhibited maximum zone of inhibition against *A. Terrus,* whereas compounds **3b** and **4f** exhibited good zone of inhibitory against *A. Flavus*.

Table 1: *In vitro* antibacterial activities of compounds 3-6

CompNo	Antibacterial activity (zone of inhibition in mm)*											
	E. Coli			*S. Aureus*			*K. Penumoniae*			*P. Aeruginosa*		
	1000	750	500	1000	750	500	1000	750	500	1000	750	500
3a	14	13	12	10	05	05	14	13	11	12	12	11
3b	13	12	12	11	04	05	08	08	05	03	03	05
3c	05	05	04	02	02	04	09	06	06	04	04	05
3d	08	08	09	02	02	02	05	05	07	09	09	09
3e	09	09	09	09	06	07	15	13	12	10	09	06
3f	02	02	05	10	05	01	14	12	12	10	07	02
3g	09	09	09	11	01	02	11	09	05	13	13	11
4a	14	13	12	08	08	01	10	10	09	09	08	05
4b	04	04	05	09	09	09	02	02	05	09	09	09
4c	06	02	03	11	04	09	09	10	04	04	09	08
4d	13	12	12	08	08	05	09	09	05	09	09	09
4e	14	12	12	10	10	11	11	09	06	11	07	07
4f	09	09	09	13	12	12	14	13	12	10	08	07
4g	09	08	08	05	05	06	15	13	11	05	06	08
5a	14	12	12	11	09	01	11	09	10	10	09	08
5b	13	12	12	02	02	05	14	12	12	05	05	08
5c	09	04	10	04	05	05	03	03	05	06	06	06
5d	08	08	09	11	08	08	05	05	06	02	02	05
5e	08	05	01	13	12	12	09	09	09	02	05	06
5f	05	04	03	09	09	05	02	02	05	00	00	00
5g	09	03	04	09	09	09	00	00	00	00	02	02
6a	02	07	05	09	06	06	06	06	08	05	05	02
6b	05	05	05	14	12	11	08	05	03	09	05	04
6c	08	04	02	15	14	14	05	05	02	10	09	09
6d	08	05	09	02	02	02	08	08	09	08	08	09
6e	05	05	03	00	00	00	10	10	04	11	07	08
6f	09	09	09	--	00	00	10	10	09	09	07	05
6g	05	05	05	02	02	05	10	10	08	10	05	03
Std	15	14	13	16	15	14	16	14	13	14	14	13

Zone of inhibition in millimeter,

Std= Streptomycin,

*Concentration in micro gm/ml

Table 2: *In vitro* antifungal activity of compounds 3-6

Comp No	Antifungal activity (zone of inhibition in mm)*											
	A. Niger			*A. Oryzae*			*A. Terrus*			*A. Flavus*		
	1000	750	500	1000	750	500	1000	750	500	1000	750	500
3a	14	12	12	10	10	08	13	12	12	09	09	10
3b	03	05	03	10	10	05	06	06	08	13	13	13
3c	13	13	11	08	08	02	02	02	03	08	10	09
3d	10	05	02	03	03	05	08	08	05	10	10	05
3e	10	09	03	05	05	08	08	06	02	11	11	09
3f	14	13	12	00	00	00	09	05	02	09	09	09
3g	10	08	04	00	00	05	10	09	01	05	05	05
4a	10	09	05	14	14	13	13	11	11	00	00	00
4b	10	05	01	09	09	06	07	05	04	00	00	00
4c	08	08	09	10	10	03	09	08	02	05	05	06
4d	03	03	08	08	08	08	09	09	09	02	02	02
4e	05	05	08	--	02	05	05	03	01	06	06	06
4f	09	05	08	00	00	02	12	12	12	14	14	12
4g	09	09	09	--	00	00	04	04	04	10	10	06
5a	10	04	02	09	09	09	09	09	10	00	00	00
5b	00	00	00	02	02	02	00	03	05	00	05	06
5c	10	09	05	10	10	05	08	08	08	00	00	00
5d	04	04	05	10	10	08	10	09	08	03	03	05
5e	08	08	08	05	05	05	12	12	12	08	08	04
5f	05	06	08	05	05	06	10	08	04	06	06	05
5g	13	12	12	02	02	02	00	00	00	03	05	08
6a	14	13	12	14	13	13	03	03	03	00	00	00
6b	09	06	03	10	10	05	13	12	12	02	02	04
6c	10	09	02	08	08	04	02	02	05	02	02	02
6d	02	09	09	03	00	00	00	05	08	11	07	04
6e	14	12	12	04	03	08	08	08	09	09	09	09
6f	--	01	01	05	04	06	10	06	02	10	10	08
6g	--	00	00	05	05	08	09	05	02	10	10	03
Std	15	14	13	15	15	14	14	14	13	15	15	14

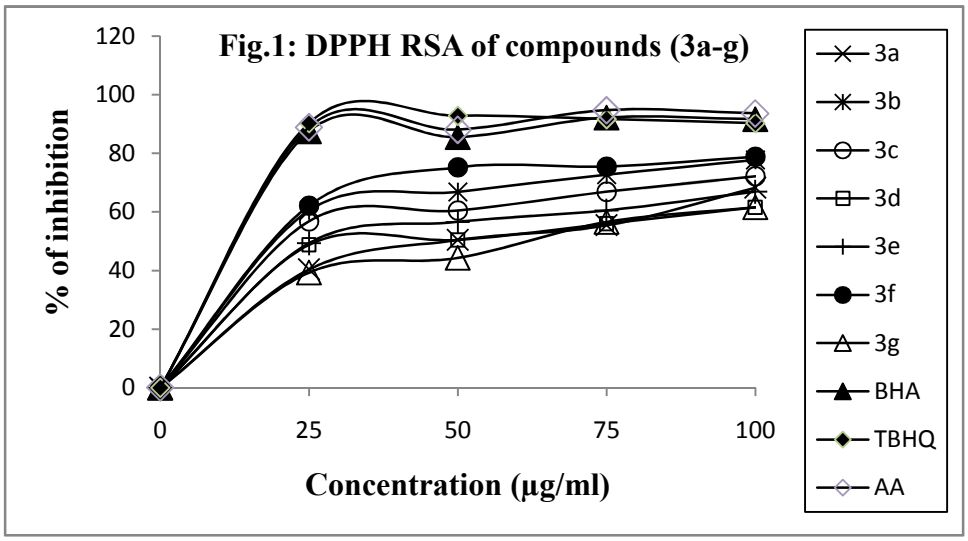
Zone of inhibition measured in millimeter,
Std= Flucanazole,
*Concentration in micro gm/ml

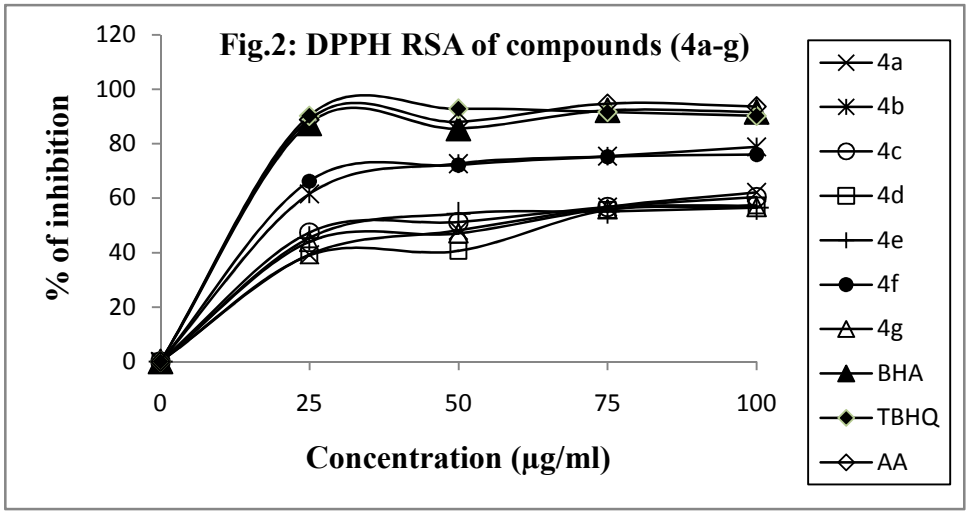
Antioxidant activities

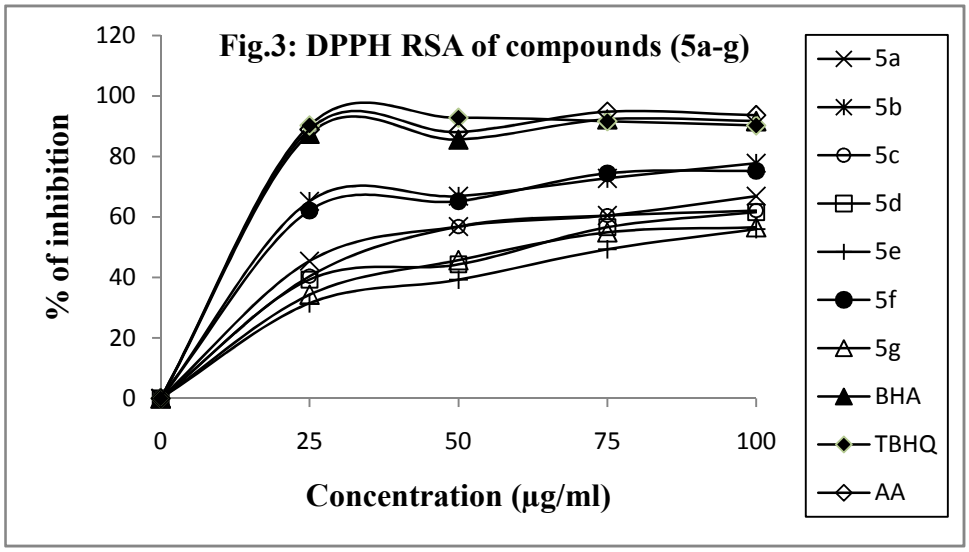
I) 1, 1-diphenyl-2-picryl hydrazyl (DPPH) radical scavenging activity (RSA)

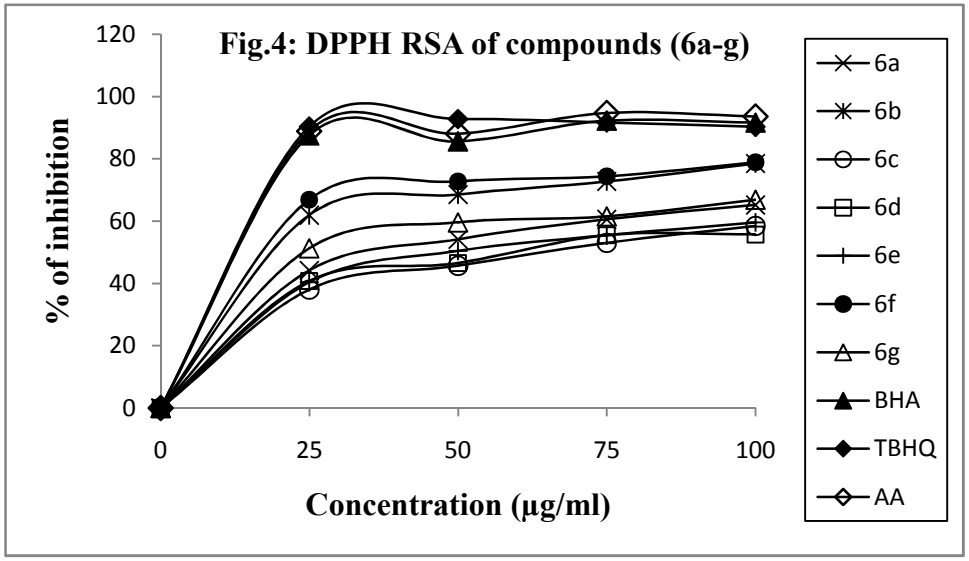
Free radicals are atomic or molecular species with unpaired electrons that are highly reactive. They take part in chemical reactions and play an important role in many chemical processes. The RSA of synthesized compounds (**3-6**) was carried out using Hatano's method[xxvi] and the result are compared with the standards 2-tert-butyl-4-methoxy phenol (butylated hydroxyl anisole, BHA), 2-(1, 1-dimethylethyl)-1, 4-benzenediol (tertiary butylated hydroquinone, TBHQ) and Ascorbic acid (AA).

The analysis of results (Figs. 1-4) indicated that, compounds **3b**, **3f**, **4b**, **4f**, **5b** and **6f** exhibited good radical scavenging activity at conc. of 50 µg/ml, compounds **3c**, **5f** and **6b** showed radical scavenging ability at conc. of 75 µg/ml. Whereas compounds **3a**, **5a** and **6g** exhibited good radical scavenging activity at conc. 100 µg/ml.







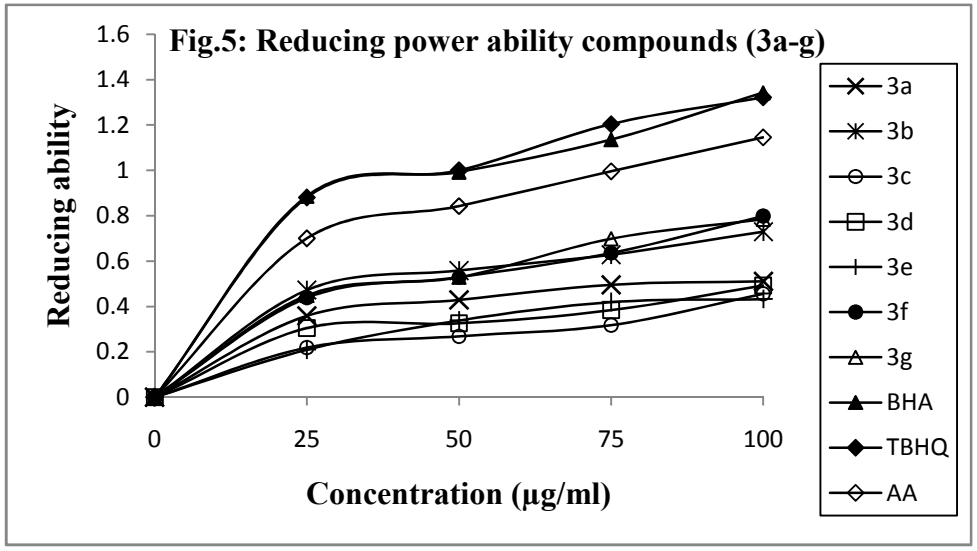


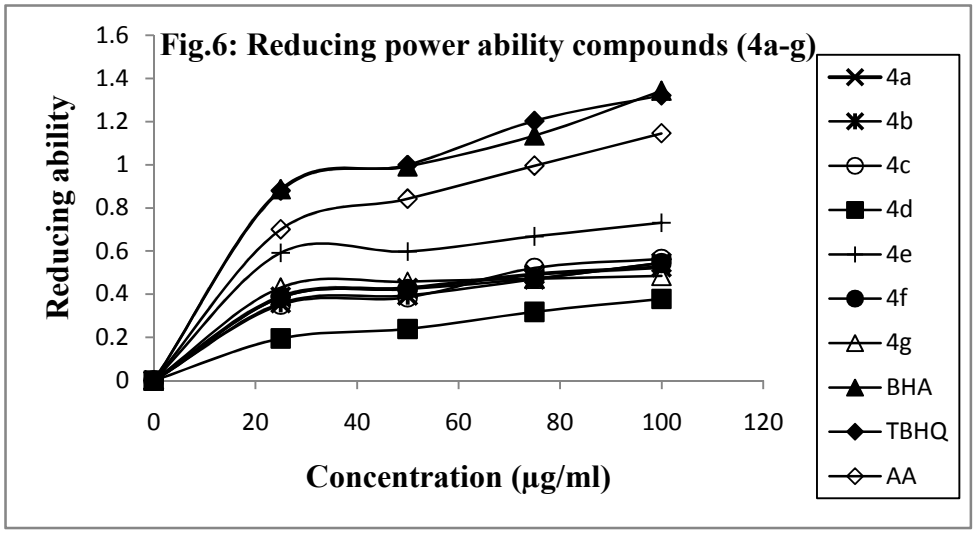
II) Ferric ions (Fe^{+3}) reducing antioxidant power (FRAP)

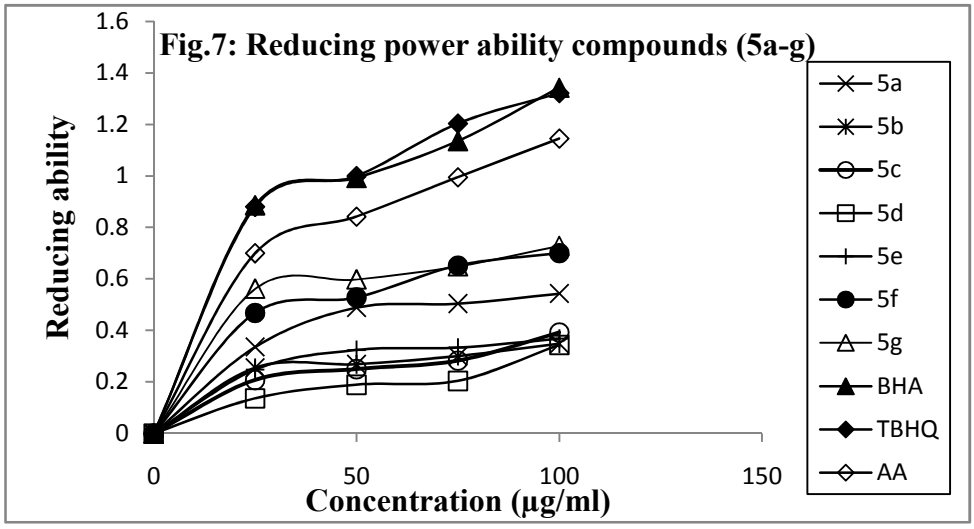
The ferric ion (Fe^{3+}) is the relatively biologically inactive form of iron. However, it can be reduced to an active Fe^{2+}, depending on condition, particularly pH[xxvii] and oxidized back through Fenton type reaction with production of hydroxyl radical or Haber-Weiss reaction with superoxide anions. Reducing power is to measure the reductive ability of an antioxidant and it is evaluated by the transformation of Fe^{3+} to Fe^{2+} by donation of an electron in the presence of test compounds. Therefore, the Fe^{2+} can be monitored by measuring the formation of Perl's Prussian blue at 700 nm.

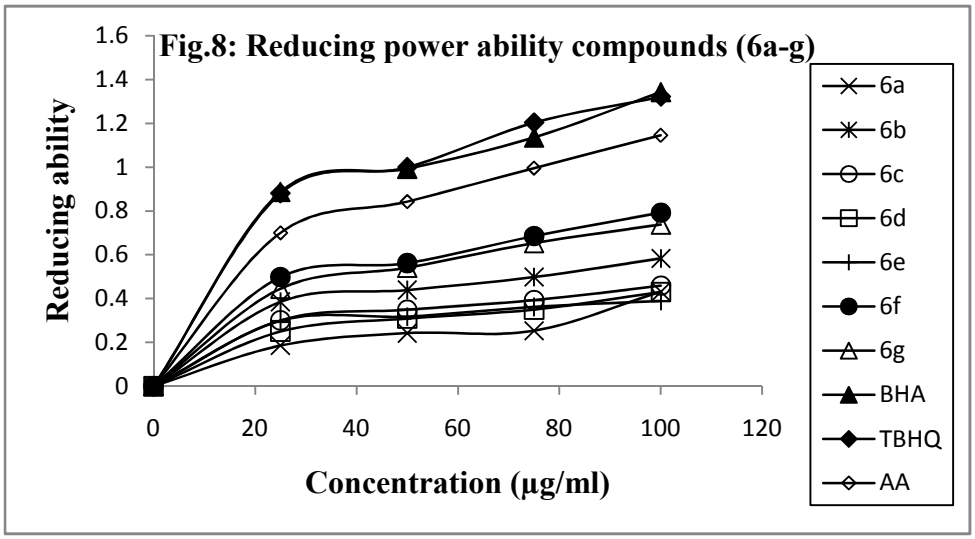
The FRAP of synthesized compounds (**3-6**) was determined at four different concentrations (25, 50, 75 and 100 µg/mL) at pH 6.6 by Oyaizu method[xxviii] using BHA, TBHQ and AA as

standards. The higher absorbance of the reaction mixture indicated greater the reducing power of the test compounds. The analysis of results (Figs. 5-8) suggested that, compounds **4e** and **5g** exhibited good reducing activity at 25 µg/ml concentration, whereas compounds **6f** and **6g** showed reducing power at 50 µg/ml concentration. Compounds **3b**, **3f**, **3g** and **5f** exhibited good reducing activity at 75 µg/ml concentration.









III) Ferrous ions (Fe^{+2}) metal chelating activity

The chelating effect of ferrous ions (Fe^{2+}) towards the test compounds (**3-6**) and standards was determined by following Dinis method[xxix] and the result were compared with standards BHA, TBHQ and AA. Ferrozine can make complex with ferrous ion. In the presence of chelating agents, complex (red colored) formation is interrupted and as a result, the red color of the complex is decreased. Thus, the chelating effect of the coexisting chelator can be determined by measuring the rate of color reduction.

The analysis of results (Figs. 9-12) indicated that, compounds **3b** and **3g** showed good metal chelating activity at 25 µg/ml concentration, whereas compound **4b** exhibited promising metal chelating activity at 50 µg/ml concentration. Compounds **3a**, **3f**, **4f**, **5b** and **6b** exhibited good metal chelating activity at 75 µg/ml concentration, whereas compounds **3c** and **4g** exhibited good metal chelating activity at 100 µg/ml concentration.

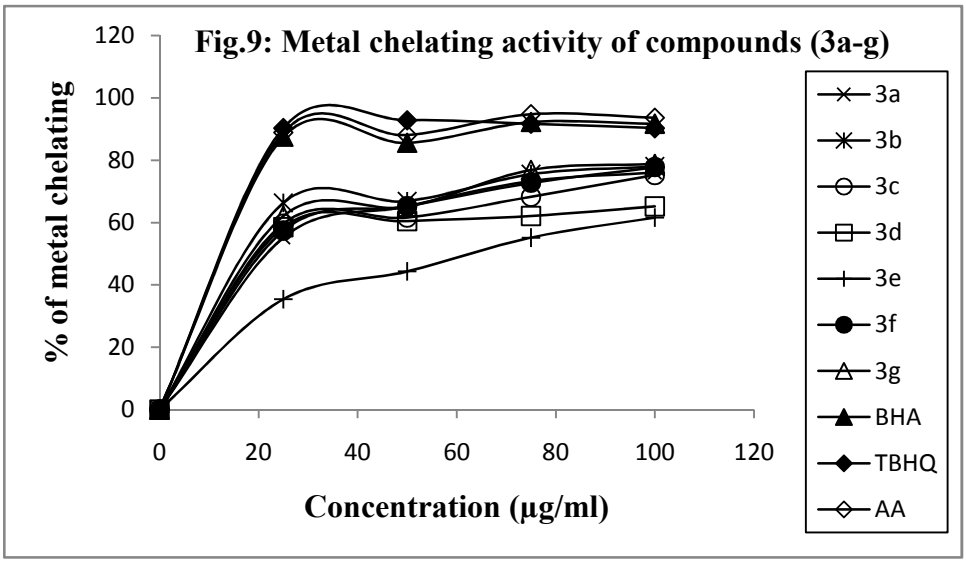


Fig.9: Metal chelating activity of compounds (3a-g)
% of metal chelating
Concentration (µg/ml)
0
20
40
60
80
100
120
3a
3b
3c
3d
3e
3f
3g
BHA
TBHQ
AA

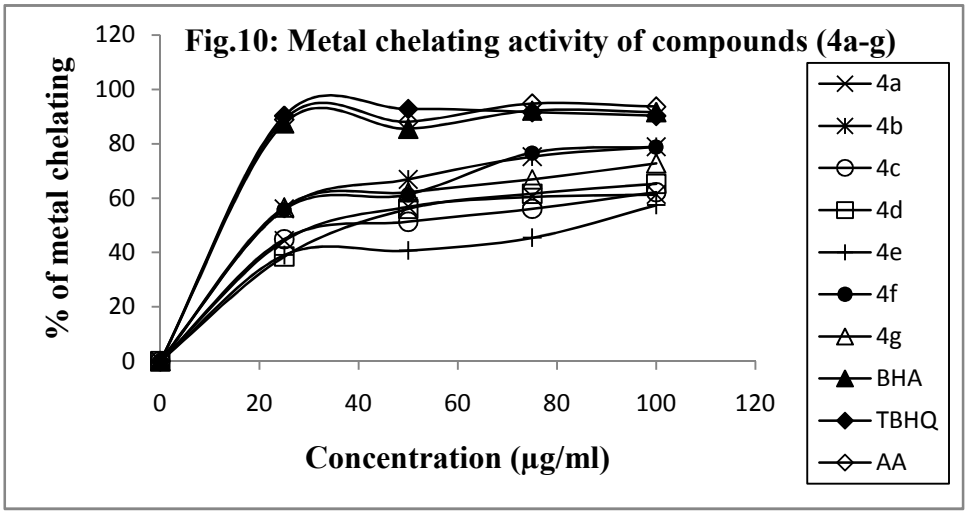


Fig.10: Metal chelating activity of compounds (4a-g)
% of metal chelating
Concentration (µg/ml)
0
20
40
60
80
100
120
4a
4b
4c
4d
4e
4f
4g
BHA
TBHQ
AA

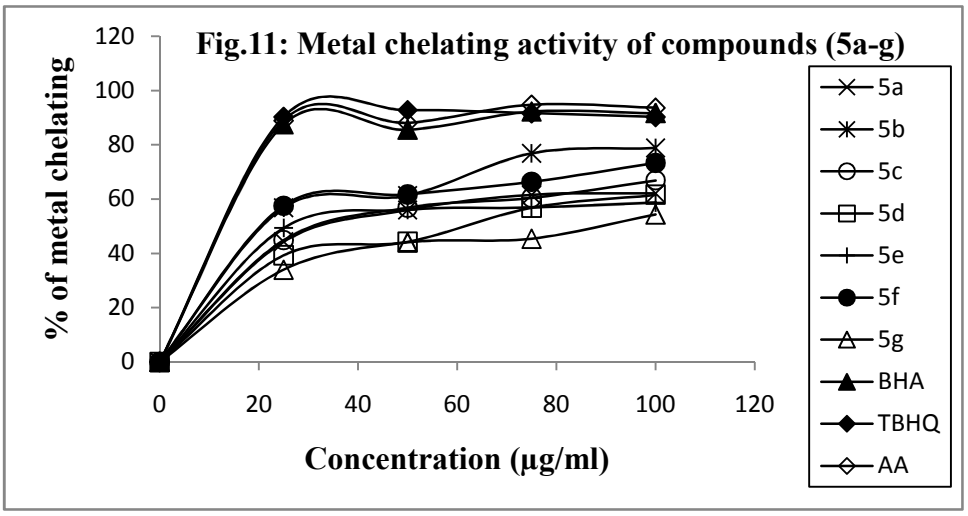
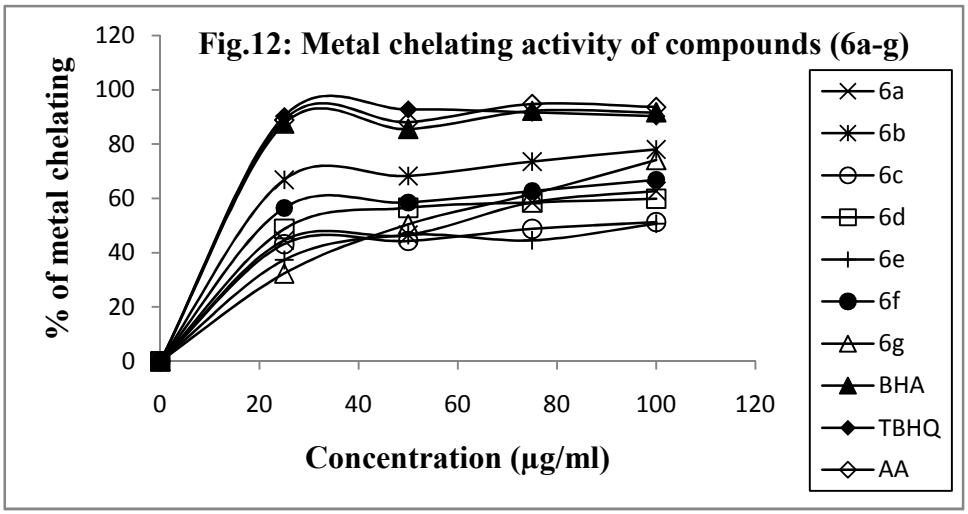


Fig.11: Metal chelating activity of compounds (5a-g)
% of metal chelating
Concentration (µg/ml)
0
20
40
60
80
100
120
5a
5b
5c
5d
5e
5f
5g
BHA
TBHQ
AA



Experimental Section

All the reagents were obtained commercially and used by further purification. Melting points were determined in open capillaries and are uncorrected. Purity of the compounds was checked by TLC using silica gel-G coated aluminium plates (Merck) and spots were visualized by exposing the dry plates to iodine vapours. The IR (KBr) spectra were recorded with a Perkin-Elmer spectrum one FT-IR spectrometer. The ^{1}H NMR (DMSO-d_6) spectra recorded on a Bruker NMR (500 MHz) and the chemical shifts were expressed in ppm (δ scale) downfield from TMS. Mass spectra were obtained on JEOL GC-MATE II GC-MS mass spectrometer. Elemental analysis was carried out using Flash EA 1112 series elemental analyzer.

Synthesis of 3-amino-2-benzoylbenzo[b]furans[xxiv] **(2)**

A mixture of salicylonitrile **1** (0.01 mol), phenacyl bromide (0.01 mol) and anhydrous potassium carbonate (30 g) was gently refluxed in anhydrous acetone for 8 hr. The mixture was cooled and poured into ice-cold water. The separated product was filtered, washed thoroughly with cold water, dried and recrystallized from ethanol to afford **2.**

5-substituted-2-phenylindol-3-carboxyaldehydes were prepared by following literature procedure[xxx]

General procedure for the synthesis of 3-substitutedmethyleneamino-2-benzoylbenzofurans (3a-g)

A solution of compound **2** (0.01 mol) and aryl or hetroaryl aldehydes (0.01 mol) in 1, 4-dioxane (40 mL) containing glacial acetic acid (2 mL) were refluxed for 8 hr. The excess of solvent was removed under reduced pressure. The residual solution after cooling to room temparature was poured into ice-cold water. The solid product thus obtained was filtered, washed thoroughly with cold water, dried and recrystallized from suitable solvent to furnish **3a-g**.

3-[(5'-Chloro-2'-phenyl-1*H*-indol-3'-yl)methyleneamino]-2-benzoylbenzofuran (3a)

Yield: 75%, mp 268-69 ºC; Rf, 0.55 ethyl acetate: ethanol (7:3) mixture; FTIR (KBr) cm^{-1}: 3434 (Indole NH), 1626 (C=O), 1574 (C=N); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.60 (s, 1H, indole

NH), 9.00 (s, 1H, N=CH), 7.30-8.20 (m, 17H, Ar-H); MS (EI): *m/z* 474 (M^+); 476 (M^++2). Anal. % $C_{30}H_{19}N_2O_2Cl$: C, 75.87; H, 4.03; N, 5.90 Found: C, 75.90; H, 4.08; N, 5.85.

3-[(5'-Methyl-2'-phenyl-1*H*-indol-3'-yl)methyleneamino]-2-benzoylbenzofuran (3b)
Yield: 66%, mp 248-49 ºC; Rf, 0.49 ethyl acetate: ethanol (1:2) mixture; FTIR (KBr) cm^{-1}: 3300 (Indole NH), 1626 (C=O), 1574 (C=N); ^1H NMR (DMSO-d_6, δ, ppm): 12.60 (s, 1H, indole NH), 8.95 (s, 1H, N=CH), 6.78-7.95 (m, 17H, Ar-H), 2.42 (s, 3H, CH_3); Anal. % $C_{31}H_{22}N_2O_2$: C, 81.91; H, 4.88; N, 6.16 Found: C, 81.88; H, 4.80; N, 6.16.

3-[(2'-Phenyl-1*H*-indol-3'-yl)methyleneamino]-2-benzoylbenzofuran (3c)
Yield: 78%, mp 292-93 ºC; Rf, 0.77 ethyl acetate: ethanol (6:4) mixture; FTIR (KBr) cm^{-1}: 3400 (Indole NH), 1600 (C=O), 1512 (C=N); ^1H NMR (DMSO-d_6, δ, ppm): 12.40 (s, 1H, indole NH), 9.00 (s, 1H, N=CH), 7.00-8.10 (m, 18H, Ar-H); Anal. % $C_{30}H_{20}N_2O_2$: C, 81.80; H, 4.58; N, 6.36 Found: C, 81.75; H, 4.50; N, 6.40.

3-Benzylideneamino-2-benzoylbenzofuran (3d)
Yield: 69%, mp 253-54 ºC; Rf, 0.67 ethyl acetate: ethanol (8:2) mixture; FTIR (KBr) cm^{-1}: 3348 (Indole NH), 1610 (C=O), 702 (C=N); ^1H NMR (DMSO-d_6, δ, ppm): 12.30 (s, 1H, indole NH), 9.10 (s, 1H, N=CH), 6.85-7.90 (m, 14H, Ar-H); Anal. % $C_{22}H_{15}NO_2$: C, 81.21; H, 4.65; N, 4.30 Found: C, 81.16; H, 4.60; N, 4.25.

3-(4-Chlorobenzylideneamino)-2-benzoylbenzofuran (3e)
Yield: 69%, mp 284-85 ºC; Rf, 0.47 ethyl acetate: ethanol (6:4) mixture; FTIR (KBr) cm^{-1}: 3318 (indoleNH), 1620 (C=O), 1538 (C=N); ^1H NMR (DMSO-d_6, δ, ppm): 12.60 (s, 1H, indole NH), 8.78 (s, 1H, N=CH), 7.00-8.08 (m, 13H, Ar-H); Anal. % $C_{22}H_{14}NO_2$: C, 73.44; H, 3.92; N, 3.89 Found: C, 73.40; H, 3.84; N, 3.80.

3-(3-Nitrobenzylideneamino)-2-benzoylbenzofuran (3f)
Yield: 65%, mp 275-76 ºC; Rf, 0.47 ethyl acetate: ethanol (4:6) mixture; FTIR (KBr) cm^{-1}: 3333 (indoleNH), 1600 (C=O), 1513 (C=N), 1473 (NO_2); ^1H NMR (DMSO-d_6, δ, ppm) 12.50 (s, 1H, indole NH), 9.00 (s, 1H, N=CH), 7.00-8.00 (m, 13H, Ar-H); Anal. % $C_{22}H_{14}N_2O_4$: C, 71.35; H, 3.81; N, 7.56 Found: C, 71.40; H, 3.73; N, 7.60.

3-[(2-Chloroquinolin-3-yl)methyleneamino]-2-benzoylbenzofuran (3g)
Yield: 60%, mp 298-99 ºC; Rf, 0.75 ethyl acetate: ethanol (7:3) mixture; FTIR (KBr) cm^{-1}: 3300 (indoleNH), 1600 (C=O), 1542 (C=N); ^1H NMR (DMSO-d_6, δ, ppm) 12.40 (s, 1H, indole NH), 9.00 (s, 1H, N=CH), 6.58-7.65 (m, 15H, Ar-H); Anal. % $C_{25}H_{15}N_2O_2Cl$: C, 73.08; H, 3.68; N, 6.82 Found: C, 72.96; H, 3.73; N, 6.89.

General procedure for synthesis of 3-(2-benzoylbenzofuran-3-yl)-2-substitutedthiazolidin-4-ones (4a-g)

Compounds **3a-g** (0.01 mol), thioglycolic acid (0.01mol) containing a pinch of anhydrous zinc chloride was refluxed in DMF (30ml) for 8 hr. The mixture was cooled and poured into ice-cold water. The separated precipitate was filtered, washed with saturated sodium carbonate solution to remove unreacted thioglycolic acid followed by cold-water, dried and recrystallized from

suitable solvent to get pure **4a-g**. Physical and spectral data of compounds are tabulated in **Table-6.3** and **6.4**.

3-(2-Benzoylbenzofuran-3-yl)-2-(5'-chloro-2'-phenyl-1*H*-indol-3'-yl)thiazolidin-4-one (4a)
Yield: 64%, mp 250-51 ºC; Rf, 0.51 ethyl acetate: ethanol (8:2) mixture; FTIR (KBr) cm^{-1}: 3434 (indoleNH), 1749 (C=O), 1626 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm): 11.70 (s, 1H, indole NH), 6.80-7.80 (m, 17H, Ar-H), 4.50 (s, 1H, N-CH), 3.80 (s, 2H, CH_2CO); MS (EI): *m/z* 548 (M^+); 550 (M^++2). Anal. % $C_{32}H_{21}N_2ClO_3S$: C, 70.00; H, 3.80; N, 5.10 Found: C, 70.08; H, 3.90; N, 5.05.

3-(2-Benzoylbenzofuran-3-yl)-2-(5'-methyl-2'-phenyl-1*H*-indol-3'-yl)thiazolidin-4-one (4b)
Yield: 74%, mp 292-93 ºC; Rf, 0.77 ethyl acetate: acetone (6:4) mixture; FTIR (KBr) cm^{-1}: 3400 (indoleNH), 1740 (C=O), 1633 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.00 (s, 1H, indole NH), 7.00-8.09 (m, 17H, Ar-H), 5.00 (s, 1H, N-CH), 3.95 (s, 2H, CH_2CO), 2.68 (s, 3H, CH_3); Anal. % $C_{33}H_{24}N_2O_3S$: C, 74.89; H, 4.58; N, 5.30. Found: C, 74.89; H, 4.65; N, 5.25.

3-(2-Benzoylbenzofuran-3-yl)-2-(2'-phenyl-1*H*-indol-3'-yl)thiazolidin-4-one (4c)
Yield: 68%, mp 248-49 ºC; Rf, 0.44 ethyl acetate: acetone (1:2) mixture; FTIR (KBr) cm^{-1}: 3430 (indoleNH), 1740 (C=O), 1628 (C=O); ^{1}H NMR (DMSO-d_6, □, ppm): 11.60 (s, 1H, indole NH), 6.80-7.80 (m, 18H, Ar-H), 4.50 (s, 1H, N-CH), 3.80 (s, 2H, CH_2CO); Anal. % $C_{32}H_{22}N_2O_3S$: C, 79.69; H, 4.31; N, 5.44. Found: C, 74.75; H, 4.25; N, 5.50.

3-(2-Benzoylbenzofuran-3-yl)-2-phenylthiazolidin-4-one (4d)
Yield: 75%, mp 254-55 ºC; Rf, 0.55 ethyl acetate: acetone (8:2) mixture; FTIR (KBr) cm^{-1}: 3365 (indoleNH), 1735 (C=O), 1628 (C=O); ^{1}H NMR (DMSO-d_6, δ ppm): 12.00 (s, 1H, indole NH), 7.00-8.10 (m, 14H, Ar-H), 4.95 (s, 1H, N-CH), 3.48 (s, 2H, CH_2CO); Anal. % $C_{24}H_{17}NO_3S$: C, 72.16; H, 4.29; N, 3.51. Found: C, 72.19; H, 4.35; N, 3.45.

3-(2-Benzoylbenzofuran-3-yl)-2-(4-chlorophenyl)thiazolidin-4-one (4e)
Yield: 81%, mp 221-22 ºC; Rf, 0.45 ethyl acetate: acetone (2:8) mixture; FTIR (KBr) cm^{-1}: 3425 (indoleNH), 1740 (C=O), 1615 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.10 (s, 1H, indole NH), 7.10-8.15 (m, 14H, Ar-H), 5.00 (s, 1H, N-CH), 3.98 (s, 2H, CH_2CO); Anal. % $C_{24}H_{16}NO_3ClS$: C, 66.43; H, 3.72; N, 3.23. Found: C, 66.39; H, 3.78; N, 3.33.

3-(2-Benzoylbenzofuran-3-yl)-2-(2-nitrophenyl)thiazolidin-4-one (4f)
Yield: 73%, mp 175-76 ºC; Rf, 0.50 ethyl acetate: acetone (3:7) mixture; FTIR (KBr) cm^{-1}: 3428 (indoleNH), 1740 (C=O), 1626 (C=O), 1479 (NO_2); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.00 (s, 1H, indole NH), 7.00-8.05 (m, 13H, Ar-H), 5.00 (s, 1H, N-CH), 4.10 (s, 2H, CH_2CO); Anal. % $C_{24}H_{16}N_2O_5S$: C, 64.86; H, 3.63; N, 6.30. Found: C, 64.78; H, 3.70; N, 6.41.

3-(2-Benzoylbenzofuran-3-yl)-2-(2-chloroquinolin-3-yl)thiazolidin-4-one (4g)
Yield: 69%, mp 188-89 ºC; Rf, 0.58 ethyl acetate: acetone (6:4) mixture; FTIR (KBr) cm^{-1}: 3420 (indoleNH), 1720 (C=O), 1630 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.00 (s, 1H, indole NH), 7.00-8.00 (m, 15H, Ar-H), 4.58 (s, 1H, N-CH), 4.00 (s, 2H, CH_2CO); Anal. % $C_{27}H_{17}N_2O_3ClS$: C, 66.87; H, 3.53; N, 5.78. Found: C, 66.40; H, 3.50; N, 5.86.

General procedure for synthesis of 1-(2-benzoylbenzofuran-3-yl)-4-substituted-3-phenylazetidin-2-ones (5a-g) and 1-(2-benzoylbenzofuran-3-yl)-4-substitutedazetidin-2-ones (6a-g).

To a solution of Schiff's base (**3a-g**) (0.02mol) in dry benzene (30ml) containing few drops of triethyl amine, phenyl acetyl chloride or acetyl chloride (0.02mol) was added drop wise with stirring during 10 mins. After the addition was over, reaction mixture was refluxed for 1 hr. Triethyl amine hydrochloride formed was filtered off and washed several times with dry benzene. The filtrate and washings were combined and concentrated under reduced pressure. On cooling the residue solution to room temperature, the product obtained was filtered, washed with petroleum ether (40:60) to remove unreacted Schiff's base and recrystallized from aqueous ethanol to afford **5a-g** and **6a-g**.

1-(2-Benzoylbenzofuran-3-yl)-4-(5'-chloro-2'-phenyl-1*H*-indol-3'-yl)-3-phenylazetidin-2-one (5a)

Yield: 69%, mp 288-89 ºC; Rf, 0.38 chloroform: ethanol (1:1) mixture; FTIR (KBr) cm^{-1}: 3435 (indoleNH), 1730 (C=O), 1626 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.60 (s, 1H, indole NH), 7.30-8.30 (m, 22H, Ar-H), 6.70 (d, 1H, N-CH), 6.00 (d, 1H, CHCO); MS (EI): *m/z* 592 (M^+); 594 (M^++2). Anal. % $C_{38}H_{25}N_2O_3Cl$: C, 76.96; H, 4.25; N, 4.72. Found: C, 76.90; H, 4.33; N, 4.66.

1-(2-Benzoylbenzofuran-3-yl)-4-(5'-methyl-2'-phenyl-1*H*-indol-3'-yl)-3-phenylazetidin-2-one (5b)

Yield: 72%, mp 80-81 ºC; Rf, 0.60 chloroform: ethanol (3:7) mixture; FTIR (KBr) cm^{-1}: 3400 (indoleNH), 1710 (C=O),1602 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.50 (s, 1H, indole NH), 7.00-8.00 (m, 23H, Ar-H), 6.48 (d, 1H, N-CH), 5.98 (d, 1H, CHCO), 2.58 (s, 3H, CH_3); Anal. % $C_{39}H_{25}N_2O_3$: C, 81.80; H, 4.93; N, 4.89. Found: C, 81.73; H, 4.89; N, 4.81.

1-(2-Benzoylbenzofuran-3-yl)-3-phenyl-4-(2'-phenyl-1*H*-indol-3'-yl)azetidin-2-one (5c)
Yield: 78%, mp 231-32 ºC; Rf, 0.55 chloroform: ethanol (6:4) mixture; FTIR (KBr) cm^{-1}: 3415 (indoleNH), 1730 (C=O), 1629 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.30 (s, 1H, indole NH), 7.00-8.30 (m, 24H, Ar-H), 6.80 (d, 1H, N-CH), 6.00 (d, 1H, CHCO); Anal. % $C_{38}H_{26}N_2O_3$: C, 81.70; H, 4.69; N, 5.01. Found: C, 81.65; H, 4.72; N, 5.10.

1-(2-Benzoylbenzofuran-3-yl)-3,4-diphenylazetidin-2-one (5d)
Yield: 65%, mp 205-06 ºC; Rf, 0.72 chloroform: ethanol (4:6) mixture; FTIR (KBr) cm^{-1}: 3400 (indoleNH), 1720 (C=O), 1608 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.38 (s, 1H, indole NH), 6.63-7.95 (m, 19H, Ar-H), 6.32 (d, 1H, N-CH), 6.00 (d, 1H, CHCO); Anal. % $C_{30}H_{21}NO_3$: C, 81.25; H, 4.77; N, 3.16. Found: C, 81.32; H, 4.81; N, 3.23.

1-(2-Benzoylbenzofuran-3-yl)-4-(4-chlorophenyl)-3-phenylazetidin-2-one (5e)
Yield: 64%, mp 243-43 ºC; Rf, 0.62 chloroform: ethanol (1:2) mixture; FTIR (KBr) cm^{-1}: 3412 (indoleNH), 1710 (C=O), 1634 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm): 12.40 (s, 1H, indole

NH), 7.10-8.20 (m, 18H, Ar-H), 6.45 (d, 1H, N-CH), 6.12 (d, 1H, CHCO); Anal. % $C_{30}H_{20}NO_3Cl$: C, 75.39; H, 4.22; N, 2.93. Found: C, 75.41; H, 4.31; N, 2.85.

1-(2-Benzoylbenzofuran-3-yl)-4-(3-nitrophenyl)-3-phenylazetidin-2-one (5f)
Yield: 71%, mp 264-65 ºC; Rf, 0.45 chloroform: ethanol (1:1) mixture; FTIR (KBr) cm^{-1}: 3400 (indoleNH), 1712 (C=O), 1628 (C=O),1457 (NO_2); ^1H NMR (DMSO-d_6, δ, ppm): 12.38 (s, 1H, indole NH), 7.00-8.10 (m, 18H, Ar-H), 6.22 (d, 1H, N-CH), 6.00 (d, 1H, CHCO); Anal. % $C_{30}H_{21}N_2O_3Cl$: C, 74.93; H, 4.00; N, 5.93. Found: C, 75.07; H, 4.10; N, 5.83.

1-(2-Benzoylbenzofuran-3-yl)-4-(2-chloroquinolin-3-yl)-3-phenylazetidin-2-one (5g)
Yield: 78%, mp 258-59 ºC; Rf, 0.77 chloroform: ethanol (3:7) mixture; FTIR (KBr) cm^{-1}: 3345 (indoleNH), 1700 (C=O), 1635 (C=O); ^1H NMR (DMSO-d_6, δ, ppm): 12.60 (s, 1H, indole NH), 6.95-8.05 (m, 20H, Ar-H), 6.52 (d, 1H, N-CH), 6.12 (d, 1H, CHCO); Anal. % $C_{33}H_{21}N_2O_3Cl$: C, 74.93; H, 4.00; N, 5.93. Found: C, 75.07; H, 4.10; N, 5.83.

1-(2-Benzoylbenzofuran-3-yl)-4-(5'-chloro-2'-phenyl-1*H*-indol-3'-yl)azetidin-2-one (6a)
Yield: 68%, mp 243-44 ºC; Rf, 0.67 benzene: methanol (1:2) mixture; FTIR (KBr) cm^{-1}: 3434 (indoleNH), 1719 (C=O), 1625 (C=O); ^1H NMR (DMSO-d_6, δ, ppm): 12.60 (s, 1H, indole NH), 7.30-8.30 (m, 17H, Ar-H), 5.80 (t, 1H, N-CH), 5.00 (d, 2H, CH_2CO); MS (EI): *m/z* 516 (M^+); 518 (M^++2). Anal. % $C_{32}H_{21}N_2O_3Cl$: C, 74.34; H, 4.09; N, 5.42. Found: C, 73.41; H, 4.18; N, 5.53.

1-(2-Benzoylbenzofuran-3-yl)-4-(5'-methyl-2'-phenyl-1*H*-indol-3'-yl)azetidin-2-one (6b)

Yield: 74%, mp 221-12 ºC; Rf, 0.54 benzene: methanol (7:3) mixture; FTIR (KBr) cm^{-1}: 3400 (indoleNH), 1725 (C=O), 1625 (C=O); ^1H NMR (DMSO-d_6, δ, ppm): 12.38 (s, 1H, indole NH), 7.10-8.00 (m, 18H, Ar-H), 5.62 (t, 1H, N-CH), 5.15 (d, 2H, CH_2CO), 2.38 (s, 3H, CH_3); Anal. % $C_{33}H_{24}N_2O_3$: C, 79.82; H, 4.87; N, 5.64. Found: C, 79.75; H, 4.80; N, 5.60.

1-(2-Benzoylbenzofuran-3-yl)-4-(2'-phenyl-1*H*-indol-3'-yl)azetidin-2-one (6c)
Yield: 64%, mp 200-01 ºC; Rf, 0.45 benzene: methanol (6:4) mixture; FTIR (KBr) cm^{-1}: 3318 (indoleNH), 1700 (C=O); ^1H NMR (DMSO-d_6, δ, ppm) 12.00 (s, 1H, indole NH), 7.00-8.10 (m, 18H, Ar-H), 5.83 (t, 1H, N-CH), 5.29 (d, 2H, CH_2CO); Anal. % $C_{32}H_{22}N_2O_3$: C, 79.65; H, 4.60; N, 5.81. Found: C, 79.58; H, 4.54; N, 5.85.

1-(2-Benzoylbenzofuran-3-yl)-4-phenylazetidin-2-one (6d)
Yield: 61%, mp 249-50 ºC; Rf, 0.71 benzene: methanol (1:1) mixture; FTIR (KBr) cm^{-1}: 3348 (indoleNH), 1700 (C=O); ^1H NMR (DMSO-d_6, δ, ppm): 12.09 (s, 1H, indole NH), 7.00-8.08 (m, 14H, Ar-H), 5.35 (t, 1H, N-CH), 5.00 (d, 2H, CH_2CO); Anal. % $C_{24}H_{17}NO_3$: C, 78.46; H, 4.66; N, 3.81. Found: C, 78.50; H, 4.70; N, 3.89.

1-(2-Benzoylbenzofuran-3-yl)-4-(4-chlorophenyl)azetidin-2-one (6e)
Yield: 59%, mp 178-79 ºC; Rf, 0.58 benzene: methanol (6:4) mixture; FTIR (KBr) cm^{-1}: 3300 (indoleNH), 1720 (C=O); ^1H NMR (DMSO-d_6, δ, ppm): 12.60 (s, 1H, indole NH), 6.78-8.00 (m, 13H, Ar-H), 5.50 (t, 1H, N-CH), 5.00 (d, 2H, CH_2CO); Anal. % $C_{24}H_{16}NO_3Cl$: C, 71.73; H, 4.01; N, 3.49. Found: C, 71.75; H, 4.10; N, 3.55.

1-(2-Benzoylbenzofuran-3-yl)-4-(3-nitrophenyl)azetidin-2-one (6f)
Yield: 65%, mp 210-11 ºC; Rf, 0.75 benzene: methanol (7:3) mixture; FTIR (KBr) cm^{-1}: 3369 (indoleNH), 1708 (C=O), 1448 (NO_2); ^1H NMR (DMSO-d_6, δ, ppm): 12.10 (s, 1H, indole NH), 7.00-8.10 (m, 13H, Ar-H), 5.38 (t, 1H, N-CH), 5.10 (d, 2H, CH_2CO); Anal. % $C_{27}H_{17}N_2O_3Cl$: C, 71.60; H, 3.78; N, 6.79. Found: C, 69.81; H, 3.85; N, 6.88.

1-(2-Benzoylbenzofuran-3-yl)-4-(2-chloroquinolin-3-yl)azetidin-2-one (6g)
Yield: 66%, mp 261-62 ºC; Rf, 0.48 benzene: methanol (3:7) mixture; FTIR (KBr) cm^{-1}: 3408 (indoleNH), 1700 (C=O); ^1H NMR (DMSO-d_6, δ, ppm): 12.28 (s, 1H, indole NH), 7.10-8.18 (m, 15H, Ar-H), 5.28 (t, 1H, N-CH), 4.95 (d, 2H, CH_2CO); Anal. % $C_{27}H_{17}N_2O_3Cl$: C, 71.60; H, 3.78; N, 6.19. Found: C, 71.53; H, 3.83; N, 6.14.

Conclusion
From the results of antimicrobial and antioxidant study revealed that, it could be assumed that, the majority of synthesized compounds having chloro substitution exhibited maximum growth inhibitory activity. The electronegative nature of the chloro group may be responsible to inhibit the growth of the microbes.

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