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Synthesis of novel N′-(2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazides *via* greener approach and their biological activities

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ABSTRACT

A novel series of N′-(2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazides was synthesized starting from substituted indoline-2,3-diones and benzofuran-2-carbohydrazide. The reaction was performed in water and the procedure was very simple and clean, as no use of any organic solvent or catalyst. This provides new opportunities for the rapid screening of a wide range of compounds, either for the development of new drugs, or original compounds for the material scientist. All the synthesized compounds were fully characterized on the basis of their detailed spectral studies and were also evaluated for their biological activities.

Keywords: Aqueous medium, Benzo[*b*]furan, Condensation reaction, Hydrazones, Indoline-2,3-diones

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INTRODUCTION

The environmental protection has become a global concern these days and therefore the synthetic organic chemists are searching the ways of developing and applying more efficient and environmentally benign strategies for sustainable future growth. One of the thrust areas for achieving this target is use of Green Chemistry Techniques in Organic Synthesis. Heterocyclic hydrazones constitute an important class of biologically active drug molecules which have attracted attention of medicinal chemists due to their wide ranging pharmacological properties [1]. They are also key intermediates for many reactions and also for the preparation of heterocyclic rings [2]. At present a broad range of methods for synthesizing imines [3] in the presence of catalysts are available: $ZnCl_2$ [4], $TiCl_2$ [5], K-10 [6], $MgSO_4$-PPTL [7] $Mg(ClO_4)_2$ [8] and also SiO_2–$NaHSO_4$ (under MW irradiation condition) [9]. More recently, ultrasound irradiation has been used to give rise to the formation of a series of Schiff bases (aryl–aryl and aryl–alkyl), under solvent-free conditions [10] or using SiO_2 as a catalyst in ethanol [11] with short reaction times (10–20 min) and high yields. For aryl-hydrazones, most reaction methods described to date involve the use of methanol as a solvent without catalysts at reflux, although ethanol and acid catalysis (or p-toluenesulfonic acid in dried toluene) are required if the carbonyl compounds bear a strong electron-withdrawing group [12]. Benzo[*b*]furan is a class of compound which is widely distributed in nature [13, 14] and its compound shown varied biological activities [15-18]. Over the last few years Benzo[*b*]furan and its derivatives has drawn considerable attention due to their profound physiological and chemotherapeutic properties such as antibacterial [19] anti-inflammatory [20] and antifungal [21]. On the other hand, indoline-2,3-dione (isatin) is a very biological active molecule containing indole as a core nucleus and known to show proconvulsant [22], anticonvulsant [23], and CNS depressant [24] activities. Isatin derivatives also possess antibacterial [25], anti-inflammatory [26], analgesic [27], anti-viral [28], antifungal [29], anti-tubercular [30] and anti-depressant [31]. So, in view of all the above observations and our interest in developing new heterocycles we have designed and synthesized some new heterocyclic hydrazone derivatives bearing benzofuran and isatin in the same molecule using water as a solvent. The reaction was carried out in very short reaction time i.e. only simple refluxing condition for 20-30 min gave the product in high yield.

MATERIALS AND METHODS

All the chemicals, reagents and solvents used were obtained from commercial sources and of analytical grade. All the reaction were monitored by thin layer chromatography (TLC) using silica gel G as stationary phase, different solvent systems as mobile phase and iodine vapours as detecting agent. Melting points were determined on an electronic apparatus and are uncorrected. IR spectra were recorded on Shimadzu model IR-435 spectrophotometer using KBr discs for solids and thin films for liquids. ^{1}H NMR and ^{13}C NMR spectra were recorded on Jeol AC (400 MHz) and Jeol AC (100 MHz) respectively in DMSO-d_6 and $CDCl_3$ using tetramethylsilane (TMS) as an internal standard. TOF ES+ Mass spectra (m/z) were recorded on Micromass Autospec LCTKC455. Substituted indol-2,3-diones were prepared by literature procedures [32], starting from the corresponding aniline and the other reactant benzofuran-2-carboxylic acid hydrazide was prepared in two steps by following the literature procedure [33].

Synthesis of ethylbenzofuran-2-carboxylate (2)

To a cooled solution of freshly ignited potassium carbonate (34.0 g) in 50 mL of dry dimethylformamide, a solution of 2-hydroxy benzaldehyde (**1**) (10 g, 81.96 mmol) in 10 mL of dry dimethylformamide was added dropwise under inert atomosphere of nitrogen. The contents were allowed to stirr at room temperature and then a solution of ethylbromoacetate (13.68 g, 81.96 mmol) in 20 mL of DMF was added to it dropwise. Stirring was continued for additional 20 minutes at this temperature. The contents were then allowed to reflux for 2 h. The progress of the reaction was monitored by using thin layer chromatography. After completion of the reaction, the reaction mixture was cooled and quenched with ice cold water and extracted with ethylacetate. The organic layer was dried over anhydrous sodium sulfate and the solvent was removed by distillation under reduced pressure to yield the desired compound **2** as yellow oil. Yield 83%; IR (film, cm^{-1})ν_{max}: 2983, 2937, 1729, 1573, 1508, 1466, 1447, 1370, 1346, 1298, 1183, 1097, 1018, 946, 868; ^{1}H NMR (δ, $CDCl_3$, 400 MHz): 7.64 (d, 1H, *J*=7.42 Hz), 7.56 (d, 1H, *J*=8.08 Hz), 7.50 (s, 1H), 7.43-7.41 (m, 1H), 7.28-7.26 (m, 1H), 4.42 (q, 2H), 1.40 (t, 3H); ^{13}C NMR (δ, $CDCl_3$, 100 MHz): 159.5, 155.6, 145.6, 127.5, 126.8, 123.6, 122.7, 113.7, 112.2, 61.4, 14.2; Mass spectral data, TOF ES+ m/z (%): 191 (M^++1).

Synthesis of benzofuran-2-carboxylic acid hydrazide (3)

The mixture of hydrazine hydrate (15 ml) and ethyl benzofuran-2-carboxylate (**2**) (2.28 g, 12 mmol) was stirred at 0-5°C for 30 min. The reaction was monitored by using thin layer chromatography. Further, the reaction mixture was stirred at room temperature to give benzofuran-2-carbohydrazide (3) as a white colored shining product. Yield 89%, mp 190-194 °C; IR (KBr, cm^{-1})ν_{max}: 3322, 3182, 3023, 2975, 1659, 1546, 1328, 1187, 1089, 822, 735; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 9.31 (s, 1H, >NH, D_2O exchangeable), 7.69 (d, 1H, *J* = 8.0 Hz), 7.54 (d, 1H, *J* = 7.44 Hz), 7.49 (s, 1H), 7.44-7.40 (m, 1H), 7.32-7.29 (m, 1H), 4.26 (brs, 2H, -NH_2, D_2O exchangeable); ^{13}C NMR (δ, DMSO-d_6, 100 MHz): 159.8, 154.8, 147.3, 127.2, 123.8, 122.7, 111.8, 111.0; Mass spectral data, TOF ES+ *m/z* (%): 177 (M^++1).

General procedure for the synthesis of N′-(2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazides (5a-j)

To the solution of benzofuran-2-carboxylic acid hydrazide **(3)** (176 mg, 1.0 mmol) in water (20 mL), indoline-2,3-dione/ substituted indoline-2,3-dione was added and the reaction mixture was refluxed. Progress of the reaction was monitored on thin layer chromatography. A solid that separated out was filtered and dried to yield the corresponding hydrazone.

N′-(5-Methyl-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5a)

Yield 95%; m.p. >280 °C; IR (KBr, cm^{-1})ν_{max}: 3440, 3216, 2925, 1721, 1665, 1600, 1541, 1481, 1311, 876, 745; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 11.72 (s, 1H, -NH, D_2O exchangeable), 10.74 (s, 1H, >NH, indole, D_2O exchangeable), 8.04 (s, 1H), 7.89-7.83 (m, 2H), 7.73 (d, 1H, *J*=8.72 Hz), 7.56-7.52 (m, 1H), 7.41-7.37 (m, 1H), 7.24 (d, 1H, *J*=8.02 Hz), 6.87-6.80 (m, 1H), 2.33 (s, 3H); ^{13}C NMR (δ, DMSO-d_6, 100 MHz): 165.2, 164.8, 155.0, 147.0, 142.4, 140.9, 133.8, 131.2, 128.2, 127.4, 124.4, 123.7, 120.0, 121.9, 115.8, 112.4, 111.0, 21.1; Mass spectral data, TOF ES+ *m/z* (%): 320 (M^++1).

N′-(2-Oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5b)

Yield 96%; m.p. >280°C; IR (KBr, cm^{-1})ν_{max}: 3445, 3234, 2926, 1720, 1668, 1606, 1578, 1340, 1259, 1164, 1009, 941, 873, 745; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 11.73 (s, 1H, -NH, D_2O exchangeable), 10.83 (s,1H,>NH, indole, D_2Oexchangeable), 8.02 (s, 1H), 7.86 (m, 2H), 7.76 (d, 1H, *J* = 8.04 Hz), 7.57-7.52 (m, 1H), 7.44-7.37 (m, 2H), 7.13-7.09 (m, 1H), 6.98-6.92 (m, 1H); ^{13}C NMR (δ, DMSO-d_6, 100 MHz): 164.9, 163.2, 154.7, 142.7, 131.4, 127.6, 126.1, 125.5, 124.8, 123.7, 122.3, 121.5, 120.3, 114.2, 111.9, 110.4, 109.3; Mass spectral data, TOF ES+ *m/z* (%): 306 (M^++1).

N′-(5-Fluoro-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5c)
Yield 92%; m.p. >280 °C; IR (KBr, cm^{-1})ν_{max}: 3426, 3278, 2924, 1742, 1672, 1610, 1577, 1445, 1339, 1179, 1079, 949, 872, 742; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 11.92 (s, 1H, -NH, D_2O exchangeable), 10.91 (s, 1H, >NH, indole, D_2O exchangeable), 8.08 (s, 1H), 7.91-7.86 (m, 2H), 7.76 (d, 1H, *J* = 8.42 Hz), 7.59 - 7.26 (m, 3H), 7.00-6.91 (m, 1H); ^{13}C NMR (δ, DMSO-d_6, 100 MHz): 165.4, 163.2, 155.8, 149.2, 141.0, 132.8, 130.7, 127.9, 127.5, 126.9, 126.0, 123.8, 123.2, 121.3, 116.7, 112.1, 111.9; Mass spectral data, TOF ES+ *m/z* (%): 324 (M^++1).

N′-(5-Chloro-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5d)
Yield 93%; m.p. >280°C; IR (KBr, cm^{-1})ν_{max}: 3443, 3246, 2924, 1748, 1708, 1616, 1573, 1510, 1468, 1273, 1168, 1025, 874, 745; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 11.61 (s, 1H, -NH, D_2O exchangeable), 10.69 (s, 1H, >NH, indole, D_2O exchangeable), 8.03 (s, 1H), 7.70-7.63 (m, 2H), 7.54 (d, 1H, *J* = 8.04 Hz), 7.49- 7.23 (m, 3H), 6.83-6.80 (m, 1H); ^{13}C NMR (δ, DMSO-d_6, 100 MHz): 164.9, 162.8, 154.6, 142.2, 140.8, 131.6, 130.1, 127.5, 127.1, 126.6, 125.8, 123.6, 123.1, 121.0, 116.1, 111.9, 111.7; Mass spectral data, TOF ES+ *m/z* (%): 341 (M^++2).

N′-(5-Bromo-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5e)
Yield 92%; m.p. 234-236°C; IR (KBr, cm^{-1})ν_{max}: 3462, 3278, 2926, 1742, 1672, 1610, 1577, 1445, 1339, 1278, 1136, 1079, 872; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 11.39 (s, 1H, -NH, D_2O exchangeable), 10.92 (s, 1H, >NH, indole, D_2O exchangeable), 8.02 (s, 1H), 7.81-7.79 (m, 2H), 7.66-7.63 (m, 1H), 7.52-7.47 (m, 2H), 7.47-7.35 (m, 1H), 6.91-6.85 (m, 1H); Mass spectral data, TOF ES+ *m/z* (%): 386 (M^++2).

N′-(5-Nitro-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5f)
Yield 92%; m.p. >280 °C; IR (KBr, cm^{-1})ν_{max}: 3462, 3234, 2925, 1735, 1686, 1618, 1573, 1515, 1341, 1274, 1165, 1026, 876, 746; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 11.73 (s, 1H, -NH, D_2O exchangeable), 10.83 (s, 1H, >NH, indole, D_2O exchangeable), 9.07 (s, 1H), 8.19-8.17 (m, 1H), 8.04 (s, 1H), 7.69 (d, 1H, *J* = 8.08 Hz), 7.55 (d, 1H, *J* = 8.76 Hz), 7.40-7.36 (m, 1H), 7.26-7.18 (m, 1H), 7.04-6.97 (m, 1H); ^{13}C NMR (δ, DMSO-d_6, 100 MHz): 170.4, 165.6, 154.7, 149.8, 147.9, 143.4, 135.0, 128.6, 128.0, 127.4, 124.1, 123.6, 122.3, 120.5, 117.1, 112.0, 111.0; Mass spectral data, TOF ES+ *m/z* (%): 351 (M^++1).

N′-(1-Methyl-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5g)
Yield 97%, m.p. 238-240 °C; IR (KBr, cm^{-1})ν_{max}: 3422, 2925, 1723, 1669, 1604, 1539, 1365, 1103, 884, 753; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 11.73 (s, 1H, -NH, D_2O exchangeable), 8.01 (s, 1H), 7.82 (d, 1H, *J* = 7.92 Hz), 7.70 (d, 1H, *J* = 7.84 Hz), 7.57-7.47 (m, 3H), 7.41-7.36 (m, 1H), 7.22-7.19 (m, 1H), 7.10-7.05 (m, 1H), 3.22 (s, 3H, -NCH_3); ^{13}C NMR (δ, DMSO-d_6, 100 MHz): 169.7, 169.4, 154.4, 139.2, 132.2, 129.3, 128.4, 126.7, 125.7, 123.3, 122.5, 118.1, 115.7, 112.2, 111.4, 108.7, 97.0, 28.6; Mass spectral data, TOF ES+ *m/z* (%): 320 (M^++1).

N′-(5-Fluoro-1-methyl-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5h)
Yield 94%; m.p. 230-232 °C; IR (KBr) ν_{max}: 3421, 2925, 1720, 1673, 1613, 1596, 1488, 1361, 1092, 890, 747; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 11.91 (s, 1H, -NH, D_2O exchangeable), 8.11 (s, 1H), 7.92-7.86 (m, 2H), 7.77 (d, 1H, *J* = 8.42 Hz), 7.60-7.39 (m, 3H), 7.23-7.14 (m, 1H), 3.22 (s, 3H, -NCH_3); Mass spectral data, TOF ES+ *m/z* (%): 338 (M^++1).

N′-(5-Chloro-1-methyl-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5i)
Yield 94 %, m.p. 192-194 °C; IR (KBr, cm^{-1})ν_{max}: 3407, 2925, 1731, 1692, 1611, 1573, 1514, 1485, 1362, 1270, 1161, 1042, 988, 841, 740; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 12.0 (s, 1H, -NH, D_2O exchangeable), 8.19 (s,1H), 7.86-7.80 (m, 2H), 7.70 (d, 1H, *J* = 8.44 Hz), 7.54-7.32 (m, 3H), 7.18-7.09 (m, 1H), 3.21 (s, 3H, -NCH_3); Mass spectral data, TOF ES+ *m/z* (%): 355 (M^++2).

N′-(5-Bromo-1-methyl-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide (5j)
Yield 93%; m.p. 149-151°C; IR (KBr, cm^{-1})ν_{max}: 3397, 2922, 1728, 1694, 1619, 1575, 1516, 1491, 1367,1274, 1161, 913, 864, 739; ^{1}H NMR (δ, DMSO-d_6, 400 MHz): 11.76 (s, 1H, -NH, D_2O exchangeable), 8.17 (s, 1H), 7.84-7.68 (m, 2H), 7.54 (d, 1H, *J* = 8.04 Hz), 7.47-7.27 (m, 3H), 7.01-6.95 (m, 1H), 3.22 (s, 3H, -NCH_3); Mass spectral data, TOF ES+ *m/z* (%): 400 (M^++2).

Biological activity
All the new compounds **5a–j** were screened for their *in vitro* antimicrobial activities to determine zone of inhibition at 100 μg/mL against three Gram-positive bacteria (*Staphylococcus aureus* MTCC 096, *Bacillus subtilis* MTCC 441 and *Staphylococcus epidermis* MTCC 435), four Gram-negative bacteria (*Escherichia coli* MTCC 443, *Pseudomonas aeruginosa* MTCC 424, *Salmonella typhi* MTCC 733, and *Klebsiella pneumoniae* MTCC 432) as well as four fungi (*Aspergillus niger* MTCC 282, *Aspergillus fumigates* MTCC 343, *Aspergillus flavus* MTCC 277,

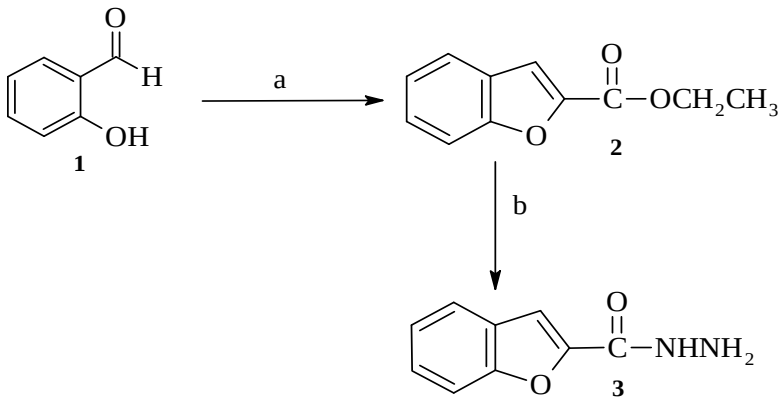
and *Candida albicans* MTCC 227) strains using Cup plate method [34,35] where inoculated Muller-Hilton agar for bacteria and Sabouraud dextrose agar for fungi was poured onto the sterilized petri dishes (25–30 mL: each petri dish). The poured material was allowed to set (30 min) and thereafter the 'CUPS' (06 mm diameter) was made by punching into the agar surface with a sterile cork borer and scooping out the punched part of the agar. Into these cups the test compound solution (0.1 mL) was added with the help of a micro pipette. The plates were incubated at 37°C for 14 h for bacteria and 30 h for fungi and the results were noted. The test solution was prepared by DMSO as solvent. Clinically antimicrobial drugs Ciprofloxacin and Miconazole were used as the positive control and DMSO was used for blank.

RESULTS AND DISCUSSION

Chemistry

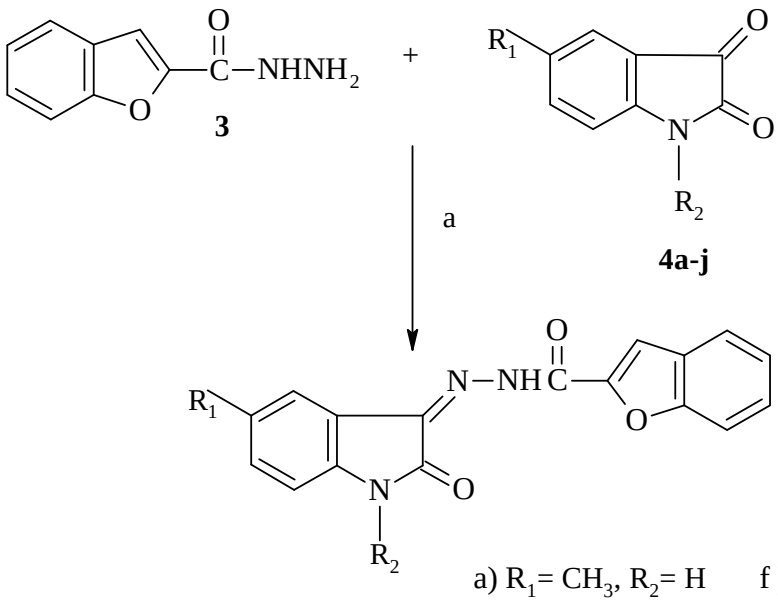
We have synthesized ten novel N′-(2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazides of biological use. The reaction of 2-hydroxy benzaldehyde (**1**) with ethylbromoacetate in dry acetone gave ethyl-2-benzofuran carboxylate (**2**) as a product and ethyl-2-benzofuran carboxylate (**2**) was then reacted with hydrazine hydrate at 0-5°C for 3 hours to give white crystalline solid as benzofuran-2-carboxylic acid hydrazide (**3**) in good yield. The structure of **3** was confirmed by its spectral data (**Scheme 1**). Now, the treatment of benzofuran-2-carboxylic acid hydrazide (**3**) with 5-methyl-indoline-2,3-dione (**4a**) (1:1) in water at refluxing condition for half an hour yielded a yellow colored solid which displayed M^++1 peak at *m/z* 320 in TOF ES+, corresponding to the molecular formula $C_{18}H_{13}N_3O_3$, thereby indicating that the two moieties have coupled together with the loss of a water molecule. Compound **5a** exhibited characteristic absorption band at 1600 cm^{-1} for >C=N stretching in its IR spectrum which indicated the formation of corresponding hydrazone. Further, broad absorption band at 3440 cm^{-1} and 3216 cm^{-1} showed the presence of -NH stretching which was also confirmed by the presence of two D_2O exchangeable broad singlets at δ 11.72 and 10.74 for the NH protons in its ^{1}H NMR spectrum. Further eight aromatic protons of the indole and benzofuran nucleus appeared at δ 8.04 (1H), 7.89-7.83 (2H), 7.73 (1H), 7.56-7.52 (1H), 7.41-7.37 (1H), 7.24 (1H) and δ 6.87-6.80 (1H). ^{1}H NMR displayed a singlet at δ 2.33 for three protons for methyl group which was also confirmed by a peak at δ 21.1 in its ^{13}C NMR spectrum. Also ^{13}C NMR spectrum of **5a** displayed characteristic two carbonyl carbon signals at δ 165.2 and 164.8 present in the molecule. In addition to this, presence of a signal at δ 131.2 for (C=N) at C-3 in the molecule finally confirmed the formation of hydrazone. Thus, on the basis of above mentioned spectral data the compound **5a** was characterized as N′-(5-methyl-2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazide. Similar set of above reactions were repeated with substituted indoline-2,3-diones to obtain in all 10 corresponding desired compounds (**Scheme 2**).

We tried the reaction of benzofuran-2-carboxylic acid hydrazide (**3**) with indoline-2,3-dione (**4b**) in different solvents under refluxing condition to obtain corresponding hydrazone and compared the percentage yield of the product synthesized in each case with the yield of product formed of the same in water. The results showed that yield was maximum when water was used as solvent. Thus, we have developed a one pot, efficient synthesis of N′-(2-oxoindolin-3-ylidene) benzofuran-2-carbohydrazides in 92-97% yield without using any catalyst or irradiation (**Figure 1**).



a: $BrCH_2COOC_2H_5$, K_2CO_3, DMF, molecular sieves, reflux, 2h; b: $NH_2NH_2.H_2O$, reflux, 3h

Scheme 1: Synthesis of benzofuran-2-carboxylic acid hydrazide



a) R_1= CH_3, R_2= H
b) R_1= H, R_2= H
c) R_1= F, R_2= H
d) R_1= Cl, R_2= H
e) R_1= Br, R_2= H
f) R_1= NO_2, R_2= H
g) R_1= H, R_2= CH_3
h) R_1= F, R_2= CH_3
i) R_1= Cl, R_2= CH_3
j) R_1= Br, R_2= CH_3

a: H_2O / reflux

Scheme 2: Synthesis of N′-(2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazides

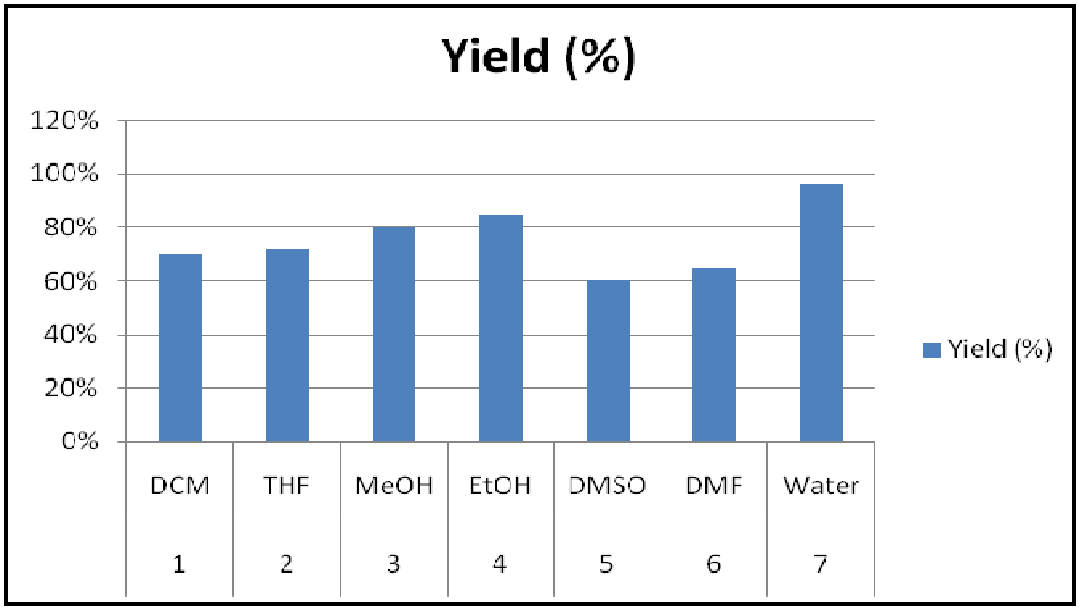


Figure 1: Graphical representation of yield of hydrazone formation during reaction of benzofuran 2-carboxylic acid hydrazide (3) with indoline-2,3-dione (4b) by using different solvents.

Biological activity

The obtained results, depicted in **Table 1**, revealed that hydrazones **5a–j** could effectively, to some extent, inhibit the growth of all tested strains *in vitro*. Compounds tested were showed significant activity towards strains of bacteria, but showed less activity against antifungal agents. In antibacterial study, except *E. coli* and *K. pneumoniae*, all of the compounds found significant active against rest of the antibacterial strains. Compounds **5h** and **5i** have shown promising antibacterial activity and comparable to the standard Ciprofloxacin against *S. aureus* while **5j** showed activity even more than the standard against *S. aureus.* **5c**, **5d,** **5f**, **5g**, **5i** and **5j** showed promising activity against *B. subtilis.* Compounds **5a**, **5b**, **5e**, **5g**, **5h** and **5i** possessed good activity against *S. epidermis* whereas

compound **5j** showed promising activity against *S. epidermis*. **5e**, **5g**, **5h**, **5i** and **5j** showed promising activity against *P. aeruginosa while* compounds **5b**, **5d, 5g, 5h** and **5i** have shown promising activity against *S. typhi.* **5j** showed activity comparable to the standard against *S. typhi.* Against the fungal pathogens, compounds were only found to be moderately active against only *A. niger*.

Table 1: Antimicrobial activity of compounds 5a-j

S. No.	Compound	Gram positive bacteria			Gram negative bacteria				Fungi			
		S. aureus	*B. subtilis*	*S. epidermis*	*E. coli*	*P. aeurginosa*	*S. typhi*	*K. pneumoniae*	*A. niger*	*A. fumigatus*	*A. flavus*	*C. albicans*
1	**5a**	16	13	15	10	12	12	11	15	14	12	12
2	**5b**	14	13	15	-[a]	13	16	11	15	12	10	13
3	**5c**	16	16	13	10	12	13	-[a]	14	14	11	12
4	**5d**	13	15	12	-[a]	13	15	11	14	12	10	11
5	**5e**	14	13	14	-[a]	16	13	12	13	12	10	11
6	**5f**	16	16	13	13	13	12	-[a]	12	12	10	13
7	**5g**	18	16	14	10	18	17	12	16	14	11	14
8	**5h**	26	14	14	11	17	17	10	16	13	12	12
9	**5i**	24	16	16	-[a]	18	18	12	16	12	10	14
10	**5j**	26	19	19	12	18	19	12	15	12	10	13
11	**Std.**[#]	**24**	**22**	**20**	**22**	**19**	**19**	**18**	**24**	**30**	**25**	**30**

-[a] Compound which does not show any activity
 # Standard drug for bacteria: Ciprofloxacin; Standard drug for fungi: Miconazole
Zone of Inhibition (Internal diameter: 6mm)
All the compounds were screened at 100 µg/mL concentration.

CONCLUSION

We have successfully synthesized ten novel N′-(2-oxoindolin-3-ylidene)benzofuran-2-carbohydrazides (**5a-j)** in good yields using green chemistry. The structures of all the compounds were confirmed by their spectral data. All the newly synthesized compounds were screened for their MIC and zone of inhibition against seven strains of bacteria and four strains of fungi. Amongst the compounds screened, most of the compounds have shown moderate to significant antibacterial and antifungal properties whereas some compounds have shown promising antibacterial properties, which were further used to determine MBC and MFC against some selected strains of bacteria and fungi. The study also suggested that 1-methyl-5-subsituted-indoline-2,3-diones derivatives are found more biological active. Compound **5j** showed very promising antibacterial activity. It showed antibacterial activity even more than the standard Miconazole against *S. aureus*, and equal to standard against *S. typhi*, so this compound can be developed as future lead molecule and therefore, it is suggested that these hydrazones are worthy for further investigations as potential antibacterial agents.

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