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Synthesis and Screening of 2-Hydroxy -N- (2, 41-Dioxospiro [Indoline-3, 21-Thiazolidin]-31-Yl)Benzamides for Anti-Bacterial Activity

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ABSTRACT

A novel synthesis of 2-hydroxy-N- (2, 41-dioxospiro[indoline-3, 21-thiazolidin]-31-yl)benzamide derivatives was synthesized by cyclization of isatin hydazones with thioglycollic acid. The synthesized compounds were characterized by spectral data (IR, 1HNMR, MASS) and evaluated for anti-bacterial activity against various strains of bacteria at the concentrations of 200 µg/ml. Among the tested compounds VI (i)is highly active against E. coli, VI (f) is active against B. subtilis, VI (l) is active against S. aureus and VI (c) is active against S. typhi.

Keywords: Iisatin, Thiazole, Anti-bacterial.

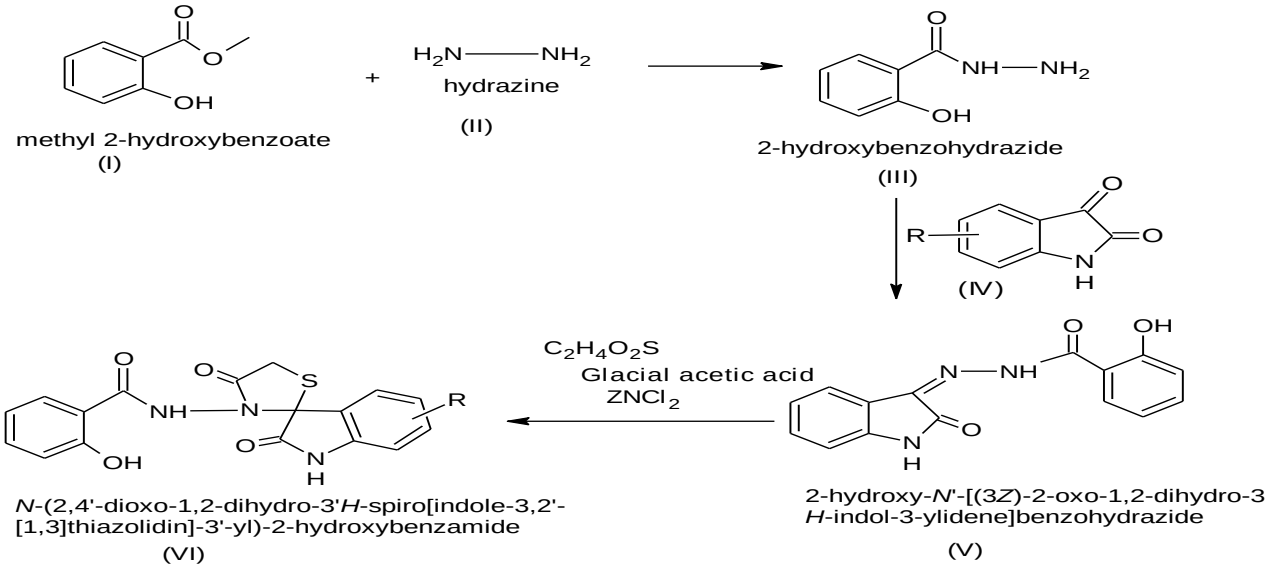
INTRODUCTION

It is evident from literature, that isatin derivatives are known to be associated with broad spectrum of biological activity like antibacterial [1], anti-inflammatory [2], analgesic [3], anti-viral [4], antifungal [5], anti-tubercular [6] and anti-depressant [7]. Isatin hydrazone have been reported to possess anti-convulsant [7] activity also [8]. In view of these fact prompted us to synthesize some new 2-hydroxy-N- (5-Chloro-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamides. All the synthesized compounds were screened for their *in vitro* anti-bacterial activity [9,10].

MATERIALS AND METHODS

All the chemicals used were of analytical grade and obtained from Himedia and SD Fine, Melting points were determined by open capillary tubes using VEEGO VMP-D Digital melting point. FTIR spectra of the powdered compounds were recorded using KBr on a JASCO FTIR 4100 series and are reported in cm^{-1} and 1H NMR spectra were recorded on a Varian Mercury YH300 (300 MHz FT NMR) spectrophotometer using TMS as an internal reference (Chemical shift represented in ppm). Purity of the compounds was checked on TLC plates using silica gel G as stationary phase and iodine vapors as the visualizing agent.

Chemistry



Scheme 1: Synthesis of Indole-2, 3-diones.

Synthesis of Indole-2, 3-diones

Isonitrosoacetanilides *(I1)*

In a 5 lit. RB flask, chloral hydrate (0.54 mol) and 1200 mL of water were placed. To this solution, crystallized sodium sulphate (1300 g) was then added followed by a solution of an appropriate aromatic amine (**I**) in 300 mL of water and concentrated hydrochloric acid (0.52 mol). Finally, a solution of hydroxylamine HCl (1.58 mol) in 500 mL of water was added. The contents of the flask were heated over a wire-gauge by a Mecker burner so that vigorous boiling begins in about 45 minutes. After 1 to 2 minutes of vigorous boiling the reaction was completed. During the heating period itself the crystals of isonitrosoacetanilides started separating out. On cooling under the current of water, the entire product was solidified. It was filtered under suction, air dried, and purified by recrystallization from suitable solvent (s).

Indole-2, 3-diones

Sulphuric acid (600 g, d, 1.84, 326 mL) were warmed at 50°C in a one liter RB flask fitted with an efficient mechanical stirrer and to this, finely powdered appropriate isonitrosoacetanilide (II, 0.46 mol) was added at such a rate so as to maintain the temperature between 60°C and 70°C but not higher. External cooling was applied at this stage so that the reaction could be carried out more rapidly. After the addition of isonitroso compound was completed the temperature of the solution was raised to 80°C and maintained at that temperature for 10 minutes, to complete the reaction. Then the reaction mixture was cooled to room temperature and poured on crushed ice (2.5 kg) while stirring. After standing for about half-an-hour, the product separated was filtered, washed several times with small portions of cold water, and dried. Purification of the compound was affected by the recrystallization from methanol.

Preparation of 2-Hydroxybenzohydrazide *(III)*

In a 500 mL of RB flask, 10 g of methyl salicylate (**I**) and 50 mL of distilled alcohol were placed and the reaction mixture was shaken for 5 minutes. To this add 20 mL of hydrazine hydrate **(II)** (99%) and the contents of the flask were refluxed for 3 hours, the completion of the reaction monitored by TLC. The resultant white crystalline solid was filtered and washed repeatedly, with small portions of cold alcohol. The product was dried and purified by recrystallization from methanol, yield 90%, m.p. 251–254°C

Synthesis of 2-Hydroxy-N- (2-oxoindolin-3-ylidene)benzohydrazide (V)

A mixture of an appropriate indole-2, 3- dione **(IV).** (0.01 mol) and 2-hydroxybenzohydrazide **(III**) (0.01 mol) was taken into methanol (50 mL) in presence of glacial acetic acid which was heated under reflux on water bath for 6-7 hours. The coloured compounds were thus obtained upon cooling, were filtered, were washed with small portions of water and recrystalize by using methanol.

Synthesis of 2-hydroxy-N- (2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide (VI)

To the above compound (V) (0.01 mol)add thioglycollic acid (0.01 mol)and add pinch of zinc chloride and reflux in presence of glacial acetic acid for about 6-7 hrs cool the reaction mixture poured into crushed ice. Then the solution is neutralized with sodium carbonate solution and filter the solution collect the compound and dry, recrystalise with methanol.

Spectral data of the synthesized compounds

2- hydroxy-N- (5-Chloro-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide

IR spectrum (KBr, cm^{-1}) 3073.01 (C-H aromatic), 1682.02 (C=Ostr), 1620.39 (C=Nstr), 1520.06 (C=C aromatic), 680.02 (S-CHstr); ^{1}H NMR (400 MHz $CDCl_3$, δ ppm): 3.44 (s, 2H, CH_2), 6.97-6.98 (s, 2H, OH), 7.04-7.05 (d, 1H, aromatic), 7.13-7.20 (m, 2H aromatic), 7.14-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide);^{13}C NMR (100 MHz, $CDCl_3$):32.4, 85.8, 115.2, 117.8, 119.8, 121.4, 124.8, 127.8, 127.8, 128.9, 129.8, 133.5, 141.1, 159.4, 164.8, 168.2, 168.8: MS: m/z:355.06 (100.0%), 356.07 (18.7%).

Elemental analysis: $C_{17}H_{13}N_3O_4S$
Calculated Values: C-57.46, H-3.69, N-11.82, S-9.02
Observed Values: C-57.15, H-3.52, N-11.72, S-9.01.

2- hydroxy-N- (5-Chloro-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide

IR spectrum (KBr, cm^{-1}) : 3069.12 (C-H aromatic), 1682.02 (C=Ostr), 1620.39 (C=Nstr), 1520.06 (C=C aromatic), 680.32 (S-CHstr);); ^{1}H NMR (400 MHz $CDCl_3$, δ ppm): 3.41 (s, 2H, CH_2), 6.95-6.97 (s, 2H, aromatic OH), 7.01-7.04 (d, 1H, aromatic), 7.10-7.18 (m, 2H aromatic), 7.38 -7.40 (m, 2H, aromatic), 7.69-7.70 (d, 1H, aromatic), 8.61 (s, 1H, amide) ^{13}C NMR (100 MHz, $CDCl_3$):-32.4, 85.3, 111.3, 117.8, 119.8, 121.4, 127.9, 128.9, 129.2, 129.6, 130.4, 133.5, 139.2, 159.4, 164.8, 168.2, 168.8. MS:m/z:389.02 (100.0%), 391.02 (36.7%), 390.03 (18.7%).

Elemental analysis: $C_{17}H_{12}ClN_30_4S$
Calculated Values: C-52.38, H-3.10, N-10.78, S-8.23
Observed Values: C-52.26, H-3.02, N-10.65, S-8.20:

2- hydroxy-N- (7-Chloro-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide

IR spectrum (KBr, cm^{-1}) : 3069.12 (C-H aromatic), 1682.02 (C=Ostr), 1620.39 (C=Nstr), 1520.06 (C=C aromatic), 680.32 (S-CHstr); ^{1}H NMR (400 MHz $CDCl_3$, δ ppm): 3.38 (s, 2H, CH_2), 6.92-6.95 (s, 2H, OH), 7.01-7.03 (d, 1H, aromatic), 7.13-7.20 (m, 2H aromatic), 7.40-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide); ^{13}C NMR (100 MHz, $CDCl_3$): 32.4, 85.3, 117.8, 119.8, 121.4, 126.2, 127.9, 128.9, 129.02, 192.2, 131.0, 133.5, 143.9, 159.4, 164.8, 168.2, 168.8. MS:m/z:389.02 (100.0%), 391.02 (36.7%).

Elemental analysis: $C_{17}H_{12}ClN_30_4S$
Calculated Values: C-52.38, H-3.10, N-10.78, S-8.23
Observed Values: C-52.35, H-3.01, N-10.68, S-8.20

2- hydroxy-N- (5-methyl-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide

IR spectrum (KBr, cm^{-1}) 3052.12 (C-H aromatic), 1678.02 (C=Ostr), 1620.39 (C=Nstr), 1520.06 (C=C aromatic), 680.32 (S-CHstr); ^{1}H NMR (400 MHz $CDCl_3$, δ ppm): 3.44 (s, 2H, CH_2), 6.97-6.98 (s, 2H, aromatic OH), 7.04-7.05 (d, 1H, aromatic), 7.13-7.20 (m, 2H aromatic), 7.14-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide) ^{13}C NMR (100 MHz, $CDCl_3$): -21.6, 32.4, 86.1, 115.3, 117.8, 119.8, 121.4, 127.7, 128.1, 128.9, 131.7, 133.5, 134.5, 138.1, 159.4, 164.8, 168.2, 168.8. MS:m/z: 369.08 (100.0%), 370.08 (21.7%).

Elemental analysis: $C_{18}H_{15}N_30_4S$
Calculated Values: C-58.53, H-4.09, N-11.38, S-8.68
Observed Values: C-58.51, H-4.05, N-11.33, S-8.62.

2- hydroxy-N- (7-methyl-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide

IR spectrum (KBr, cm^{-1}) 3069.12 (C-H aromatic), 1682.02 (C=Ostr), 1620.39 (C=Nstr), 1520.06 (C=C aromatic), 680.32 (S-CH.str); ^{1}H NMR (400 MHz $CDCl_3$, δ ppm): 3.44 (s, 2H, CH_2), 6.97-6.98 (s, 2H, aromatic OH), 7.04-7.05 (d, 1H, aromatic), 7.13-7.20 (m, 2H aromatic), 7.14-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide); ^{13}CNMR (100 MHz, $CDCl_3$): 17.3, 32.4, 86.1, 117.8, 119.8, 121.4, 124.7, 126.8, 127.7, 128.9, 129.6, 131.3, 133.5, 141.1, 159.4, 164.8, 168.2, 168.8. MS:m/z:369.08 (100.0%), 370.08 (21.7%).

Elemental analysis: $C_{18}H_{15}N_30_4S$
Calculated Values: C-58.53, H-4.09, N-11.38, S-8.68
Observed Values: C-58.50, H-4.06, N-11.33, S-8.61.

2- hydroxy-N- (5-fluoro-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide

IR spectrum (KBr, cm^{-1}): 3078.12 (C-H aromatic), 1689.02 (C=Ostr), 1625.39 (C=Nstr), 1527.06 (C=C, aromatic), 685.32 (S-CHstr);^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 3.47 (s, 2H, CH_2), 6.98-7.0 (s, 2H, aromatic OH), 7.04-7.05 (d, 1H, aromatic), 7.15-7.26 (m, 2H aromatic), 7.14-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide); ^{13}CNMR (100 MHz, $CDCl_3$): 32.4, 85.8, 111.1, 114.6, 116.8, 117.8, 119.8, 121.4, 128.9, 129.4, 133.5, 136.7, 159.0, 159.4, 164.8, 168.2, 168.8. MS:m/z: 373.05 (100.0%), 374.06 (18.7%), 375.05 (4.7%).

Elemental analysis: $C_{18}H_{16}FN_3O_4S$
Calculated Values: C-54.69, H-3.24, N-11.25, S-8.59
Observed Values: C-54.65, H-3.22, N-11.23, S-8.52.

2- hydroxy-N- (7-fluoro-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide

IR spectrum (KBr, cm^{-1}): 3072.12 (C-H aromatic), 1682.02 (C=Ostr), 1620.39 (C=Nstr), 1520.06 (C=C aromatic), 680.32 (S-CHstr); ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 3.41 (s, 2H, CH_2), 6.97-6.98 (s, 2H, aromatic OH), 7.10-7.12 (d, 1H, aromatic), 7.17-7.20 (m, 2H aromatic), 7.14-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide); ^{13}CNMR (100 MHz, $CDCl_3$): 32.4, 85.8, 114.6, 116.8, 117.8, 119.8, 121.4, 125.4, 126.4, 128.9, 129.1, 133.5, 159.4, 163.3, 164.8, 168.2, 168.8. MS:m/z:373.05 (100.0%), 374.06 (18.7%), 375.05 (4.7%).

Elemental analysis: $C_{18}H_{16}FN_3O_4S$
Calculated Values: C-54.69, H-3.24, N-11.25, S-8.59:
Observed Values: C-54.64, H-3.20, N-11.23, S-8.57.

2- hydroxy-N- (5-Bromo-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide:

IR spectrum (KBr, cm^{-1}) : 3069.12 (C-H aromatic), 1685.02 (C=Ostr), 1625.39 (C=Nstr), 1520.06 (C=Caromatic), 685.32 (S-CHstr); ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 3.42 (s, 2H, CH_2), 6.97-6.98 (s, 2H, aromatic OH), 7.01-7.03 (d, 1H, aromatic), 7.13-7.20 (m, 2H aromatic), 7.14-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide) ^{13}CNMR (100 MHz, $CDCl_3$): 32.4, 85.1, 117.8, 119.2, 119.8, 121.4, 124.3, 128.9, 130.0, 130.7, 133.5, 134.6, 140.1, 159.4, 164.8, 168.2, 168.8.

MS:m/z: 434.97 (100.0%), 432.97 (98.0%), 435.97 (20.02%), 433.98 (18.3%), Elemental analysis: $C_{17}H_{12}BrN_3O_4S$ Calculated Values: C-47.02, H-2.79, N-9.68, S-7.38: Observed Values: C-47.0, H-2.75, N-9.62, S-7.33:

2- hydroxy-N- (5, 6-Dichloro-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide: IR spectrum (KBr, cm^{-1}) : 3062.12 (C-H aromatic), 1688.02 (C=Ostr), 1628.39 (C=Nstr), 1529.06 (C=C aromatic), 681.32 (S-CHstr); ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 3.44 (s, 2H, CH_2), 6.97-6.98 (s, 2H, aromatic OH), 7.04-7.05 (d, 1H, aromatic), 7.13-7.20 (m, 2H aromatic), 7.14-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide) ^{13}CNMR (100 MHz, $CDCl_3$): 32.4, 85.3, 117.8, 119.8, 121.4, 123.9, 127.3, 128.1, 128.9, 130.1, 131.0, 133.5, 140.6, 159.4, 164.8, 168.2, 168.8. MS:m/z: 422.98 (100.0%), 424.98 (68.5%), 423.99 (18.7%), 426.98 (13.4%);

Elemental analysis: $C_{17}H_{11}Cl_2N_3O_4S$
Calculated Values: C-48.13, H-2.61, N-9.90, S-7.56:
Observed Values: C-48.10, H-2.59, N-9.89, S-7.52:

2- hydroxy-N- (5-Nitro-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl)benzamide

IR spectrum (KBr, cm^{-1}): 3069.12 (C-H aromatic), 1682.02 (C=Ostr), 1620.39 (C=Nstr), 1520.06 (C=C aromatic), 680.32 (S-CHstr); ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 3.44 (s, 2H, CH_2), 6.97-6.98 (s, 2H, aromatic OH), 7.04-7.05 (d, 1H, aromatic), 7.13-7.20 (m, 2H aromatic), 7.14-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide) ^{13}CNMR (100 MHz, $CDCl_3$): 32.4, 84.8, 109.3, 117.8, 119.8, 121.4, 123.0, 126.2, 128.7, 128.9, 133.5, 144.0, 147.2, 159.4, 164.8, 168.2, 168.8MS:m/z:400.05 (100.0%), 401.05 (19.6%), 402.04 (4.5%), 402.05 (3.3%), 401.04 (1.5%)

Elemental analysis: $C_{17}H_{12}N_4O_6S$
Calculated Values: C-51.00, H-3.02, N-13.99, S-8.01
Observed Values: C-50.98, H-3.00, N-13.96, S-8.00

2- hydroxy-N- (7-Nitro-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl) benzamide

IR spectrum (KBr, cm^{-1}): 3058.12 (C-H aromatic), 1682.02 (C=Ostr), 1645.39 (C=Nstr), 1532.06 (C=C aromatic), 668.32 (S-CHstr); ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 3.34 (s, 2H, CH_2), 6.54-6.55 (s, 2H, aromatic OH), 7.04-7.05 (d, 1H, aromatic), 7.20-7.22 (m, 2H aromatic), 7.34-7.36 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide) ^{13}CNMR (100 MHz, $CDCl_3$): 32.4, 84.8, 117.8, 119.8, 121.4, 124.2, 125.7, 128.7, 128.9, 130.6, 133.5, 135.9, 138.9, 159.4, 164.8, 168.2, 168.8. MS:m/z:400.05 (100.0%), 401.05 (19.6%).

Elemental analysis: $C_{17}H_{12}N_4O_6S$
Calculated Values: C-51.0, H-3.02, N-13.99, S-8.01
Observed Values: C-50.98, H-3.01, N-13.97, S-8.00.

2-hydroxy-N- (5-Hydroxy-2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl) benzamide
IR spectrum (KBr, cm^{-1}) :3069.12 (C-H aromatic), 1682.02 (C=Ostr), 1620.39 (C=Nstr), 1520.06 (C=C aromatic), 680.32 (S-CHstr); ^{1}HNMR (400 MHz, $CDCl_3$, δ, ppm): 3.44 (s, 2H, CH_2), 6.97-6.98 (s, 2H, aromatic OH), 7.04-7.05 (d, 1H, aromatic),

7.13-7.20 (m, 2H aromatic), 7.14-7.46 (m, 2H, aromatic), 7.69-7.7 (d, 1H, aromatic), 8.61 (s, 1H, amide) ^{13}CNMR (100 MHz, $CDCl_3$): 32.4, 86.1, 111.9, 115.0, 115.5, 117.8, 119.8, 121.4, 128.9, 129.2, 133.5, 133.7, 153.1, 159.4, 164.8, 168.2, 168.8. MS:m/z:371.06 (100.0%), 372.06 (19.5%), 373.05 (4.5%).

Elemental analysis: $C_{17}H_{13}N_3O_5S$.
Calculated Values: C-54.98, H-3.53, N-11.31, S-8.63:
Observed Values: C 54.96-, H-3.51, N-11.28, S-8.60.

Biological activities

In vitro anti-bacterial by using the results were depicted in Table 1.

Table 1: Physical data of the newly synthesized compounds (VIIa–j).

S. No.	Compound	R	Mol. F	Mol. Wt.	M.P (°C)	%Yield
1	VIa	H	$C_{17}H_{13}N_3O_4S$	355	260-262	75
2	VIb	5-Cl	$C_{17}H_{12}ClN_30_4S$	389	285-287	67.26
3	VIc	7-Cl	$C_{17}H_{12}ClN_30_4S$	389	290-292	70
4	VId	5-CH_3	$C_{18}H_{15}N_30_4S$	369	302-304	57
5	VIe	7-CH_3	$C_{18}H_{15}N_30_4S$	369	270-272	62
6	VIf	5-F	$C_{18}H_{16}FN_3O_4S$	389	250-252	73.19
7	VIg	7-F	$C_{18}H_{16}FN_3O_4S$	389	198-200	66.49
8	VIh	5-Br	$C_{17}H_{12}BrN_3O_4S$	434	320-322	75
9	VIi	5, 6-Dichloro	$C_{17}H_{11}Cl_2N_3O_4S$	424	310-312	60
10	VIj	5-NO_2	$C_{17}H_{12}N_4O_6S$	400	294-296	58
11	VIk	7-NO_2	$C_{17}H_{12}N_4O_6S$	400	333-335	62
12	VIl	5-OH	$C_{17}H_{13}N_3O_5S$	371	275-277	67

Evaluation of anti-bacterial activity

In vitro antibacterial activity was done by the disk diffusion technique [10]. The microorganisms used were purchased from (1) N-broth i.e., Nutrient broth medium (Sigma aldrich). (2) Sabouraud's dextrose broth medium (Sigma Aldrich). (3) Anti-bacteriological grade Agar-Agar (HIMEDIA, Mumbai). The tested compounds solution were prepared in dimethylformamide (DMF) and evaluated them for their *in vitro* antibacterial activity against *Bacillus subtilis* NCIM 2250, *Staphylococcus aureus* NCIM 2079, *Escherichia coli* NCIM 2109, *S. typhi*, respectively. All bacteria were grown on Mueller-Hinton agar (Hi-Media) plates (37°C, 24 h) The results were established by the presence of clear zone of inhibition around the active compounds. Suspensions of each microorganism were prepared to contain approximately 106 colony forming units (cfu)/ mL and applied to plates. The surface of the medium was allowed to dry. The 200 µg/ mL (in DMSO) compound impregnated discs were applied to the surface of inoculated plates. The Petri plates were incubated at 37 °C for antibacterial activity. The petri plates were examined for antibacterial activity after 18-24 h of incubation.

Table 2: *In vitro* anti-bacterial activity.

Compounds	R	*E. coli*	*B. subtillis*	*S. aureus*	*S. typhi*
VIa	H	NS	NS	NS	NS
VIb	5-Cl	6.5	9.5	9	10
Vic	7-Cl	7	11	10.2	6
VId	5-CH_3	NS	7	NS	NS
Vie	7-CH_3	NS	NS	7	12
VIf	5-F	6	6	8.6	10.6
VIg	7-F	8	10.6	NS	NS
VIh	5-Br	NS	NS	4.5	10
VIi	5, 6-Dichloro	5.5	8.5	5.8	6.2
VIj	5-NO_2	7	8.5	NS	7.5
VIk	7-NO_2	NS	NS	6	NS
VIl	5-OH	NS	6.2	NS	NS
Penicillin (10 µg/disc)		9	12	11	13

Note: NS: Not significant

RESULTS AND DISCUSSION

Some of the new isatin derivatives were obtained by cyclization of 2-hydroxy –N'[(3Z)-2-oxo-1, 2-dihydro-3H-indol-3-ylidene] benzohydrazide with thioglycollic acid in presence of glacial acetic acid depicted in Scheme 1. Physical data of all the synthesized compounds are shown in Table 1.

Anti-bacterial activity

The newly synthesized compounds were screened for anti-bacterial at the concentrations of 200 µg/ml. The results of antibacterial screening are presented in Table 2. Among the tested compounds VI (i)is highly active against *E. coli*, VI (f) is active against *B. subtilis*, VI (l) is active against *S. aureus* and VI (c) is active against *S. typhi.*

CONCLUSION

The present study involves synthesis and evaluation of 2-hydroxy-N- (2, 4^1-dioxospiro[indoline-3, 2^1-thiazolidin]-3^1-yl) benzamides for anti-bacterial activity. The title compounds have shown potent anti-bacterial activities.

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