IJPSR (2019), Volume 10, Issue 8 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 23 November 2018; received in revised form, 19 March 2019; accepted, 29 March 2019; published 01 August 2019

SYNTHESIS AND SCREENING *N*-(2, 4'-DIOXO-1, 2-DIHYDRO-3'*H*-SPIRO [INDOLE-3, 2'-[1,3]THIAZOLIDIN]-3'-YL)-2-HYDROXYBENZAMIDES FOR ANTI-BACTERIAL ACTIVITY

N. Saritha Devi [*1], B. Srinivas [2] and Manda Sarangapani [3]

Medicinal Chemistry Division [1], Faculty of Pharmaceutical Sciences [3], University College of Pharmaceutical Sciences, Kakatiya University, Warangal - 506009, Telangana, India.
Department of Chemistry [2], Guru Nanak Institutions Technical Campus, Hyderabad - 501506, Telangana, India.

Keywords:

Antibacterial, Isatin, Penicillin, Thiazolidinone

Correspondence to Author:
N. Saritha Devi

Research Scholar,
Medicinal Chemistry Division,
University College of Pharmaceutical Sciences, Kakatiya University, Warangal - 506009, Telangana, India.

E-mail: nellutlasaritha@gmail.com

ABSTRACT: A novel synthesis of *N*-(2, 4'-dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3] thiazolidin]-3'-yl)-2 -hydroxybenzamide derivatives were synthesized by cyclization of isatin hydrazones with thioglycolic acid. The synthesized compounds were characterized by spectral data (IR, ^{1}H-NMR, Mass) and evaluated for antibacterial activity against various strains of bacteria at the concentrations of 200 µg/ml. Among the tested compounds X(i) is highly active against *E. coli*, X(f) is active against *B. subtilis*, X(h) is active against *S. aureus* and X(c) is active against *S. typhi*.

INTRODUCTION: It is evident from literature, that isatin derivatives are known to be associated with a broad spectrum of biological activity like antibacterial [1], anti-inflammatory [2], analgesic [3], antiviral [4], anti-fungal [5], anti-tubercular [6] and anti-depressant [7]. Isatin hydrazone has been reported to possess anticonvulsant [8, 9] activities also. Given this fact prompted us to synthesize some new *N*-(2,4'-Dioxo-1, 2-dihydro-3'*H*-spiro[indole-3, 2'-[1,3]thia zolidin]- 3'- yl)- 2- hydroxybenzamides. All the synthesized compounds were screened for their *in-vitro* antibacterial activity.

MATERIALS AND METHODS: All the chemicals used were of analytical grade and obtained from Himedia and SD Fine,

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.10(8).3850-55

The article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.10(8).3850-55

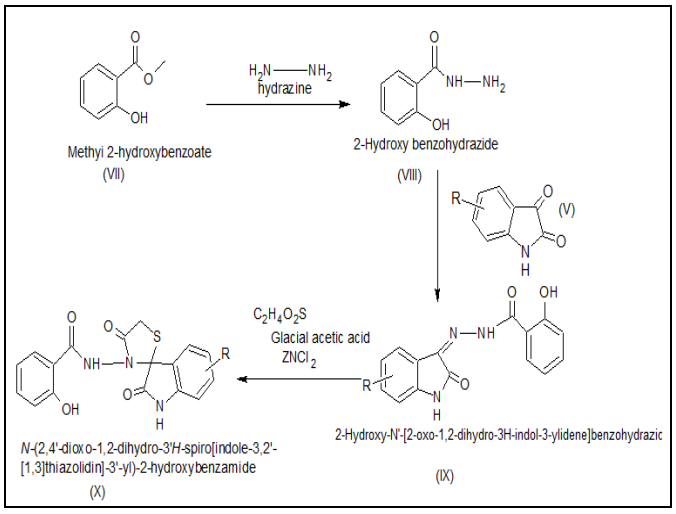
Melting points were determined by open capillary tubes using VEEGO VMP-D Digital melting point. FTIR spectra of the powdered compounds were recorded using KBr on a JASCO FTIR 4100 series and are reported in $cm^{-1,}$ and ^{1}H-NMR spectra were recorded on a Varian Mercury YH300 (400 MHz FT NMR) spectrophotometer using TMS as an internal reference (Chemical shift represented in ppm). The purity of the compounds was checked on TLC plates using silica gel G as the stationary phase and iodine vapors as the visualizing agent.

Chemistry:

Synthesis of Indole-2,3-diones:

Isonitrosoacetanilides: In a 5 lit RB flask, chloral hydrate (0.54 mol) and 1200 ml of water were placed. To this solution, crystallized sodium sulfate (1300 g) was then added followed by a solution of an appropriate aromatic amine (I) in 300 ml of water and concentrated hydrochloric acid (0.52mol). Finally, a solution of hydroxylamine HCl (1.58mol) in 500 ml of water was added. The contents of the flask were heated over a wire-gauge

of a Mecker burner so that vigorous boiling begins in about 45 min. After 1 to 2 min of vigorous boiling, the reaction was completed. During the heating period itself, the crystals of isonitroso-acetanilides were started separating. On cooling under the current of water, the entire product was solidified. It was filtered under suction, air dried and purified by recrystallization using a suitable solvent(s).



SCHEME 1: *N*-(2,4'-Dioxo-1,2-dihydro-3'*H*-spiro[indole-3,2'-[1,3]thiazolidin]-3'-yl)-2-hydroxybenzamide

Indole-2,3-diones(V): Sulphuric acid (600 g, d, 1.84, 326 mL) was warmed at 50 ºC in a one liter RB flask fitted with an efficient mechanical stirrer and to this, finely powdered appropriate isonitroso-acetanilide (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 min, 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 done by the recrystallization from methanol.

Preparation of 2-Hydropxybenzohydrazide (VIII): In a 500 ml of RB flask, 10 g of methyl salicylate (VII) and 50 ml of distilled alcohol were placed, and the reaction mixture was shaken for 5 minutes. To it 20 ml of hydrazine hydrate (99%) was added and the contents of the flask were refluxed for 3 h, the completion of the reaction was 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) benzohydrazides (IX(a-l)): A mixture of an appropriate indole-2,3-dione (V)(0.01 mol) and 2-hydroxybenzohydrazide (0.01mol) was taken into methanol (50 ml) in the presence of glacial acetic acid which was heated under reflux on water bath for 6-7 h. The colored compounds thus obtained upon cooling, were filtered, washed with small portions of cold methanol, and were dried. They were purified by recrystallization from alcohol.

TABLE 1: PHYSICAL DATA OF THE NEWLY SYNTHESIZED COMPOUNDS (X(a–l))

S. no.	Compound	R	Mol. F	Mol. Wt.	M.P(°C)	%Yield
1	Xa	H	$C_{17}H_{13}N_3O_4S$	355	260-262	75
2	Xb	5-Cl	$C_{17}H_{12}ClN_30_4S$	389	285-287	67.26
3	Xc	7-Cl	$C_{17}H_{12}ClN_30_4S$	389	290-292	70
4	Xd	5-CH_3	$C_{18}H_{15}N_30_4S$	369	302-304	57
5	Xe	7-CH_3	$C_{18}H_{15}N_30_4S$	369	270-272	62
6	Xf	5-F	$C_{18}H_{16}FN_3O_4S$	389	250-252	73.19
7	Xg	7-F	$C_{18}H_{16}FN_3O_4S$	389	198-200	66.49
8	Xh	5-Br	$C_{17}H_{12}BrN_3O_4S$	434	320-322	75
9	Xi	5,6-Dichloro	$C_{17}H_{11}Cl_2N_3O_4S$	424	310-312	60
10	Xj	5-NO_2	$C_{17}H_{12}N_4O_6S$	400	294-296	58
11	Xk	7-NO_2	$C_{17}H_{12}N_4O_6S$	400	333-335	62
12	Xl	5-OH	$C_{17}H_{13}N_3O_5S$	371	275-277	67

Synthesis of *N*-(2,4'-Dioxo-1,2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3]thiazolidin]-3'-yl)-2-hydroxy benzamides (X(a-l)): To the above compound (0.01mol), thioglycolic acid (0.01mol), pinch of $ZnCl_2$ and 10 ml of glacial acetic acid were added and refluxed for 6 h. Then the reaction mixture was

cooled and poured into crushed ice. To its 10% sodium carbonate solution was added to neutralize the acid. Then filter the reaction mixture and the product obtained was washed thoroughly with cold water and dried. The compound was purified by recrystallisation from methanol.

Spectral Data of the Synthesized Compounds:

X(a) *N*-(2,4'-Dioxo-1,2-dihydro-3'*H*-spiro[indole -3, 2'-[1, 3] thiazolidin]-3'- yl)- 2- hydroxy benzamide: IR spectrum (KBr, cm^{-1}): 3459.01 (OH), 3124.06 (ISATIN NH), 3102.05(N-H), 3061.90 (C-H aromatic), 1767.20 (C=O), 1639.07 (C=O); ^{1}H NMR (400MHz CDCl3, 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),7.71(d, 1H, Indole ArH), 10.04(s, 1H, Phenolic OH); ^{13}CNMR (100MHz, CDCl3): 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: 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. MS: m/z: 355.06 (100.0%), 356.07 (18.7%).

X(b) *N*-(5-Chloro-2,4'-Dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3]thiazolidin]-3'-yl) -2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3458.21 (OH), 3123.56 (ISATIN NH), 3100.45 (N-H), 3063.23 (C-H aromatic), 1764.50 (C=O), 1637.35 (C=O); ^{1}H NMR (400MHz CDCl3, 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, Indole ArH), 9.85(s, 1H, Phenolic OH); ^{13}C NMR(100MHz,$CDCl_3$):-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. 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: MS: m/z: 389.02 (100.0%), 391.02 (36.7%), 390.03(18.7%).

X(c) *N*-(7-Chloro-2, 4'-Dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3] thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3460.11 (OH), 3125.06 (ISATIN NH), 3103.35 (N-H), 3065.46(C-H aromatic), 1763.23 (C=O), 1639.32 (C=O); ^{1}H NMR (400MHz $CDCl_3$, 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, Indole ArH), 10.04 (s, 1H, Phenolic OH); ^{13}C NMR (100MHz,$CDCl_3$): 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. 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: MS: m/z: 389.02(100.0%), 391.02 (36.7%).

X(d) *N*-(5-Methyl-2, 4'-Dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3]thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}) 3459.34 (OH), 3126.27 (ISATIN NH), 3105.32 (N-H), 3062.44 (C-H aromatic), 1760.26 (C=O), 1640.34 (C=O); ^{1}H NMR (400MHz $CDCl_3$, 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, Indole ArH), 10.04 (s, 1H, Phenolic OH) ^{13}C-NMR (100MHz,$CDCl_3$): -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. 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. MS: m/z: 369.08 (100.0%), 370.08 (21.7%).

X(e) *N*-(7-Methyl-2,4'-Dioxo-1, 2-dihydro-3'*H*-spiro[indole-3, 2'-[1, 3] thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3457.24 (OH), 3125.22 (ISATIN NH), 3101.33 (N-H), 3060.42 (C-H aromatic), 1758.26 (C=O), 1642.34 (C=O); ^{1}H NMR (400MHz $CDCl_3$, 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, Indole ArH),9.85(s, 1H, Phenolic OH); ^{13}C-NMR (100MHz,$CDCl_3$): 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. 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. MS: m/z: 369.08 (100.0%), 370.08 (21.7%).

X(f) *N*-(5-Fluoro-2, 4'-Dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3]thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3460.41(OH), 3129.20 (ISATIN NH), 3104.31(N-

H), 3062.41 (C-H aromatic), 1760.24 (C=O), 1645.31 (C=O); ^{1}H-NMR (400MHz, $CDCl_3$, 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, Indole ArH), 9.85 (s, 1H, Phenolic OH); ^{13}C-NMR (100MHz,$CDCl_3$): 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. 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. MS: m/z: 373.05 (100.0%), 374.06 (18.7%), 375.05 (4.7%).

X(g) *N*-(7-Fluoro-2, 4'-Dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3] thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3458.21 (OH), 3127.20 (ISATIN NH), 3100.41 (N-H), 3060.31 (C-H aromatic), 1757.22 (C=O), 1641.31 (C=O); ^{1}HNMR (400MHz, CDCl3, 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, Indole ArH), 10.04(s, 1H, Phenolic OH); ^{13}C-NMR (100MHz, $CDCl_3$): 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. 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. MS: m/z: 373.05 (100.0%), 374.06 (18.7%), 375.05 (4.7%).

X(h) *N*-(5-Bromo-2, 4'-Dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3] thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3461.32 (OH), 3129.20 (ISATIN NH), 3106.51 (N-H), 3059.33 (C-H aromatic), 1759.19 (C=O), 1644.21 (C=O); ^{1}HNMR (400MHz, $CDCl_3$, 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, Indole ArH), 10.04 (s, 1H, Phenolic OH) ^{13}CNMR (100MHz, $CDCl_3$): 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.

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. MS: m/z: 434.97 (100.0%), 432.97 (98.0%), 435.97 (20.02%), 433.98 (18.3%).

X(i) *N*-(5, 6-Di chloro-2, 4'-Dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3] thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3443.22 (OH), 3103.10 (ISATIN NH), 3100.41 (N-H), 2922.31 (C-H aromatic), 1786.29 (C=O), 1621.11 (C=O); ^{1}HNMR (400MHz, CDCl3, 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, Indole ArH), 9.85(s, 1H, Phenolic OH) ^{13}C-NMR(100MHz, $CDCl_3$): 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. 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, MS: m/z: 422.98 (100.0%), 424.98 (68.5%), 423.99 (18.7%), 426.98 (13.4%).

X(j) *N*-(5-Nitro-2, 4'-Dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3] thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3466.32 (OH), 3124.17 (ISATIN NH), 3101.21 (N-H), 3059.11 (C-H aromatic), 1760.24 (C=O), 1642.15 (C=O); ^{1}HNMR (400MHz, $CDCl_3$, 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, Indole ArH), 9.85 (s, 1H, Phenolic OH) ^{13}C-NMR (100MHz, $CDCl_3$): 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, 168.8, 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, MS: m/z: 400.05 (100.0%), 401.05 (19.6%), 402.04 (4.5%), 402.05 (3.3%), 401.04 (1.5%).

X(k) *N*-(7-Nitro-2, 4'-Dioxo-1, 2-dihydro-3'*H*-spiro[indole-3, 2'-[1, 3] thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3462.11 (OH), 3123.27 (ISATIN NH), 3104.31 (N-H), 3063.21 (C-H aromatic), 1758.34 (C=O), 1644.35 (C=O); ^{1}H-NMR (400MHz, $CDCl_3$, 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, Indole ArH), 9.85 (s, 1H, Phenolic OH) ^{13}C-NMR(100MHz,$CDCl_3$): 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. 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, MS: m/z: 400.05 (100.0%), 401.05 (19.6%).

X(l) *N*-(5-Hydroxy-2, 4'-Dioxo-1, 2-dihydro-3'*H*-spiro [indole-3, 2'-[1, 3] thiazolidin]-3'-yl)-2-hydroxybenzamide: IR spectrum (KBr, cm^{-1}): 3461.21 (OH), 3124.47 (ISATIN NH), 3100.21 (N-H), 3060.11 (C-H aromatic), 1765.32 (C=O), 1645.35 (C=O); ^{1}H-NMR (400MHz, $CDCl_3$, 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, Indole ArH), 10.04 (s, 1H, Phenolic OH) ^{13}C-NMR (100MHz, CDCl3): 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. 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: C54.96, H-3.51, N-11.28, S-8.60, MS: m/z: 371.06 (100.0%), 372.06 (19.5%), 373.05(4.5%).

Biological Activity: *In-vitro* antibacterial activity results were depicted in **Table 2**.

TABLE 2: *IN-VITRO* ANTIBACTERIAL ACTIVITY

Compound	R	*E. coli*	*B. subtilis*	*S. aureus*	*S. typhi*
Xa	H	NS	NS	NS	NS
Xb	5-Cl	6.5	9.5	9	10
Xc	7-Cl	7	11	10.2	6
Xd	5-CH_3	NS	7	NS	NS
Xe	7-CH_3	NS	NS	7	12
Xf	5-F	6	6	8.6	10.6
Xg	7-F	8	10.6	NS	NS
Xh	5-Br	NS	NS	4.5	10
Xi	5,6-Dichloro	5.5	8.5	5.8	6.2
Xj	5-NO_2	7	8.5	NS	7.5
Xk	7-NO_2	NS	NS	6	NS
Xl	5-OH	NS	6.2	NS	NS
Penicillin(10 µg/disc)		9	12	11	13

NS: Not significant.

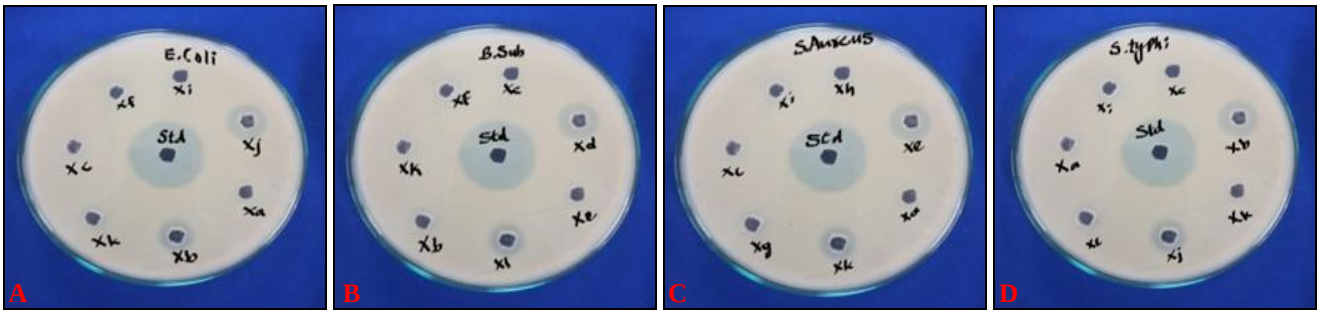


FIG. 1: (A) *E. COLI* (B) *B. SUBTILIS* (C) *S. AURES* (D) *S. TYPHI*

Evaluation of Antibacterial 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 *Baccillus subtillis* 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, 24h). The results were established by the presence of a clear zone of inhibition around the active compounds. Suspensions of each micro-organism were prepared to contain approximately 10^6 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.

RESULTS AND DISCUSSION: Some of the new isatin derivatives were obtained by cyclization of 2-hydroxy -N' [2-oxo -1, 2-dihydro -3H -indol-3-ylidene] benzohydrazide with thioglycolic acid in the presence of glacial acetic acid depicted in **Scheme 1**. Physical data of all the synthesized compounds are shown in **Table 1**.

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

CONCLUSION: The present study involves synthesis and evaluation of *N*-(2, 4'-dioxo-1, 2-dihydro-3'*H*-spiro [indole-3,2'-[1, 3] thiazolidin]-3'-yl)-2-hydroxybenzamides for anti-bacterial activity. The title compounds have shown potent anti-bacterial activities.

ACKNOWLEDGEMENT: The authors are very grateful to the Principal, University College of Pharmaceutical Sciences for providing facilities to perform the work. The authors are also thankful to IICT Hyderabad for providing the spectral data.

CONFLICT OF INTEREST: The authors declared no conflict of interest.

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How to cite this article:
Devi NS, Srinivas B and Sarangapani M: Synthesis and screening *N*-(2, 4'-dioxo-1, 2-dihydro-3'*H*-spiro[indole-3,2'-[1,3]thiazolidin]-3'-yl)-2-hydroxybenzamides for anti-bacterial activity. Int J Pharm Sci & Res 2019; 10(8): 3850-55. doi: 10.13040/IJPSR.0975-8232. 10(8).3850-55.