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Synthesis of some substituted azetidinonyl and thiazolidinonyl-1,3,4-thiadiazino[6,5-*b*]indoles as prospective antimicrobial agents

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Several 2-[(3-chloro-2-substituted phenyl)-4-azetidinon-3-yl]-1,3,4-thiadiazino[6,5-*b*]indoles and 2-[(2-substituted phenyl)-4-thiazolidinon-3-yl]-1,3,4-thiadiazino[6,5-*b*]indoles have been synthesized. The structures of the synthesized compounds are characterized by elemental and spectral analysis. These compounds are also evaluated for their antimicrobial susceptibility test against *S.aureus, E.coli, K.pneumoniae, P.vulgaris* and *A.fumigatus, C.albicans, A. albicans ATCC, C. krusei G03* respectively. Compounds **4c** and **5e** showed the most potent antibacrerial and antifungal activities. These two compounds are devoid of any toxicity.

Keywords: Benzylidenaminoindoles, azetidinon-3-yl-1,3,4-thiadiazino[6,5-*b*] indoles, antibacterial activity, antifungal activity

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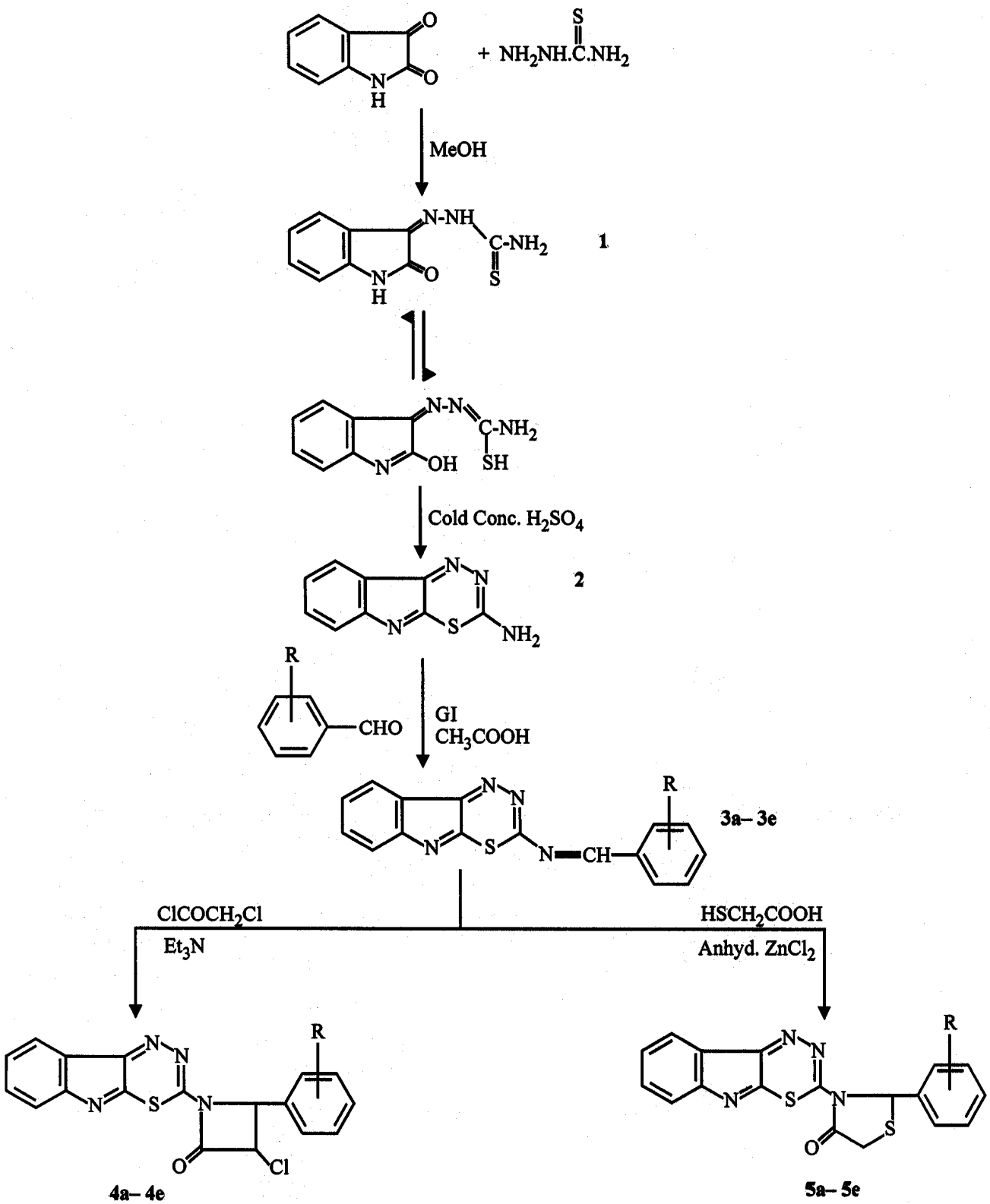
Bacterial resistance to the antibiotics is a big blow to humanity and continual search for newer chemotherapeutic agents is the only way to fortify against this awful threat. Indole and its analogs constitute the active class of the compounds possessing wide spectrum of biological activities[1-2]. fungicidal[3], bactericidal[4] and tuberculostatic[5]. Various indole derivatives exhibited antidepressive[3], anti-inflammatory[4], fungicidal[5], bactericidal[6] and tuberculostatic[7] activities. Further azetidinones and thiazolidinones are well famed for their antimicrobial[8-11] activities. In the light of above reports and also in continuation of our laboratory work on chemoselective reaction of indole derivatives, a drug strategy has been planned to synthesize several indole derivatives possessing azetidinone and thiazolidinone moieties with the hope to possess better antimicrobial activity. All the synthesized compounds were screened for their antibacterial and antifungal activities against some selected microbes.

Result and Discussion

The chemical synthesis initiates with the reaction of indole-2,3-dione with thiosemicarbazide to yield 3-thiosemicarbazidoindole-2-one **1**. 2-Amino-1,3,4-thiadiazino[6,5-*b*]indole **2** was prepared by the cyclization of compound **1** with cold, conc. sulphuric acid. Treatment of different aromatic aldehydes in presence of gl. acetic acid with compound **2** yielded 2-substituted arylidenamino-1,3,4-thiadiazino[6,5-*b*]-indoles **3a-e**. 2-[(3-chloro-2-substituted phenyl)-4-azetidinon-3-yl]-1,3,4-thiadiazino[6,5-*b*]indoles **4a-e** were sysnthesized by reacting compounds **3a-e** with chloro acetyl chloride in presence of triethyl amine. Compounds **3a-e** were refluxed with thioglycolic acid in presence of anhydrous $ZnCl_2$ to yield 2-[(2-substituted phenyl)-4-thiazolidinon-3-yl]-1,3,4-thiadiazino-[6,5-*b*] indoles **5a-e** (**Scheme I)**. The structure of all the newly indole derivatives were confirmed on the basis of spectral and analytical data.

Antimicrobial activity

Preliminary antimicrobial susceptibility tests for all the synthesized indole derivatives were performed by using cup plate method[12] at a concentration of 250 μg/mL against some selected pathogenic strains. *S. aureus, E.coli., P. vulgaris, K.pneumoniae* were used for bactericidal activity and *A. fumigatus, C.albicans, C.albicans* ATCC, *C.crusei* G03 for fungicidal activity. Prepared nutrient agar (Qualigen Fine Chem., Mumbai, India) was used to subculture differ-



R=H, *p*-OCH_3, *o*-OH, *m*-OCH_3 & *p*-OH, *p*-n$(CH_3)_2$

Scheme I

ent strains of bacteria while SDA (Sabouraud Dextrose Agar-Himedia Labs., Mumbai) to subculture selected fungal strains. Plates incubated 24 hr for bactricidal and 48 hr for fungicidal activity. The inhibition zone for testing compounds was measured in mm **(Table I)**.

Acute Toxicity

Lethal dose (LD_{50}) of compounds was determined in albino mice. After 24 hr of drug administration, mortality in each group was observed and from the data obtained LD_{50} was calculated by the method of Carrol[13]. Data revealed that compound **4a** and **5e** do not show any toxicity up to dose of 10.25 mg/kg and 12.50 mg/kg body weight in mice.

The synthesized molecules in **Scheme I** were screened for antibacterial and antifungal activity. The results are summarized in **Table I**. Compound **1** on screening showed poor bioactivity. Cyclization of compound **1** yielded compound **2**, exhibited slight increase in bacterial inhibition. The characteristic feature of compounds **3a-e** was the presence of azomethine(-N=CH-) linkage. Observation of results cleared that the order of bioactivity was **3c**>**3b**>**3e**>**3d**>>**3a**. As compound **3c** and **3b** showed equipotent inhibitory effect. Compounds **4a-e** were characterized by the presence of substituted azetidinone moiety. The order of biological activity for these compounds **4a-e** was found **4c**>**4e** >**4d** >**4b**> **4a**. Compound **4c** was found to possess most inhibitory effect against *S.aureus. E.coli* respectively. Conversion of compounds **3a-e** lead to different thiazolidinones **5a-e**. They showed their inhibitory property in order of **5e**> **5d**> **5c**>**5b**>> **5a**. Compound **5a** devoid of any biological activity. Compound **5b** showed poor while **5c** and **5d** exhibited moderate activity. It was **5e** which demonstrated comparable antifungal activity in comparison to used standard. Considering the potency of these two compounds (**4c** and **5e)**, these further revaluated at lower concentration to determine the MIC_{90} by serial tube dilution method[14] against *E. coli* and *C .albicans*. The MIC_{90} levels of the compound **4c** were 0.025 μg/mL against *E.coli* while 1.25 μg/mL for compound **5e** against *C .albicans*.

Discussion

On the basis of structure activity relationship, it is concluded that incorporation of S atom 2 brings an increase in bactericidal inhibition. Azomethine **3a-e** linkage enhances antibacterial and antifungal activity. *p*-Methoxy substituted azetidinone **4c** and *o*-hydroxy substituted thiazolidinone **5e** moieties claim most potent antibacterial and antifungal activity. It is interesting to point out that compound **4c** showed much potency than the used ampicillin and gatifloxacin standards and compound **5e** possessed comparable inhibitory effect to fluconazole.

Experimental Section

The melting points of the compounds were determined in open glass capillaries with the help of thermonic melting point apparatus and are uncorrected. The homogeneity of all the newly synthesized compounds was routinely checked by TLC on silica gel G plates and spots were located by using iodine chamber.

Elemental analysis of all the synthesized compounds were determined by a Perkin-Elmer 2400 elemental analyzer, and results were found within the ± 0.4% of theoretical values. IR spectra were recorded in KBr on a Perkin-Elmer-Spectrum RX-I, spectrometer. ^{1}H NMR spectra were recorded by Bruker AC-300 F instrument using DMSO–d_6 as solvent and tetramethylsilane (TMS) as internal reference standard. All chemical shift values were recorded as δ (ppm). Mass spectra were determined on a VG–70-S instrument.

3-Thiosemicarbazido indole-2-one 1. A mixture of indole-2, 3-dione (2 g), thiosemicarbazide (1.23 g) in methanol (50 mL) was refluxed for 1 hr. The completion of reaction was checked by TLC and excess of methanol distilled out. The cooled, refluxed residual was poured into ice water, filtered, washed with water, dried and recrystallized from methanol to obtain compound **1** (80%), m.p. 200ºC; IR (KBr, cm^{-1}): 1200, 1610, 1682, 1710, 3144, 3419; ^{1}H NMR ($CDCl_3$+DMSO-d_6,): δ 6.75-6.95 (d, $1H_d$), 7.02-7.10 (t, $1H_c$), 7.22-7.30 (t, $1H_b$), 7.5707.62 (d, $1H_a$), 8.90 (bs, 2H), 9.36 (bs, 1H) ppm. Anal. Calcd for $C_9H_8N_4SO$: C, 49.09; H, 3.63; N, 25.45. Found: C, 49.38; H, 3.41; N, 25.60%. MS: $[M]^+$ at m/z 220.

2-Amino-1,3,4-thiadiazino(6,5-*b*)indole 2. Compound **1** (3 g) was mixed with small quantity of cold and conc. H_2SO_4 (1.52 mmole). The reaction mixture was left at room temp for 16 hr. After this, reaction mixture was poured into ice-cold water, neutralized with liquid ammonia to obtain solid mass, which was filtered, washed with water, dried and recrystallized from methanol to yield compound **2** (65%), m.p.

Table I — Antibacterial and antifungal activity of the synthesized compounds

Compd	R	Bacterial growth inhibition (diameter in mm)				Fungal growth inhibition (diameter in mm)			
		S. aureus	*E. coli*	*P. vulgaris*	*K. pneumoniae*	*A. fumigatus*	*C. albicans*	*C. albicans ATCC*	*C. Krusei G03*
1	-	6	-	-	8	-	5	-	-
2	-	7	5	-	8	-	-	-	-
3a	H	-	-	-	-	-	-	-	-
3b	*m*-OCH_3 & *p*-OH	-	8	10	-	-	-	9	-
3c	*p*-OCH_3	8	18	-	18	8	14	10	-
3d	*p*-$N(CH_3)_2$	15	-	-	-	-	-	-	-
3e	*o*-OH	7	16	-	8	10	15	12	-
4a	H	16	16	-	-	12	17	10	10
4b	*m*-OCH_3 & o-OH	14	-	14	9	-	15	15	14
4c	*p*-OCH_3	30	36	-	6	12	18	16	10
4d	*p*-$N(CH_3)_2$	16	16	-	-	13	16	18	10
4e	*o*-OH	33	34	-	-	15	-		
5a	H			-	-	-	-	-	-
5b	*m*-OCH_3 & *p*-OH	12	-	5	-	-	-	-	-
5c	*p*-OCH_3	15	18	-	-	-	-	-	-
5d	*p*-$N(CH_3)_2$	12	15	-	10	10	10	-	8
5e	*o*-OH	18	16	-	8	25	26	-	18
Ampicillin		20	18	18	14	-	-	-	-
Gattifloxacin		25	22	20	21	-	-	-	-
Fluconazole		-	-	-	-	-	29	25	19

*250 μg/mL - Drug concentration.

230ºC; IR(KBr, cm^{-1}): 672, 1295, 1611, 1683, 3144, 3420; ^1H NMR ($CDCl_3$+DMSO-d_6): δ 6.89-6.97 (d,1H_d), 7.00-7.05 (t,1H_c), 7.26-7.31 (t,1H_b), 7.56-7.59 (d,1H_a), 8.58 (bs,2H) ppm. Anal. Calcd for $C_9H_6N_4S$: C, 53.46; H, 2.97; N, 27.72. Found: C, 53.26; H, 3.15; N, 27.94%. MS: $[M]^+$ at m/z 202.

Benzylidenamino-1,3,4-thiadiazino[6,5-*b*]indole 3a. The equimolar mixture (.01 mole) of compound **2** and benzaldehyde (.01 mole) in methanol (50 mL) was refluxed for 6 hr in presence of gl. acetic acid. The completion of reaction was checked by TLC and excess of methanol distilled off. After this, refluxed reaction mixture was poured into ice-water, filtered, washed with water and dried. Dried mass was recrystallized from ethanol to yield compound **3a** (68%) m.p. 224ºC; IR (KBr, cm^{-1}) 672, 1296, 1611, 1682, 31; ^1H NMR ($CDCl_3$+DMSO-d_6,): δ 6.47-6.68 (m,5H), 6.86-6.96 (d,1H_d), 7.02-7.12 (t,1H_c), 7.23-7.28 (t,1H_b), 7.56-7.60 (d,1H_a), 8.29 (s,1H) ppm. Anal. Calcd for $C_{16}H_{10}N_4S$: C, 66.20; H, 3.44; N, 19.31. Found: C, 65.96; H, 3.61; N, 19.18%. MS: $[M]^+$ at m/z 290.

2-[4-Hydroxy-3-methoxybenzylidenamino]-1, 3, 4-thiadiazino[6,5-*b*]indole 3b. m.p. 245ºC (methanol-water); IR (KBr, cm^{-1}): 673, 1062, 1297, 1612, 1680, 3145, 3420; ^1H NMR ($CDCl_3$+DMSO-d_6): δ 3.72 (s, 3H), 6.72 (s, 1$H_{a'}$), 6.90-6.92 (d, 1$H_{d'}$), 7.01-7.06 (t, 1H_c), 7.27-7.32 (t, 1H_b), 7.54-7.56 (d, 1H_a), 7.76-7.79 (d, 1$H_{b'}$), 7.87-7.90 (d,1$H_{c'}$), 8.25 (s,1H), 12.78(ss,1H) ppm. Anal. Calcd for $C_{17}H_{12}N_4O_2S$: C, 60.71; H, 3.57; N, 16.66. Found: C, 60.50; H, 3.32; N, 16.39%. MS: $[M]^+$ at m/z 336.

2-[4-Methoxybenzylidenamino]-1, 3, 4-thiadiazino[6,5-*b*]indole 3c. m.p. 232-33ºC (ethanol-water); IR (KBr, cm^{-1}): 673, 1060, 1297, 1610, 1681, 31448; ^1H NMR ($CDCl_3$+DMSO-d_6): δ 3.68 (s,3H), 6.52-6.75 (m,4H), 6.92-6.93 (d,1H_d), 7.00-7.04 (t,1H_c), 7.26-7.31 (t, 1H_b), 7.36-7.37 (d,1H_a), 8.31 (s, 1H) ppm. Anal. Calcd for $C_{17}H_{12}N_4SO$: C, 63.75; H, 3.75; N, 17.50. Found: C, 63.49; H, 3.50; N, 17.74%. MS: $[M]^+$ at m/z 320.

2-[4-*N*, *N*-Dimethyl benzylidenamino]-1, 3, 4-thiadiazino[6, 5-*b*]indole 3d. m.p. 212-13 ºC (DMF-Water); IR (KBr, cm^{-1}): 673, 1297, 1610, 1683,

3144; ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 2.15 (s, 6H) 6.63-6.78 (m, 4H), 6.88-6.90 (d,1H_d), 6.998-7.02 (t,1H_c), 7.28-7.30 (t,1H_b), 7.36-7.39 (d,1H_a), 8.29 (s,1H) ppm. Anal. Calcd for $C_{18}H_{15}N_5S$: C, 64.86; H, 4.50; N, 21.02. Found: C, 64.98; H, 4.27; N, 21.30% MS: at m/z 333.

2-[2-Hydroxy benzylidenamino]-1, 3, 4-thiadiazino[6,5-*b*]indole 3e. m.p. 239-40ºC. (DMF-Water); IR (KBr, cm^{-1}): 672, 1294, 1611, 1683, 3142, 3421; ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 6.60-6.76 (m, 4H), 6.92-6.94 (d, 1H_d), 7.02-7.07 (t, 1H_c), 7.28-7.33 (t, 1H_b), 7.37-7.39 (d, 1H_a), 8.30 (s, 1H), 12.81 (ss, 1H) ppm. Anal. Calcd for $C_{16}H_{10}N_4SO$: C, 62.74; H, 3.26; N, 18.30. Found: C, 63.02, H, 3.12; N, 18.47%. MS: $[M]^+$ at m/z 306.

2- [3-Chloro-2-phenyl)-4-azetidinon-3-yl]-1, 3, 4-thiadiazino[6,5-*b*]indole 4a. To the ethanolic solution of the synthesized compound **3a** (0.01 mole), chloro acetyl chloride (.01 mole) was added dropwise with constant stirring in presence of triethyl amine (.01 mole) at 0-5ºC. The reaction mixture was refluxed for 8 hr. The completion of reaction was checked by TLC and excess of ethanol distilled off. The resulting residual mass was cooled, poured into ice water, filtered, washed with water, dried and recrystallized from methanol to yield compound **4a** (65%), m.p. 249-50ºC; IR (KBr, cm^{-1}) 672, 1295, 1610, 632, 1675, 1712, 3153; ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 4.87-4.91 (d, 1H), 6.56-6.68 (d, 1H), 6.69-6.82 (m, 5H), 6.91-6.92 (d, 1H_d), 7.08-7.11 (t, 1H_c), 7.27-7.30 (t, 1H_b), 7.36-7.39 (d, 1H_a) ppm. Anal. Calcd for $C_{18}H_{11}N_4SOCl$: C, 59.01; H, 3.00; N, 15.30. Found: C, 59.34; H, 3.20; N, 15.17%. MS: $[M]^+$ at m/z 366.

2 - [{3-Chloro-2-(4-hydroxy-3-methoxyphenyl)}-4-azetidinon-3-yl]-1, 3, 4-thiadiazino[6,5-*b*]indole 4b. m.p. 235-36ºC (ethanol-water); IR (KBr, cm^{-1}): 633, 673, 1205, 1296, 1617, 1676, 1711, 3153; ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 3.84 (s, 3H), 4.87-4.91 (d, 1H), 6.56-6.70 (d, 1H), 6.83(s, 1$H_{a'}$), 6.94-6.97 (d, 1H_d), 6.70-7.05 (t, 1H_c), 7.26-7.31 (t, 1H_b), 7.54-7.56 (d, 1H_a), 7.81-7.89 (d, 1$H_{b'}$), 8.02-8.17 (d, 1$H_{a'}$), 12.74 (ss, 1H) ppm. Anal. Calcd for $C_{19}H_{13}N_4SO_3Cl$: C, 55.33; H, 3.15; N, 13.59. Found: C, 54.98; H, 2.94; N, 13.30%. MS: $[M]^+$ at m/z 412.

2 - [{3-Chloro-2-(4-methoxyphenyl)}- 4- azetidinon-3-yl] -1, 3, 4-thiadiazino[6, 5-*b*]indole 4c. m.p. 226-27ºC (DMF-water); IR (KBr, cm^{-1}) 633, 673, 1206, 1294, 1617, 1675, 1710, 3154; ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 3.78 (s, 3H), 4.86-4.88 (d, 1H), 6.48-6.55 (d, 1H), 6.58-6.78 (m, 4H), 6.93-6.95 (d, 1H_d), 7.07-7.10(t, 1H_c), 7.25-7.30 t, 1H_b), 7.35-7.39 (d, 1H_a) ppm. Anal. Calcd for $C_{19}H_{13}N_4SO_2Cl$: C, 57.57; H, 3.28; N,14.14. Found: C, 57.64; H, 3.38; N, 13.92%. MS: $[M]^+$ at m/z 396.

2-[{3-Chloro-2-(4-N, N-Dimethylphenyl)}-4-azetidin-3-yl]-1,3,4-thiadi-azino[6,5-*b*]indole 4d. m.p. 241-42ºC (methanol); IR (KBr, cm^{-1}): 633, 673, 1206, 1294, 1615, 1674, 1710, 3153; ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 2.151(s,6H), 4.80-4.84 (d,1H), 6.50-6.56 (d,1H), 6.60-6.79(4H), 6.86-6.90(d, 1H_d), 7.11-7.19(t, 1H_c),7.25-7.28 (t, 1H_b), 7.31-7.40 (d, 1H_a) ppm. Anal. Calcd for $C_{20}H_{16}N_5SOCl$: C, 58.67; H, 3.91; N, 17.11. Found: C, 58.84; H, 4.12; N, 17.25%. MS: $[M]^+$ at m/z 409.

2-[{3-Chloro-2-(4-hydroxy-3-methoxy phenyl)}-4-azetidinon-3-yl]-1,3,4-thiadia-zino[6,5-*b*]indole 4e. m.p. 229-30ºC (ethanol-water); IR (KBr, cm^{-1}): 633, 672, 1296, 1615, 1675, 1710, 3153, 3421; ^{1}H NMR ($CDCl_3$ + DMSO-d_6): δ 4.76-4.78 (d, 1H), 6.51-6.58 (d, 1H), 6.63-6.83 (m, 4H), 6.86-6.89 (d, 1H_d), 7.10-7.17(t, 1H_c), 7.25-7.28 (t, 1H_b), 7.31-7.39 (d, 1H_a), 12.79 (ss, 1H) ppm. Anal. Calcd for $C_{18}H_{11}N_4SO_2Cl$: C, 56.54; H, 2.87; N, 14.64. Found: C, 56.64; H, 3.02; N, 14.47%. MS: $[M]^+$ at m/z 382.

2-[2-Phenyl-4-thiazolidinon-3-yl]-1, 3, 4-thiadiazino[6,5-*b*]indole 5a. To a solution of compound **3a** in methanol (50 mL), thioglycolic acid (.02 mole) was added dropwise in presence of anhydrous zinc chloride and this mixture was refluxed for 8 hr. The completion of the reaction was checked by TLC. The excess of methanol was distilled off. The cooled residual mass was diluted with ice-water, filtered, washed with water, dried and recrystallized from suitable ethanol-water to yield compound **5a** (62%), m.p. 214-15ºC; IR (KBr, cm^{-1}): 672, 1293, 1525, 1611, 1685, 1690, 3145; ^{1}H NMR ($CDCl_3$+DMSO-d_6): δ 3.85 (s, 2H), 6.51 (s, 1H), 6.68-6.77 (m, 5H), 6.90-6.93 (d, 1H_d), 7.11-7.15 (t, 1H_c), 7.28-7.31 (t, 1H_b), 7.57-7.62 (d, 1H_a) ppm. Anal. Calcd for $C_{18}H_{12}N_4S_2O$: C, 59.34; H, 3.29; N, 115.38. Found: C, 59.56; H, 3.40; N, 15.19%. MS: $[M]^+$ at m/z 364.

2 - [2-(4-Hydroxy-3-methoxyphenyl)-4-thiazolidinon-3-yl]-1,3,4-thiadiazino[6,5-*b*]indole 5b. m.p. 231-32ºC (methanol-water); IR (KBr, cm^{-1}): 672.2, 1060.4, 1293, 1525, 1611, 1684, 1690, 3145, 3418; ^{1}H NMR ($CDCl_3$+DMSO-d_6,): δ 3.57 (s, 3H), 3.89 (s, 2H), 6.51 (s, 1H), 6.86 (s, 1$H_{a'}$), 6.89-6.92 (d, 1H_d),

7.01-7.06 (t, $1H_c$), 7.30-7.32 (t, $1H_b$), 7.57-7.59 (d, $1H_a$), 7.88-7.97 (d, $1H_{b'}$), 8.13-8.16 (d, $1H_c$), 12.72 (ss, 1H) ppm. Anal. Calcd for $C_{19}H_{14}N_4S_2O_3$: C, 55.60; H, 3.41; N, 13.65. Found: C, 55.37; H, 3.29; N, 13.80%. MS: $[M]^+$ at m/z 410.

2-[2-(4-Methoxyphenyl)-4-thiazolidinon-3-yl]-1, 3, 4-thiadiazino[6, 5-*b*]indole 5c. m.p. 239-40ºC(DMF-water); IR (KBr, cm^{-1}) 671, 1061, 1294, 1525, 1611, 1685, 1691, 3146; ^1H NMR ($CDCl_3$+DMSO-d_6): δ 3.63 (s, 3H), 3.85 (s, 2H), 6.59 (s, 1H), 6.70-6.80 (m, 4H), 6.86-6.90 (d, $1H_d$), 7.07-7.13 (t, $1H_c$), 7.27-7.31 (t, $1H_b$), 7.59-7.63 (d, $1H_a$) ppm. Anal. Calcd for $C_{19}H_{14}N_4S_2O_2$: C, 57.86; H, 3.55; N, 14.21. Found: C, 57.51; H, 3.29; N, 14.47%. M S: $[M]^+$ at m/z 394.

2-[2-(4-*N*, *N*-Dimethylphenyl)-4-thiazolidinon-3-yl]-1,3,4-thiadiazino[6,5-*b*]indole 5d. m.p. 197-98ºC (ethanol); IR (KBr, cm^{-1}): 672, 1293, 1525, 1611, 1684, 1690, 3146; ^1H NMR ($CDCl_3$+DMSO-d_6): δ 2.14 (s,6H), 3.79 (s, 2H), 6.61 (s, 1H), 6.68-6.79 (m, 4H), 6.85-6.88 (d, $1H_d$), 7.04-7.10 (t, $1H_c$), 7.27-7.29 (t, $1H_b$), 7.57-7.60 (d, $1H_a$) ppm. Anal. Calcd for $C_{20}H_{17}N_5S_2O$: C, 58.96; H, 4.17; N, 17.19. Found: C, 58.70; H, 4.37; N, 17.40%. MS: $[M]^+$ at m/z 407.

2 - [2-(2-Hydroxyphenyl)-4-thiazolidinon-3-yl] - 1,3,4-thiadiazino[6,5-*b*]indole 5e. m.p. 227-28ºC (DMF-Water); IR (KBr, cm^{-1}): 673, 1294, 1525, 1610, 1684, 1690, 3145; ^1H NMR ($CDCl_3$+DMSO-d_6): δ 3.85 (s,2H), 6.632 (s,1H), 6.67-6.76 (m, 4H), 6.86-6.89 (d, $1H_d$), 7.06-7.10 (t, $1H_c$), 7.27-7.32 (t, $1H_b$), 7.51-7.58 (d, $1H_a$), 12.71 (ss, 1H) ppm. Anal. Calcd for $C_{18}H_{12}N_4S_2O_2$: C, 56.84; H, 3.15; N, 14.73. Found: C, 56.60; H, 3.29; N, 14.58%. MS: $[M]^+$ at m/z 380.

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