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Synthesis and anti-microbial screening of some new 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl)-2-(4'-substitutedbenzylidine)-3-(4-nitrophenylamino) thiazoloquinazoline derivatives

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Abstract
A series of some new 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl)-2-(4'-fluorobenzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline (4a-4d) and 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxy phenyl)-2-(4'-substituted benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline (5a-5d) derivatives were synthesized. The *in vitro* anti-bacterial and anti-fungal activities were determined by paper disk diffusion method. The minimum inhibitory concentrations (MIC) of the compounds were also determined by agar streak dilution method. Most of the synthesized compounds exhibited significant anti-bacterial and anti-fungal activities. Among the synthesized compounds 6,7,8,9-Tetra hydro-5*H*-5-(2'-hydroxy phenyl)-2-(4'-methoxy benzylidine)-3-(4-nitro phenyl amino)thiazolo quinazoline 5a, 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxy phenyl)-2-(3',4'-dimethyl benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline 5b and 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl)-2-(4'-fluoro benzylidine)-3-(4-nitro phenylamino) thiazolo quinazoline 5d exhibited most potent *in vitro* antimicrobial activity with MIC of (9.4, 10.2, 10.4, 10.2, 11.3, 12.1, 12.7, 14.6, 18.7), (10.3, 14.2, 11.6, 13.4, 13.6, 13.8, 14.6, 13.1, 14.5) and (12.5, 10.3, 14.1, 10.6, 13.4, 19.8, 17.8, 11.2, 13.6) at 100 μg mL^{-1} against *Staphylococcus aureus, Staphylococcus epidermidis, Micrococcus luteus*, *Bacillus cereus, Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, Aspergillus niger* and *Candida albicans.*

Key words: Thiazoloquinazoline, Benzylidine thiazoloquinazoline, Nitrophenyl amino Thiazoloquinazoline, Dimethyl group substitution, anti-bacterial, anti-fungal.

Introduction

Bacterial infections such as food poisoning, rheumatic, salmonellosis and diarrhea are caused by multidrug-resistant Gram -positive and Gram-negative pathogens. Principal players among these problematic organisms are isolates of methicillin resistant Staphylococcus aureus, Staphylococcus pyogenes, Salmonella typhimurium and Escherichia coli. Million of people in the subtropical regions of the world are infected and 20,000 deaths every year due to these parasitic bacterial infections. Amoxicillin, norfoxacin, ciprofoxacin are the principal drugs of choice in the treatment of bacterial infect ion since they are effective against extra intestinal and intestinal wall infection, but these are associated with several side effects such as nausea, metallic taste, dizziness, hypertension, etc. as well as resistance have been reported. The present strategy for new drug development is directed towards identifying the essential enzyme system in the bacterial and developing molecules to in-

hibit them on our going medicinal chemistry research activity. We have found that quinazolines and condensed quinazolines are classes of fused heterocycles that are of considerable interest because of the diverse range of their biological properties. Among a wide variety of nitrogen heterocycles that have been explored for developing pharmaceutically important molecules. Many derivatives of quinazoline are used in the pharmaceutical industry, in medicine and in agriculture due to their antimicrobial (1-3), anti-infammatory (4, 5), diuretic (6), anti-convulsant (7), anti-allergic (8), anti-hypertensive (9, 10) and anti-parkinsonism efects (11). Some of the quinazolines induced mutagenic activity (12,13). As documented in the literature, many quinazolines act as anticancer active agents (14-17). Our analogue-based design encompasses the synthesis of 6,7,8,9-Tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-substituted benzylidine)-3-(4-nitrophenylamino)thiazoloquinazoline derivatives intended to be tested for their *in vitro* antimicrobial properties against Gram positive and Gram negative bacteria and fungi.

Materials and Methods

Materials: Synthetic starting compounds, reagents and solvents were of analytical reagent grade or of the highest quality commercially available and were purchased from Aldrich Chemical Co., Merck Chemical Co. and were dried when necessary. The melting points were taken in open capillary tube and are uncorrected. IR spectra were recorded with KBr pellets (ABB Bomem FT-IR spectrometer MB 104 ABB Limited, Bangaluru, India). Proton (^{1}H) NMR spectra (Bruker 400 NMR spectrometer) were recorded with TMS as internal standard. Mass spectral data were recorded with a quadrupol mass spectrometer (Shimadzu GC MS QP 5000), and microanalyses were performed using a *vario EL* V300 *elemental* analyzer (Elemental Analysensysteme). The purity of the compounds was checked by TLC on pre-coated silica gel (HF_{254}, 200 mesh) aluminium plates (E.Merck) using ethyl acetate: benzene (1:3) and visualized in UV chamber. IR, ^{1}H-NMR, mass spectral datas and elemental analysis were consistent with the assigned structures.

Experimental methods: The synthetic strategy leading to the key intermediate and the target compounds are illustrated in Scheme. 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl)-thiazolo (2,3-*b*) quinazolin-3(2*H*)-one 3 prepared by taking the equimolar quantities of each (0.039 mol) of cyclohexanone and salicylaldehyde (0.039 mol) then it in a beaker, to this sodium hydroxide solution was added to make the solution alkaline, this was shaken and kept aside. The solid thus obtained, was filtered, washed with water and recrystallized from absolute ethanol. A mixture of 2-Hydroxybenzylidine cyclohexanone 1 (0.039 mol) thiourea (0.03 mol) and potassium hydroxide (2.5g) in ethanol (100 ml) was heated under reflux for 3h. The reaction mixture was concentrated to half of its volume, diluted with water, then acidified with dilute acetic acid and kept overnight. The solid thus obtained was filtered, washed with water and recrystallized from ethanol to give 4-hydroxyphenyl 3,4,5,6,7,8-Hexahydro quinazolin-2-thione **2**. The chloroacetic acid (0.096 mol) was melted on a water bath and thione (0.009 mol) added to it portion wise to maintain its homogeneity. The homogeneous mixture was further heated on a water bath for 30 min and kept overnight. The solid thus obtained was washed with water and crystallized from ethanol to give 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxy phenyl) thiazolo (2, 3-*b*) quinazolin-3-(2*H*)-one 3 (18).

A mixture of 3 (0.002 mol), substituted benzaldehyde (0.002 mol) and anhydrous sodium acetate (0.002 mol) in glacial acetic acid (10 ml)

was heated under reflux for 4h. The reaction mixture was kept overnight and the solid, thus separated was filtered, washed with water and recrystallized from ethanol to furnish 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl)-2-(4'-substituted benzylidine) thiazolo (2,3-*b*) quinazolin-3-(2*H*)-one (4a-4d). Equimolar quantities (0.004 mol) of compounds 4a-4d treated with thionyl chloride and DMF to get chloro derivative and then coupled with *p*-nitroaniline in DMF at 80^0C and quenched in ice-water to get the products, which were separated by filtration, vaccum dried and recrystallized from warm ethanol to yield 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxy phenyl)-2-(4'-substituted benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazolines (5a-5d). The spectral data IR, ^{1}H NMR, mass spectroscopy and elemental analyses were used to ascertain the structures of all the compounds.

^{1}H NMR spectra were recorded for all the target compounds. The ^{1}H NMR spectra were recorded for the representative key intermediate 3. The 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxy phenyl) thiazolo (2, 3-*b*) quinazolin-3-(2*H*)-one. Yield: 71%; m.p.153-155°C, IR (KBr, cm^{-1}): 3402 (phenolic OH), 3046 (Ar-CH), 1719 (C=O), 1462 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$) ä: 9.91 (s, 1H; Ar-OH), 6.61-6.89 (m,4H Ar-H), 5.71 (s, 1H; -CH) 3.76 (s, 2H; -CH_2) 1.6-2.42 (m, 8H; 4XCH_2).EI-MS m/z [M]+: 300 (Calcd for $C_{16}H_{16}N_2O_2S$; 300.38). Anal. Calcd for $C_{16}H_{16}N_2O_2S$; C, 63.98; H, 5.37; N, 9.32; Found: C, 63.92; H, 5.28; N, 9.30.

6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl)-2-(4'-methoxybenzylidine) thiazolo(2,3-*b*) quinazolin-3-(2*H*)-one (4a): Pale yellow solid; Yield: 78%; mp. 183-185°C, IR : 3476 (O-H), 3096 (Ar-CH), 1728 (C=O), 1468 (C=C) cm^{-1}. ^{1}H-NMR ($CDCl_3$): ä 9.84 (s, 1H, Ar-OH), 6.96-7.54 (m, 8H, Ar-H), 6.67 (s, 1H, =CH), 5.83 (s, 1H, H-5), 3.75 (s, 3H –OCH_3), 1.58-2.62 (m, 8H, 4 × CH_2); EI-MS (m/z, %): 418 [M]+; (Calcd for $C_{24}H_{22}N_2O_3S$; 418.51). Anal. Calcd for $C_{24}H_{22}N_2O_3S$, C, 68.88; H, 5.30; N, 6.69; Found: C, 68.90; H, 5.33; N, 6.72.

6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl) -2-(3',4'-dimethylbenzylidine) thiazolo(2,3-*b*) quinazolin-3-(2*H*)-one (4b): Solid; Yield: 79%; mp. 181-183 °C, IR : 3450 (O-H), 3051 (Ar-CH), 1724 (C=O), 1437 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$): ä 6.89-7.76 (m, 7H, Ar-H), 6.74 (s, 1H, =CH), 5.78 (s, 1H, H-5), 9.84 (s, 1H, Ar-OH), 2.23 (s, 6H 2×CH_3), 1.62-2.32 (m, 8H, 4×CH_2); EI-MS (m/z, %): 416 [M]+; (Calcd for $C_{25}H_{24}N_2O_2S$; 416.16). Anal. Calcd for $C_{25}H_{24}N_2O_2S$; C, 72.09; H, 5.81; N, 6.73; Found: C, 72.12; H, 5.79; N, 6.75.

6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl)-2-(4'-methylbenzylidine) thiazolo(2,3-*b*) quinazolin-3-(2*H*)-one (4c): Cream solid; Yield: 76%; mp. 186-188°C, IR : 3448 (O-H), 3049 (Ar-CH), 1721 (C=O), 1434 (C=C) cm^{-1}; ^{1}H-NMR ($CDCl_3$): ä 6.86-7.74 (m, 8H, Ar-H), 6.72 (s, 1H, =CH), 5.76 (s, 1H, H-5), 9.76 (s, 1H, Ar-OH), 2.20 (s, 3H –CH_3), 1.62-2.32 (m, 8H, 4 × CH_2); EI-MS (m/z, %): [M]+ 402; (Calcd for $C_{24}H_{22}N_2O_2S$; 402.14). Anal. Calcd for $C_{24}H_{22}N_2O_2S$; C, 71.00; H, 5.51; N, 6.96; Found: C, 69.87; H, 5.32; N, 6.74.

6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl)-2-(4'-fluorobenzylidine) thiazolo(2,3-*b*) quinazolin-3(2*H*)-one (4d). Pale yellow solid; Yield: 69%; mp. 153-155°C, IR : 3437 (O-H), 3026 (Ar-CH), 1729 (C=O), 1522 (C=C), 826 (C-F) cm^{-1}; ^{1}H-NMR ($CDCl_3$): ä 9.94 (s, 1H, Ar-OH),6.63-7.32 (m, 8H, Ar-H), 6.38 (s, 1H, =CH), 5.87 (s, 1H, H-5), 1.34-2.33 (m, 8H, 4 × CH_2); EI-MS (m/z, %): [M]+406; (Calcd for $C_{23}H_{19}FN_2O_2S$; 406.12). Anal. Calcd

for $C_{23}H_{19}FN_2O_2S$; C, 67.96; H, 4.71; N, 6.89; Found: C, 67.97; H, 4.73; N, 6.87.

6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl) -2-(4'-methoxybenzylidine)-3-(4-nitrophenyl amino)thiazoloquinazoline (5a): Pale yellow solid; Yield: 76%; mp. 156-158°C, IR : 3464 (O-H), 3027 (Ar-CH), 1494 (C=C), 1306 (N-H bending), 3396 (N-H stretching) cm^{-1}; ^{1}H-NMR ($CDCl_3$): ä 9.87 (s, 1H, Ar-OH), 6.72-7.23 (m, 12H, Ar-H), 6.36 (s, 1H, =CH),5.62 (s, 1H, H-5), 4.46 (s, 1H, thiazole), 3.78 (s, 3H –OCH_3), 7.26 (s, 1H, N-H), 1.46-2.42 (m, 8H, 4 × CH_2); EI-MS (m/z, %): [M]+ 540; (Calcd for $C_{30}H_{28}N_4O_4S$; 540.18). Anal. Calcd for $C_{30}H_{28}N_4O_4S$; C, 66.65; H, 5.22; N, 10.36; Found: C, 66.67; H, 5.25; N, 10.38.

6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl) -2-(3',4'-dimethylbenzylidine)-3-(4-nitrophenyl amino)thiazoloquinazoline (5b): Yellow solid; Yield: 77%; mp. 181-183°C, IR : 3429 (O-H), 3027 (Ar-CH), 1413 (C=C), 1334 (N-H bending), 3313 (N-H stretching) cm^{-1}; ^{1}H-NMR ($CDCl_3$): ä 9.93 (s, 1H, Ar-OH), 6.79-7.24 (m, 12H, Ar-H), 6.26 (s, 1H, =CH), 5.74 (s, 1H, H-5), 4.39 (s, 1H, thiazole), 2.34 (s, 6H, 2XCH_3), 7.62 (s, 1H, N-H), 1.36-2.41 (m, 8H, 4 × CH_2); EI-MS (m/z, %): [M]+ 538; (Calcd for $C_{31}H_{31}N_4O_3S$; 538.2). Anal. Calcd for $C_{31}H_{31}N_4O_3S$; C, 69.12; H, 5.61; N, 10.40; Found: C, 69.14; H, 5.63; N, 10.43.

6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl) -2-(4'-methylbenzylidine)-3-(4-nitrophenyl amino)thiazoloquinazoline (5c): Cream solid; Yield: 76%; mp. 193-192°C, IR : 3438 (O-H), 3024 (Ar-CH), 1412 (C=C), 1322 (N-H bending), 3310 (N-H stretching) cm^{-1}; ^{1}H-NMR ($CDCl_3$): ä 9.82 (s, 1H, Ar-OH), 6.69-7.24 (m, 12H, Ar-H), 6.28 (s, 1H, =CH), 5.72 (s, 1H, H-5), 4.45 (s, 1H, thiazole), 2.28 (s, 3H, –CH_3), 7.69 (s, 1H, N-H), 1.36-2.41 (m, 8H, 4 × CH_2); EI-MS (m/z, %): [M]+ 524; (Calcd for $C_{30}H_{28}N_4O_3S$; 524.19). Anal. Calcd for $C_{30}H_{28}N_4O_3S$; C, 68.68; H, 5.38; N, 10.68; Found: C, 68.65; H, 5.36; N, 10.70.

6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl) -2-(4'-fluorobenzylidine)-3-(4-nitrophenyl amino)thiazoloquinazoline (5d): Cream solid; Yield: 89%; mp. 184-186°C, IR : 3449 (O-H), 3026 (Ar-CH), 1524 (C=C), 1316 (N-H bending), 3319 (N-H stretching), 821 (C-F) cm^{-1}; ^{1}H-NMR ($CDCl_3$): ä 9.96 (s, 1H, Ar-OH), 6.74-7.32 (m, 12H, Ar-H), 6.23 (s, 1H, =CH), 5.84 (s, 1H, H-5), 4.42 (s, 1H, thiazole), 7.34 (s,1H, N-H), 1.24-2.32 (m, 8H, 4 × CH_2); EI-MS (m/z, %): [M]+ 528; (Calcd for $C_{29}H_{25}FN_4O_3S$; 528.16). Anal. Calcd for $C_{29}H_{25}FN_4O_3S$; C, 65.89; H, 4.77; N, 10.60; Found: C, 65.91; H, 4.79; N, 10.62.

Antimicrobial Screening: All the synthesized compounds were screened for anti-bacterial and anti-fungal activities by paper disc diffusion technique. The anti-bacterial activity of the compounds were evaluated against four gram positive bacteria (*Staphylococcus aureus* ATCC 9144*, Staphylococcus epidermidis* ATCC 155*, Micrococcus luteus* ATCC 4698 and *Bacillus cereus* ATCC 11778) and three gram negative bacteria (*Escherichia coli* ATCC 25922*, Pseudomonas aeruginosa* ATCC 2853, *and Klebsiella pneumoniae* ATCC 11298*)*. The anti-fungal activities of the synthesized compounds were evaluated against two fungi (*Aspergillus niger* ATCC 9029 and *Candida albicans* ATCC 2091). The observed data on the antimicrobial activity of the synthesized compounds and standard drugs are given in Table 1.

Paper Disc Diffusion Technique: The sterilized (19) (autoclaved at 120°C for 30 minutes) medium (40-50°C) was inoculated (1 mL/100 mL of medium) with the suspension (10^5 cfu mL^{-1})

of the microorganism (matched to McFarland barium sulphate standard) and poured into a petridish to give a depth of 3-4 mm. The paper impregnated with the test compounds (μg mL^{-1} in dimethyl formamide) was placed on the solidified medium. The plates were pre-incubated for 1 h at room temperature and incubated at 37°C for 24 and 48 h for anti-bacterial and anti-fungal activities, respectively. Ciprofloxacin (Dr. Reddy's Laboratories, Batch No: IC666E04, India) and Ketoconazole (Wuhan Shengmao Corporation, Batch No: SBML/403, China) were used as standard for anti-bacterial and anti-fungal activities, respectively. The observed zone of inhibition is presented in table-1 and figures.

Minimum Inhibitory Concentration (MIC): MIC (20) of the compound was determined by agar streak dilution method. A stock solution of the synthesized compound (100 μg mL^{-1}) in dimethylformamide was prepared and graded quantities of the test compounds were incorporated in specified quantity of molten sterile agar (nutrient agar for anti-bacterial activity and sabouraud dextrose agar medium for antifungal activity). A specified quantity of the medium (40-50°C) containing the compound was poured into a petridish to give a depth of 3-4 mm and allowed to solidify. Suspension of the microorganism were prepared to contain approximately 10^5 cfu mL^{-1} and applied to plates with serially diluted compounds in dimethylformamide to be tested and incubated at 37°C for 24 h and 48 h for bacteria and fungi, respectively. The MIC was considered to be the lowest concentration of the test substance exhibiting no visible growth of bacteria or fungi on the plate. The observed MIC is presented in table-1.

Statistical Analysis: Student's *t*-test was used to determine a significant difference between the control.

Results and Discussion

The synthesized series of heterocycles, 4a-4d and 5a-5d by the reaction of 3 with appropriate aromatic aldehydes and *p* –nitro aniline in the presence of anhydrous sodium acetate and DMF as presented in Scheme. The IR, ^{1}H-NMR, mass spectroscopy and elemental analysis for the new compound is in accordance with the assigned structures. The IR spectra of compounds 4a-4d showed stretching bands of keto group at 1715-1740 cm^{-1}. In 5a-5d stretching and bending NH bands of thiazolo quinazoline moiety appear at 3300-3400 cm^{-1}, 1300-1350 cm^{-1} respectively. The recorded IR spectra of representative compounds 5a-5d showed missing of keto group bands. This clearly envisages that the keto group of 4a-4d is converted in to secondary NH. The proton magnetic resonance spectra of thiazoloquinazoline and their corresponding derivatives have been recorded in $CDCl_3$. In this 5a-5d NH signal of 3-(4-nitro phenyl) amino thiazolo quinazoline moiety appear at 7.26 (s), 7.62 (s), 7.69 (s), 7.34 (s) ppm respectively. The position and presence of NH signal in the ^{1}H-NMR spectra of final compounds conforms the secondary NH proton in thiazoloquinazoline moiety. This clearly envisages that thiazole-3-one moiety involve in 3-(4-nitro phenyl) amino formation. All these observed facts clearly demonstrate that 3rd position of keto group in thiazole ring is converted in to secondary amino group as indicated in figures- 1,2 and 3, it conforms the proposed structure 5a -5d.

All the synthesized compounds exhibited moderate to good anti-bacterial and anti-fungal activity. Among the synthesized compounds, compound 5a, 5b and 5d were found to possess significant anti-bacterial and anti-fungal activity when compared to standard drug Ciprofloxacin and Ketoconazole for anti-bacterial and anti-fungal activity respectively. Compound 5d displayed moderate anti-microbial activity where as the remain-

ing compounds 4a, 4b, 4c and 4d shown lesser activity. The MIC of the synthesized compounds was established screened by agar streak dilution method with an MIC range of 9.4-27.4 μg mL^{-1}. 6,7,8,9-Tetrahydro-5*H*-5-(2'-hydroxyphenyl)-2-(4'-methoxy benzylidine)-3-(4-nitrophenyl amino) thiazoloquinazoline 5a and 6,7,8,9-Tetra hydro-5*H*-5-(2'-hydroxy phenyl)-2-(3',4'-dimethyl benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline 5b was found to exhibit the highest anti-bacterial activity against *S.aureus* (9.4 μg mL^{-1}), *S.epidermidis* (9.6 μg mL^{-1}), *M.luteus* (10.4 μg mL^{-1}), *B.cereus* ('10.2 μg mL^{-1}), *E.coli* (11.3 μg mL^{-1}), *P.aeruginosa* (12.1 μg mL^{-1}), *K.pneumoniae* (12.7 μg mL^{-1}), 6,7,8,9-Tetra hydro-5*H*-5-(2'-hydroxy phenyl)-2-(4'-fluoro benzylidine)-3-(4-nitrophenyl amino) thiazolo quinazoline 5d exhibited highest anti-fungal activity against *A.niger* (MIC: 11.2 μg mL^{-1}) and *C.albicans* (MIC: 13.9 μg mL^{-1}).The synthesized compounds were active against all the tested micro-organisms with a range of MIC values for *S.aureus* (9.4-23.6 μg mL^{-1}), *S.epidermidis* (9.6-25.2 μg mL^{-1}), *M.luteus* (10.4-26.7 μg mL^{-1}), *B.cereus* (10.2-22.2 μg mL^{-1}), *E.coli* (11.3-24.9 μg mL^{-1}), *P.aeruginosa* (12.1-23.9 μg mL^{-1}), *K.pneumoniae* (12.7-22.9 μg mL^{-1}), *A.niger* (MIC: 11.2-27.4 μg mL^{-1}) and *C.albicans* (MIC: 13.9-26.6 μg mL^{-1}).The potent anti-microbial activity exhibited by 5a and 5b may be due to the incorporation of electron donating groups like, methoxy and dimethyl (at 4th position of the arylidine ring). The interesting results we observed that both electrons donating as well as electrons withdrawing groups was found to increase the anti-microbial properties, whereas *p*-nitro anilines unsubstituted derivatives exhibited lesser degree of activity. The compound 5a and 5b was found to possess anti-bacterial activity almost equivalent to standard drug and considerable anti-fungal activity, all the observed zone of inhibition clearly indicated in figure-4.

Conclusion

In conclusion, the present study highlights the importance of phenyl hydrazine substitution at 3rd position of the thiazoloquinazoline ring features responsible for the anti-microbial property and therefore may serves as a lead molecule to obtain clinically useful novel entities in the new millennium.

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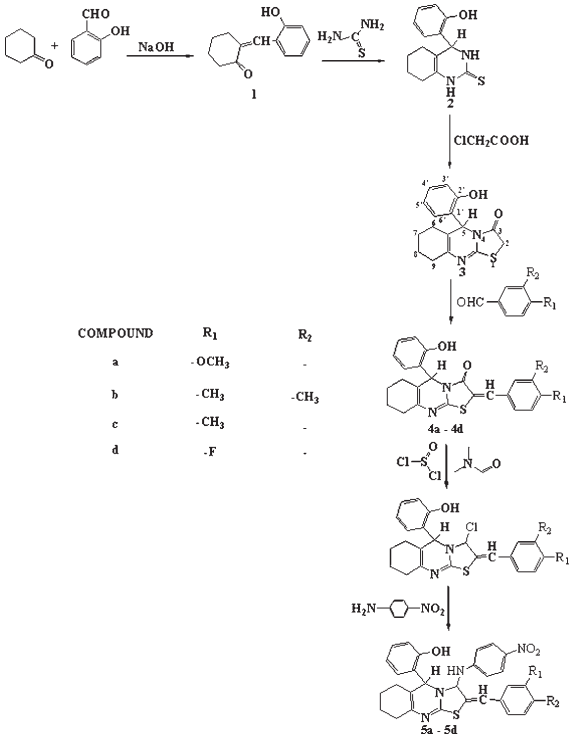

COMPOUND	R_1	R_2
a	$-OCH_3$	-
b	$-CH_3$	$-CH_3$
c	$-CH_3$	-
d	-F	-

SCHEME

Synthesis of 6,7,8,9-Tetra hydro-5*H*-5-(2'-hydroxy phenyl)-2-(4'-substitutedbenzylidine)-3-(4-nitrophenylamino)thiazoloquinazoline

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