



Research Article

SYNTHESIS AND ANTI-MICROBIAL ACTIVITY OF NOVEL THIAZOLO QUINAZOLINE DERIVATIVES

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ABSTRACT

A series of 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-some substituted benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (**5a-h**) derivatives were synthesized and tested for anti-microbial activity. All the newly synthesized compounds chemical structures were confirmed by IR, ¹H-NMR, mass spectroscopy and elemental analyses. The results of studies indicate that the compound 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-fluoro benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone **5f** showed potent antimicrobial activities.

Key words: Thiazolo quinazoline, Thiazolo quinazoline phenyl hydrazone, Aromatic aldehydes substitution, Benzylidene thiazolo quinazoline phenyl hydrazone, Antimicrobial

INTRODUCTION

Bacterial infections such as food poisoning, rheumatic, salmonellosis and diarrhea are caused by multidrug-resistant Gram-positive and Gram-negative pathogens. The 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, norfloxacin, ciprofloxacin are the principal drugs of choice in the treatment of bacterial infection since they are effective against extra intestinal and intestinal wall infection¹, but these are associated with several side effects such as nausea, metallic taste, dizziness, hypertension, etc. as well as resistance have been reported². The present strategy for new drug development is directed towards identifying the essential enzyme system in the bacterial and developing molecules to inhibit them on our going medicinal chemistry research activity. We have found that quinazolines and condensed quinazolines exhibit potent pharmacological activities³⁻⁹. On the other hand, the considerable biological and medicinal activities of thiazole and their derivatives have attracted continuing interest over the years because of their varied biological activities^{10,11} recently found application in drug development for the treatment of allergies¹², hypertension¹³, schizophrenia¹⁴, bacterial¹⁵, HIV infections¹⁶, hypnotics¹⁷ and more recently for the treatment of pain¹⁸. These observation led to the conception that a novel series of 6,7,8,9 tetra hydro-5H-5-(2'-hydroxyphenyl)-2-(4'-some substituted benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone derivatives were synthesized using phenyl hydrazine and different aromatic aldehydes by condensation and their chemical structure were confirmed by IR, ¹H-NMR, mass spectral and elemental analyses. These compounds were screened for their anti-microbial activity.

MATERIALS AND METHODS

General procedure

The synthesis of compounds starting compound 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl) thiazolo (2, 3-b) quinazolin-3(2H)-one **3** prepared by the equimolar quantities of each (0.039 mol) of cyclohexanone and salicylaldehyde (0.039 mol) were taken 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-hydroxy benzylidene cyclohexanone ring **1** (0.039 mol) thiourea (0.03 mol) and potassium hydroxide (2.5g) in ethanol (100 ml) was heated under reflux for 3 h. 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-hydroxy phenyl **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 until neutralized and crystallized from ethanol to give 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl) thiazolo (2, 3-b) quinazolin-3(2H)-one **3**¹⁹. A mixture of **3** (0.002 mol), treated with phenyl hydrazine (0.002 mol) anhydrous sodium acetate (0.002 mol) and glacial acetic acid (10 ml) were dissolved in 10ml of warm ethanol and refluxed for 30 min. After standing for approximately 24 h at room temperature, the product were separated by filtration, vacuum dried and recrystallized from warm ethanol to yields 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone **4**. Equimolar quantities (0.002 mol) of compound **4** clubbed with substituted benzaldehyde (0.002 mol) and anhydrous sodium acetate (0.002 mol) in glacial acetic acid (10 ml) was heated under reflux for 4 h. The reaction mixture was kept overnight and the solid, thus separated, was filtered, washed with water and recrystallized from ethanol to furnish of 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy

phenyl)-2-(4'-some substituted benzylidene) thiazolo (2,3-b) quinazolin-3-phenyl hydrazone (**5a-h**). The spectral data IR, ¹H NMR, mass spectroscopy and elemental analyses were used to ascertain the structures of all the compounds. Other characteristic data for compounds are given in Table 1.

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 (¹H) NMR spectra (Bruker 400 NMR

spectrometer Mumbai, India) were recorded with TMS as internal references. Mass spectral data were recorded with a quadrupole mass spectrometer (Shimadzu GC MS QP 5000, Chennai, India), and microanalyses were performed using a *vario EL V300 elemental analyzer* Element Analysensysteme GmbH Chennai, India). The purity of the compounds was checked by TLC on pre-coated SiO₂ gel (HF₂₅₄, 200 mesh) aluminium plates (E. Merck) using ethyl acetate: benzene (1:3) and visualized in UV chamber. IR, ¹H-NMR, mass spectral data and elemental analyses were consistent with the assigned structures.

Table 1 Formula and Physical constants for 5a-h

Compounds	M.P (°C)	Yields	Molecular formula	Molecular weight
4	183-185	84.12	C ₂₂ H ₂₆ N ₄ OS	390.5
5a	187-189	82.18	C ₂₉ H ₂₆ N ₄ O ₂ S	494.18
5b	190-194	78.42	C ₃₀ H ₂₈ N ₄ O ₂ S	508.63
5c	212-214	76.23	C ₃₀ H ₂₈ N ₄ O ₂ S	492.63
5d	250-252	74.41	C ₃₁ H ₃₀ N ₄ OS	506.66
5e	264-266	65.16	C ₃₁ H ₃₁ N ₅ OS	521.22
5f	183-185	72.46	C ₂₉ H ₂₅ FN ₄ OS	496.6
5g	179-181	79.16	C ₂₉ H ₂₅ ClN ₄ OS	513.05
5h	180-182	76.11	C ₂₉ H ₂₅ BrN ₄ OS	557.5

The ¹H NMR spectra were recorded for the representative key intermediate **3**. The 6,7,8,9 tetra hydro-5H-5-(2'-hydroxyphenyl) thiazoloquinazolin-3-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; ¹H-NMR (CDCl₃): δ: 6.61-6.89 (m,4H Ar-H), 5.71 (s, 1H; -CH) 9.91 (s, 1H; Ar-OH), 3.76 (s, 2H; -CH₂) 1.6-2.42 (m, 8H; CH₂, CH₂, CH₂, CH₂). EI-MS *m/z* (M⁺): 300 (Calcd for C₁₆H₁₆N₂O₂S; 300.38). Anal. Calcd for C₁₆H₁₆N₂O₂S; C, 63.98; H, 5.37; N, 9.32. Found: C, 63.81; H, 5.28; N, 9.43.

6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (4). IR : 3467 (O-H), 3064 (Ar-CH), 1541 (C=C), 1610 (C=N), 1333 (N-H bending), 3378 (N-H stretching) cm⁻¹; ¹H-NMR (CDCl₃): δ: 6.98-7.36 (m, 9H, Ar-H), 5.82 (s, 1H, H-5), 9.74 (s, 1H, H-2', Ar-OH), 7.12 (s, 1H, N-H), 2.97 (s, 2H, thiazole), 1.59-2.47 (m, 8H, 4 × CH₂); EI-MS (*m/z*, %): 390 (M⁺); (Calcd for C₂₂H₂₂N₄O₂S; 390.5). Anal. Calcd for C₂₂H₂₂N₄O₂S; C, 67.67; H, 5.68; N, 14.32. Found: C, 67.56; H, 5.59; N, 14.43.

6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-hydroxybenzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (5a). IR : 3415 (O-H), 3060 (Ar-CH), 1534 (C=C), 1619 (C=N), 1312 (N-H bending), 3310 (N-H stretching) cm⁻¹; ¹H-NMR (CDCl₃): δ: 6.98-7.36 (m, 13H, Ar-H), 6.53 (s, 1H, =CH), 5.82 (s, 1H, H-5), 9.74 (s, 1H, H-2', Ar-OH), 5.12 (s, 1H, H-4", Ar-OH), 7.78 (s, 1H, N-H), 1.59-2.47 (m, 8H, 4 × CH₂); EI-MS (*m/z*, %): 494 (M⁺); (Calcd for C₂₉H₂₆N₄O₂S; 494.18). Anal. Calcd for C₂₉H₂₆N₄O₂S; C, 70.42; H, 5.30; N, 11.33; Found: C, 70.12; H, 5.02; N, 11.54.

6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-methoxy benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (5b). IR : 3464 (O-H), 3027 (Ar-CH), 1494 (C=C), 1626 (C=N), 1306 (N-H bending), 3396 (N-H stretching) cm⁻¹; ¹H-NMR (CDCl₃): δ: 6.72-7.23 (m, 13H, Ar-H), 6.36 (s, 1H, =CH), 5.62 (s, 1H, H-5), 9.87 (s, 1H, H-2', Ar-OH), 3.78 (s, 3H - OCH₃), 7.26 (s, 1H, N-H), 1.46-2.42 (m, 8H, 4 × CH₂); EI-MS (*m/z*, %): 508 (M⁺); (Calcd for C₃₀H₂₈N₄O₂S; 508.63). Anal. Calcd for C₃₀H₂₈N₄O₂S; C, 70.84; H, 5.55; N, 11.02. Found: C, 70.75; H, 5.46; N, 11.21.

6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-methyl benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (5c). IR : 3438 (O-H), 3024 (Ar-CH), 1412 (C=C), 1632 (C=N), 1322 (N-H bending), 3310 (N-H stretching) cm⁻¹;

5.72 (s, 1H, H-5), 9.82 (s, 1H, H-2', Ar-OH), 2.28 (s, 3H, -CH₃), 7.69 (s, 1H, N-H), 1.36-2.41 (m, 8H, 4 × CH₂); EI-MS (*m/z*, %): 492 (M⁺); (Calcd for C₃₀H₂₈N₄O₂S; 492.63). Anal. Calcd for C₃₀H₂₈N₄O₂S; C, 73.14; H, 5.73; N, 11.37. Found: C, 73.26; H, 5.57; N, 11.19.

6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(3',4'-dimethyl benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (5d). IR : 3429 (O-H), 3019 (Ar-CH), 1413 (C=C), 1648 (C=N), 1334 (N-H bending), 3313 (N-H stretching) cm⁻¹; ¹H-NMR (CDCl₃): δ: 6.79-7.24 (m, 12H, Ar-H), 6.26 (s, 1H, =CH), 5.74 (s, 1H, H-5), 9.93 (s, 1H, H-2', Ar-OH), 2.34 (s, 6H, -CH₃), 7.62 (s, 1H, N-H), 1.36-2.41 (m, 8H, 4 × CH₂); EI-MS (*m/z*, %): 506 (M⁺); (Calcd for C₃₁H₃₀N₄O₂S; 506.66). Anal. Calcd for C₃₁H₃₀N₄O₂S; C, 73.49; H, 5.97; N, 11.06. Found: C, 73.28; H, 5.82; N, 11.18.

6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-nitro dimethyl benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (5e). IR : 3441 (O-H), 3035 (Ar-CH), 1417 (C=C), 1653 (C=N), 1336 (N-H bending), 3376 (N-H stretching) cm⁻¹; ¹H-NMR (CDCl₃): δ: 6.72-7.23 (m, 13H, Ar-H), 6.46 (s, 1H, =CH), 5.74 (s, 1H, H-5), 9.86 (s, 1H, H-2', Ar-OH), 2.28 (s, 6H, -CH₃), 7.89 (s, 1H, N-H), 1.39-2.43 (m, 8H, 4 × CH₂); EI-MS (*m/z*, %): 521 (M⁺); (Calcd for C₃₁H₃₁N₅O₂S; 521.68). Anal. Calcd for C₃₁H₃₁N₅O₂S; C, 71.37; H, 5.99; N, 13.42. Found: C, 71.49; H, 5.86; N, 13.31.

6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-fluoro benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (5f). IR : 3449 (O-H), 3026 (Ar-CH), 1524 (C=C), 1639 (C=N), 1316 (N-H bending), 3319 (N-H stretching), 821 (C-F) cm⁻¹; ¹H-NMR (CDCl₃): δ: 6.74-7.32 (m, 13H, Ar-H), 6.23 (s, 1H, =CH), 5.84 (s, 1H, H-5), 9.96 (s, 1H, H-2', Ar-OH), 7.34 (s, 1H, N-H), 1.24-2.32 (m, 8H, 4 × CH₂); EI-MS (*m/z*, %): 496 (M⁺); (Calcd for C₂₉H₂₅FN₄O₂S; 496.6). Anal. Calcd for C₂₉H₂₅FN₄O₂S; C, 70.14; H, 5.07; N, 11.28. Found: C, 70.25; H, 5.19; N, 11.10.

6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-chloro benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (5g). IR : 3446 (O-H), 3013 (Ar-CH), 1526 (C=C), 1646 (C=N), 1348 (N-H bending), 3336 (N-H stretching), 824 (C-Cl) cm⁻¹; ¹H-NMR (CDCl₃): δ: 6.71-7.33 (m, 13H, Ar-H), 6.24 (s, 1H, =CH), 5.86 (s, 1H, H-5), 9.74 (s, 1H, H-2', Ar-OH), 7.31

(s,1H, N-H), 1.21-2.31 (m, 8H, 4 × CH₂); EI-MS (*m/z*, %): 515 (M+2); (Calcd for C₂₉H₂₅ClN₄O₅; 513.05). Anal. Calcd for C₂₉H₂₅ClN₄O₅; C, 67.89; H, 4.91; N, 10.92. Found: C, 67.59; H, 4.72; N, 10.74.

6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-bromo benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone (5h). IR : 3447 (O-H), 3021 (Ar-CH), 1519 (C=C), 1641 (C=N),1327 (N-H bending), 3352 (N-H stretching), 818 (C-Br) cm⁻¹; ¹H-NMR (CDCl₃): δ 6.81-7.36 (m, 13H, Ar-H), 6.49 (s, 1H, =CH), 5.84 (s, 1H, H-5), 9.81 (s, 1H, H-2', Ar-OH), 7.79 (s, 1H, N-H), 1.29-2.34 (m, 8H, 4 × CH₂); EI-MS (*m/z*, %): 559 (M+2); (Calcd for C₂₉H₂₅BrN₄O₅; 557.5). Anal. Calcd for C₂₉H₂₅BrN₄O₅; C, 62.48; H, 4.52; N, 10.05. Found: C, 62.52; H, 4.18; N, 10.26.

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 2.

Paper Disc Diffusion Technique

The sterilized²⁰ (autoclaved at 120°C for 30 min) medium (40-50°C) was inoculated (1 mL/100 mL of medium) with the suspension (10⁵ 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 2.

Minimum Inhibitor Concentration (MIC)

MIC²¹ 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 10⁵ 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 2.

Table 2: Anti-microbial activity of the synthesized compounds (100 μg/ml)

Compounds	In vitro activity - zone of inhibition (MIC)								
	<i>S.aureus</i>	<i>S.epidermidis</i>	<i>M.luteus</i>	<i>B.cereus</i>	<i>E.coli</i>	<i>P.aeruginosa</i>	<i>K.pneumoniae</i>	<i>A.niger</i>	<i>C.albicans</i>
5a	21(10.4)	22(9.6)	23(11.2)	19(12.1)	21(14.8)	20(16.8)	20(13.9)	20(12.4)	19(16.6)
5b	15(23.6)	19(20.4)	15(26.7)	16(19.2)	18(24.9)	17(19.8)	14(19.6)	18(21.1)	19(16.6)
5c	19(19.3)	18(21.2)	15(16.3)	17(15.3)	18(19.2)	18(18.6)	15(22.9)	19(27.4)	16(19.9)
5d	17(13.2)	16(25.2)	17(20.6)	15(16.7)	17(19.0)	17(19.7)	17(16.6)	18(24.3)	17(26.6)
5e	18(13.6)	16(14.8)	18(12.4)	17(22.2)	16(14.4)	16(23.9)	19(13.8)	17(13.8)	18(14.2)
5f	24(9.4)	27(10.2)	22(10.4)	20(10.2)	23(11.3)	23(12.1)	26(12.7)	19(14.6)	19(18.7)
5g	22(10.3)	25(14.2)	24(11.6)	21(13.4)	25(13.6)	21(13.8)	25(14.6)	18(13.1)	18(14.5)
5h	19(12.5)	20(10.3)	19(14.1)	18(10.6)	19(13.4)	18(19.8)	16(17.8)	24(11.2)	22(13.6)
Ciprofloxacin	25	29	27	23	29	25	27	-	-
Ketoconazole	-	-	-	-	-	-	-	29	26
DMF	-	-	-	-	-	-	-	-	-

Zone of inhibition in mm, MIC in μg/ml.

Statistical Analysis

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

RESULTS AND DISCUSSION

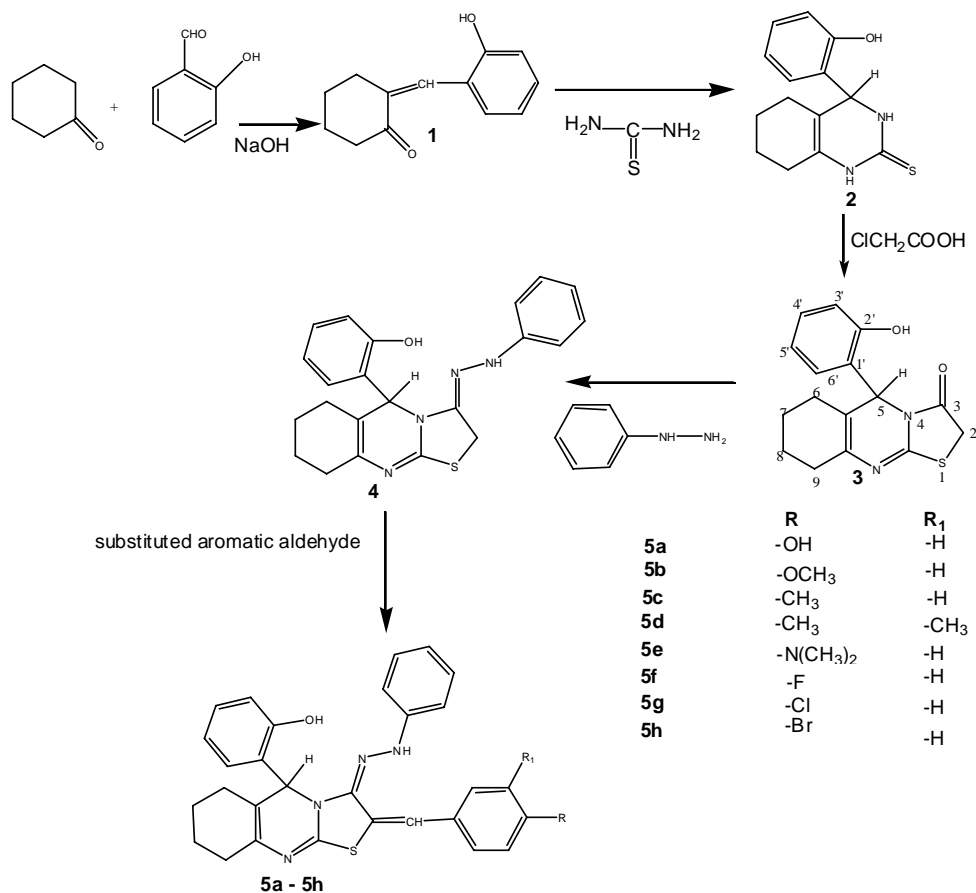
Chemistry

The synthesized series of heterocycles, **5a-h** by the reaction of **3** with appropriate phenyl hydrazine and aromatic aldehydes

in the presence of anhydrous sodium acetate and glacial acetic acid as presented in **Scheme**. The IR, ¹H-NMR, mass spectroscopy and elemental analyses for the new compound is in accordance with the assigned structures. The IR spectrum of compound **3** showed stretching bands of keto group at 1715-1740 cm⁻¹. In **4**, stretching and bending NH bands of thiazolo quinazoline moiety appear at 3300-3400 cm⁻¹, 1300-1350 cm⁻¹ respectively. The absence of keto group absorption at 1715-1740 cm⁻¹ and appearance of a strong intensity band in the IR spectra of compounds **4** in the range of 1610-1655 cm⁻¹

attributable to C=N provides a strong evidence for the condensation and also confirms the formation of the azomethine **4**. The proton magnetic resonance spectra of thiazolo quinazoline and their corresponding derivatives have been recorded in CDCl₃. In this **5a-h** NH signal of thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone moiety appear at 7.78 (s), 7.26 (s), 7.69 (s), 7.62 (s), 7.89 (s), 7.34 (s) 7.31 (s), 7.79 (s) ppm respectively. The position and presence of NH signal in the ¹H-NMR spectra of final compounds conforms the secondary NH proton in thiazolo quinazoline moiety. This clearly envisages that thiazole-3-one moiety involve in thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone formation. All these observed facts clearly demonstrate that 3rd position of keto

SCHEME



lesser activity. The MIC of the synthesized compounds was screened by agar streak dilution method with an MIC range of 9.4-27.4 µg mL⁻¹. 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-fluoro benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone **5f** and 6,7,8,9 tetra hydro-5H-5-(2'-hydroxy phenyl)-2-(4'-chloro benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone **5g**, 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-5H-5-(2'-hydroxy phenyl)-2-(4'-bromo benzylidene) thiazolo (2, 3-b) quinazolin-3-phenyl hydrazone **5h** 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 microorganisms with a range of MIC values for *S.aureus* (9.4-

group in thiazole ring is converted in to secondary amino group as indicated in **Scheme** and conforms the proposed structure (**5a-h**).

Anti-microbial activity

All the synthesized compounds exhibited moderate to good anti-bacterial and anti-fungal activity. Among these synthesized compounds, compound **5f**, **5g** and **5h** 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 respectively. Compound **5a** displayed moderate antimicrobial activity where as the remaining compounds **5b**, **5c**, **5d** and **5e** shown

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: 13.6-26.6 µg mL⁻¹). The potent anti-microbial activity exhibited by **5f**, **5g** and **5h** may be due to the incorporation of electron withdrawing groups e.g. 4-fluorine, 4-chlorine and 4-bromine (at 4th position of the arylidene ring). The interesting results we observed that the electrons withdrawing groups was found to increase the antimicrobial properties, where as donating groups like 4-methoxy, 4-methyl, 3,4-dimethyl, 4-dimethyl amino exhibited lesser degree of activity. In exceptional case, 4-hydroxy, substituted analog (**5a**) was found better in activity. The compound **5f** and **5h** was found to possess anti-bacterial activity almost equivalent to standard drug and considerable anti-fungal activity.

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