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Synthesis, characterization and biological evaluation of some novel heterocyclic compounds having sulphamido moiety

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ABSTRACT

*4-Amino-N-[4-(4-chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidin-2-yl]- benzensulfonamide **(2)** was prepared by the hydrolysis of N-{4-[4-Chloro-phenyl}-6-(3,4-dimethyl-phenyl)-pyrimidin-2-ylsulfamoyl]-phenyl}-acetamide **(1)**.It was on-facile condensation reaction with various aromatic aldehydes yields Schiff bases /anils/azomethines (**3a-h**). These anils on cyclo condensation reaction with thio glycolic acid (mercapto acetic acid) and thio lactic acid yields 4-thiazolidinoes (**4a-h**) and 5-Methyl 4-Thiazolidinones (**5a-h**) respectively. The newly synthesized compounds were evaluated for their antibacterial and antifungal activities.*

Keywords: 4-Thiazolidinoes, 5-Methyl 4-thiazolidinones, Cyclo-condensation reaction, facile condensation.

INTRODUCTION

The development of sulphonamides is one of the most fascinating and informative fields in medicinal chemistry, highlighting the roles of skillful planning and serendipity in drug research. The discovery of sulphonamides marked the beginning of the chemotherapeutic area by making possible a direct attack on microbial infections [1]. Sulphonamides antibacterials continued to be used because they are effective, inexpensive and free of super infection problems of the broad-spectrum antibiotic [2].As a part of surge of interest in heterocyclic that have been explored for developing pharmaceutically important molecule 4-thiazolidinoes [3-5] and 5-Methyl 4-Thiazolidinones [6-8] have played an important role in medicinal chemistry. Moreover, they have been studied extensively because of their ready accessibility, diverse chemical reactivity, and broad spectrum of biological activities.

Pyrimidine derivatives occupy a unique position as leiodynamic agents, both as essential components of nucleic acids and also as therapeutic agents [9-10].During the past years considerable evidence has been accumulated to demonstrate the efficiency of substituted 4-thiazolidinones and sulphonamides [11-15]

Keeping in view of biological importance of this group, we replace them by pyrimidine moiety at **N1**-position of sulphanilamide and 4-Thiazolidinoes/5-Methyl 4-Thiazolidinones at **N4**-position in sulphanilamide and our approach clearly shows the biological importance of the coupled products. The research work is scanned in scheme.

Antibacterial Activity

Antibacterial activities of all compounds were studied against Gram positive (*Bacillus subtillis* and S*taphylococcus aureus*) and Gram negative bacteria (*E. coli* and *Salmonella typhi*) at a concentration of 50 µg/ml by agar cup plate method[16]. Methanol system was used as control in this method. Under similar condition us in of penicillin and sulphanilamide as a standard comparison carried out control experiment. The area of inhibition of zone is measured in centimeters. Compounds **4b, 4c, 4f, 5b, 5f** were found more active against the above microbes. Other compounds found to be less or moderate active than the standards (**Tables I and II**).

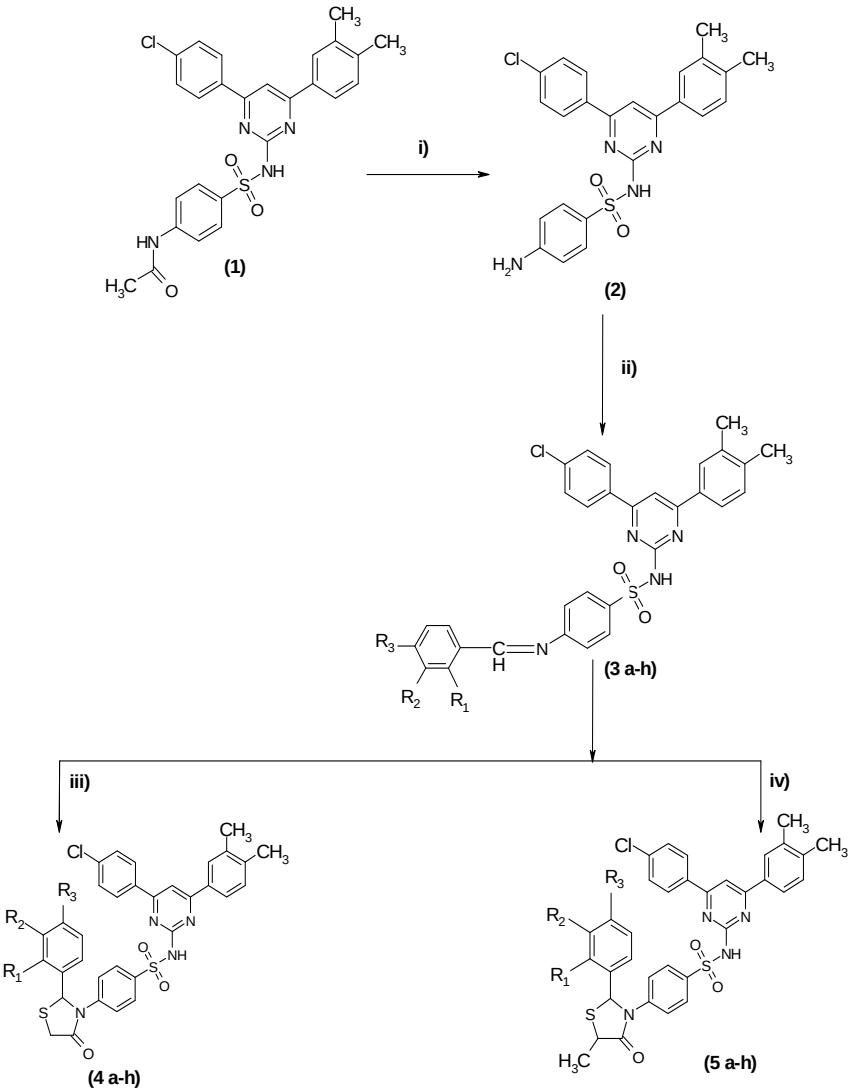
Antifungal Activity

The compounds (**4a-h**) and (**5a-h**) were tested for in vitro antifungal activity against Candida. Albicans and Aspergillus. Niger. The standard drug used was Griseofulvin. The investigation antifungal screening is reported in **Tables I and II**. Compounds **4e, 4g**, **5b, 5g** Shows good activity against C. Albicans fungal strain.

MATERIALS AND METHODS

Melting points were determined in open capillary tubes and are uncorrected. The IR spectra were recorded in KBr pellets on a Nicolet 400D spectrometer and 1 H NMR spectra in CDCl3 on Hitachi R-1500, 60 MHz spectrometer using TMS as an internal standard. The required N-Acetyl Sulphanilyl chlorides (N-ASC) were prepared by reported method [17]. All chemicals used were of laboratory grade.

Preparation of N-{4-[4-Chloro-phenyl}-6-(3,4-dimethyl-phenyl)-pyrimidin-2-ylsulfamoyl]-phenyl}-acetamide **(1)** was prepared according to the reported method [18]



Scheme 1 *Reagents and conditions :* ***i)*** *Hydrolysis/NaOH;* ***ii)*** *Ethanol /Substituted benzaldehyde / 8hr;* ***iii)*** *THF/Anhydrous $ZnCl_2$ /Thio- glycolic acid ;* ***iv)*** *THF/Anhydrous $ZnCl_2$ / Thio-lactic acid*

(a) *R_1 =R_2=R_3=H;* ***(b)*** *R_1 =R_2= H, R_3=OCH_3;* ***(c)*** *R_1 =R_2= H, R_3=OH;* ***(d)*** *R_1 =OH, R_2= R_3=H;* ***(e)*** *R_1 =R_2= H, R_3=CH_3;* ***(f)*** *R_1 = H R_2=R_3= -O-CH_2-O-;* ***(g)*** *R_1 =H,R_2= OCH_3, R_3=OH;* ***(h)*** *R_1 =H,R_2= OCH_2CH_3, R_3= OCH_2CH_3;*

Preparation of 4-Amino-N-[4-(4-chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidin-2-yl]-benzensulfonamide (2)

General procedure

N-{4-[4-Chloro-phenyl}-6-(3,4-dimethyl-phenyl)-pyrimidin-2-ylsulfamoyl]-phenyl}-acetamide **(1)** was hydrolyzed by refluxing 0.5-1.0 molar solution containing 2.5 equivalents of sodium hydroxide for two hours. After this period, the mixture was cooled to room temperature and neutralized with concentrated HCl pH by approximately 6.0. The mixture was cooled in the ice bath until the total precipitation of the product, the filtered vacuum, washed with small volume

of water ice and purification by recrystallization from ethanol to give white product **(2)** in 40-45% yield.

m.p 196-197°C; IR(KBr,cm^{-1}): 3410 (-NH_2), 1600 (C=C), 1310, 1150 (-SO_2-), 3290 (Ar-H); ^{1}H NMR: δ 6.12-7.6 (m,5H,Ar-H), 7.9 (s,1H,pyrimidine ring proton), 6.2 (s,2H,NH_2); A*nal* Cald.for $C_{24}H_{21}N_4O_2SCl$ (464.96): C,62.00; H,4.55; N,12.05; S,6.90; Cl,7.62; Found: C,61.90; H,4.50; N,12.05; S,6.80; Cl,7.60; Yield 67%;

Preparation of 4-(Arylidine-amino-N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidin-2-yl]-benzensulfonamide (3 a-h)

General procedure

A mixture of equimolar amount (0.01 mol) of 4-Amino-N-[4-(4-chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidin-2-yl]- benzensulfonamide (2) and the Substituted Benzaldehydes in absolute ethanol (50 ml) and piperidine (0.4 ml) was refluxed for 8 h in a water bath. The reaction mixture was concentrated, cooled and poured into ice cold water the solid obtained was filtered and Recrystallized from absolute ethanol to give white Schiff base (**3 a-h)**. It was obtained in 55-60% yield.

4-(Benzylidene-amino)-N-[4-(4-chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidin-yl]-benzenesulfonamide (3a).

m.p 191-192°C; IR(KBr cm^{-1}): 3030(Aromatic stretching), 1600(C=C),1375,1150 (-SO2-), 1640(-CH=N-); ^{1}H NMR: 7.8 (s,1H,H-5- of the pyrimidine ring), 6.12-7.5(17H,m,Aromatic); ^{13}CNMR: 115-129 (Benzene), 134 (Ar-Cl), 160 (-CH=N-); A*nal* Cald.for $C_{31}H_{25}N_4O_2SCl$ (553.07): C,67.32; H,4.56; N,10.13; S,5.80; Cl,6.41 Found: C,67.20; H,4.50; N,10.10; S,5.70; Cl,6.30; Yield 55%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[(4-methoxy-benzylidene)-amino]-benzenesulfonamide (3b)

m.p 189-190°C; IR(KBr cm^{-1}): 3030(Aromatic stretching), 1600(C=C), 1375,1150(-SO2-), 1640(-CH=N-),1200(Ar-O-alkyl) ; ^{1}H NMR:, 7.8 (s,1H,H-5- of the pyrimidne ring) , 3.85 (3H,s,-OCH3) , 6.12-7.5(16H,m,Aromatic); ^{13}CNMR: 163 (–C-O-), 115-129 (Benzene), 160 (-CH=N-), 56 (-CH_3), A*nal* Cald.for $C_{32}H_{27}N_4O_3SCl$ (583.09): C,65.91; H,4.67; N,9.61; S,5.50; Cl,6.08 Found: C,65.80; H,4.53; N,9.50; S,5.40; Cl,6.00; Yield 57%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[(4-hydroxy-benzylidene)-amino]-benzenesulfonamide (3c)

m.p 194-195°C; IR(KBr cm^{-1}): 3030(Aromatic stretching), 1600(C=C), 1375,1160(-SO2-), 1640(-CH=N-); ^{1}H NMR: 7.8 (s,1H,H-5- of the pyrimidne ring), 3.83 (3H,s,-OH) 6.12-7.5(16H,m,Aromatic); ^{13}CNMR: 163 (–C-O-), 115-129 (Benzene), 160 (-CH=N-); A*nal* Cald.for $C_{31}H_{25}N_4O_3SCl$ (569.07): C,65.43; H,4.43; N,9.85; S,5.63; Cl,6.23 Found: C,65.30; H,4.40; N,9.80; S,5.63; Cl,6.15; Yield 65%;

TABLE I Antibacterial Activity and Anti fungal activity of compounds (**4 a-h**)

Compounds	Antibacterial Activity				Anti fungal activity	
	% Zone of Inhibition					
	Gram +ve		Gram -ve			
	B.Subtillis	S.Aureus	E.Coli	Ps.Aeruginosa	C. Albicans	A. Niger
4a	48	40	45	61	43	40
4b	78	69	74	65	41	56
4c	55	45	41	53	51	44
4d	71	65	69	74	53	55
4e	62	59	59	60	65	75
4f	77	77	71	74	38	40
4g	57	59	56	48	63	71
4h	48	39	59	62	45	67
Penicillin	83	66	77	74	-	-
sulphanilamide	79	72	83	70	-	-
Griseofulvin	-	-	-	-	78	82

TABLE II Antibacterial Activity and Anti fungal activity of compounds **(5 a-h)**

Compounds	Antibacterial Activity					Anti fungal activity	
	% Zone of Inhibition						
	Gram +ve		Gram -ve				
	B.Subtillis	S.Aureus	E.Coli	Ps.Aeruginosa	C. Albicans	A. Niger
5a	57	42	43	52	44	40
5b	61	59	62	55	65	76
5c	51	46	57	48	51	44
5d	41	57	41	43	53	44
5e	45	50	46	59	41	56
5f	78	68	71	79	38	40
5g	57	54	55	44	62	73
5h	43	40	58	63	46	41
Penicillin	83	66	77	74	-	-
sulphanilamide	79	72	83	70	-	-
Griseofulvin	-	-	-	-	78	82

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[(2-hydroxy-benzylidene)-amino]-benzenesulfonamide (3d)

m.p 185-186°C; IR(KBr cm^{-1}): 3030(Aromatic stretching), 1600(C=C), 1375,1150(-SO2-), 1640(-CH=N-); ^{1}H NMR: 7.8 (s,1H,H-5- of the pyrimidne ring), 3.83 (3H,s,-OH) 6.12-7.5(16H,m,Aromatic); $^{13}CNMR$: 163 (–C-O-), 115-129 (Benzene), 160 (-CH=N-), A*nal* Cald.for $C_{31}H_{25}N_4O_3SCl$ (569.07): C,65.43; H,4.43; N,9.85; S,5.63; Cl,6.23 Found: C,65.30; H,4.40; N,9.80; S,5.63; Cl,6.15; Yield 61%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[(4-methyl-benzylidene)-amino]-benzenesulfonamide(3e)

m.p 192-193°C; IR(KBr cm^{-1}): 3030(Aromatic stretching), 1600(C=C), 1375,1150(-SO2-), 1630(-CH=N-) ; ^{1}H NMR: 7.8 (s,1H,H-5- of the pyrimidne ring), 2.34 (3H,s,-CH_3), 6.12-

7.5(16H,m,Aromatic); ^{13}CNMR: 163 (–C-O-), 115-129 (Benzene), 160 (-CH=N-), 20.9(Ar-CH3); A*nal* Cald.for $C_{32}H_{27}N_4O_2SCl$ (567.10) : C,67.77; H,4.80; N,9.88; S,5.65; Cl,6.25 Found: C,67.60; H,4.70; N,9.85; S,5.60; Cl,6.22; Yield 57%;

4-[(Benzo[1,3]dioxol-5ylmethylene)-amino]-N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-benzenesulfonamide (3f)

m.p 199-200°C; IR(KBr cm^{-1}): 3030(Aromatic stretching), 1600(C=C), 1370,1150(-SO2-), 1640(-CH=N-) ; ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring) ,6.12-7.5(15H,m,Aromatic), 6.07 (2H, S, -O-CH_2-O-); ^{13}CNMR: 115-129 (Benzene), 160 (-CH=N-), 101 (-O-CH_2-O-); A*nal* Cald.for $C_{32}H_{25}N_4O_4SCl$ (597.09): C,64.37; H,4.22; N,9.38; S,5.37; Cl,5.94 Found: C,64.31; H,4.2; N,9.30; S,5.37; Cl,5.72; Yield 55%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[(4-hydroxy-3-methoxy-benzylidene)-amino]-benzenesulfonamide (3g)

m.p 190-191°C; IR(KBr cm^{-1}): 3370(-OH),3030(Aromatic stretching), 1600(C=C), 1375,1160 (-SO2-), 1640(-CH=N-) cm^{-1}; ^{1}H NMR:, 7.8 (s,1H,H-5- of the pyrimidne ring) ,3.36 (3H,s,-OCH3), 3.85 (1H,s,-OH), 6.12-7.5(15H,m,Aromatic); ^{13}CNMR: 56.3 (–OCH3), 115-129 (Benzene),160 (-CH=N-); A*nal* Cald.for $C_{32}H_{27}N_4O_4SCl$ (599.09): C,64.15; H,4.54; N,9.35; S,5.35; Cl,5.92 Found: C,64.00; H,4.50; N,9.30; S,5.23; Cl,5.81; Yield 59%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[(3,4-diethoxy-benzylidene)-amino]-benzenesulfonamide (3h)

m.p 188-189°C; IR(KBr cm^{-1}): 3370(-OH), 3030(Aromatic stretching), 1600(C=C), 1375,1150 (-SO2-), 1640(-CH=N-), cm^{-1}; ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 3.36 (3H,s,-OCH3), 3.85 (1H,s,-OH), 6.12-7.5(15H,m,Aromatic); ^{13}CNMR: 56.3 (–OCH3), 149 (-C-O-), 115-129 (Benzene), 160 (-CH=N-); A*nal* Cald.for $C_{35}H_{33}N_4O_4SCl$ (641.17): C,64.56; H,5.19; N,8.74; S,5.00; Cl,5.53 Found: C,64.37; H,5.10; N,8.70; S,5.00; Cl,5.50; Yield 60%;

Preparation of N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-(4-oxo-2-aryl-thiazolidin-3-yl)-benzenesulfonamide (4a-h)

General procedure

A mixture of Schiff base (**3 a-h**) (0.01 mol) and Tetrahydrofuran (THF) (40 ml) was and thio glycolic acid (mercapto acetic acid) (0.01 mol) with a pinch of anhydrous ZnCl2 was refluxed for 12 hr in an oil bath. The solvent was then removed to get a residue, the residue washed with (10%) sodium bicarbonate solution and then product crystallized from absolute ethyl alcohol to give (**4 a-h**). 50-60% yield.

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-(4-oxo-2-phenyl-thiazolidin-3-yl)-benzenesulfonamide (4a)

m.p 184-185°C; IR(KBr cm^{-1}): 3350(-NH-),1370,1150(-SO2-), 1690(β Lactum (C=O)), 754(C-S-C Str.); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring) ,6.12-7.56 (17H,m,Aromatic), 3.9(s,2H,S-CH2-), 6.44 (1H,s,-N-CH-), 4.00 (2H,s,Cyclic -CO-CH2-S-); ^{13}CMR:171.2(C=O), 33.5(-CH2-thiazolidine ring), 72.6(-CH-thiazolidine ring); A*nal* Cald.for $C_{33}H_{27}N_4O_3S_2Cl$ (627.19): C,63.14; H,4.34; N,8.93; S,10.23; Cl,5.65 Found: C,63.10; H,4.31; N,8.82; S,10.12; Cl,5.61; Yield 52%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[2-(4-methoxy-phenyl)4-oxo-thiazolidin-3-yl)-benzenesulfonamide (4b)
m.p 188-189°C; IR(KBr cm^{-1}): 3350(-NH-), 1200 (Ar-O-CH_3), 1375,1150(-SO2-), 1685(β Lactum (C=O)), 754(C-S-C Str.); ^{1}H NMR: 7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.56 (16H,m,Aromatic), 4.0(s,2H,S-CH2), 6.45 (1H,s,-N-CH-), 4.30 (2H,s,Cyclic -CO-CH2-S-); ^{13}CMR:171.2(C=O), 33.5(-CH2-thiazolidine ring), 72.6(-CH-thiazolidine ring), 56(-CH_3)A*nal* Cald.for $C_{34}H_{29}N_4O_4S_2Cl$ (657.20): C,62.14; H,4.45; N,8.53; S,9.76; Cl,5.39 Found: C,62.10; H,4.30; N,8.42; S,9.68; Cl,5.30 ; Yield 55%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[2-(4-hydroxy-phenyl)4-oxo-thiazolidin-3-yl)-benzenesulfonamide (4c)
m.p 191-192°C; IR(KBr cm^{-1}): 3350(-NH-), 1370,1150(-SO2-), 1685(β Lactum (C=O)), 754(C-S-C Str.); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.56 (16H,m,Aromatic), 4.0 (s,2H,S-CH2), 6.45 (1H,s,-N-CH-), 4.30 (2H,s,Cyclic -CO-CH2-S-), 5.95 (1H,s,Cyclic -S-CH-N-), 5.35 (1H,S,-OH); ^{13}CMR:171.2(C=O), 33.5(-CH2-thiazolidine ring), 72.6(-CH-thiazolidine ring); A*nal* Cald.for $C_{33}H_{27}N_4O_4S_2Cl$ (643.17): C,61.62; H,4.23; N,8.71; S,9.97; Cl,5.51 Found: C,61.60; H,4.23; N,8.65; S,9.90; Cl,5.50; Yield 56%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[2-(2-hydroxy-phenyl)4-oxo-thiazolidin-3-yl)-benzenesulfonamide (4d)
m.p 194-195°C; IR(KBr cm^{-1}): 3350(-NH-), 1370,1150(-SO2-), 1685(β Lactum (C=O)), 754(C-S-C Str.); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.5 (16H,m,Aromatic), 3.90(s,2H,S-CH2),6.44 (1H,s,-N-CH-), 4.30 (2H,s,Cyclic -CO-CH2-S-), 5.95 (1H,s,Cyclic -S-CH-N-), 5.35 (1H,S,-OH); ^{13}CMR:171(C=O), 33.5(-CH2-thiazolidine ring), 72.6(-CH-thiazolidine ring); A*nal* Cald.for $C_{33}H_{27}N_4O_4S_2Cl$ (643.17): C,61.62; H,4.23; N,8.71; S,9.97; Cl,5.51 Found: C,61.62; H,4.23; N,8.60; S,9.90; Cl,5.48 ; Yield 61%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-(4-oxo-2-p-tolyl-thiazolidin-3-yl)-benzenesulfonamide (4e)
m.p 199-200°C; IR(KBr cm^{-1}): 3350(-NH-),1370,1150 (-SO2-), 1685(β Lactum (C=O)), 754(C-S-C Str.); ^{1}H NMR: 7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.56 (16H,m,Aromatic), 3.90(s,2H,S-CH2), 6.45(1H,s,-N-CH-), 4.30 (2H,s,Cyclic -CO-CH2-S-), 5.95 (1H,s,Cyclic -S-CH-N-), 2.34 (1H,S,-CH3); ^{13}CMR:171.2(C=O), 33.5(-CH2-thiazolidine ring), 72.6(-CH-thiazolidine ring), 18,21.3 (-CH_3); A*nal* Cald.for $C_{34}H_{29}N_4O_3S_2Cl$ (641.20) : C,63.69; H,4.56; N,8.74; S,10.00; Cl,5.53 Found: C,63.69; H,4.52; N,8.72; S,10.00; Cl,5.40; Yield 60%;

4-(2-(benzo[d][1,3]dioxol-5-yl)-4-oxothiazolidin-3-yl)-N-(4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)pyrimidin-2-yl)benzenesulfonamide (4f)
m.p 196-197°C; IR(KBr cm^{-1}): 3350(-NH-), 1370,1150(-SO2-), 1685(β Lactum (C=O)), 754(C-S-C Str.); ^{1}H NMR: 7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.5 (15H,m,Aromatic), 4.0(s,2H,S-CH2), 6.45(1H,s,-N-CH-), 4.30 (2H,s,Cyclic -CO-CH2-S-), 5.95 (1H,s,Cyclic -S-CH-N-); ^{13}CMR:171.2(C=O), 33.5 (-CH2-thiazolidine ring), 72.6 (-CH-thiazolidine ring); A*nal* Cald.for $C_{34}H_{27}N_4O_5S_2Cl$ (671.20) : C,60.84; H,4.05; N,8.35; S,9.05; Cl,5.28 Found: C,60.70; H,3.86; N,8.27; S,9.38; Cl,5.20; Yield 57%

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[2-(4-hydroxy-3-methoxy-phenyl)4-oxo-thiazolidin-3-yl)-benzenesulfonamide (4g)

m.p 184-185°C; IR(KBr cm^{-1}): 3350(-NH-), 1370,1150(-SO2-), 1685(β Lactum (C=O)), 754(C-S-C Str.),cm^{-1}; ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.5 (15H,m,Aromatic), 3.90(s,2H,S-CH2), 6.45 (1H,s,-N-CH-), 4.30 (2H,s,Cyclic -CO-CH2-S-), 5.95 (1H,s,Cyclic -S-CH-N-), 5.35 (1H,s,-OH), 3.83 (3H,s,-OCH3); ^{13}CMR: 171.2(C=O), 33.5(-CH2-thiazolidine ring), 72.6(-CH-thiazolidine ring); A*nal* Cald.for $C_{34}H_{29}N_4O_5S_2Cl$ (673.20) : C,60.66; H,4.34; N,8.32; S,9.53; Cl,5.27 Found: C,60.61; H,4.34; N,8.30; S,9.53; Cl,5.20; Yield 59%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[(3,4-diethoxy-phenyl)-4-oxo-thiazolidin-3-yl)-benzenesulfonamide (4h)

m.p 196-197°C; IR(KBr cm^{-1}): 3350(-NH-), 1370,1150(-SO2-),1685(β Lactum (C=O)), 754(C-S-C Str.),cm^{-1}; 1H NMR:7.8 (s,1H,H-5- of the pyrimidne ring) ,6.12-7.5 (15H,m,Aromatic) 3.90 (s,2H,S-CH2), 6.45 (1H,s,-N-CH-),4.30 (2H,s,Cyclic -CO-CH2-S-),5.95 (1H,s,Cyclic -S-CH-N-),4.10 (4H,q,2CH2), 1.32 (6H,t,2CH3), 13CMR:171.2(C=O),33.5(-CH2-thiazolidine ring),72.6 (-CH-thiazolidine ring),65 (OCH_2); A*nal* Cald.for $C_{37}H_{35}N_4O_5S_2Cl$ (715.28) : C,62.13; H,4.93; N,7.83; S,8.97; Cl,4.96 Found: C,62.13; H,4.90; N,7.81; S,8.80; Cl,4.92; Yield 57%;

Preparation of N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-(5-methyl-4-oxo-2-aryl-thiazolidin-3-yl)-benzenesulfonamide (5a-h)

General procedure

A mixture of Schiff base (**3 a-h**) (0.01 mol) and Tetrahydrofuran (THF) (40 ml) was and thio lactic acid (0.01 mol) with a pinch of anhydrous ZnCl2 was refluxed for 12 hr in an oil bath. The solvent was then removed to get a residue, the residue washed with (10%) sodium bicarbonate solution and then product crystallized from absolute ethyl alcohol to give (**5 a-h**). 50-65% yield.

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-(5-methyl-4-oxo-2-phenyl-thiazolidin-3-yl)-benzenesulfonamide (5a)

m.p 188-189°C; IR(KBr cm^{-1}): 3350(-NH-),1360,1140(-SO2-), 1685(β Lactum (C=O)), 754 (-C-S-C Str.-); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.6 (17H,m,Aromatic), 1.40 (d,3H,-CH-CH3), 6.44 (1H,s,-N-CH-), 3.65 (q,1H,-CH-CH3); ^{13}CMR:174(C=O), 42.4 (-C_5H-thiazolidine ring), 70.1 (-C_2H-thiazolidine ring); A*nal* Cald.for $C_{34}H_{29}N_4O_3S_2Cl$ (641.20): C,63.69; H,4.56; N,8.74; S,10.00; Cl,5.53 Found: C,63.69; H,4.56; N,8.74; S,10.00; Cl,5.53; Yield 62%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[2-(4-methoxy-phenyl)-5-methyl-4-oxo-thiazolidin-3-yl)-benzenesulfonamide (5b)

m.p 185-186°C; IR(KBr cm^{-1}): 3350(-NH-),1360,1140(-SO2-), 1685(β Lactum (C=O)), 754 (-C-S-C Str.-); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.6 (17H,m,Aromatic), 1.40 (d,3H,-CH-CH3), 6.44 (1H,s,-N-CH-), 3.65 (q,1H,-CH-CH3); ^{13}CMR:174(C=O), 42.4 (-C_5H-thiazolidine ring), 70.1 (-C_2H-thiazolidine ring); A*nal* Cald.for $C_{35}H_{31}N_4O_4S_2Cl$ (671.22): C,62.63; H,4.66; N,8.35; S,9.55; Cl,5.28 Found: C,62.52; H,4.66; N,8.30; S,9.55; Cl,5.22; Yield 53%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[2-(4-hydroxy-phenyl)-5-methyl-4-oxo-thiazolidin-3-yl)-benzenesulfonamide (5c)

m.p 199-200°C; IR(KBr cm^{-1}): 3350(-NH-),1360,1140(-SO2-), 1685(β Lactum (C=O)), 754 (-C-S-C Str.-); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.6 (17H,m,Aromatic), 1.40 (d,3H,-CH-CH3), 6.44 (1H,s,-N-CH-), 3.65 (q,1H,-CH-CH3); ^{13}CMR:174(C=O), 42.4 (-C_5H-thiazolidine ring), 70.1 (-C_2H-thiazolidine ring); A*nal* Cald.for $C_{34}H_{29}N_4O_4S_2Cl$ (657.20): C,62.14; H,4.45; N,8.53; S,9.76; Cl,5.39 Found: C,62.10; H,4.45; N,8.51; S,9.50; Cl,5.10; Yield 52%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[2-(2-hydroxy-phenyl)-5-methyl-4-oxo-thiazolidin-3-yl)-benzenesulfonamide (5d)

m.p 205-206°C; IR(KBr cm^{-1}): 3350(-NH-),1360,1140(-SO2-), 1685(β Lactum (C=O)), 754 (-C-S-C Str.-); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.6 (17H,m,Aromatic), 1.40 (d,3H,-CH-CH3), 6.44 (1H,s,-N-CH-), 3.65 (q,1H,-CH-CH3); ^{13}CMR:174(C=O), 42.4 (-C_5H-thiazolidine ring), 70.1 (-C_2H-thiazolidine ring); A*nal* Cald.for $C_{34}H_{29}N_4O_4S_2Cl$ (657.20): C,62.14; H,4.45; N,8.53; S,9.76; Cl,5.39 Found: C,62.14; H,4.45; N,8.51; S,9.50; Cl,5.10; Yield 59%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-(-5-methyl-4-oxo-2-p-tolyl-thiazolidin-3-yl)-benzenesulfonamide (5e)

m.p 181-182°C; IR(KBr cm^{-1}): 3350(-NH-),1360,1140(-SO2-), 1685(β Lactum (C=O)), 754 (-C-S-C Str.-); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.6 (17H,m,Aromatic), 1.40 (d,3H,-CH-CH3), 6.44 (1H,s,-N-CH-), 3.65 (q,1H,-CH-CH3); ^{13}CMR:174(C=O), 42.4 (-C_5H-thiazolidine ring), 70.1 (-C_2H-thiazolidine ring); A*nal* Cald.for $C_{35}H_{31}N_4O_3S_2Cl$ (655.22): C,64.16; H,4.77; N,8.55; S,9.79; Cl,5.41 Found: C,64.16; H,4.77; N,8.50; S,9.73; Cl,5.30; Yield 63%;

4-(2-(benzo[d][1,3]dioxol-5-yl)-5-methyl-4-oxothiazolidin-3-yl)-N-(4-(4-chlorophenyl)-6-(3,4-dimethylphenyl)pyrimidin-2-yl)benzenesulfonamide (5f)

m.p 197-198°C; IR(KBr cm^{-1}): 3350(-NH-),1360,1140(-SO2-), 1685(β Lactum (C=O)), 754 (-C-S-C Str.-); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.6 (17H,m,Aromatic), 1.40 (d,3H,-CH-CH3), 6.44 (1H,s,-N-CH-), 3.65 (q,1H,-CH-CH3); ^{13}CMR:174(C=O), 42.4 (-C_5H-thiazolidine ring), 70.1 (-C_2H-thiazolidine ring); A*nal* Cald.for $C_{34}H_{28}N_4O_3S_2Cl_2$ (675.64): C,60.44; H,4.18; N,8.29; S,9.49; Cl,10.49 Found: C,60.40; H,4.10; N,8.22; S,9.45; Cl,10.49 ; Yield 56%

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[2-(4-hydroxy-3-methoxy-phenyl)-5-methyl-4-oxo-thiazolidin-3-yl)-benzenesulfonamide (5g)

m.p 199-200°C; IR(KBr cm-1): 3350(-NH-),1360,1140(-SO2-), 1685(β Lactum (C=O)), 754 (-C-S-C Str.-); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.6 (17H,m,Aromatic), 1.40 (d,3H,-CH-CH3), 6.44 (1H,s,-N-CH-), 3.65 (q,1H,-CH-CH3); ^{13}CMR:174(C=O), 42.4 (-C_5H-thiazolidine ring), 70.1 (-C_2H-thiazolidine ring); A*nal* Cald.for $C_{35}H_{31}N_4O_5S_2Cl$ (687.22): C,61.17; H,4.55; N,8.15; S,9.33; Cl,5.16 Found: C,61.17; H,4.55; N,8.15; S,9.30; Cl,5.05; Yield 57%;

N-[4-(4-Chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidn-2-yl]-4-[(3,4-diethoxy-phenyl)-5-methyl-4-oxo-thiazolidin-3-yl)-benzenesulfonamide (5h)
m.p 204-205°C; IR(KBr cm-1): 3350(-NH-),1360,1140(-SO2-), 1685(β Lactum (C=O)), 754 (-C-S-C Str.-); ^{1}H NMR:7.8 (s,1H,H-5- of the pyrimidne ring), 6.12-7.6 (17H,m,Aromatic), 1.40 (d,3H,-CH-CH3), 6.44 (1H,s,-N-CH-), 3.65 (q,1H,-CH-CH3); ^{13}CMR:174(C=O), 42.4 (-C_5H-thiazolidine ring), 70.1 (-C_2H-thiazolidine ring); A*nal* Cald.for $C_{38}H_{37}N_4O_5S_2Cl$ (729.30): C,62.58; H,5.11; N,7.68; S,8.79; Cl,4.86 Found: C,62.50; H,5.10; N,7.62; S,8.71; Cl,4.86; Yield 61%;

RESULTS AND DISCUSSION

Since the antibacterial effect of sulphanilamide has been attributed to the presence of a sulphonamide groups (-SO_2 NH_2-) and NH_2 group in para position, it is of interest to study the effect of fixation of these groups to the pyrimidine moiety. This interest has also prompted us to extend this study to include the effect of the introduction of the well known antibacterial nucleus (Thiazolidinone) instead of NH2 group into the sulfa-pyrimidine nucleus.

The starting material, N-{4-[4-Chloro-phenyl}-6-(3,4-dimethyl-phenyl)-pyrimidin-2-ylsulfamoyl]-phenyl}-acetamide **(1)** was prepared by according to the reported method [18]. It can be hydrolyzed to 4-Amino-N-[4-(4-chloro-phenyl)-6-(3,4-dimethyl-phenyl)-pyrimidin-2-yl]-benzensulfonamide **(2)** by sodium hydroxide solution. It is characterized by the elemental analysis, IR spectral studies, and NMR spectral studies. The strong absorptions at 1370 and 1160 were due to the presences of sulphonyl group. The structure of (**2**) was established by spectroscopic evidence.

This hydrolyzed product (**2**) was dissolved in absolute ethanol and was reacted with aromatic aldehyde in the presence of piperidine to yield Schiff bases (**3 a-h)** were then characterized by the elemental analysis, IR spectral studies, and NMR spectral studies. The IR spectra of Schiff bases show the prominent band at 1630 cm-1 for the azomethine group[19]. All the compounds show the NMR signals for different kinds of protons at their respective positions. It is characterized by the elemental analysis, IR spectral studies, and NMR spectral studies.

These Schiff bases on Cyclo condensation reaction with thio glycolic acid (mercapto acetic acid) afford 4-thiazolidinoes (**4 a-h)** and with thio lactic acid afford 5-Methyl 4-Thiazolidinones (**5 a-h)** respectively. The structures of these compounds have been confirmed by elemental analysis, IR spectral studies, and NMR spectral studies. These compounds shows the band at 1685 cm-1 for cyclic (C=O of thiazolidinone ring) group [19]. All the compounds show the NMR signals for different kinds of protons at their respective positions.

The antibacterial activities of both the series (**4 a-h)** and (**5 a-h)** respectively, have been carried out against some strain of bacteria. The results show that the prepared compounds are toxic against the bacteria. The comparison of the antibacterial activity of these compounds with penicillin and sulphanilamide shows that these compounds have almost similar activity.

CONCLUSION

The clubbing of sulfa pyrimidine and thiazolidinone has been done successfully into one molecule. Both the moieties have important applications in medicinal use; the produced compounds may be act as good biological compounds.

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