Formation and Biological evaluation of 4-thiazolidinone derivatives for their pharmacological activity

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ABSTRACT. Thiazolidin-4-one is a versatile lead molecule for designing potential bioactive agents. An expeditious method for preparation of 4-thiazolidinones 7(a-h) are an important class of heterocycles, having potential biological importance due to their unique features. The process of convert of imine (Schiff's base) to 4-thiazolidinone through an intermediate of THF mercapto acetic acid with anhydrous zinc chloride is important synthetic method for preparation of 4-thiazolidinone. The structures of the synthesized compounds were confirmed by IR, ¹H-NMR, ¹³C NMR and Mass spectral studies. The compounds were screened for their antimicrobial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* was determined by disc diffusion technique. All the synthesized compounds exhibited promising antimicrobial activity against the studied set of microorganisms.

1. INTRODUCTION

4-thiazolidinone embraces the most important position among pharmaceutically significant natural products and synthetic compounds. The role of 4-thiazolidinone nucleus in the field of medicinal chemistry provoked us to keep on working on synthesize novel derivatives having this moiety. The incredible ability of 4-thiazolidinones, to serve equally as biomimetics and reactive pharmacophore, makes up them an extremely considerable class of compounds. In view of the general observation that pharmacological activity is invariably associated with a large variety of heterocyclic compounds, the investigation of some heterocycles such as thiazolidinone derivatives has been undertaken. 4-thiazolidinones are derivatives of thiazolidine with a carbonyl group at the 4 position. Several methods for syntheses are available. The literature survey revealed that 4-thiazolidinone and their derivatives were possessed a wide range of pharmacological activities such as anti-inflammatory, analgesic, anticonvulsant, antimicrobial, local and spinal anesthetics, CNS stimulants, hypnotics, anti HIV, hypoglycemic, anticancer, FSH receptor agonist and CFTR inhibitor etc [1-2]. Derivatives of these compounds are reported to possess a wide spectrum of biological activities which include anti-inflammatory, analgesic, antitumour, antihypertensive, anticonvulsant and antimicrobial activity. Owing to the importance and established physiological activity of these thiazolidinones it was thought to synthesize and investigate compounds with comparable structures [3-8]. 4-thiazolidinone nucleus has also occupied a unique place in the field of medicinal chemistry due to wide range of biological activities like antischistosomal, antibacterial, anticancer, potassium channel inhibitor, cardiovascular [9], local anesthetic, sedative, cholorectic, anti-tubercular [10], antiviral, anti-tumor, CNS depressant [11], antihypertensive, hypoglycaemic [12], anti allergic [13], hypertensive, antihelminthic, antiinflammatory, anti-parkinsonian [14], hypnotic [15], antithyroidal, fungicidal [16], cysticidal, anti-leukemic [17], and anti-oxidant activities of thiazadiazole, 4-thiazolidinone. The synthetic route of the abovementioned compounds is shown in reaction scheme.

Reaction Scheme

Reaction reagent and condition

A= 40% KOH, OH⁻

B= Guinidine Hydrochloride,

C= -H₂O, -H₂

D= P-Acetyl-aminobenzenesulphonyl chloride and pyridine

E= Hydrolysis

F= Different Aldehyde (5a-h)

G= THF anhydrous/ SNCH₂COOH

Table 1: The benzaldehyde derivatives (5a-h) used for Schiff bases formation of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

No.	Benzaldehyde derivative	Structure
5a	Benzaldehyde
5b	4-Methoxy benzaldehyde
5c	4-Hydroxy benzaldehyde
5d	2-Hydroxy benzaldehyde
5e	4-Methyl benzaldehyde
5f	3,4-Methylenedioxy benzaldehyde (i.e. Veretral)
5g	4-Hydroxy-3-methoxy benzaldehyde
5h	3,4-Diethoxy benzaldehyde

Table 2: Physical characterisation constant of 4-(benzylideneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (6 a-h)

Com. No	Molecular Formula	-Ar	Molecular Weight	Elemental analysis, Cal/Found			
				%C	%H	%N	%S
6a	C ₃₄ H ₂₄ Cl ₂ N ₄ O ₂ S	Phenyl	622.10 gm/mole	65.49 65.19	3.88 3.57	8.99 8.89	5.14 5.10
6b	C ₃₅ H ₂₆ Cl ₂ N ₄ O ₃ S	4-Methoxy phenyl	652.11 gm/mole	64.32 64.12	4.01 3.92	8.57 8.51	4.91 4.86
6c	C ₃₄ H ₂₄ Cl ₂ N ₄ O ₃ S	4-Hydroxy phenyl	638.09 gm/mole	63.85 63.55	3.78 3.65	8.76 8.56	5.01 5.00
6d	C ₃₄ H ₂₄ Cl ₂ N ₄ O ₃ S	2-Hydroxy phenyl	638.09 gm/mole	63.85 63.55	3.78 3.65	8.76 8.56	5.01 5.00
6e	C ₃₄ H ₂₆ Cl ₂ N ₄ O ₂ S	4-Methyl phenyl	636.12 gm/mole	63.93 63.73	4.11 4.01	8.89 8.79	5.03 5.00
6f	C ₃₅ H ₂₄ Cl ₂ N ₄ O ₄ S	3,4-Methylenedioxy phenyl	666.09 gm/mole	62.97 62.81	3.62 3.55	8.39 8.32	4.80 4.70
6g	C ₃₅ H ₂₆ Cl ₂ N ₄ O ₄ S	4-Hydroxy-3-methoxy phenyl	668.11 gm/mole	62.78 62.68	3.91 3.76	8.37 8.30	4.79 4.73
6h	C ₃₈ H ₃₂ Cl ₂ N ₄ O ₄ S	3,4-Diethoxy phenyl	710.19 gm/mole	64.13 64.00	4.53 4.48	7.87 7.81	4.51 4.44

Table 3: Physical characterisation constant of N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-oxo-2-phenylthiazolidin-3-yl)benzenesulfonamide (7a-h)

Com. No	Molecular Formula	-Ar	Molecular Weight	Elemental analysis, Cal/Found			
				%C	%H	%N	%S
7a	C ₃₆ H ₂₆ Cl ₂ N ₄ O ₃ S ₂	Methylbenzene	696.09 gm/mole	61.98 61.80	3.76 3.71	8.03 8.00	9.19 9.01
7b	C ₃₇ H ₂₈ Cl ₂ N ₄ O ₄ S ₂	1-Methoxy-4-methylbenzene	726.09 gm/mole	61.07 61.00	3.88 3.75	7.70 7.62	8.81 8.60
7c	C ₃₆ H ₂₆ Cl ₂ N ₄ O ₄ S ₂	4-Methylphenol	712.19 gm/mole	60.59 60.46	3.67 3.60	7.85 7.80	8.99 8.78
7d	C ₃₆ H ₂₆ Cl ₂ N ₄ O ₄ S ₂	2-Methylphenol	712.19 gm/mole	60.59 60.48	3.67 3.55	7.85 7.77	8.99 8.79
7e	C ₃₇ H ₂₈ Cl ₂ N ₄ O ₃ S ₂	1,4-Dimethylbenzene	710.10 gm/mole	62.44 62.40	3.97 3.93	7.87 7.83	9.01 8.89
7f	C ₃₇ H ₂₆ Cl ₂ N ₄ O ₅ S ₂	5-Methyl-1,3-benzodioxole	740.17 gm/mole	59.92 59.89	3.53 3.50	7.55 7.50	8.65 8.61
7g	C ₃₇ H ₂₈ Cl ₂ N ₄ O ₅ S ₂	2-Methoxy-4-methylphenol	742.09 gm/mole	59.76 59.70	3.79 3.73	7.53 7.48	8.62 8.60
7h	C ₄₀ H ₃₄ Cl ₂ N ₄ O ₅ S ₂	1,2-Diethoxy-4-methylbenzene	784.13 gm/mole	61.14 61.03	4.36 4.31	7.13 7.10	8.16 8.03

2. METHODOLOGY

Synthesis of 3-(2,4-dichlorophenyl)-1-(6-methylnaphthalen-2-yl)prop-2-en-1-one (1)

To a well stirred solution of 2,4-dichloro benzaldehyde (0.01 mole) and 1-(6-methylnaphthalen-2-yl)ethanone (0.01 mole) in ethanol (35 ml), 40% KOH added till the solution become basic. The reaction mixture was stirred for 24 hrs. The contents were poured into ice, acidified, filtered and crystallized from ethanol.

Synthesis of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (2)

A mixture of Chalcone (0.01 mole) in 25 ml of absolute alcohol, add Guanidine Hydrochloride (0.015 mole) and sodium hydroxide (0.045 mole in 2 ml of water) was refluxed in water bath at temp 80-90°C for 8 hr. The reaction mixture was poured into ice. The product was isolated and crystallized from ethanol.

Synthesis of N-(4-(N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)sulfamoyl)phenyl)acetamide (3)

The derivative was prepared by reactions of amino pyrimidine (2) (0.01 mole) with *P*-Acetylamino-benzenesulfonyl chloride (0.012 mole) in dry pyridine (30 ml) was heated to 70-75°C on a water bath for 5 hr. the cold reaction mixture was acidified with dil. hydrochloric acid. The solid that separated was filtered, washed several times with hot water, dried and crystallized from proper solvent.

4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

N-(4-(N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)sulfamoyl)phenyl)acetamide (3) was hydrolysed by refluxing 0.5-1.0 molar solution containing 3.5 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.

Synthesis of 4-(benzylideneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (6 a-h)

The various Schiff bases (6a-h) of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4) have been prepared in the similar manner. The procedure is as follow:

A mixture of equimolar amount (0.01 mole) of of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4) and the Substituted Benzaldehydes (5) in absolute ethanol (70 ml) and piperidine (0.5 ml) was refluxed for 10 hr. 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.

Synthesis of N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-oxo-2-phenylthiazolidin-3-yl)benzenesulfonamide (7a-h)

A mixture of Schiff bases (6a-h) (0.01 mole) in THF (30ml) and mercapto acetic acid (thioglycolic acid) (0.01 mole) with a pinch of anhydrous ZnCl₂ was refluxed for 12 hours. The solvent was then removed to get a residue, which was dissolved in benzene and passed through column of silica gel using benzene: chloroform (8:2; v/v) mixture as eluent. The eluate was concentrated and the product crystallized from alcohol to give 4-thiazolidinones (7a-h), which were obtained in 50-60% yield.

3. RESULTS AND DISCUSSION

SPECTRAL STUDIES:

IR spectra of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

Sulfa Pyrimidine is a heterocyclic compound. It is an aromatic compound thus it provides the IR frequencies. The bands due to pyrimidine are at $3220\text{--}3440\text{ cm}^{-1}$ and $1610\text{--}1640\text{ cm}^{-1}$ corresponds to N-H (str.) and C=N groups. The peak at 1630 cm^{-1} is indicative of C=N, 1600 cm^{-1} due to C=C cm^{-1} , and 1310 cm^{-1} and 1150 cm^{-1} diagnostic for the presence of the sulphonamido group ($-\text{SO}_2\text{NH}-$) also The corresponding N-H in plane and out of plane bending vibrations occurs at 1630 and 699 cm^{-1} respectively.

NMR spectra of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

The signal at 4.0 ppm is responsible for N-H proton of pyrimidine $-\text{SO}_2\text{NH}-$, signal at 6.35 ppm is responsible for $-\text{NH}_2$ proton, and multiple signals between 6.15-7.8 ppm are responsible for aromatic proton. While signal at 2.30 due to two $-\text{CH}_3$ on benzene ring.

CMR spectra of 4-amino-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (4)

The signals at 101.7 (C_5), 162.5 (C_4), 165.4 (C_6) and 169.3 (C_2) ppm are responsible for pyrimidine multiple signals between 114-140 ppm are responsible for aromatic segments. While signal at 18.8 and 19.1 are due to two $-\text{CH}_3$.

Finally the structure of compound conform by LC-MS compound (4) shows peak of (m/Z) at 534.07 which consistent with the calculated molecular weight of Compound (4) i.e. 534.07.

Spectral Studies of compound 6a-6h

4-(benzylideneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 6a

Yield: 60%, MP 193°C , Infrared Spectral Features around cm^{-1} 3030, 1500, Aromatic C-H stretching, 1600- 1641 - $\text{CH}=\text{N}-$, 1315-1375 $-\text{SO}_2-$, 3250-3330 $-\text{NH}-$ of $-\text{SO}_2\text{NH}-$, PMR spectral Features (δ Ppm) 6.5-8.5 multiplet, aromatic+ CH of $\text{CH}=\text{N}$ protons + H of Pyrimidine + H of $\text{SO}_2\text{NH}+$), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene, 134- Ar-Cl, 160- $\text{CH}=\text{N}$, 162-169- pyrimidine.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-methoxybenzylideneamino)benzenesulfonamide 6b

Yield: 61%, MP 197°C , Infrared Spectral Features around cm^{-1} 3030, 1500, Aromatic C-H stretching, 1600-1640 $-\text{CH}=\text{N}-$, 1315-1375 $-\text{SO}_2-$, 3250-3330 $-\text{NH}-$ of $-\text{SO}_2\text{NH}-$, 1200- Ar-O-alkyl, PMR spectral Features (δ Ppm) 6.5-8.6 (multiplet, aromatic+ CH of $\text{CH}=\text{N}$ protons + H of Pyrimidine + H of SO_2NH) 3.85 (3H, singlet, OCH_3), ^{13}CMR spectral Features (δ Ppm) 114-131- Benzene, 134- Ar-Cl, 160 - $\text{CH}=\text{N}$, 162-169 - pyrimidine, 163-C-O, 56 - CH_3

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-hydroxybenzylideneamino)benzenesulfonamide 6c

Yield: 60%, MP 199°C , Infrared Spectral Features around cm^{-1} 3370-OH, 3030, 1500, Aromatic C-H stretching, 1600-1640 $-\text{CH}=\text{N}-$, 1315-1375- SO_2- , 3250-3330 $-\text{NH}-$ of $-\text{SO}_2\text{NH}-$, PMR spectral Features (δ Ppm) 6.5-8.6 (multiplet, aromatic + CH of $\text{CH}=\text{N}$ protons + H of Pyrimidine + H of SO_2NH) 3.85 (3H, singlet, OCH_3), ^{13}CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - $\text{CH}=\text{N}$, 162-169 - pyrimidine, 163 -C-O.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(2-hydroxybenzylideneamino)benzenesulfonamide 6d

Yield: 62%, MP 191°C , Infrared Spectral Features around cm^{-1} 3370-OH, 3030, 1500, Aromatic C-H stretching, 1600-1640 $-\text{CH}=\text{N}-$, 1315-1375- SO_2- , 3250-3330- $\text{NH}-$ of $-\text{SO}_2\text{NH}-$, PMR spectral Features (δ Ppm) 6.5-8.6 (multiplet, aromatic + CH of $\text{CH}=\text{N}$ protons + H of Pyrimidine + H of SO_2NH) 3.85 (3H, singlet, OCH_3), ^{13}CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - $\text{CH}=\text{N}$, 162-169 - pyrimidine, 163 -C-O.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-methylbenzylideneamino)benzenesulfonamide 6e

Yield: 62%, MP 193⁰C, Infrared Spectral Features around cm⁻¹ 2950, 1370 - CH₃, 3030, 1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1375 -SO₂-, 3250-3330 -NH- of -SO₂NH-, PMR spectral Features (δ Ppm) 6.5-8.7 (multiplet, aromatic + CH of CH=N protons + H of Pyrimidine + H of SO₂NH) 2.34 (3H, singlet, CH₃), ¹³CMR spectral Features (δ Ppm) 114-131- Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 - pyrimidine, 21-CH₃.

4-(benzo[d][1,3]dioxol-5-ylmethyleneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 6f

Yield: 60%, MP 201⁰C, Infrared Spectral Features around cm⁻¹2920, 2850 - CH₂-, 1450, 3030, 1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1365 -SO₂-, 3250-3330 -NH- of -SO₂NH-, PMR spectral Features (δ Ppm) 6.5-8.7 (multiplet, aromatic + CH of CH=N protons + H of Pyrimidine + H of SO₂NH) 6.07 (2H, singlet, -O-CH₂-O-), ¹³CMR spectral Features (δ Ppm) 101.2 -CH₂-O-, 114-131-Benzene, 134- Ar-Cl, 160 -CH=N, 162-169 - pyrimidine, 21 -CH₃.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(3-hydroxy-4-methoxybenzylideneamino)benzenesulfonamide 6g

Yield: 57%, MP 199⁰C, Infrared Spectral Features around cm⁻¹ 3370 -OH, 2950,1370 -CH₃, 3030,1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1375 -SO₂-, 3250-3330 -NH- of -SO₂NH-, PMR spectral Features (δ Ppm) 6.5-8.7 (multiplet, aromatic + CH of CH=N protons + H of Pyrimidine + H of SO₂NH) 3.83 (3H, singlet, -O-CH₃) 5.35 (1H, Singlet, -OH), ¹³CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 -pyrimidine, 149-151 -C - O, 56-OCH₃.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(3,4-diethoxybenzylideneamino)benzenesulfonamide 6h

Yield: 60%, MP 190⁰C, Infrared Spectral Features around cm⁻¹ 2950,2820, -CH₂-, 1450,3030,1500, Aromatic C-H stretching, 1600-1640 -CH=N-, 1315-1375 -SO₂-, 3250-3330 -NH- of -SO₂NH-, PMR spectral Features (δ Ppm) 6.5-8.7 (multiplet, aromatic + CH of CH=N protons + H of Pyrimidine + H of SO₂NH) 4.0 (4H, quartet, 2CH₂) 1.33 (6H, triplet, 2CH₃), ¹³CMR spectral Features (δ Ppm) 114-131-Benzene, 134- Ar-Cl, 160 - CH=N, 162-169 - pyrimidine, 149-151 -C-O.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-oxo-2-phenylthiazolidin-3-yl)benzenesulfonamide 7a

Yield: 64%, MP 198-99⁰C, Infrared Spectral Features around cm⁻¹3030, 1500, Aromatic C-H stretching, 1600-1641 -CH=N, 1315-1375 -SO₂-, 3250-3330-NH- of -SO₂NH-, 1690 C=O of thiazolidinone, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimidine), 3.9-4.0 (2H of CH₂ for thiazolidinone), 6.44 (H of C₂H for thiazolidinone), 11.34 (H of SO₂NH), ¹³CMR spectral Features (δ Ppm) 114-131- Benzene, 134- Ar-Cl, 163-169- pyrimidine, 171.2 C=O, 33.5 CH₂, 65.6 CH.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(2-(4-methoxyphenyl)-4-oxothiazolidin-3-yl)benzenesulfonamide 7b

Yield: 60%, MP 191-92⁰C, Infrared Spectral Features around cm⁻¹3030, 1500, Aromatic C-H stretching, 1600-1641 -CH=N, 1315-1375 -SO₂-, 3250-3330 -NH- of -SO₂NH-, 1690 C=O of thiazolidinone, 1200 Aryl-alkyl ether, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimidine + H of SO₂NH), 6.44 (H of C₂H for thiazolidinone), 3.83 (3H, singlet, OCH₃) 11.34 (H of SO₂NH), ¹³CMR spectral Features (δ Ppm) 114-131- Benzene, 163-169- pyrimidine, 171.2 C=O, 33.5 CH₂, 65.6 CH, 158-159 -C-O, 56 CH₃.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(2-(4-hydroxyphenyl)-4-oxothiazolidin-3-yl)benzenesulfonamide 7c

Yield: 55%, MP 189-90⁰C, Infrared Spectral Features around cm⁻¹ 3030, 1500, Aromatic C-H stretching, 1600-1641 -CH=N, 1315-1375 -SO₂-, 3250-3330 -NH- of -SO₂NH-, 1690 C=O of thiazolidinone, 3200,2600 -OH Phenolic (broad), 2880,2920,1400 CH₂, 1200 Aryl-alkyl ether, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimidine + H of SO₂NH), 6.44 (H

of C₂H for thiazolidinone), 11.34 (H of SO₂NH), 5.35 (H of OH), ¹³CMR spectral Features (δ Ppm) 114-131- Benzene, 134 Ar-Cl, 163-169- pyrimidine, 171.2- C=O, 33.5 CH₂, 65.6 CH.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(2-(2-hydroxyphenyl)-4-oxothiazolidin-3-yl)benzenesulfonamide 7d

Yield: 59%, MP 186-86⁰C, Infrared Spectral Features around cm⁻¹ 3030, 1500, Aromatic C-H stretching, 1600-1641 -CH=N, 1315-1375 -SO₂-, 3250-3330 -NH- of -SO₂NH-, 1690 C=O of thiazolidinone, 3200,2600 -OH Phenolic (broad), 2880,2920,1400 CH₂, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimidine + H of SO₂NH), 6.44 (H of C₂H for thiazolidinone), 3.9-4.0 (2H of CH₂ for thiazolidinone), 11.34 (H of SO₂NH), 5.35 (H of OH), ¹³CMR spectral Features (δ Ppm) 114-131- Benzene, 134 Ar-Cl, 163-169- pyrimidine, 171.2- C=O, 33.5 CH₂, 65.6 CH.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-oxo-2-p-tolylthiazolidin-3-yl)benzenesulfonamide 7e

Yield: 60%, MP 195-96⁰C, Infrared Spectral Features around cm⁻¹ 3030, 1500, Aromatic C-H stretching, 1600-1641 -CH=N, 1315-1375 -SO₂-, 3250-3330 -NH- of -SO₂NH-, 1690 C=O of thiazolidinone, 3200,2600 -OH Phenolic (broad), 2880,2920,1400 CH₂, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimidine + H of SO₂NH), 6.44 (H of C₂H thiazolidinone), 3.9-4.0 (2H of CH₂ for thiazolidinone), 11.34 (H of SO₂NH), 2.34 (3H, singlet, CH₃), ¹³CMR spectral Features (δ Ppm) 114-131- Benzene, 134 Ar-Cl, 163-169- pyrimidine, 171.2- C=O, 33.5 CH₂, 18- 21.3 CH₃.

4-(2-(benzo[d][1,3]dioxol-5-yl)-4-oxothiazolidin-3-yl)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide 7f

Yield: 61%, MP 188-89⁰C, Infrared Spectral Features around cm⁻¹ 3030, 1500, Aromatic C-H stretching, 1600-1641 -CH=N, 1690 C=O of thiazolidinone, 2880,2920,1400 CH₂, 2950, 1370 -CH₃, 1315-1365 -SO₂-, 3250-3330 -NH- of -SO₂NH-, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimidine + H of SO₂NH), 6.44 (H of C₂H thiazolidinone), 3.9-4.0 (2H of CH₂ for thiazolidinone), 6.10 (2H for CH₂ of -O- CH₂-O-), ¹³CMR spectral Features (δ Ppm) 114-131- Benzene, 134 Ar-Cl, 163-169- pyrimidine, 171.2- C=O, 33.5 CH₂, 65.6 CH, 101.2 O- CH₂-O-.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(2-(4-hydroxy-3-methoxyphenyl)-4-oxothiazolidin-3-yl)benzenesulfonamide 7g

Yield: 62%, MP 191-92⁰C, Infrared Spectral Features around cm⁻¹ 3030, 1500, Aromatic C-H stretching, 1600-1641 -CH=N, 1690 C=O of thiazolidinone, 2880,2920,1400 CH₂, 2950, 1370 -CH₃, 1315-1365 -SO₂-, 3250-3330 -NH- of -SO₂NH-, 1200 Aryl-alkyl ether, PMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimidine + H of SO₂NH), 6.44 (H of C₂H thiazolidinone), 3.9-4.0 (2H of CH₂ for thiazolidinone), 5.35 (H of OH), 3.83(3H for OCH₃), ¹³CMR spectral Features (δ Ppm) 114-131- Benzene, 134 Ar-Cl, 163-169- pyrimidine, 171.2- C=O, 33.5 CH₂, 65.6 CH, 56.1 OCH₃.

N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(2-(3,4-diethoxyphenyl)-4-oxothiazolidin-3-yl)benzenesulfonamide 7h

Yield: 60%, MP 199-00⁰C, Infrared Spectral Features around cm⁻¹ 3030, 1500, Aromatic C-H stretching, 1600- 1641 -CH=N, 1690 C=O of thiazolidinone, 2880,2920,1400 CH₂, 2950, 1370 -CH₃, 1315-1365 -SO₂-, 3250-3330 -NH- of -SO₂NH-, 1200 Aryl-alkyl ether, NMR spectral Features (δ Ppm) 6.5-7.9 (multiplet, aromatic + H of Pyrimidine + H of SO₂NH), 6.44 (H of C₂H thiazolidinone), 3.9-4.0 (2H of CH₂ for thiazolidinone), 5.35 (H of OH), 1.32 (6H for 2 CH₃), 4.10 (4H for 2 CH₂), ¹³CMR spectral Features (δ Ppm) 114-131- Benzene, 134 Ar-Cl, 163-169- pyrimidine, 171.2- C=O, 33.5 CH₂, 65.6 CH.

4. MICROBIAL ACTIVITY

The compounds tested for antimicrobial activity are listed in table 4 standard drugs of compound, 5 and 6 show the size of zone of inhibition of bacterial growth procedure by test compounds for broad range of antimicrobial activity inhibiting growth of Gram-positive bacterial strains *B.Subtillis* and *S.Aureus*, and Gram-negative bacterial strains *E.Coli* and *Ps. Aeruginosa*.

Table 4: Antimicrobial activity of Standards and Solvent (DMF)

No.	Name of compound	Zone of inhibition (in mm)			
		Gram positive		Gram negative	
		<i>B.Subtillis</i>	<i>S.Aureus</i>	<i>E.Coli</i>	<i>Ps.Aeruginosa</i>
1	DMF	8	5	6	7
2	Ampicillin	15	12	20	20
3	Tetracyclin	21	22	15	18
4	Gentamycin	20	19	18	22
5	Chloramphenicol	21	23	17	24

Table 5: Antimicrobial activity of 4-(arylideneamino)-N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)benzenesulfonamide (6a-h)

Compound (Designation)	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	<i>B.Subtillis</i>	<i>S.Aureus</i>	<i>E.Coli</i>	<i>Ps.Aeruginosa</i>
6a	12	13	08	12
6b	10	12	10	10
6c	14	14	15	10
6d	10	10	08	09
6e	06	16	12	20
6f	13	11	10	14
6g	21	19	14	16
6h	14	14	18	17

Table 6: Antimicrobial activity Synthesis of N-(4-(2,4-dichlorophenyl)-6-(6-methylnaphthalen-2-yl)pyrimidin-2-yl)-4-(4-oxo-2-phenylthiazolidin-3-yl)benzenesulfonamide (7a-h).

Compound (designation)	Zone of Inhibition (in mm)			
	Gram positive		Gram negative	
	<i>B.Subtillis</i>	<i>S.Aureus</i>	<i>E.Coli</i>	<i>Ps.Aeruginosa</i>
7a	09	12	11	17
7b	14	09	13	09
7c	13	12	08	08
7d	14	10	20	13
7e	18	14	14	09
7f	22	20	18	20
7g	14	16	15	13
7h	15	15	19	21

5. CONCLUSIONS

In conclusion, a new series of compound 6(a-h) and 7(a-h) were synthesized, compounds screened for their spectral study and biological study. The investigation of antimicrobial activities data revealed that the compounds (7d), (7e), (7f), (7g) and (7h), displayed excellent activity, the compounds (7a), (7b) and (7e) showed moderate activity and rested compounds showed less activity compared with standard drugs.

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