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Note

Synthesis of pyrimidine based thiazolidinones and azetidinones: Antimicrobial and antitubercular agents

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Several 2-aryl-3-[4-(4-chlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl-ureido]-4-thiazolidinones **5a-j** and 1-[4-(4-chlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl-ureido]-3-chloro-4-aryl-2-azetidinones **6a-j** have been synthesized and tested for their antibacterial, antifungal and antituberculosis activities against different microorganisms. The structures of novel synthesized compounds have been established on the basis of elemental analyses, ^{1}H NMR and IR spectral data.

Keywords: Pyrimidine, thiazolidinone, antimicrobial activity, antitubercular activity

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Literature survey reveals that most of the compounds having pyrimidine or thiazolidinone and azetidinone nucleus possess pharmacological action[1-3]. A wide spectrum of biological activities like anti-inflammatory[4], antibacterial[5], antifungal[6], antitubercular[7], analgesic and hypothermic[8] are found to be associated with compounds having pyrimidine moiety. 4-Thiazolidinone and its derivatives are known to possess a variety of physiological properties viz. analgesic, local[9] and spiral[10] anesthetic, CNS stimulant[11], hypnotics[12], antibacterial[13], antifungal[14], antitubercular[15], anticancer and anti-HIV[16]. Azetidinone and its derivatives are also a very good antibacterial[17], antitubercular[18] and antifungal[19] agents as well as possess pharmacological properties[20,21].

The required starting compound 2-amino-4-(4-chlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidine **1** was prepared by known method[22]. Pyrimidine **1**, which on treatment with chloromethylformate yielded 4-(4-chlorophenyl)-6-(3, 4, 5-trimethoxyphenyl)pyrimidin-2-yl-carbamate[23] **2** followed by condensation with hydrazine hydrate gave 4-[4-(4-chlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl]semicarbazide[24] **3**. This semicarbazide **3** was transformed into semicarbazones[25] **(4a-j, Table I)** by condensation with substituted aromatic aldehydes. These semicarbazones **4a-j** were converted into 2-aryl-3-[4-(4-chlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl-ureido]- 4 - thiazolidinones[26] **(5a-j, Table I)** and 1-[4-(4-chlorophenyl)-6-(3, 4, 5 - trimethoxyphenyl)pyrimidin -2-yl-ureido]-3-chloro-4-aryl-2-azetidinones[27] **(6a-j, Table I, Scheme I)**.

Experimental Section

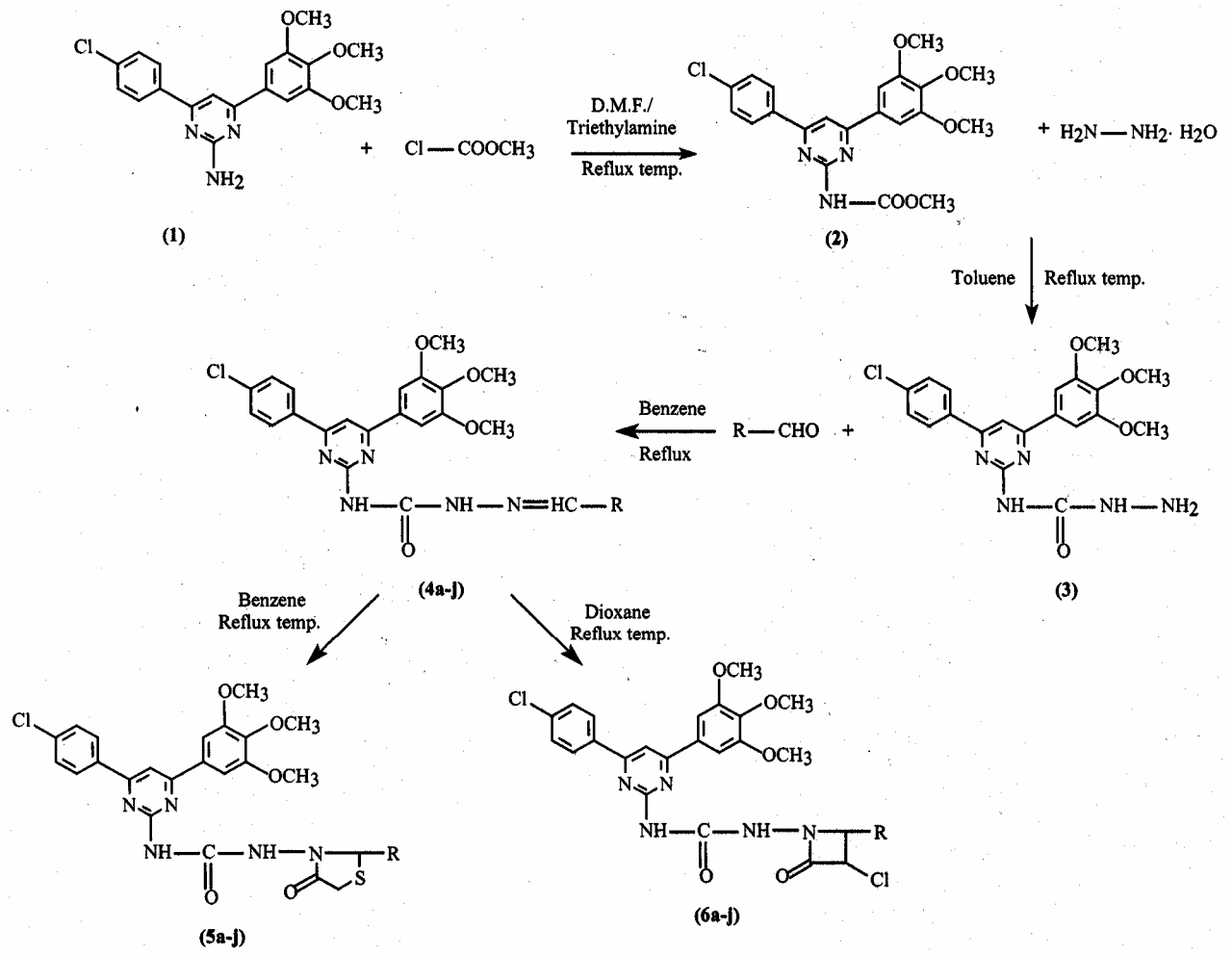
General. Melting points were determined in open capillary tubes and are uncorrected. IR spectra (γ_{max} in cm^{-1}) were recorded on a FT BOMMEN IR spectrophotometer; ^{1}H NMR spectra on a Hitachi 300MHz using TMS as internal standard (chemical shifts in δ, ppm) and elemental analyses were done on Haraeus Rapid Analyser.

4-(4-Chlorophenyl)-6-(3,4,5-trimethoxyphenyl)-pyrimidin-2yl-carbamate[23] **2.** To a solution of pyrimidine **1** (0.1 mole, 37.15g) and triethylamine (0.15 mole, 15.15g, 20.84 mL) in DMF (150 mL) was added methylchloroformate (0.15 mole, 14.18 g, 11.59 mL) dropwise at 0-5°C. Then, the reaction mixture was refluxed for 15 hr on oil-bath. Progress of the reaction was monitored by TLC using toluene-ethyl acetate (80:20) as eluent. After completion of reaction, it was poured into dil. HCl (160 mL, 50% v/v) with stirring. The solid obtained was filtered and dried. The crude product was purified by crystallization from absolute alcohol to give **2**, m.p. 145°C, yield 60% (Found: N, 9.55. $C_{21}H_{20}O_5N_3Cl$ requires N, 9.78%).

4-[4-(4-Chlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2yl]semicarbazide[24] **3.** The mixture of **2** (0.1 mole, 43 g) and hydrazine hydrate (0.43 mole, 21.5 g, 20.87 mL) in toluene (43 mL) was gently heated in oilbath for 18 hr. Progress of the reaction was checked by TLC using toluene-ethyl acetate (80:20) as eluent. Then, the reaction mixture was cooled to give white crystals. After the completion of reaction, the reaction mass was filtered and dried. The crude product was purified by crystallization from absolute alcohol to give **3**, m.p. 130°C, yield 75% (Found: N, 16.00. $C_{20}H_{20}O_4N_5Cl$ requires N, 16.29%).

Table I — Characterization data of the compounds **4a-j, 5a-j** and **6a-j**

Compd	R	Mol. formula	Yield (%)	m.p. ºC	Calcd (Found) %		
					C	H	N
4a	3-$NH_2C_6H_4$	$C_{27}H_{25}O_4N_6Cl$	74	165-67	60.85 (60.47	4.69 4.43	15.77 15.62)
4b	4-$N(CH_3)_2C_6H_4$	$C_{29}H_{29}O_4N_6Cl$	80	160	62.09 (62.00	5.17 5.00	14.99 14.75)
4c	2-$NO_2C_6H_4$	$C_{27}H_{23}O_6N_6Cl$	65	177-78	57.60 (57.30	4.09 3.92	14.93 14.67)
4d	2-ClC_6H_4	$C_{27}H_{25}O_4N_5Cl_2$	67	145-47	58.69 (58.49	4.17 4.01	12.68 12.48)
4e	2,4-$(Cl)_2C_6H_3$	$C_{27}H_{22}O_4N_5Cl_3$	61	150	55.24 (55.10	3.75 3.59	11.94 11.59)
4f	4-FC_6H_4	$C_{27}H_{23}O_4N_5ClF$	64	157-58	60.50 (60.40	4.29 4.07	13.07 12.91)
4g	2-$OCH_3C_6H_4$	$C_{28}H_{26}O_5N_5Cl$	76	175-77	61.37 (61.07	4.75 4.47	12.78 12.59)
4h	4-$OCH_3C_6H_4$	$C_{28}H_{26}O_5N_5Cl$	72	135	61.37 (61.14	4.75 4.61	12.78 12.65)
4i	3,4,5-$(OCH_3)_3C_6H_2$	$C_{30}H_{30}O_7N_5Cl$	80	139-40	59.36 (59.15	4.95 4.65	11.52 11.28)
4j	2-OHC_6H_4	$C_{27}H_{24}O_5N_5Cl$	70	179-81	60.73 (60.42	4.50 4.22	13.12 13.07)
5a	3-$NH_2C_6H_4$	$C_{29}H_{27}O_5N_6SCl$	82	161-63	57.27 (57.38	4.25 4.45	13.60 13.85)
5b	4-$N(CH_3)_2C_6H_4$	$C_{31}H_{31}O_5N_6SCl$	74	180	58.43 (58.63	4.62 4.88	13.01 13.24)
5c	2-$NO_2C_6H_4$	$C_{29}H_{25}O_7N_6SCl$	66	148-49	54.54 (54.67	3.80 3.93	13.03 13.20)
5d	2-ClC_6H_4	$C_{29}H_{25}O_5N_5SCl_2$	73	150	55.39 (55.59	3.70 3.99	11.05 11.18)
5e	2,4-$(Cl)_2C_6H_3$	$C_{29}H_{24}O_5N_5SCl_3$	75	165-67	52.40 (52.69	3.35 3.63	10.30 10.60)
5f	4-FC_6H_4	$C_{29}H_{25}O_5N_5SClF$	68	172-75	56.95 (57.09	3.95 4.10	11.19 11.48)
5g	2-$OCH_3C_6H_4$	$C_{30}H_{28}O_6N_5SCl$	79	166-67	57.72 (57.92	4.27 4.50	11.02 11.26)
5h	4-$OCH_3C_6H_4$	$C_{30}H_{28}O_6N_5SCl$	60	145	57.82 (57.92	4.33 4.50	11.06 11.26)
5i	3,4,5-$(OCH_3)_3C_6H_2$	$C_{32}H_{32}O_8N_5SCl$	71	149-50	56.17 (56.35	4.45 4.70	10.09 10.27)
5j	2-OHC_6H_4	$C_{29}H_{26}O_6N_5Cl$	64	153	57.11 (57.28	4.03 4.28	11.32 11.52)
6a	3-$NH_2C_6H_4$	$C_{29}H_{26}O_5N_6Cl_2$	68	159-60	57.01 (57.14	4.18 4.27	13.49 13.79)
6b	4-$N(CH_3)_2C_6H_4$	$C_{31}H_{30}O_5N_6Cl_2$	78	195-97	58.28 (58.40	4.54 4.71	13.07 13.19)
6c	2-$NO_2C_6H_4$	$C_{29}H_{24}O_7N_6Cl_2$	70	156	54.30 (54.46	3.53 3.76	13.03 13.14)
6d	2-ClC_6H_4	$C_{29}H_{24}O_5N_5Cl_3$	76	187-89	55.22 (55.37	3.60 3.82	11.00 11.14)
6e	2,4-$(Cl)_2C_6H_3$	$C_{29}H_{23}O_5N_5Cl_4$	63	200-202	52.22 (52.49	3.25 3.47	10.28 10.56)
6f	4-FC_6H_4	$C_{29}H_{24}O_5N_5Cl_2F$	65	197	56.54 (56.86	3.66 3.92	11.19 11.44)
6g	2-$OCH_3C_6H_4$	$C_{30}H_{27}O_6N_5Cl_2$	80	210-12	57.39 (57.69	4.05 4.33	11.09 11.22)
6h	4-$OCH_3C_6H_4$	$C_{30}H_{27}O_6N_5Cl_2$	70	199	57.45 (57.69	4.10 4.33	11.01 11.22)
6i	3,4,5-$(OCH_3)_3C_6H_2$	$C_{32}H_{31}O_8N_5Cl_2$	73	203-04	56.03 (56.14	4.42 4.53	10.02 10.23)
6j	2-OHC_6H_4	$C_{29}H_{25}O_6N_5Cl_2$	71	220-23	56.98 (57.05	4.00 4.10	11.37 11.48)



Scheme I

1-(3-Aminobenzylidene)-4 - [4-(4-chlorophenyl)-6 - (3, 4, 5 - trimethoxyphenyl)pyrimidin-2-yl]semicarbazide[25] **4a.** A mixture of **3** (0.01 mole, 4.3g), 3-aminobenzaldehyde (0.015 mole, 1.82g) and hydrochloric acid (35% w/v, 0.002 mole, 0.20g, 0.18 mL) in benzene (86 mL) was refluxed for 4 hr. Dean-Stark apparatus removed the water formed during the reaction azeotropically. Progress of the reaction was checked by TLC using toluene-ethyl acetate (80:20) as eluent. After the completion of reaction, benzene was removed by distillation to give solid, which was dissolved in methanol (70 mL). This solution was warmed and treated with sodium bisulphite solution to remove unreacted aldehyde. The solid obtained was filtered, washed with water, dried and crystallized from absolute alcohol to give **4a**, m.p. 165°C, yield 74% (Found: C, 60.47; H, 4.43; N, 15.62. $C_{27}H_{25}O_4N_6Cl$ requires C, 60.85; H, 4.69; N, 15.77%).

Similarly, other members **4b-j** were prepared and their physical data are given in **Table I**.

2 - (3-Aminophenyl) – 3 - [4-(4-chlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-yl-ureido]-4-thiazolidinone[26] **5a.** A mixture of **4a** (0.005 mole, 2.66g) and thioglycolic acid (0.005 mole, 0.46g) in dry benzene (80 mL) was refluxed for 6 hr. Water formed during the reaction was removed azeotropically by Dean-Stark apparatus. Progress of the reaction was checked by TLC using benzene-ether (70:25) as eluent. After the completion of reaction, benzene was removed by distillation to give solid, which was dissolved in methanol (70 mL). This solution was warmed and treated with sodium bicarbonate solution to remove unreacted acid. The solid obtained was filtered, washed with ether and purified by crystallization from methanol to give **5a**, m.p. 161°C, yield 82% (Found: C, 57.27; H, 4.25; N, 13.60. $C_{29}H_{27}O_5N_6Cl$ requires C, 57.38; H, 4.45; N, 13.85%).

Similarly, other members **5b-j** were prepared and their physical and spectral data are recorded in **Table I**.

Table II — Antimicrobial screening results of the compounds synthesized

Compd	Antibacterial activity in mm (Zone of inhibition at 50μg/ mL)					Antifungal activity μg/ mL	Antitubercular activity μg/ mL
	E.coli	*S.aureus*	*S.paratyphi B*	*P.vulgaris*	*Enterobacter*	*C.albicans*	$H_{37}Rv$ strain of *M.tuberculosis*
5a	---	22	13	10	09		
5b	15	09	---	13	12	200	---
5c	20	10	16	14	21	---	100
5d	13	10	10	15	09		
5e	16	16	10	10	14	100	---
5f	---	16	---	11	---	---	200
5g	09	20	---	---	---	200	---
5h	---	17	11	12	09	---	100
5i	---	12	15	---	14	---	200
5j	---	20	---	---	16	200	100
6a	---	10	15	16	15	200	100
6b	---	10	---	21	---	200	100
6c	10	10	---	---	09	---	---
6d	---	13	14	---	---	100	---
6e	---	20	14	---	---	100	200
6f	---	11	---	19	16	---	100
6g	12	15	---	10	17	---	---
6h	---	20	---	---	18	---	---
6i	---	14	09	20	---	200	200
6j	---	10	10	---	14		
Standard drugs	Norfloxacine	Althrocine	Sparfloxacine	Tetracycline	Phexine	Miconazole	INH
	36	24	32	28	36	6.25	0.05

1-[4-(4-Chlorophenyl)-6-(3,4,5-trimethoxyphenyl)-pyrimidin-2-yl-ureido]-3-chloro-4-(3-aminophenyl)-2-azetidinone[27] **6a.** To a solution of **4a** (0.005 mole, 2.66g) in dioxane (20 mL), chloroacetyl chloride (0.006 mole, 0.678g, 0.48 mL) was added dropwise at room temperature with constant stirring. Then, triethylamine (0.001 mole, 0.1g, 0.14 mL) was added and reaction mixture was refluxed for 12 hr. Progress of the reaction was checked by TLC using benzene-acetone (95:5) as eluent. After completion of reaction, it was poured in water. The solid was filtered, dried and crystallized from absolute alcohol to give **6a**, m.p. 159°C, yield 68% (Found: C, 57.01; H, 4.18; N, 13.49. $C_{29}H_{26}O_5N_6Cl_2$ requires C, 57.14; H, 4.27; N, 13.79%).

Similarly, other members **6a-j** were prepared and their physical and spectral data are recorded in **Table I**.

The spectral data of the novel synthesized compounds **5a-j** and **6a-j** are given below.

5a; m/z: 605 (M^+); IR (KBr): 1614, 1508 (-C=N-), 3490 (-NH-), 3350, 3400 ($-NH_2$), 1224 (Ar-OCH_3), 1780 (>C=O, cyclic), 1690 (-CONH-), 688 (-C-S-C-); ^{1}H NMR (DMSO –d_6, δ): 3.73 (s, 3H, -OCH_3), 3.90 (s, 6H, Ar-OCH_3), 6.75 (s, 1H, -CONH-), 5.75 (s, 1H, Ar-NH-CO-), 7.51-8.28 (m, 11H, Ar-H), 2.7 (s, 2H, Ar-NH_2), 3.32 (d, 1H, *J*=2.0, >CH-), 4.10 (s, 2H, -CH_2-). **5b**; 3.73 (s, 3H, -OCH_3), 3.90 (s, 6H, 2Ar-OCH_3), 6.75 (s, 1H, -CONH-), 5.75 (s, 1H, Ar-NH-CO-), 7.51-8.28 (m, 11H, Ar-H), 1.20 (t, 6H, *J*=7.2, -$N(CH_3)_2$), 3.32 (d, 1H, *J*=1.9, >CH-), 4.10 (s, 2H, -CH_2-). **5d**; 3.72 (s, 3H, -OCH_3), 3.91 (s, 6H, 2Ar-OCH_3), 6.76 (s, 1H, -CONH-), 5.74 (s, 1H, Ar-NH-CO-), 7.51-8.28 (m, 11H, Ar-H), 3.33 (d, 1H, *J*=1.4, >CH-), 4.11 (s, 2H, -CH_2-). **5f**; 3.71 (s, 3H, -OCH_3), 3.89 (s, 6H, 2Ar-OCH_3), 6.75 (s, 1H, -CONH-), 5.76 (s, 1H, Ar-NH-CO-), 7.51-8.28 (m, 11H, Ar-H), 3.31 (d, 1H, *J*=1.8, >CH-), 4.10 (s, 2H, -CH_2-). **5g**; 3.75 (s, 6H, 2-OCH_3), 3.93 (s, 6H, 2Ar-OCH_3), 6.75 (s, 1H, -CONH-), 5.75 (s, 1H, Ar-NH-CO-), 7.51-8.28 (m, 11H, Ar-H), 3.30 (d, 1H, *J*=2.1, >CH-), 4.11 (s, 2H, -CH_2-). **5h**; 3.71 (s, 6H, 2-OCH_3), 3.92 (s, 6H, 2Ar-OCH_3), 6.76 (s, 1H, -CONH-), 5.74 (s, 1H, Ar-NH-CO-), 7.51-8.28 (m, 11H, Ar-H), 3.31 (d, 1H, *J*=2.0,

>CH-), 4.12 (s, 2H, -CH_2-). **5i**; 3.70 (s, 6H, -OCH_3), 3.93 (s, 12H, 4Ar-OCH_3), 6.73 (s, 1H, -CONH-), 5.74 (s, 1H, Ar-NH-CO-), 7.51-8.28 (m, 11H, Ar-H), 3.34 (d, 1H, *J*=2.1, >CH-), 4.10 (s, 2H, -CH_2-). **5j**; 3.74 (s, 3H, -OCH_3), 3.91 (s, 6H, 2Ar-OCH_3), 6.74 (s, 1H, -CONH-), 5.74 (s, 1H, Ar-NH-CO-), 7.51-8.28 (m, 11H, Ar-H), 3.31 (d, 1H, *J*=1.8, >CH-), 4.10 (s, 2H, -CH_2-), 6.79 (s, 1H, -OH). **6a**; m/z: 608 (M^+); IR (KBr): 1612, 1531 (-C=N-), 3426 (-NH-), 3340, 3400 (-NH_2), 1222 (Ar-OCH_3), 1720 (>C=O, cyclic), 1683 (-CONH-), 713 (C-Cl); ^{1}H NMR (DMSO –d_6, δ): 3.73 (s, 3H, -OCH_3), 3.90 (s, 6H, 2Ar-OCH_3), 6.75 (s, 1H, -CONH-), 7.51-8.28 (m, 12H, Ar-H, Ar-NH-CO-),2.7 (s, 2H, Ar-NH_2), 3.31 (d, 1H, *J*=1.5, >CH-Cl), 3.34 (d, 1H, *J*=5.6, >CH-). **6b**; 3.70 (s, 3H, -OCH_3), 3.89 (s, 6H, 2Ar-OCH_3), 6.74 (s, 1H, -CONH-), 7.51-8.28 (m, 12H, Ar-H, Ar-NH-CO-), 1.21 (t, 6H, *J*=7.0, -$N(CH_3)_2$), 3.32 (d, 1H, *J*=1.4, >CH-Cl), 3.35 (d, 1H, *J*=5.5, >CH-). **6c**; 3.73 (s, 3H, -OCH_3), 3.90 (s, 6H, 2Ar-OCH_3), 6.75 (s, 1H, -CONH-), 7.51-8.28 (m, 12H, Ar-H, Ar-NH-CO-), 3.31 (d, 1H, *J*=1.6, >CH-Cl), 3.34 (d, 1H, *J*=5.6, >CH-). **6e**; 3.73 (s, 3H, -OCH_3), 3.90 (s, 6H, 2Ar-OCH_3), 6.75 (s, 1H, -CONH-), 7.51-8.28 (m, 11H, Ar-H, Ar-NH-CO-), 3.31 (d, 1H, *J*=1.4, >CH-Cl), 3.34 (d, 1H, *J*=5.7, >CH-). **6f**; 3.73 (s, 3H, -OCH_3), 3.90 (s, 6H, 2Ar-OCH_3), 6.75 (s, 1H, -CONH-), 7.51-8.28 (m, 12H, Ar-H, Ar-NH-CO-), 3.31 (d, 1H, *J*=1.2, >CH-Cl), 3.34 (d, 1H, *J*=5.4, >CH-). **6h**; 3.71 (s, 6H, 2-OCH_3), 3.91 (s, 6H, 2Ar-OCH_3), 6.76 (s, 1H, -CONH-), 7.51-8.28 (m, 12H, Ar-H, Ar-NH-CO-), 3.30 (d, 1H, *J*=1.5, >CH-Cl), 3.33 (d, 1H, *J*=5.4, >CH-). **6i**; 3.76 (s, 6H, 2-OCH_3), 3.93 (s, 12H, 4Ar-OCH_3), 6.72 (s, 1H, -CONH-), 7.51-8.28 (m, 12H, Ar-H, Ar-NH-CO-), 3.32 (d, 1H, *J*=1.6, >CH-Cl), 3.34 (d, 1H, *J*=5.2, >CH-). **6j**; 3.73 (s, H, -OCH_3), 3.90 (s, 6H, 2Ar-OCH_3), 6.75 (s, 1H, -CONH-), 7.51-8.28 (m, 12H, Ar-H, Ar-NH-CO-), 6.80 (s, 1H, -OH), 3.31 (d, 1H, *J*=1.4, >CH-Cl), 3.34 (d, 1H, *J*=5.5, >CH-).

Antimicrobial activity

The activity was determined using cup-plate agar diffusion method[28] by measuring the inhibition zones in mm. All compounds were screened for their antimicrobial activity against a variety of bacterial strains such as *S.aureus*, *E.coli*, *P.vulgaris*, *S.paratyphi B* and *Enterobacter*, fungi such as *C.albicans* and antitubercular activity against $H_{37}Rv$ strain of *M.tuberculosis*. Known antibiotics like Phexine, Norfloxacine, Althrocine, Sparfloxacine, Tetracycline, Miconazole and INH were used for comparisons. All the compounds reported in **Table II** were tested against number of bacteria, fungi and $H_{37}Rv$ strain of *M.tuberculosis*.

The present paper is focused on the synthesis of novel heterocyclic compounds as possible antibacterial, antifungal and antitubercular agents. The antimicrobial screening of the series revealed the following points.

Ten ureido linkages connecting with 4-thiazolidinone and 2-amino-4,6-diarylpyrimidine derivatives have been synthesized. It was not active up to 100 to 200 μg/mL against *C.albicans* and $H_{37}Rv$ *strain of M.tuberculosis*. Out of ten compounds synthesized, three compound (**5c**, **5a**, **5d**) showed very good zone of inhibition on different type of microorganisms. Compound **5c** showed 20mm, 16mm and 21mm zone of inhibition for *E.coli*, *S.paratyphi B* and *Enterobacter*, compound **5a** showed 22mm zone of inhibition for *S.aureus* and compound **5d** showed 15mm zone of inhibition for *P.vulgaris*.

The structural variations such as -NH_2 group at 3-position on phenyl ring against *S.aureus*, -Cl group at 2-position on phenyl ring against *P.vulgaris*, and -NO_2 at 2-position on phenyl ring against *E.coli*, *S.paratyphi B*, *Enterobacter* exhibited excellent antibacterial activity.

Various β-lactam derivatives were connected to the parent compound 2-amino-4-(4-chlorophenyl)-6-(3,4,5-trimethoxyphenyl)pyrimidine through ureido linkage. The parent compound showed no activity against *E.coli*, *S.aureus*, *S.paratyphi B*, *P.vulgaris* and *Enterobacter*. It was not active up to 100-200 μg/mL against *C.albicans* and *H37Rv strain of M.tuberculosis,* but presence of various β-lactam ring connected to the parent compound by means of ureido linkage showed moderate to excellent activity against all the microorganisms. Presence of ureido linkage showed increase in biological activity of the parent compound. Five compounds (**6a**, **6b**, **6e**, **6g** and **6h**) have exhibited excellent activity against *E.coli*, *S.aureus*, *S.paratyphi B*, *P.vulgaris* and *Enterobacter* i.e 12-21mm zone of inhibition.

The structural variations such as 3-amino substituted phenyl ring against *S.paratyphi B*, 2-methoxy substituted phenyl ring against *E.coli*, 2,4-dichloro and 4-methoxy substituted phenyl ring against *S.aureus* and *Enterobacter* and 4-N,N-dimethylamino substituted phenyl ring against *P.vulgaris* has exhibited excellent activity.

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References

1 Dave C V & Shukla M C, *Indian J Chem,* 39B, **2000**, 210.
2 Patel R B & Chikhalia K H, *J Indian Chem Soc,* 80, **2003**, 138.
3 Singh A K & Birendra Kumar, *Asian J Chem,* 9(2), **1997**, 234.
4 Menozzi G & Filippelli W, *Farmaco,* 49(2), **1994**, 115; *Chem Abstr,* 121, **1994**, 205269h.
5 Barot V M, *Asian J Chem*, 8(4), **1996**, 802.
6 Khan M H & Nizamuddin, *J Food Agric Chem*, 43, **1995**, 2719.
7 Gangiee A & Adaer G, *J Med Chem*, 42, **1999**, 2447.
8 Ahluwalia V K & Gupta C, *Heterocycles,* 32(5), **1991**, 907.
9 Trautman H D & Longe L M, *J Am Chem Soc,* 70, **1948**, 3436.
10 Surray A R, *J Am Chem Soc,* 71, **1949**, 3354.
11 French G, *Chem Abstr,* 65, **1966**, 4439.
12 Doran W J & Sholen H A, *J Org Chem,* 3, **1938**, 193.
13 Sayed Bayoumy B, *Acta Pol Pharma* (Poland), 13, **1991**, 48.
14 Srivastav S K & Srivastav S D, *Indian J Chem,* 39B, **2000**, 104.
15 Oza H, Joshi D & Parekh H, *Indian J Chem,* 37B, **1998**, 822.
16 Shah B R, Desai N C & Trivedi P B, *Indian J Heterocycl Chem,* 2(4), **1993**, 249.
17 Riaz F A & Furh H K, *J Med Chem,* 18(6), **1975**, 625.
18 Trivedi P B, Undavia N K & Desai N C, *Indian J Chem,* 32B, **1993**, 760.
19 Sharma S D & Khurana J P S, *Indian J Chem,* 28B, **1989**, 97.
20 Srivastav V K & Shanker K, *Indian J Chem*, 26B, **1987**, 652.
21 Shrenik K & Shah B, *Eur Pat Appl EP*, 360 199, **1986**; *Chem Abstr,* 110, **1989**, 173073u.
22 Mahmoud M R & Radwan A M, *Indian J Chem,* 35B, **1996**, 915.
23 Ram S & Townsend L B, *J Med Chem,* 35(3), **1992**, 539.
24 Mallakpour S & Taghizadeh H A, *Molecules,* 8, **2003**, 359.
25 Dimmock J R & Stable J P, *Eur J Med Chem,* 35, **2000**, 241.
26 Mystafa A & Shobby M E E, *J Org Chem,* 23, **1958**, 1992.
27 Sharma S D & Bose A K, *Indian J Chem,* 33B, **1994**, 624.
28 Barry A L, *The antimicrobial susceptibility test, principle and practices*, edited by Illus Lea & Febiger 180, *Biol Abstr*, 64, **1977**, 25183.