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Research Article

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Synthesis and antimicrobial activity of 2-{4'-[(6"-aryl)2"-amino-3",4"-dihydro-pyrimidine-4"-yl]-phenyl amino}-6-[bis (2'"-chloroethyl) amino]-4-methoxy-1,3,5-triazine

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ABSTRACT

The titled compounds (5a-5k) have been synthesized by the condensation of 2-{4'-[(3"-aryl)-2"-Propene-1"-one]-Phenyl amino}-6-[Bis-2""-chloroethyl) amino]-4-methoxy-1,3,5-triazine with guanidine hydrochloride in the presence of alcoholic potassium hydroxide. The biological activities of these compounds have been examined against various Gram +ve, Gram –ve bacteria and fungi. The structure of the products was confirmed by IR, ^1H NMR, Mass spectra and elemental analysis.

Key words : Amino pyrimidines, S-Triazine, Antibacterial screening, Antifungal screening.

INTRODUCTION

Antimicrobial activity

Amino pyrimidines (5a-5k) were evaluated in vitro for antimicrobial activity against *B. Mega, B. Subtillis, E. Coli, P. Fluoresences* and for antifungal activity against *A. awamori* using DMF as solvent at 50 µg concentration by cup-plate method[8]. After 24 hrs. of incubation at 37 ^{0}C temp., the zone or inhibition were measured in mm. The activity was compared with the known antibiotics e.g. Ampicillin, chloramphenicol, Norfloaxacin, Griseofulvin at same concentration which is represented in Table-I and comparable anti microbial activity represented in Table no. II

EXPERIMENTAL SECTION

All the melting points were taken in open glass capillaries and are uncorrected. IR absorption spectra were recorded on a Shimadzu-FT-IR 8400 Spectrophotometer using KBr pellet and ^{1} H NMR spectra on a Bruker DPX-200 spectrometer (300 MHz) using DMSO as solvent and TMS as internal standard.

Experimental and spectral section:

Synthesis of 2–(4'–Acetyl phenyl amino)–4,6–dichloro–1,3,5-triazine (1) :

A mixture of 2,4,6–trichloro–S–triazine (1.845 gm, 0.01 m), 4-amino acetophenone (1.35 gm, 0.01 m) in acetone (25 ml) and aq. NaOH solution till solution basic. The reaction mixture was stirring at 0 $^\circ$C temp. for 5 hrs. The content was poured into crushed ice, filltered and washed with water. The isolated product was crystallized from dioxane yield : 82%, MP. 112 $^\circ$C. (Found : C, 46.61 , H, 2.79, N, 19.75, $C_{11}H_8N_4OCl_2$ required C, 46.64, H, 2.82, N, 19.79%). IR : (cm^{-1}) : 2952 (C–H str. asym.), 2870 (C–H Str. Sym), 1420 (C–H def.), 3056 (C–H str. aromatic), 1509 (C=C str.), 1118 (C–N str.), 1620 (N–H bend), 768 (C–Cl Str.), 1700 (C=O str.) ^{1} H NMR : (δ ppm) : 3.10–3.20 (s, 3H, Ar–$COCH_3$); 6.50–6.63 (m, 4H, Ar–H), 9.95 (s, 1H, N–H). Mass : (m/z) 77, 103, 139, 145, 172, 198, 221, 240, 259.

Synthesis of 2–(4'–Acetyl phenyl amino)–6–chloro–4–methoxy–1,3,5–triazine (2) :
A mixture of 2–(4'–acetyl phenyl amino)–4,6–dichloro–1,3,5–triazine (2.83 gm, 0.01 m); sodium methoxide (0.56 gm, 0.01 m) in methanol. The reaction mixture was stirring at room temp. for 7 hrs. The content was poured into crushed ice, filltered and wash with water. The isolated product was crystallized from dioxane. yield : 86%, M. P. 178^0C. (Found C, 51.65

H, 3.91, N, 20.09, $C_{12}H_{11}N_4O_2Cl$ required C, 51.70, H, 3.94, N, 20.10%), IR : (cm^{-1}) : 2950 (C–H str. asym), 2871 (C–H Str. Sym.) 1421 (C–H def.), 3051 (C–H str. aromatic), 1510 (C=C str.) 1120 (C–N Str.), 1618 (–NH Str.), 1244 (C–O–C Str.), 761(C–Cl str),1702 (C=O str.) ^{1}H NMR : (δ ppm) 3.10–3.20 (s, 3H, Ar–$COCH_3$), 3.62–3.86 (s, 3H, Ar–OCH_3), 7.10–7.03 (D.D. 4H Ar Hb, Hc), 9.95 (s, 1H, N–Hf) Mass : (m/z) 77, 103, 136, 145, 174, 202, 221, 240, 264, 278.

Synthesis of 2–(4'–Acetyl phenyl amino)–6–[Bis (2"–chloroethyl) amino]–4–methoxy–1,3,5 triazine. (3) :
A mixture of 2–(4'–acetyl phenyl amino)–6–chloro–4–metholy–1,3,5–triazine (2.78 gm, 0.01 m), 2,2'–di chloro diethyl amine hydrochloride (1.43 gm, 0.01m); dioxane (25 ml) and aq. NaOH. The reaction mixture was refulx at 110 °C temp. for 6 hrs. The content was cooled and poured into crushed ice, Filltered and washed with water. The isolated product was crystallized from dioxane. yield 79%, M. P. 249 °C. (Found : C, 49.88, H, 4.91, N, 18.19, $C_{16}H_{19}N_5O_2Cl_2$ required C, 50.00, H, 4.94, N, 18.22%) IR : (cm^{-1}): 2921 (C–H str. asym), 2850 (C–H str. sym.), 1431 (C–H def.), 3062 (C–H str. aromatic), 1166 (C–H i.p. def.), 842 (C–H, o.p. def.), 1511 (C=C Str.) 1121 (C–N str.), 3342 (N–H Str.) 1242 (C–O–C Str.), 1702 (C=O str.) ^{1}H NMR : (δ ppm) 3.10–3.22 (s, 3H, Ar–$COCH_3$), 3.62–3.86 (s, 3H, –OCH_3), 7.01–7.03 (D.D. 4H, (Ar-H), 4.79–4.80 (t, 4H, –CH_2–Cl), 9.95 (s, 1H, –NH), Mass : (m/z) 77, 103, 145, 172, 210, 228, 265, 282, 302, 326, 355, 370.

Synthesis of 2–{4'–[3''–(4''''–Methoxy phenyl)–2''–propene–1''–one]phenyl amino}–6–[Bis(2'''–chloro ethyl amino] –4–methoxy–1,3,5–triazine. (4e) :
A mixture or 2–(4'–acetyl phenyl amino)–6–[Bis(2"–chloro ethyl) amino]–4–methoxy– 1,3,5–triazine((3.84 gm, 0.01 m), 4–methoxy benzaldehyde (1.36 gm, 0.01 m), methanol (25 ml). and 40% aq. NaOH solution till becomes basic medium. The reaction mixture was stirring 24 hrs. at room temp. The contents were poured into crushed ice, acidified, filltered and crystalized from dioxane. yield 79%, M. P. : 198 °C. (Found C, 57.31, H, 4.90, N, 13.91, $C_{24}H_{25}O_3N_5Cl_2$ required C, 57.37, H, 4.98, N, 13.94%) IR : (cm^{-1}) : 2923 (C–H str. asym.), 2852 (C–H str. sym), 1436 (C–H str. asym), 1371 (C–H str. sym) 3097 (C–H str. aromatic) 1276 (C–H i.p. def.), 821 (C–H, o.o.p. def.), 1677 (C=O str.), 1118 (C–N Str.), 3311 (N–H str.) 3045 (C=C str.), 1245 (C–O–C Str.), 768 (C–Cl str.) ^{1}H NMR : (δ ppm) 3.62–3.86 (s, 6H, Ar-OCH_3), 7.01–7.03 (D. D. 4H, Ar–Hb), 8.08–8.72 (D. D. 4H, Ar– Hc), 4.79–4.80 (t, 4H, CH_2–Cl), 2.50–2.51 (t, 4H, -NCH_2), 9.95 (s, 1H, –NHf), 4.80–4.83 (s, 2H, CH=CHg) Mass : (m/z) 112, 130, 156, 212, 262, 271, 280, 285, 325, 335, 371, 428, 461, 502.

Similarly other chalcones (4a – 4k) where prepared and their physical data and antimicrobial activities data already established.

Synthesis of 2–{4'–[6"–(4''''–Methoxy phenyl)–2"–amino-3",4"-dihydro-pyrimidine-4"-yl]-phenyl amino}–6–[Bis(2""–chloroethyl) –amino]–4–methoxy–1,3,5-–triazine(5e):
A mixture of 2-{4'-[3"-(4""-methoxy Phenyl) – 2" – Propene – 1"-one] Phenyl amino}-6-[Bis (2"'-chloro ethyl) amino]-4-methoxy – 1,3,-5 – triazine (5.02 gm., 0.01 M) and guanidine hydrochloride (0.95 g, 0.01M) was refluxed at 110º C for 12 hrs. in presence of alcoholic KOH in methanol. The reaction mixture was poured into crushed ice filtered, dried and crystallized from dioxane. Yield : 80%. M.P. : 153º C (Found : C : 55.21; H : 5.13; N : 20.61; $C_{25}H_{28}O_2N_8Cl_2$, required C: 55.24; H : 5.15; N : 20.62%). IR : (cm^{-1}) : 2925 (C–H str. asym), 2876 (C–H str. sym.) 1460 (C–H def. asym), 1355 (C–H def. sym.), 3081 (C–H str. aromatic) 1180 (C–H i. p. def.), 806 (C–H o.o.p. def.), 1473 (C=C str), 1141 (C–N str.), 1589 (C=N str.), 3407 (N–H str.)s 1247 (C–O– C str. asym.), 1068 (C–O– C str. sym.), 767 (C–Cl str.), 3350 (N–H str.), 1116 (C–N str.), 1616 (C=N str.). ^{1}H NMR : (δ ppm) 3.50 – 3.69 (s, 6H, Ar–OCH_3), 7.49-7.90 (DD, 4H, Ar-H_b), 7.92-9.27 (D.D. 4H, Ar–H_C), 4.62-4.65 (t, 4H, -CH_2–Cl), 2.32-2.92 (t, 4H, -NCH_2), 9.69 (s, 2H, Ar–NH), 9.78 (s, 2H, Ar-NH_2 -). Mass : (m/z) 143, 141, 151, 157, 188, 247, 279, 337, 347, 388, 424, 452, 543.

Similarly other (5a – 5k) have been synthesized and their physical data represented in Table no. I.

REACTION SCHEME

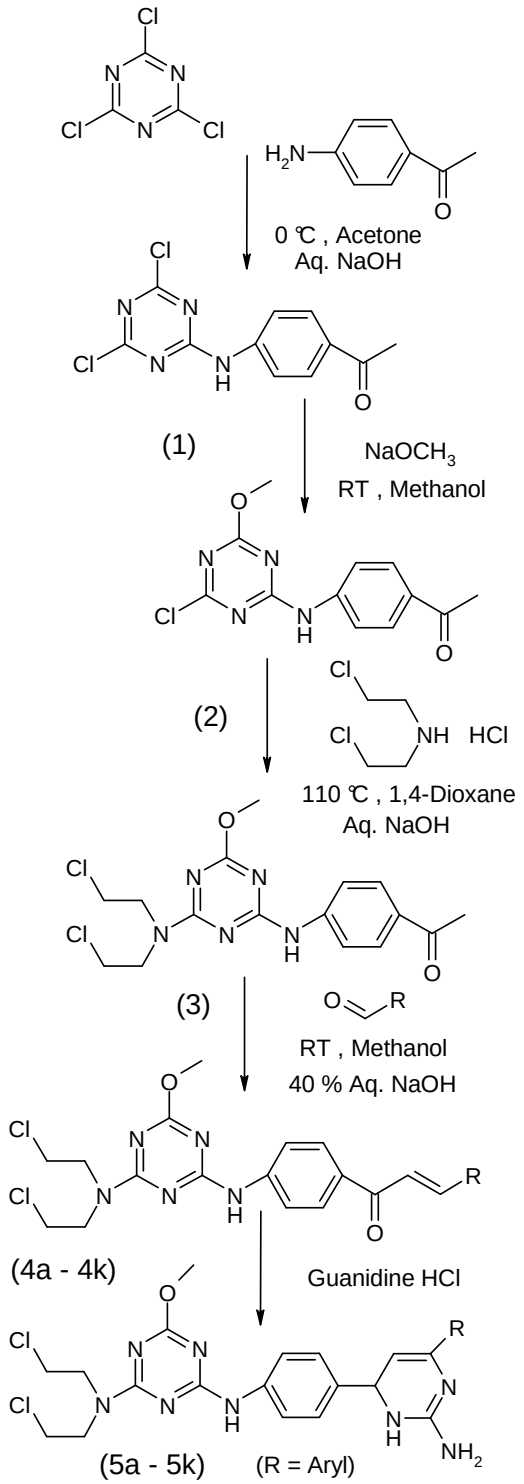

Table-I: The physical data and antimicrobial activity of compounds (5a -5k)

Compd	R	Mol. Formula	M.P. ^{0}C	Yield (%)	N(%)		Antibacterial activity				Antifungal Activity
					Calc.	Found	*B. Mega*	*B. Subtillis*	*E. Coli.*	*P. Fluoroscens*	*A. awamori*
5a	C_6H_5	$C_{24}H_{26}Cl_2N_8O$	189	78	21.82	21.80	20	12	18	21	15
5b	2-OH C_6H_4	$C_{24}H_{26}Cl_2N_9O_2$	180	81	21.16	21.14	22	14	17	24	14
5c	3-OH C_6H_4	$C_{24}H_{26}Cl_2N_8O_2$	212	69	21.16	21.15	18	19	21	20	18
5d	4-OH C_6H_4	$C_{24}H_{26}Cl_2N_8O_2$	239	73	21.16	21.13	24	20	19	23	19
5e	4-OCH3 C_6H_4	$C_{25}H_{28}Cl_2N_8O_2$	153	80	20.62	20.61	18	15	20	18	20
5f	4-OH, 3-OCH_3 C_6H_4	$C_{25}H_{28}Cl_2N_8O_3$	149	72	20.03	20.01	17	17	16	17	17
5g	4-Br, C_6H_4	$C_{24}H_{25}BrCl_2N_8O$	264	79	18.92	18.99	19	16	22	19	22
5h	3-NO_2 C_6H_4	$C_{24}H_{25}Cl_2N_9O_3$	253	81	22.57	22.56	20	18	19	16	18
5i	4-NO_2 C_6H_4	$C_{24}H_{25}Cl_2N_9O_3$	211	83	22.57	22.55	23	22	18	22	21
5j	4-N,N$(CH_3)_2$ C_6H_4	$C_{26}H_{31}Cl_2N_9O$	236	78	22.65	22.62	21	18	23	23	20
5k	C_4H_3O (Furfuryl)	$C_{22}H_{24}Cl_2N_8O_2$	197	77	22.26	22.21	16	17	19	16	22

Table-II Antimicrobial activity compared with known standard drugs.

	Compd	*B. Mega*	*B. Subtillis*	*E. Coil*	*P. Fluorescens*	*A. awamori*
	5a-5k	5d, 5i, 5j	5c, 5d, 5i	5c, 5g, 5j	5b, 5d, 5j	5g, 5i, 5k
1	Ampicillin (50 µg)	23	18	17	27	-
2	Chloramphenicol (50 µg)	24	19	25	26	-
3	Norfloxacin (50 µg)	24	19	25	26	-
4	Griseofulvin (50 µg)	-	-	-	-	23

CONCLUSION

The titled compounds (5a – 5k) have been synthesisid and evaluated in vitro their antimicrobial screening. The compounds 5c, 5d, 5i, 5j showed moderated comparable antibacterial and antifungal activity then other synthesized compounds which are compare with known standard drugs e.g. Ampicillin , Chloramphenicol, Norfloxacin, Griseofulvin at same concentration (50 µg/ml)

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REFERENCES

[1] AyselG, SeretD, GultazeC. Kevser E; Kamil V., *Ear. J. med, Chem*. **2000**, 35, PP 359-64.
[2] Archana Shrivastva V. K.; Chandra Ramesh Kumar Ashok. *Indian J. Chem.* **2002**, 41(1), PP 75; *Chem. Abstr*, **2003**, 138, PP 271582.
[3] Panda J; Srinivas S. V.; Rao M. E., *J. Ind. Chem. Soc*., **2002**, 79(9), 770-1; *Chem. Abstr*, **2003**, 138, PP 153499n.
[4] Roman, *Pharmazie* **1990**, 45, PP 214.
[5] Ashok Kumar, Verma R. S. and Jagu B. P. *J. Ind. Chem. Soc*., **1990**, 67, PP 120.
[6] Ronald W. I.; Advianv A., *Chem. Abstr*., **1997**, 126, PP 181346f.
[7] Mokhta H. M.; Faidailab H. M., *Pharmazie*, **1987**, 42, PP 42.
[8] A. D. Sagar ; M. V. Yadav, *J. Chem. Pharm. Res*., **2011,** 3(6) : 1103-1108
[9] M. H. Mistry ; S.J.Paramar ; G.C.Desai , *J. Chem. Pharm. Res*., **2011**, 3(4) : 831-837
[10] P.P.Singh ; S.B.Sharma ; K. Singh , *J. Chem. Pharm. Res*., **2010**, 2(5) : 193-205
[11] N.Haque ; N.Parvez ; S.Yadav ; R.Khalel, *J. Chem. Pharm. Res*., **2010**, 2(5) : 161-168
[12] Barry A. L., "The Antimicrobial Susceptibility Test, Principle and Practices, 4th edn (ELBS) **1976**, PP 180.