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SYNTHESIS AND MICROBIAL STUDIES OF SOME NOVEL SCHIFF BASE CONTAINING PYRIMIDINE

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ABSTRACT

6-chloro 2, 4-diamino pyrimidine reacts with various aromatic aldehyde. Finally, the product was characterized by conventional and instrumental methods. Their structures were determined and important therapeutic properties were studied.

INTRODUCTION: Azomethines are generally known as Schiff bases to honour Hugo Schiff, who synthesized such compounds. These are the compounds containing characteristic -C=N- group. Several methods have been reported for the preparation of azomethines. Selvam *et.al*[1] have prepared sulfonamide and its derivatives as anti-HIV agents. More *et. al* have marked the biological activity of Schiff bases synthesized from aminothiazoles. Ernst Bayer has reported some metallocomplex Schiff bases derived from *o*-amino phenol. Schiff bases can be synthesized from an aromatic amine and a carbonyl compound by nucleophilic addition forming a hemiaminal, followed by a dehydration to generate an imine. They are well known intermediates for the preparation of azetidinones, thiazolidinones, oxadiazolines and many other derivatives. Azomethines exhibit a wide range of pharmacological activities like antimicrobial, antiparasitic, anti-inflammatory, anticancer *etc*. Pyrimidine and their derivatives posseses several interesting biological activity such as antimicrobial [2-4], antitumor, antifungal activities. Many pyrimidine derivatives are used for thyroid drugs and leukemia.

MATERIALS AND METHODS: The reagent grade chemicals were obtained from commercial sources and purified by either distillation or recrystallization before use. Purity of synthesized compounds has been checked by thin layer chromatography. Melting points were determined by open capillary method and are uncorrected. IR spectra are recorded on FT-IR Bruker with KBr disc. ^{1}H NMR spectra are recorded in DMSO-d6 on a Bruker DRX-400 MHz using TMS as internal standard. The chemical shift are reported as parts per million (ppm) and mass spectra were determined on Jeol-SX-102(FAB) spectrometer.

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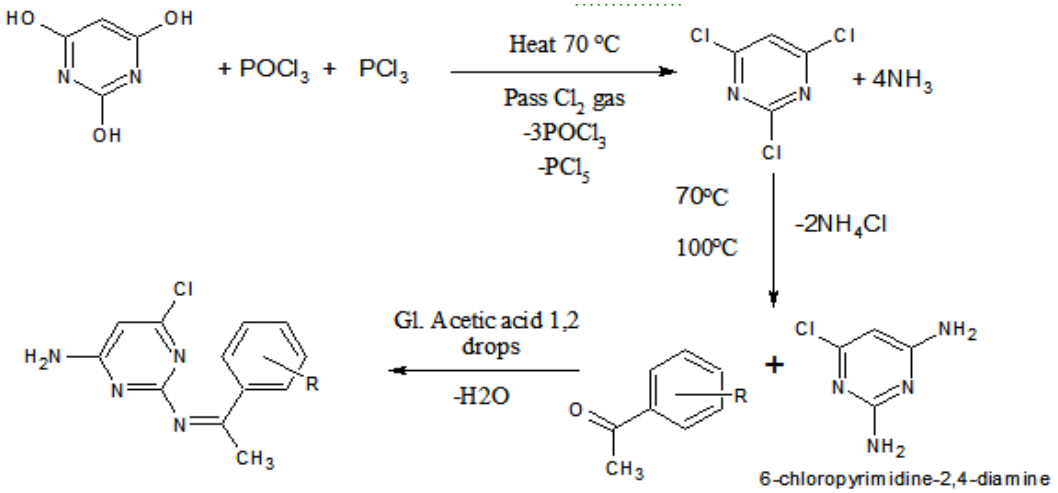
Synthetic Procedures:

Preperation of 6-chloro 2, 4-diamino pyrimidine: Take 3 neck flask, T.P, Stirrer, Purger, Charge Barbutiric acid, POCl3 and PCl3, now heat the R.M. till 70°C temperature, now pass Cl2 gas and temperature rise up to 100°C so, three Hydroxyl group replace by three chlorine group, progress of the reaction was monitored by TLC. So, here formation of 2, 4, 6 tri chloro pyrimidine. Now, in autoclave taken Liq. NH3 and cool it 0°C temperature, now add 2, 4, 6 tri chloro pyrimidine slowly into it, now heat the RM till 70°C temp. and maintain for 1-2 hrs., then raise the temp., till 100°C and maintain for 1-2 hrs. Progress of the reaction was monitored by TLC. After the completion of the reaction, filter it and W/C washed with water, suck dry well, then purified in Methanol.

Preparation of 6-chloro-N2-[(Z)-phenylmethylidene] pyrimidine-2,4-diamine: To a mixture of 6-chloro pyrimidine-2,4-diamine (0.1 mol.) and substituted aromatic acetophenone (0.1 mol.) in ethanol, 1 ml. of glacial acetic acid added then the resultant mixture was refluxed for (5-6 hours), progress of the reaction was monitored by TLC. After the completion of the reaction, the obtained product was poured into crushed ice stirred well; solid obtained was recrystallized from suitable solvent. Their Analytical data and synthetic procedure shown in **Tabel 1 and Scheme 1**.



Scheme-I

FIGURE 1: SYNTHETIC ROUTE OF SCHIFF BASE DERIVATIVES

TABLE 1: PHYSICAL CONSTANTS AND ELEMENTAL ANALYSIS OF SCHIFF-BASE

Comp. No.	-R	Molecular Formula	M.P. °C	Yield %	% of C Found, (calcd.)	% of H Found (calcd.)	% of N Found (calcd.)
SP_V-1	4-NH_2-C_6H_4	$C_{12}H_{12}$ Cl N_5	62	71	55.08 (55.07)	4.63 (4.62)	26.77 (26.76)
SP_V -2	3-OCH_3-4-OH-C_6H_3	$C_{13}H_{13}ClN_4O_2$	65	74	53.36 (53.34)	4.49 (4.48)	19.16 (19.14)
SP_V -3	3-F-C_6H_4	$C_{12}H_{10}ClFN_4$	68	79	54.46 (54.45)	3.80 (3.81)	21.19 (21.17)
SP_V -4	3-OH-C_6H_4	$C_{12}H_{11}ClN_4O$	61	80	54.88 (54.87)	4.23 (4.22)	21.35 (21.33)
SP_V -5	2,4-$(OH)_2$-C_6H_3	$C_{12}H_{11}ClN_4O_2$	58	84	51.74 (51.72)	3.99 (3.98)	20.12 (20.10)
SP_V -6	2,4-$(Cl)_2$-5-F-C_6H_2	$C_{12}H_8Cl_3FN_4$	60	73	43.24 (43.21)	2.40 (2.42)	16.83 (16.80)
SP_V -7	2,6-$(Cl)_2$-3-F-C_6H_2	$C_{12}H_8Cl_3FN_4$	72	75	43.22 (43.21)	2.41 (2.42)	16.84 (16.80)
SP_V -8	3-Cl-4-F-C_6H_3	$C_{12}H_9Cl_2FN_4$	69	79	48.19 (48.18)	3.01 (3.03)	18.75 (18.73)
SP_V -9	3-F-C_6H_4	$C_{12}H_{10}ClFN_4$	63	81	54.46 (54.45)	3.82 (3.81)	21.19 (21.17)
SP_V -10	2-Br-4-F-C_6H_3	$C_{12}H_9BrClFN_4$	66	69	41.97 (41.95)	2.65 (2.64)	16.30 (16.31)

RESULTS AND DISCUSSION:

Therapeutic Study:

Antibacterial activity: Antibacterial activity was carried out by browth dilution method [5]. The compounds SP_v-1-10 were screened for their antibacterial activity against *Escherichia coli, Staphylocous aureus, Pseudomonas aeruginosa* and *Staphyloccous pyogenes* of concentrations of 1000, 500, 200, 100, 50, 25, 12.5 µg/mL respectively.

Antibacterial activity results showed that, compound SP_V-03 and SP_V-04 were good active

Antifungal activity: Same compounds were tested for antifungal activity against *C. albicans A. niger* and *A. clavatus* of a concentrations of 1000, 500, 200, 100 µg/mL respectively. The results are recorded in the form of primary and secondary screening. Each synthesized drug was diluted to obtain 1000 µg/mL concentration, as a stock solution.

The data of antifungal activity of this series indicated that, compounds were not showing potential activity against any species. Their Antifungal data are given in **Table 2**.

TABLE 2:ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY DATA

Sr. No.	MINIMAL BACTERICIDAL CONCENTRATIONS (MBC) IN µg / ml				MINIMAL FUNGICIDAL CONCENTRATIONS (FBC) in µg/ml	
	E. coli MTCC 443 µg / ml	*P. aeruginosa* MTCC 1688 µg / ml	*S. aureus* MTCC 96 µg / ml	*S. pyogenus* MTCC 442 µg / ml	*C. albicans* MTCC 227 µg/ml	*A. niger* MTCC 282 µg/ml
SP_V-01	250	250	250	250	200	1000
SP_V-02	200	100	200	125	1000	1000
SP_V-03	125	62.5	125	250	1000	1000
SP_V-04	62.5	100	62.5	500	500	500
SP_V-05	50	100	125	500	>1000	>1000
SP_V-06	250	500	250	250	1000	>1000
SP_V-07	100	125	50	100	500	500
SP_V-08	500	1000	500	500	>1000	1000
SP_V-09	250	250	500	500	500	1000
SP_V-10	200	200	250	250	1000	500

CONCLUSION: The Schiff base were synthesized and characterized for their structure elucidation. Various chemical and Spectral data supported the structure thought of Antibacterial and Antifungal studies of these compounds indicated that SP_v-03 and SP_v-04 were good active against all bacteria while all compounds were not showing potential antifungal activity against any species.

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