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Research Article

Biological Screening of Some Novel Pyrimidine Compounds

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Abstract

Some novel pyrimidine compounds have been synthesized and their biological screening is done in DMSO using Gram positive and Gram negative bacterial and fungal strains. It is observed that inhibition depends on strain as well as structure of compounds.

Keywords: S. typhimurium; C. glabrata; C. neoformans

Introduction

The extensive use of antibiotics has led to the appearance of multidrug resistant microbial pathogens [1]. In recent years, multiple drug resistance has developed due to indiscriminate use of existing antimicrobial drugs in the treatment of infectious diseases. Further, antibiotics are sometimes associated with adverse effects on the host-like hypersensitivity. Therefore, there is a need to develop alternative antimicrobials drugs for the treatment of infectious diseases from other sources.

The biological activity spectrum of a compound represents the pharmacological effects, physiological and biochemical mechanisms of action, specific toxicity that can be revealed in compound's interaction with biological system. Further, it describes the intrinsic properties of the compound, which depends on its structure.

Pyrimidines are always an attraction point for researchers because of its efficiency towards various pharmacological usages. These compounds are known to possess various biological activities [2-10]. Literature survey shows that various fused pyrimidine derivatives are known to exhibit anti-tubercular [11,12], anti-proliferative [13,14], anti-HIV [15,16], anti-microbial [17], anti-analgesic [18], anti-inflammatory [19] and anti-malarial [20] activities. Compounds containing imidazo [2, 1-b] thiazole derivatives are also of great interest among medicinal chemists as these compounds have also been reported for a wide spectrum of other biological properties [21-26].

In the present paper, some novel pyrimidines compounds have been synthesized. The antimicrobial activities of synthesized compounds have been screened against some bacterial (both Gram positive and Gram negative) and fungal strains in DMSO. The results are reported as minimum inhibitory concentrations and minimum bactericidal concentration for all the synthesized compounds.

Experimental

A variety of different pyrimidine compounds are synthesized.

Synthesis of 2, 4-disubstituted Pyrimidine derivatives (BKD-1 to BKD-12): In n-butanol, Equimolar mixture of 2, 4-dichloropyrimidine (DCP), 4-((1H-1, 2, 4-triazol-1-yl) methyl) aniline (TMA) and 0.012 mole of N, N-diisopropyl ethyl amine was refluxed for 3 hr. The completion of reaction was confirmed by analytical thin layer chromatography using as a 9.6:0.4.

Dichloromethane: Methanol mobile phase. After completion of reaction, reaction mixture was cooled. The resulting solid was filtered, washed with cold water and dried under vacuum to give crude product.

This resulting product was refluxed for 3 hr with ethanolic solution of different aromatic amines (0.011 mol) using glacial acetic acid as catalyst. The completion of reaction was monitored using TLC (100% ethyl acetate + NH3 atmosphere as a mobile phase). After completion of reaction, the reaction mixture was cooled, and the resulting solid was filtered, washed with cold ethanol and dried under vacuum to give crude product. The obtained crude product was purified by trituration with diethyl ether.

The reaction scheme is:

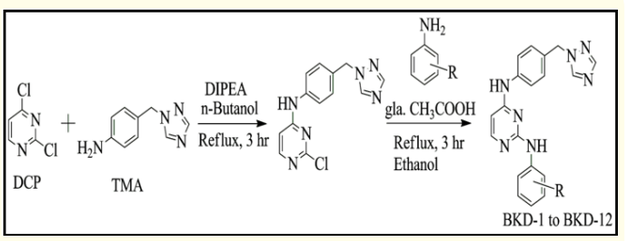

Figure 1

Synthesis of 2, 4-disubstituted pyrimidine derivatives (KDB-1 to KDB-9): Equimolar mixture of 2,4-dichloropyrimidine (DCP), 1-Naphthol (NTL) and 0.015 mole of Potassium carbonate (K_2CO_3) in DMF was refluxed for 4 hr. The completion of reaction was confirmed by analytical thin layer chromatography (TLC) using (7:3–Hexane: Ethyl acetate) as mobile phase. After completion of reaction, the reaction mixture was cooled, and the resulting solid was filtered, washed with cold water and dried under vacuum to give crude product.

This resulting product (0.01 mol) was refluxed for 4 - 5 hr with ethanolic solution of different aromatic amines (0.012 mol) using hydrochloric acid as catalyst. The completion of reaction was confirmed by TLC using (7.5:2.5-Hexane: Ethyl acetate) mobile phase. After completion of reaction, the reaction mixture was cooled. The resulting solid was filtered, washed with cold ethanol and dried under vacuum to give crude product. The obtained crude product was purified by trituration with diethyl ether.

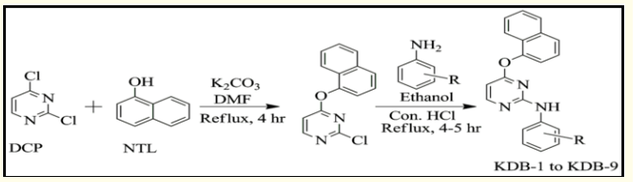

Figure 2

The physical constants of all synthesized compounds are listed in table 1.

	BKD-series				
Compound Code	**Substitution R**	**M. F.**	**M. Wt. (g/mol)**	**Yield (%)**	**R_f value**
BKD-1	4-Cl	$C_{19}H_{16}ClN_7$	377.83	88	0.44
BKD-2	4-CH_3	$C_{20}H_{19}N_7$	357.41	92	0.46
BKD-3	4-F	$C_{19}H_{16}FN_7$	361.38	79	0.45
BKD-4	3-CF_3	$C_{20}H_{16}F_3N_7$	411.38	89	0.48
BKD-5	3-Cl, 4-F	$C_{19}H_{15}ClFN_7$	395.82	78	0.41
BKD-6	4-OCH_3	$C_{20}H_{19}N_7O$	373.41	87	0.39
BKD-7	3-Cl	$C_{19}H_{16}ClN_7$	377.83	77	0.43
BKD-8	3,4-dichloro	$C_{19}H_{15}C_{l2}N_7$	412.28	89	0.40
BKD-9	4-CF_3	$C_{20}H_{16}F_3N_7$	411.38	90	0.47
BKD-10	3-CH_3	$C_{20}H_{19}N_7$	357.41	92	0.47
BKD-11	2-CH_3	$C_{20}H_{19}N_7$	357.41	76	0.41
BKD-12	2-F	$C_{19}H_{16}FN_7$	361.38	74	0.40
	KDB-series				
KDB-1	4-Cl	$C_{20}H_{14}ClN_3O$	347.08	78	0.55
KDB-2	4-CH_3	$C_{21}H_{17}N_3O$	327.38	71	0.52
KDB-3	4-F	$C_{20}H_{14}FN_3O$	331.11	81	0.42
KDB-4	3-CF_3	$C_{21}H_{14}F_3N_3O$	381.35	86	0.58
KDB-5	3-Cl, 4-F	$C_{20}H_{13}ClFN_3O$	365.79	78	0.54
KDB-6	4-OCH_3	$C_{21}H_{17}N_3O_2$	343.38	77	0.50
KDB-7	3, 4-dichloro	$C_{20}H_{13}Cl_2N_3O$	382.24	80	0.54
KDB-8	3-Cl	$C_{20}H_{14}ClN_3O$	347.80	77	0.52
KDB-9	2-F	$C_{20}H_{14}FN_3O$	331.11	70	0.53

Table 1: Physical constants of 2,4-disubsstitutedpyrimidine derivatives.

Synthesis of substituted and fused Pyrazolopyrimidines (TC-1 to TC-16)

Ist Step: Synthesis of substituted Acetoacetanilide derivatives (AAA) (Intermediate-I): Equimolar mixture of substituted aromatic amine (I), 1, 3-diketone (II) and catalytic amount of potassium hydroxide (KOH) in 1, 4-dioxane was refluxed for 4 - 5 hr. The progress of the reaction was monitored by thin layer chromatography. After completion of reaction, reaction mixture was allowed to cool at room temperature and was poured into crushed ice. The obtained solid was filtered and was purified by trituration with hexane to get pure product (Intermediate-I).

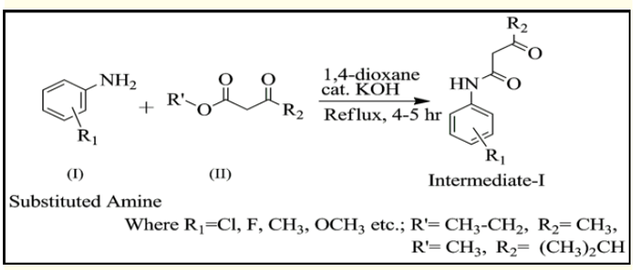

Figure 3

IInd Step: Synthesis of 5-Amino-3-(methylthio)-1H-pyrazole-4-carbonitrile (Intermediate-II): A mixture of malano nitrile (0.01 m mol) and dry K2CO3 (0.012 m mol) were stirred in dry DMF at room temperature for 30 minutes, 0.02 mole carbon disulphide (CS2) was drop wise added in reaction mixture. Then, the reaction mixture was stirred for an additional 2.5 hr at same temperature. The reaction mixture was then cooled at 0 - 5°C and dimethyl sulphate (0.02 mol) was added. The solution was stirred at room temperature for another 5 - 6 hr and was poured into crushed ice to give solid product. The resulting solid was filtered, washed with cold water and was dried under vacuum to give crude product.

This resulting crude product (0.01 mol) was refluxed with hydrazine hydrate (0.01 mol) for 30 minutes. in isopropyl alcohol (IPA). After completion of reaction, the reaction mixture was cooled and poured into crushed ice. The resulting solid was filtered, washed with water and dried under vacuum to give crude product (Intermediate-II). The obtained crude product was purified by trituration with hexane and used in next step without further purification.

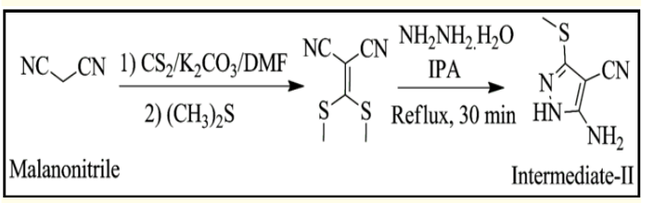

Figure 4

IIIrd Step: Synthesis of substituted and fused Pyrazolo pyrimidines (TC-1 to TC-16): A mixture of Int.-I (0.01 mol), Int.-II (0.015 mol) and different substituted aldehyde (0.01 mol) was heated at 140 - 150°C for 25 - 30 minutes. in presence 3 - 4 drops of DMF. The completion of reaction was confirmed by analytical thin layer chromatography (TLC). After completion of reaction, reaction mixture was allowed to cool at room temperature and poured into crushed ice. The resulting solid was filtered, washed with water and dried under vacuum which was then purified by trituration with methanol.

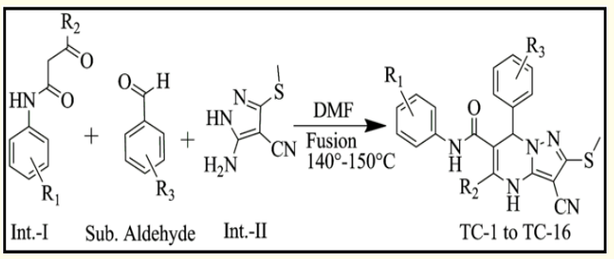

Figure 5

Synthesis of substituted and fused Pyrazolopyrimidines (KD-1 to KD-12): An ethanolic solution of different substituted aromatic aldehyde (0.01 mol), Int.-II (0.015 mol) and malano nitrile (0.01 mol) was refluxed for 3 - 5 hr using sodium hydroxide as catalyst. The reaction mass was cooled and resulting solid was filtered, washed with cold ethanol and dried. The crude product was purified by trituration with diethyl ether.

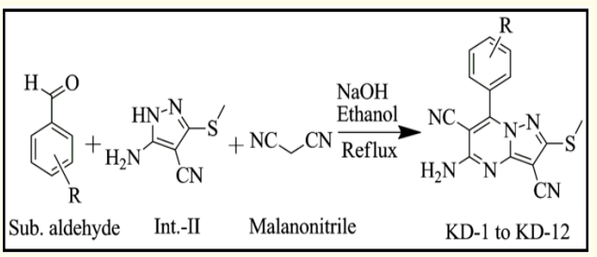

Figure 6

The physical constants of all synthesized compounds are listed in table 2.

TC- series							
Comp. Code	Substitutions			M.F.	M. Wt.	Yield (%)	R_f value
	R_1	R_2	R_3				
TC-1	4-Cl	$(CH_3)_2CH$-	4-Cl	$C_{24}H_{21}Cl_2N_5OS$	498.43	68	0.61
TC-2	3-Cl	$(CH_3)_2CH$-	4-Cl	$C_{24}H_{21}Cl_2N_5OS$	498.43	59	0.63
TC-3	3,4-di Cl	$(CH_3)_2CH$-	4-Cl	$C_{24}H_{20}Cl_3N_5OS$	532.87	66	0.65
TC-4	3-Cl,4-F	$(CH_3)_2CH$-	4-Cl	$C_{24}H_{20}Cl_2FN_5OS$	516.42	56	0.69
TC-5	4-F	$(CH_3)_2CH$-	4-Cl	$C_{24}H_{21}ClFN_5OS$	481.87	70	0.70
TC-6	4-CH_3	$(CH_3)_2CH$-	4-Cl	$C_{25}H_{24}ClN_5OS$	477.14	65	0.70
TC-7	4-CF_3	$(CH_3)_2CH$-	4-Cl	$C_{25}H_{21}ClF_3N_5OS$	531.98	62	0.69
TC-8	4-Cl	$(CH_3)_2CH$-	4-OCH_3	$C_{25}H_{24}ClN_5O_2S$	493.01	62	0.68
TC-9	3,4-di Cl	$(CH_3)_2CH$-	4-OCH_3	$C_{25}H_{23}Cl_2N_5O_2S$	527.09	59	0.66
TC-10	4-OCH_3	-CH_3	4-OCH_3	$C_{24}H_{23}N_5O_3S$	461.15	70	0.63
TC-11	4-Cl	-CH_3	4-Cl	$C_{22}H_{17}Cl_2N_5OS$	469.05	55	0.69
TC-12	4-F	-CH_3	4-Cl	$C_{22}H_{17}ClFN_5OS$	453.08	66	0.64
TC-13	4-Br	-CH_3	4-Cl	$C_{22}H_{17}BrClN_5OS$	514.83	69	0.65

TC-14	4-Br	$-CH_3$	$4-OCH_3$	$C_{23}H_{20}BrN_5O_2S$	509.04	67	0.63
TC-15	4-F	$-CH_3$	$4-OCH_3$	$C_{23}H_{20}FN_5O_2S$	449.13	70	0.64
TC-16	4-Cl	$-CH_3$	$4-OCH_3$	$C_{23}H_{20}ClN_5O_2S$	465.96	68	0.66
KD- series							
Compd. Code	**Substitution R**			**M.F.**	**M. wt.**	**Yield (%)**	**R_f value**
KD-1	$4-OCH_3$			$C_{16}H_{12}N_6OS$	336.37	72	0.41
KD-2	3,4-di OCH_3			$C_{17}H_{14}N_6O_2S$	366.40	71	0.40
KD-3	4-Cl			$C_{15}H_9ClN_6S$	340.79	69	0.47
KD-4	4-F			$C_{15}H_9FN_6S$	324.34	67	0.49
KD-5	-H			$C_{15}H_{10}N_6S$	306.35	69	0.48
KD-6	3-Cl			$C15H_9ClN_6S$	340.79	64	0.47
KD-7	3-Br			$C_{15}H_9BrN_6S$	385.24	73	0.49
KD-8	2,5-di-OCH_3			$C_{17}H_{14}N_6O_2S$	366.40	72	0.39
KD-9	$3-OCH_3$			$C_{16}H_{12}N_6OS$	336.37	71	0.46
KD-10	$4-N(CH_3)_2$			$C_{17}H_{15}N_7S$	349.41	69	0.48
KD-11	$4-CH_3$			$C_{16}H_{12}N_6S$	320.37	67	0.51
KD-12	3,4,5-tri OCH_3			$C_{18}H_{16}N_6O_3S$	396.42	61	0.37

Table 2: Physical constants of Pyrazolopyrimidine derivatives.

Synthesis of Imidazothiazole derivatives (TP-1 to TP-9)

Ist Step: Synthesis of Ethyl 2-aminothiazole-5-carboxylate (Int.-1): Equimolar mixture of ethyl chloro acetate and ethyl formate were added drop wise to a suspension of 0.01 mol solution of sodium ethoxide in dry toluene, maintained at a temperature between 0 - 5°C for 2 hr. Then, the reaction mixture was stirred at 0°C for another 2.5 hr. The contents were diluted with water and the layers were separated. The aqueous phase was acidified with concentrated hydrochloric acid.

Compound Code	Substitution R	M. F.	M. Wt. (g/mol)	Yield (%)	R_f value
TP-1	$4-OCH_3$	$C_{15}H_{14}N_2O_3S$	302.35	64	0.41
TP-2	4-Cl	$C_{14}H_{11}ClN_2O_2S$	306.77	66	0.49
TP-3	4-Br	$C_{14}H_{11}BrN_2O_2S$	351.22	70	0.48
TP-4	3,4-di-F	$C_14H_{10}F_2N_2O_2S$	308.30	61	0.49
TP-5	-H	$C_{14}H_{12}N_2O_2S$	272.32	69	0.50
TP-6	4-F	$C_{14}H_{11}FN_2O_2S$	290.31	72	0.47
TP-7	2,4-di-Cl	$C_{14}H_{10}C_{l2}N_2O_2S$	341.21	69	0.46
TP-8	$4-NO_2$	$C_{14}H_{11}N_3O_4S$	317.32	67	0.43
TP-9	$4-CH_3$	$C_{15}H_{14}N_2O_2S$	286.35	63	0.48

Table 3: Physical constants of Imidazothiazole derivatives.

In this acidified solution, 0.013 mole of aqueous thio urea solution was added and the solution was refluxed for 2.5 hr. The completion of reaction was confirmed by analytical thin layer chromatography (TLC) using (100% Ethyl acetate) as mobile phase. After completion of reaction, the reaction mass was cooled and neutralized with sodium hydroxide solution. An amber colored solid was precipitated, which was filtered and dried to get desired product ethyl 2-aminothiazole-5-carboxylate.

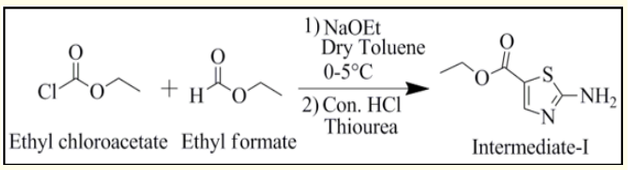

Figure 7

IInd Step: Synthesis of Imidazothiazole derivatives (TP-1 to TP-9): A mixture of ethyl 2-amino thiazole-5-carboxylate (Int.-1) (0.01 mol), different substituted phenacyl bromide (0.012 mol) and 10% aqueous solution of 1, 4-diazabicyclo [2.2.2] octane (DABCO) was refluxed for 1 hr. The completion of reaction was confirmed by analytical thin layer chromatography (TLC) using (8:2-Hexane: Ethyl acetate) as mobile phase. After completion of reaction, the reaction mixture was cooled. The resulting solid was filtered, washed with cold water and dried. The obtained crude product was purified by trituration with mixture of methanol and ethyl acetate.

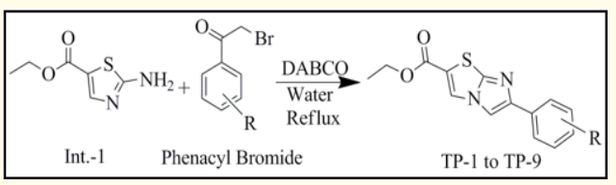

Figure 8

Synthesis of fused Tetrazolopyrimidines derivatives (K-1 to K-14)

Synthesis of substituted aceto acetanilide derivatives (AAA) (Intermediate-I): Given above (of TC series).

Synthesis of fused Tetrazolopyrimidines derivatives (K-1 to K-14): All the compounds (K-1 to K-14) were synthesized according to synthesis of fused pyrazolopyrimidines (TC series).

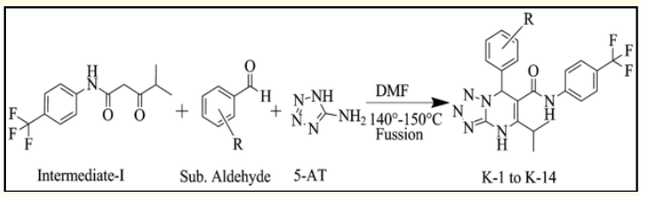

Figure 9

The physical constants of all synthesized compounds are listed in table 4.

Compound Code	Substitutions R	M. F.	M. Wt (g/mol)	Yield (%)	R_f value
K-1	-H	$C_{21}H_{19}F_3N_6O$	428.41	51	0.44
K-2	3,4-di-OCH_3	$C_{23}H_{23}F_3N_6O_3$	488.46	59	0.39
K-3	4-Cl	$C_{21}H_{18}ClF_3N_6O$	462.86	62	0.42
K-4	4-F	$C_{21}H_{18}F_4N_6O$	446.40	63	0.44
K-5	3-OH	$C_{21}H_{19}F_3N_6O_2$	444.41	69	0.35
K-6	4-OCH_3	$C_{22}H_{21}F_3N_6O_2$	458.44	55	0.41
K-7	3-Cl	$C_{21}H_{18}ClF_3N_6O$	462.86	59	0.46
K-8	4-$OCHF_2$	$C_{22}H_{19}F_5N_6O_2$	494.42	54	0.40
K-9	3-Br	$C_{21}H_{18}BrF_3N_6O$	507.31	66	0.43
K-10	4-CH_3	$C_{22}H_{21}F_3N_6O$	442.44	67	0.45
K-11	3-OCH_3	$C_{22}H_{21}F_3N_6O_2$	458.44	68	0.42
K-12	2,5-di-OCH_3	$C_{23}H_{23}F_3N_6O_3$	488.46	66	0.43
K-13	2- OCH_3	$C_{22}H_{21}F_3N_6O_2$	458.44	64	0.41
K-14	2-Cl	$C_{21}H_{18}ClF_3N_6O$	462.86	52	0.46

Table 4: Physical constants of Tetrazolopyrimidine derivatives.

The formation of compounds was checked by TLC (Performed on aluminum coated TLC plates gel-G60 F_{254} and accomplished on 0.5-mm (E. Merck)). Visualization of spot was made with UV light (254 and 365 nm), an iodine vapor and other visualizing reagent. The melting point was determined in open capillary tubes and was uncorrected. IR spectra were recorded on KBr discs, using FT-IR, (Shimadzu spectrophotometer Model no.-8400). 1H-NMR spectra were taken on a Bruker AVANCE II 400. In all the cases, 1H NMR spectra were obtained in DMSO-d6 using TMS as an internal standard. The NMR signals are reported in δ ppm. Mass spectra were determined using direct inlet probe on a GCMS-QP-2010 mass spectrometer.

Biological Screening

The antibacterial and antifungal activities of all synthesized compounds were studied in DMSO. All the synthesized compounds were recrystallized prior to use and DMSO was purified by standard method [27]. For all the compounds, agar well diffusion method was used.

Following Strains were used for the antimicrobial screening:

Gram positive bacteria

1. *Corynebacterium rubrum* ATCC14898 (*CR*)
2. *Staphylococcus albus* NCIM2178 (*SAL*)
3. *Staphylococcus aureus* ATCC25923 (*SA*)

Gram negative bacteria

1. *Enterobacter aerogenes* ATCC13048 (*EA*)
2. *Escherichia coli* NCIM2931 (*EC*)
3. *Salmonella typhimurium* ATCC23564 (*ST*)

Fungi(Yeast)

1. *Candida albicans* ATCC2091 (*CA*)
2. *Candida neoformans* NCIM3542 (*CN*)
3. *Candida glabrata* NCIM3448 (*CG*)

All these strains were obtained from National Chemical Laboratory (NCL), Pune, India. The bacterial and fungal strains were maintained on nutrient agar and MGYP medium (Hi Media, India) respectively while *E. coli* were maintained on Luria medium (Hi Media, India) at 4°C and sub cultured before use.

Minimum inhibitory concentration (MIC) refers to the lowest concentration of the antimicrobial agent which is required for the inhibition of visible growth of the tested microorganism [28]. The antimicrobial activity of an agent is usually quantified by determining the MIC values which serve as a guide for treatment of most infections. MIC values were calculated using INT dye. The MBC is interpreted as the lowest concentration that can completely remove the microorganisms.

Preparation of solution of compounds for (MIC) and (MBC) study: All the compounds dissolved in DMSO were first diluted to highest concentration (20 mg ml^{-1}) to be tested and then serial two-fold dilution was made in a concentration range from (0.156 to 20 mg ml^{-1}).

Preparation of bacterial inocula for MIC and MBC study: The inocula of the test organisms were prepared using the colony suspension method [29]. Colonies picked from 24h old cultures grown on nutrient agar were used to make suspension of the test organisms in saline solution to give an optical density of approximately 0.1 at 600 nm. The suspension was then diluted 1:100 by transfer of 0.1 ml of the bacterial suspension to 9.9 ml of sterile nutrient broth before use to yield 6 × 105 CFU ml^{-1}.

Determination of the minimum inhibitory concentrations (MIC): The MIC was determined by the micro well dilution method [30] with some modification. This test was performed in sterile flat bottom micro test plates (Tarsons Products Pvt. Ltd.). 150 µl volume of Mueller Hinton broth (MHB) was dispensed into each well and 20 µl of various concentrations of the compounds was added in decreasing order along with 30 µl of the test organism suspension. The final volume in each well was 200 µl (150 µl Mueller Hinton broth, 30 µl of the test organism suspension

and 20 µl compound). Two control wells were maintained for each test batch; sterility control (MHB and DMSO) and organism control (MHB, test organism and DMSO). Plates were then incubated at 37°C for 24h. Experiments were carried out in duplicate. After incubation, 40 µl of INT (2-(4-Iodo phenyl)-3-(4-nitro phenyl)-5-phenyltetrazolium chloride) solution (0.2 mg ml-1) dissolved in sterile distilled water was added to each well [31]. The plates were incubated for further 30 minutes and were estimated visually for change in color to pink indicating reduction of the dye due to bacterial growth. The highest dilution (lowest concentration) that remained clear corresponded to the MIC.

Determination of the minimum bactericidal concentration (MBC): Minimum bactericidal concentration (MBC) was determined from all wells showing no growth as well as from the lowest concentration showing growth in the MIC assay for all the samples. Bacterial cells from the MIC test plate were sub cultured on freshly prepared solid nutrient agar plates by making streaks on the surface of the agar. The plates were incubated at 37°C for 24h overnight. Plates that did not show growth were considered to be the MBC for the compounds used [32]. The experiment was carried out in duplicate.

Results and Discussion

2, 4-disubstituted Pyrimidine derivatives (BKD and KDB series)

The MIC and MBC values of BKD compounds are presented in table 5. The compounds exhibited concentration dependent inhibition of growth. All the compounds showed varied levels of MIC and MBC values against studied microorganism. In sterility control (MBH and DMSO), DMSO had no inhibitory effect on the tested organisms. For the Gram positive bacterial strains MIC and MBC varied from < 0.156 mg ml^{-1} to > 20 mg ml^{-1} and 0.250 mg ml^{-1} to > 20 mg ml^{-1} respectively for BKD series whereas for KDB series, MIC and MBC varied from < 0.156 mg ml-1 to > 20 mg ml^{-1} and 10 mg ml^{-1} to > 20 mg ml^{-1} respectively.

Compd. code	Gram positive bacteria						Gram positive bacteria						Fungi (yeast)					
	SAL		SA		CR		EA		EC		ST		CA		CG		CN	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
BKD -1	> 20	> 20	1.25	20	5	> 20	5	> 20	10	> 20	10	> 20	0.312	> 20	< 0.156	10	1.25	> 20
BKD -2	> 20	> 20	5	> 20	2.5	> 20	5	> 20	5	> 20	10	> 20	0.625	> 20	1.25	10	1.25	> 20
BKD -3	> 20	> 20	5	> 20	5	> 20	10	> 20	10	> 20	10	> 20	1.25	> 20	5	> 20	< 0.156	5
BKD -4	> 20	> 20	< 0.156	10	5	> 20	10	> 20	10	> 20	10	> 20	1.25	> 20	0.625	> 20	0.312	> 20
BKD -5	> 20	> 20	2.5	> 20	10	> 20	20	> 20	10	> 20	10	> 20	1.25	> 20	10	> 20	< 0.156	2.5
BKD -6	> 20	> 20	< 0.156	0.250	5	> 20	> 20	> 20	10	> 20	20	> 20	2.5	> 20	0.625	> 20	1.25	> 20
BKD -7	> 20	> 20	10	> 20	5	> 20	10	> 20	20	> 20	10	> 20	2.5	> 20	2.5	10	2.5	> 20
BKD-8	> 20	> 20	2.5	> 20	2.5	> 20	20	> 20	20	> 20	10	> 20	1.25	> 20	2.5	10	2.5	> 20
BKD-9	> 20	> 20	0.312	10	1.25	> 20	10	> 20	10	> 20	10	> 20	1.25	> 20	2.5	10	2.5	> 20
BKD -10	> 20	> 20	0.312	20	0.625	20	5	> 20	10	> 20	5	> 20	1.5	> 20	0.65	10	2.5	> 20
BKD-11	> 20	> 20	0.312	20	5	> 20	10	> 20	10	> 20	10	> 20	2.5	> 20	2.5	> 20	2.5	> 20
BKD -12	> 20	> 20	0.625	> 20	0.625	> 20	10	> 20	10	> 20	10	> 20	> 20	> 20	> 20	> 20	5	> 20

Table 5: Antibacterial activity data (MIC and MBC in mg ml^{-1}) of BKD series compounds against Gram positive bacteria, Gram negative bacteria and fungal strains.

Against *S. albus*, all compounds showed MIC and MBC values > 20 mg ml-1. Against *S. aureus*, compound BKD-4 and BKD-6 showed lowest MIC (< 0.156 mg ml^{-1}) whereas maximum is obseved by BKD-7 having value of 10 mg ml^{-1}. The lowest MBC value is 0.250 mg ml^{-1} for BKD-6 followed by BKD-4 and BKD-9 (having value 10 mg ml^{-1}). BKD-10 and BKD-12 had minimum MIC value of 0.625 mg ml^{-1} against *C. rubrum* whereas MBC values were 20 mg ml^{-1} for all the studied BKD compounds.

For all the selected Gram negative bacterial strains, MBC values are > 20 for all the BKD compounds. The MIC values are minimum i.e., 5 mg ml^{-1} for KDB-1, KDB-2 and KDB-10 against *E. aerogenes.* For *E. coli* also, KDB-2 has minimum value of 5 mg ml-1 whereas a value of 5 mg ml^{-1} is for BKD-10 against *S. typhimurium* which is minimum as comparison to other compounds.

For different fungal strains, all the compounds showed varied levels of MIC and MBC values. Against *C. albicans*, minimum value of MIC is for BKD-1 and maximum is for BKD-12. MBC values were > 20 mg ml^{-1} for all the studied BKD compounds. The lowest MIC values (< 0.156 mg ml-1) shown by BKD-1 (against *C. glabrara*) and BKD-3 and BKD-5 against *C. neoformans*. The minimum MBC values are 10 mg ml^{-1} and 5 mg ml^{-1} respectively for these two fungal strains.

The inhibition depends on solvent, compound structure and strain. In the present study, solvent is same throught so this parameter is not considered. Table 1 shows that different R groups in these compounds. These compounds have same central nucleus but different substitution. These substitutions are aryl ring with different functional groups. Thus, different substitutions affect different strains differently. In BKD series, BKD-4 and BKD-6

contains 3-CF_3 and 4-OCH_3 respectively. Thus, 3-CF_3 and -OCH_3substitutions are more effective against *S. aureus.* Whereas 4-chloro present in compound BKD-1 is more effective against fungal strain *C. glabrara*. Against *C. neoformans*, BKD-3 and BKD-5 compounds are more effective containing 4-fluoro and 3-chloro, 4-fluoro respectively. For Gram negative bacteria, the studied BKD compounds are not very effective. Thus, these selected Gram-negative bacteria are most resistant. Among Gram positive bacteria, *S. albus* is most resistant.

Table 6 shows that all the KDB compounds have > 20 mg ml^{-1} value of MIC against *S. albus.* However, *S. aureus*, KDB-4 and KDB-8 showed lowest MIC (< 0.156 mg ml^{-1}) and MBC (10 mg ml^{-1}) values. Thus, for this bacteria, 4-CF3 and 3-Cl are most effective. For *C. rubrum*, MBC values were > 20 mg ml^{-1} for all the studied KDB compounds but MIC values are minimum (2.5 mg ml^{-1}) for KDB-9.

Compd. code	Gram positive bacteria						Gram positive bacteria						Fungi (yeast)					
	SAL		SA		CR		EA		EC		ST		CA		CG		CN	
	MIC	MBC	MIC	MBC	MIC	MBC	CA	CG	CN	CA	CG	MBC	MIC	MBC	MIC	MBC	MIC	MBC
KDB -1	> 20	> 20	5	> 20	5	> 20	10	> 20	10	> 20	5	> 20	2.5	> 20	2.5	> 20	> 20	> 20
KDB -2	> 20	> 20	10	> 20	1.25	> 20	> 20	> 20	10	> 20	5	> 20	1.25	20	2.5	> 20	> 20	> 20
KDB -3	> 20	> 20	5	> 20	5	> 20	10	> 20	10	> 20	5	> 20	0.312	5	2.5	> 20	0.625	> 20
KDB -4	> 20	> 20	< 0.156	10	10	> 20	20	> 20	20	> 20	20	> 20	5	> 20	5	> 20	5	> 20
KDB -5	> 20	> 20	2.5	> 20	5	> 20	5	> 20	2.5	> 20	5	> 20	2.5	> 20	2.5	> 20	> 20	> 20
KDB -6	> 20	> 20	1.25	20	5	> 20	10	> 20	10	> 20	10	> 20	2.5	> 20	5	> 20	1.25	> 20
KDB -7	> 20	> 20	2.5	> 20	10	> 20	5	> 20	2.5	> 20	2.5	> 20	5	> 20	5	> 20	1.25	> 20
KDB -8	> 20	> 20	< 0.156	10	10	> 20	> 20	> 20	2.5	> 20	5	> 20	0.312	> 20	0.312	> 20	< 0.156	> 20
KDB -9	> 20	> 20	2.5	20	2.5	> 20	10	> 20	5	> 20	10	> 20	2.5	> 20	2.5	> 20	2.5	> 20

Table 6: Antimicrobial activity data (MIC and MBC in mg ml^{-1}) of KDB series compounds against Gram positive bacteria, Gram negative bacteria and fungal strains.

Thus, 2-flouro substitution is most effective for this strain. All the compounds showed varied and moderate MIC values against *E. coli, E. aerogenes* and *S. Typhimurium*. However, MBC values are > 20 for all the compounds. For the fungal strains, MIC and MBC varied from < 0.156 mg ml^{-1} to > 20 mg ml^{-1} and 5 mg ml^{-1} to >20 mg ml^{-1} respectively. Minimum MIC is for KDB-9 containing 2-flouro against *C. neoformans*.

Fused Pyrimidine derivatives (TC, KD and K series)

Table 7 shows the MIC and MBC values of TC series. TC-9 showed minimum value of MIC (> 0.156 mg ml^{-1}) followed by TC-1 (> 0.425 mg ml^{-1}) against *S. albus*. Whereas TC-5, TC-7, TC-8 and TC-10 compounds are more effective against *S. aureu*. For *C. rubrum*, TC-2 and TC-15 showed minimum MIC value of 1.25 mg ml^{-1}. The MBC values are > 20 mg ml^{-1} for all the compounds against *S. albus* and *C. rubrum*. Only TC-7, TC-8 and TC-15 had MBC value of 10 mg ml^{-1}.

Compd. code	Gram positive bacteria						Gram negative bacteria						Fungi (yeast)					
	SAL		SA		CR		EA		EC		ST		CA		CG		CN	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
TC-1	> 0.425	> 20	5	> 20	5	> 20	> 20	> 20	10	> 20	5	> 20	5	> 20	2.5	> 20	> 0.450	> 20
TC-2	> 20	> 20	10	> 20	1.25	> 20	< 0.156	0.300	10	> 20	5	> 20	5	20	2.5	> 20	> 20	> 20
TC-3	> 20	> 20	5	> 20	5	> 20	10	> 20	10	> 20	5	> 20	10	5	2.5	> 20	> 20	> 20
TC-4	> 20	> 20	2.5	> 20	5	> 20	5	> 20	2.5	> 20	5	> 20	2.5	> 20	< 0.156	> 20	> 20	> 20
TC-5	> 20	> 20	< 0.156	20	5	> 20	0.260	> 20	10	> 20	10	> 20	2.5	> 20	5	> 20	2	> 20
TC-6	10	> 20	2.5	> 20	10	> 20	5	> 20	2.5	> 20	2.5	> 20	5	> 20	5	> 20	5	> 20
TC-7	> 20	> 20	< 0.260	10	> 20	> 20	> 20	> 20	2.5	> 20	5	> 20	0.380	> 20	3.5	> 20	< 0.250	> 20
TC-8	> 20	> 20	< 0.156	10	10	> 20	20	> 20	20	> 20	20	> 20	5	> 20	5	> 20	5	> 20

TC-9	> 0.156	> 20	2.5	20	2.5	> 20	10	> 20	5	> 20	10	> 20	2.5	> 20	2.5	> 20	2.5	> 20
TC-10	> 20	> 20	< 0.325	20	5	> 20	< 0.156	> 20	10	> 20	20	> 20	2.5	> 20	5	> 20	1.25	> 20
TC-11	> 20	> 20	1.25	20	5	> 20	15	> 20	10	> 20	10	> 20	0.450	> 20	< 0.200	> 20	1.25	> 20
TC-12	> 20	> 20	5	> 20	2.5	> 20	5	> 20	5	> 20	10	> 20	0.600	> 20	1.25	> 20	1.25	> 20
TC-13	> 20	> 20	10	> 20	5	> 20	10	> 20	< 0.156	> 20	10	> 20	2.5	> 20	2.5	> 20	2.5	> 20
TC-14	> 2.5	> 20	2.5	> 20	2.5	> 20	20	> 20	20	> 20	10	> 20	1.25	> 20	2.5	> 20	2.5	> 20
TC-15	> 20	> 20	2.5	10	1.25	> 20	10	> 20	10	> 20	10	> 20	1.25	> 20	2.5	> 20	< 0.156	> 20
TC-16	5	> 20	10	20	2.5	20	5	> 20	10	> 20	5	> 20	1.25	> 20	0.625	> 20	2.5	> 20

Table 7: Antimicrobial activity data (MIC and MBC in mg ml^{-1}) of TC series compounds against Gram positive bacteria, Gram negative bacterial and fungal strains.

As shown in table 2, TC compounds have same central nucleus but different R_1, R_2 and R_3 groups. TC-9 contains 3, 4-di chloro, $(CH_3)_2CH$- and 4-OCH_3 whereas TC-1 contains 4- chloro, (CH3)2CH- and 4- chloro groups at R_1, R_2 and R_3 positions respectively. Thus, it is observed that when 4- chloro and 4-OCH3 groups are present at R_3 MIC is minimum. In TC-2, TC-5, TC-7, TC-8, TC-10 and TC-15 compounds also, 4-chloro and 4-OCH_3 groups are present at R_3 which causes a decrease in MIC values against *S. aureu* and *C. rubrum.*

Against Gram negative bacterial strains, when R1 is 3- chloro, 4-F and 4-OCH3 groups, compounds are more effective against *E. aerogenes*. TC-13 containing 4-chloro (R1), –CH3 (R2) and 4–Br (R3) shows lowest MIC value against *E. coli* whereas against S. typhimurium, not a single compound was effective. Against *E. coli* and *S. typhimurium*, all the compounds have MBC values > 20 mg ml^{-1}. Only TC-2 has lowest MBC of 0.300 mg ml^{-1} against *E. aerogenes.*

For fungal strains, TC-7 for *C. albicans*, TC-4 and TC-11-CF_3 (R_1) and - chloro (R_3) groups are present at 4- position in compound TC-7 against *C. glabrata* and TC-7 and TC-15 for *C. neoformans* have minimum MIC values. Comparison of different groups at R_1, R_2 and R_3 positions shows that when 4-F group is at R1 position as in TC-4 and TC-15, it is more effective.

This is followed by 4-CF3 (as in TC-7) and 4- chloro (as in TC-11) at R_1 position. In all these four effective compounds, R_3 is 4- chloro or 4-OCH_3. The R_2 position is found to be not very effective. However, all these TC compounds have > 20 mg ml^{-1} MBC values.

Table 8 shows MIC and MBC values of KD series against different bacterial and fungal strains. For this series also, MBC values are not very significant against all the bacterial strains. However, among the three fungal strains, against *C. glabrata*, KD-7 to KD-12 compounds has MBC value of 10 mg ml-1. For other two strains, values are > 20 mg ml^{-1} for all the compounds.

Compd. Code	Gram positive bacteria						Gram negative bacteria						Fungi (yeast)					
	SAL		SA		CR		EA		EC		ST		CA		CG		CN	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
KD-1	> 10	> 20	2.5	> 20	20	> 20	10	> 10	2.5	> 20	2.5	> 20	10	> 20	5	> 20	2.5	> 20
KD-2	> 20	> 20	2.5	> 20	10	> 20	5	> 20	2.5	> 20	2.5	> 20	5	> 20	5	> 20	1.25	> 20
KD-3	> 20	> 20	10	10	10	> 20	> 20	> 20	2.5	> 20	5	> 20	0.280	> 20	10	> 20	> 20	> 20
KD-4	< 0.156	> 20	10	10	10	> 20	20	> 20	20	> 20	20	> 20	5	> 20	5	> 20	5	> 20
KD-5	> 20	> 20	2.5	20	10	< 20	10	> 20	5	> 20	10	> 20	2.5	> 20	5	> 20	2.5	> 20
KD-6	> 10	> 20	< 0.156	10	5	> 20	> 20	> 20	10	> 20	20	> 20	2.5	> 20	0.500	> 20	1.25	> 20
KD-7	5	> 20	1.25	20	5	> 20	5	> 20	10	> 20	10	> 20	0.350	> 20	< 0.156	10	1.25	> 20
KD-8	> 20	> 20	5	> 20	2.5	> 20	5	> 20	5	> 20	10	> 20	2.5	> 20	1.25	10	1.25	> 20
KD-9	< 0.156	> 20	10	> 20	5	> 20	10	> 20	20	> 20	2.5	> 20	10	> 20	2.5	10	2.5	> 20
KD-10	> 20	> 20	2.5	> 20	2.5	> 20	20	> 20	20	> 20	10	> 20	1.25	> 20	2.5	10	2.5	> 20
KD-11	> 20	> 20	0.312	10	1.25	> 20	10	> 20	10	> 20	10	> 20	1.25	> 20	2.5	10	10	> 20
KD-12	> 20	> 20	0.312	20	0.625	20	5	> 20	10	> 20	5	> 20	1.25	> 20	0.625	10	2.5	> 20

Table 8: Antimicrobial activity data (MIC and MBC in mg ml^{-1}) of KD series compounds against Gram positive bacteria, Gram negative bacteria and fungal strains.

KD-4, KD-6, KD-9, KD-11 and KD-12 compounds show lowest MIC values against Gram positive bacterial strains. For fungal strains, compounds KD-3, KD-6, KD-7 and KD-12 are most effective. However, all the compounds had little effect against Gram negative bacterial strains.

Table 2 shows the general structure of these derivatives along with different R groups. KD-4 and KD-9 containing 4-F and 3-OCH_3 groups, affect *S. albus.* Against *S. aureus*, KD-6, KD-11 and KD-12 containing 3- chloro, -4CH_3 and 3, 4, 5-tri OCH_3 groups are found to be most effective.

Against Gram negative bacteria, overall methoxy and chloro groups at different positions are found to be a little bit effective.

Against fungal strains, 4- chloro and 3-Br containing compounds KD-3 and KD-7 are effective against *C. albicans*. However, *C. glabrata* is most inhibited by compound KD-6, KD-7 and KD-12 containing 3-Cl, 3-Br and 3,4,5-tri OCH_3 respectively. Against *C. neoformans,* some compounds show minimum value of MIC to be 2.5 mg ml^{-1}. Thus, for KD series, the selected Gram negative bacteraia are most resistant. Among the studied Gram positive bacteria and fungal strains, *C. rubrum* and *C. neoformans* are most resistant for this series.

Table 9 shows the antimicrobial activity data of tetrazolopyrimidine derivatives (K-1 to K-14) against bacterial as well as fungal strains. It is evident from table 4 that against *S. albus*, MIC value is 5 mg ml^{-1} for K-13 which is lowest as comparison to other compounds.

Compd. Code	Gram positive bacteria						Gram negative bacteria						Fungi (yeast)					
	SAL		SA		CR		EA		EC		ST		CA		CG		CN	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
K-1	> 20	> 20	5	> 20	5	> 20	10	> 20	10	> 20	5	> 20	2.5	> 20	2.5	> 20	> 20	> 20
K-2	10	> 20	< 0.156	> 20	10	> 20	> 20	> 20	1.25	> 20	5	> 20	5	20	2.5	> 20	> 20	> 20
K-3	> 20	> 20	5	> 20	5	> 20	10	> 20	10	> 20	5	> 20	0.310	5	2.5	> 20	< 0.156	> 20
K-4	> 20	> 20	2.5	> 20	5	> 20	< 0.156	> 20	2.5	> 20	5	> 20	2.5	> 20	2.5	> 20	> 20	> 20
K-5	> 20	> 20	1.25	20	5	> 20	10	> 20	10	> 20	10	> 20	2.5	> 20	5	> 20	1.25	> 20
K-6	> 20	> 20	< 0.156	> 20	10	> 20	5	> 20	2.5	> 20	2.5	> 20	5	> 20	5	> 20	1.25	> 20
K-7	> 20	> 20	5	10	10	> 20	> 20	> 20	2.5	> 20	5	> 20	0.325	> 20	0.360	> 20	0.250	> 20
K-8	> 20	> 20	2.5	10	10	> 20	20	> 20	20	> 20	20	> 20	5	> 20	5	> 20	5	> 20
K-9	2.5	> 20	2.5	20	2.5	> 20	10	> 20	5	> 20	5	> 20	2.5	> 20	2.5	> 20	1.5	> 20
K-10	> 20	> 20	> 20	0.250	5	> 20	> 20	> 20	10	> 20	20	> 20	2.5	> 20	0.600	> 20	2.5	> 20
K-11	> 20	> 20	10	> 20	5	> 20	< 0.156	> 20	10	> 20	10	> 20	15	> 20	< 0.156	10	5	> 20
K-12	> 20	> 20	5	> 20	2.5	> 20	5	> 20	5	> 20	10	> 20	5	> 20	1.25	10	1.25	> 20
K-13	5	> 20	2.5	> 20	5	> 20	10	> 20	20	> 20	10	> 20	2.5	> 20	2.5	10	2.5	> 20
K-14	> 20	> 20	10	> 20	2.5	> 20	20	> 20	20	> 20	10	> 20	10	> 20	2.5	10	2.5	> 20

Table 9: Antimicrobial activity data (MIC and MBC in mg ml^{-1}) of KD series compounds against Gram positive bacteria, Gram negative bacteria and fungal strains.

Table 2 shows the different substitutions in these compounds. Thus, different substitution affect different strain differently. So, 2-OCH_3 group present in K-13, is most effective MIC values are minimum for K-2 and K-6 against *S. aureus*. Both these compounds again contain methoxy groups at different positions. Thus, methoxy group is most effective against *S. aureus* also. For *C. rubrum*, 2.5 mg ml^{-1} MIC is found to for few compounds; K-9, K-12 and K-14. Thus, for this bacterial strain, 3-Br, 2, 5-di OCH_3 and 2-Cl groups are found to be most effective.

Against different Gram negative bacterial strains, K-4 and K-11 compounds are more effective against *E. aerogenes.* Other compounds had no signifacnt effect against *E. coli* and *S. typhimurium.* Thus, 4-F and 3-OCH_3 are most effective against *E. aerogenes.*

Against fungal strains, compounds, only K-3 and K-11 compounds exhibited minimum MIC value of < 0.156 against *C. neoformans* and *C. glabrata* respectively. K-3 also has lowest MIC values (0.310 mg ml^{-1}) against *C. albicans.* Thus, 4-chloro (as in K-3) and 3-OCH_3 (as in K-11) groups are most effective against *C. neoformans* and *C. glabrata* respectively.

Table 10 shows the MIC and MBC values of imidazothiazole derivatives (TC-1 to TC-9) against nine bacterial and fungal strains. It is observed that among the three Gram positive bacteria, TP-2 and TP-3 against *S. albus* and TP-7 and TP-8 compounds (2.5 mg ml^{-1}) against *S. aureus* showed lowest MIC as compared to other compounds. Against *C. rubrum*, TP-7 has minimum MIC of 1.25 mg ml^{-1}. The general structure of these compounds of TP series along with different substitutions (R) are given in figure 4. Thus, 4-chloro and 4-bromo are most effective against *S. albus,* 2,4-di chloro and 4-NO_2 against *S. aureus* and 2,4-di chloro against *C. rubrum* gives better results. In case of Gram negative bacteria, not a single compound gave significant MIC against E.

coli. For Whereas TP-7 compound also exhibited better results for two fungal strains. The MBC values are > 20 mg ml^{-1} for all the compounds against *S. albus* and *S. aureus.* However, TP-7 having 2, 4-dichloro substitution, exhibited lowest MBC against *C. rubrum.*

In Gram negative bacterial strains, TP-8 having 4-NO_2 shows the lowest MIC value (2.5 mg ml^{-1}) against *E. aerogenes* and *S. typhimurium.* For *S. typhimurium*, TP-2 and TP-3 also show lowest MIC values (2.5 and 1.25 mg ml^{-1}). Thus, again 4-Chloro and

Compd. Code	Gram positive bacteria						Gram negative bacteria						Fungi(yeast)					
	SAL		SA		CR		EA		EC		ST		CA		CG		CN	
	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
TP-1	> 20	> 20	10	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20
TP-2	5	> 20	10	> 20	5	> 20	5	> 20	> 20	> 20	2.5	> 20	> 20	> 20	> 20	> 20	> 20	> 20
TP-3	5	> 20	5	> 20	2.5	> 20	5	> 20	> 20	> 20	1.25	> 20	> 20	> 20	> 20	> 20	> 20	> 20
TP-4	> 20	> 20	> 20	> 20	20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20
TP-5	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20
TP-6	> 20	> 20	> 20	> 20	20	> 20	5	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20
TP-7	> 20	> 20	2.5	> 20	1.25	1.25	5	> 20	> 20	> 20	5	> 20	2.5	5	1.25	5	> 20	> 20
TP-8	20	> 20	2.5	> 20	2.5	> 20	2.5	> 20	> 20	> 20	2.5	> 20	> 20	> 20	> 20	> 20	> 20	> 20
TP-9	20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20	> 20

Table 10: Antimicrobial activity data (MIC and MBC in mg ml^{-1}) of TP series compounds against Gram positive bacteria, Gram negative bacteria and fungal strains.

4-bromo groups are most effective. For *E. coli,* not a single compound has minimum MIC value. Further, MBC values for all TP compounds are > 20 mg ml^{-1}.

Against fungal strains, onlt TP-7 containing 2,4-dichloro groups exhibited better results of MIC and MBC against *C. albicans* and *C. glabrata* fungal strains. Other compounds have > 20 mg ml^{-1} values for both MIC and MBC against these strains. For *C. neoformans,* these TP series compounds are not effective.

Thus, among the studied bacterial and fungal strains, *E. coli* and *C. neoformans* are most resistant for this series.

Conclusion

Thus, it is concluded that some of the studied compounds in different series can be used as a lead molecule for further biological study, since these compounds exhibited better activity against different strains.

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