Synthesis, Spectral Characterization, and Biological Screening of Pyrimidine-Linked Thioxotetrahydropyrimidine Carboxamides

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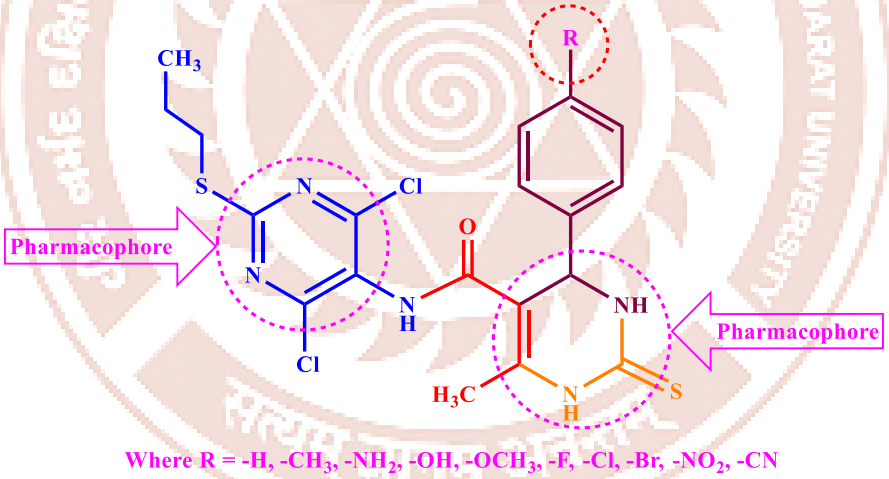
Abstract:

A novel series of compounds (5a-5j) derived from *N*-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-6-methyl-4-substituted phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide was synthesized and systematically characterized. The synthesized molecules were confirmed through spectroscopic techniques including FT-IR, 1H-NMR, 13C-NMR, and mass spectrometry, along with elemental analysis, to validate their structural features. Antimicrobial evaluation was carried out to explore the biological potential of these derivatives. The compounds 5d and 5f exhibited promising antibacterial activity against selected Gram-positive and Gram-negative strains, with certain derivatives showing enhanced potency compared to standard drugs. Furthermore, antifungal assays indicated moderate to good inhibitory effects against the tested fungal pathogens. Structure–activity relationship (SAR) analysis suggested that the nature and position of substituents on the phenyl ring significantly influenced the antimicrobial efficacy. Overall, the study demonstrates that this scaffold holds considerable potential for the development of new antibacterial and antifungal agents.

Graphical Abstract:



Introduction:

Pyrimidine is found as a core structure in a large variety of compounds that exhibit important biological activity.[1] Pyrimidines, being an integral part of DNA and RNA in it, play an essencial role in several biological processes and have considerable chemical and pharmacological importance.[2] Numerous researchers have explored the synthetic pathways and investigated the diverse biological activities of these compounds. These efforts have culminated in the synthesis and pharmacological assessment of dihydropyrimidines (DHPMs).[3],[4]

The 1,4-dihydropyridine structure is a crucial component in several antihypertensive drugs [5,6], such as nitrodipine[7] and nifedipine [8], which act by blocking calcium channels.

More recently, compounds featuring the 1,4-dihydropyridine ring have also demonstrated promising antitubercular [9,10,11] and anticancer properties [12]. This class of compounds was originally synthesized by Hantzsch in 1886 through a multicomponent reaction approach [13, 14.]

Among these, substituted pyrimidines bearing thioxotetrahydropyrimidine moieties have garnered considerable interest for their potential as therapeutic agents, owing to their structural versatility and ability to interact with diverse biological targets. In the ongoing search for novel antimicrobial agents, especially in light of increasing resistance to conventional antibiotics, the design and synthesis of hybrid molecules that incorporate multiple pharmacophores have emerged as a promising strategy.

In this study, we report the synthesis of a novel series of compounds (5a–5j) based on the N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-6-methyl-4-substituted phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide scaffold. To assess the biological relevance of the synthesized derivatives, antimicrobial screening was performed against selected Gram-positive and Gram-negative bacterial strains, as well as fungal pathogens. Notably, compounds 5d and 5f exhibited significant antibacterial activity, in some cases surpassing the efficacy of standard drugs. The antifungal evaluation also revealed moderate to good inhibitory effects, further highlighting the therapeutic promise of these molecules.

A structure–activity relationship (SAR) analysis was conducted to examine the influence of various substituents on the phenyl ring, revealing that both the nature and position of these groups played a critical role in modulating antimicrobial activity. These findings support the potential of pyrimidine-linked thioxotetrahydropyrimidine carboxamides as lead compounds for the development of new antimicrobial agents.

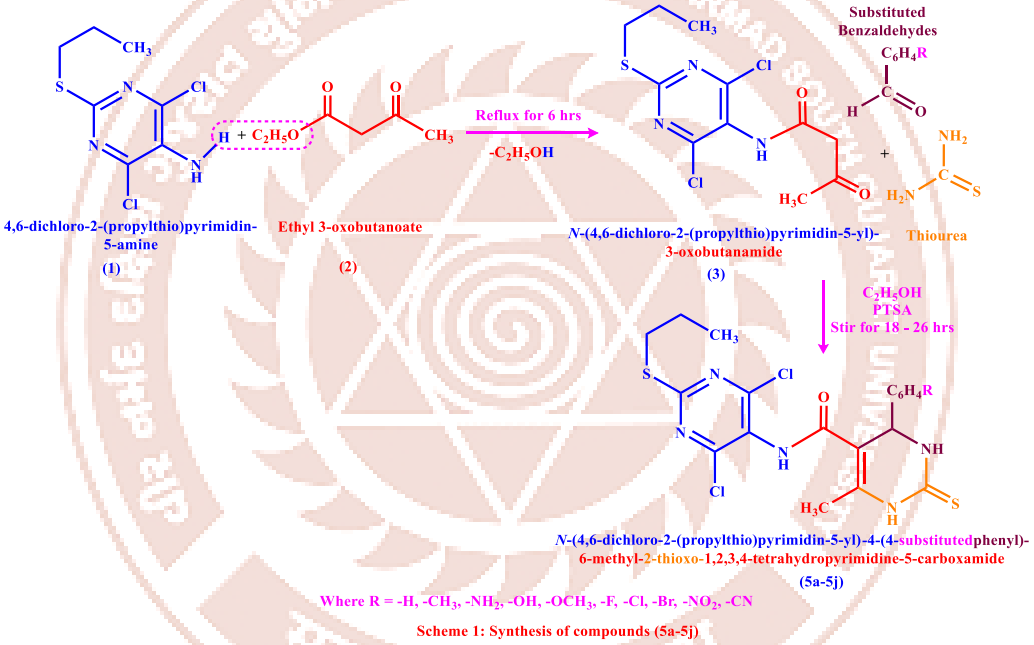
Material and Experimental Methods:

Synthesis of *N*-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-3-oxobutanamide (3):

4,6-Dichloro-2-(propylthio)pyrimidin-5-amine (1) (0.01 M) was reacted with ethyl 3-oxobutanoate (2) (0.01 M) under reflux for about six hours in a 250 mL round-bottom flask. During the process, the generated ethanol was removed by heating the reaction mixture in a water bath. Upon completion, the reaction mixture was cooled, leading to the separation of crude crystals. These crystals were purified by stirring with chilled diethyl ether for approximately 10 minutes using a mechanical stirrer. The mixture was then kept undisturbed for 20 minutes, followed by filtration, which afforded the purified product, N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-3-oxobutanamide (3) [22].

Synthesis of N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-4-(4-substitutedphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5a-5j):

A reaction mixture comprising N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-3-oxobutanamide (3) (0.005 M), thiourea (0.0075 M), and the appropriate aldehyde (0.005 M) was stirred in 10 mL of ethanol in the presence of a catalytic quantity of p-toluenesulfonic acid (PTSA) for 18–26 hours. Reaction progress was monitored by thin-layer chromatography (TLC) using a solvent system of petroleum ether and ethyl acetate (70:30, v/v). After completion, the mixture was refrigerated, and the precipitated solid was separated by filtration. The collected solid was washed thoroughly with water to remove unreacted thiourea and subsequently dried. The crude material was purified by recrystallization from ethanol to afford the final compounds **(5a–5j)**, as illustrated in **Scheme 1** [22].



Scheme 1: Synthesis of compounds (5a-5j)

RESULT AND DISCUSSION:

SPECTRAL DATA:

[1]N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-6-methyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5a):

FT-IR (KBr, cm^{-1}): 731 (>C-Cl), 1237 (>C-N of pyrimidine ring), 1330 ((>C=S stretching), 1532 (>C=N of pyrimidine ring), 1656 (>C=O stretching in -CONH- group), 2980 (>C-H of methyl group), 3034 (>C-H stretching of the pyrimidine ring), 3252 (>N-H of -CONH-). **^{1}H-NMR** (DMSO-d_6 δ ppm): 0.97 (s, -CH_3), 1.40 (m,-CH_2), 2.24 (s, -CH_3), 3.15 (t, -CH_2), 5.40 (s, - CH), 7.20-7.32(m, Ar-H), 9.22 (s, -NH), 9.80 (s, -NH), 9.98 (s, -NH). **^{13}C-NMR** (100 MHz, DMSO-d_6 δ ppm): 173.9, 162.8, 162.2, 159.2, 150.2, 139.7, 127.4, 126.9, 126.0, 106.4,

57.9, 38.3, 22.6, 17.9, 12.9. **m/z:** 467.04 M^+ calculated, 465.4 found. Elemental Analysis: $C_{19}H_{19}Cl_2N_5OS_2$, C, 48.72; H, 4.09; Cl, 15.14; N, 14.95; O, 3.42; S, 13.69.

[2]N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-4-(4-methylphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5b):

FT-IR (KBr, cm-1): 725 (>C-Cl), 1211 (>C-N of pyrimidine ring), 1340 ((>C=S stretching), 1523 (>C=N of pyrimidine ring), 1655 (>C=O stretching in -CONH- group), 2990 (>C-H of methyl group), 3040 (>C-H stretching of the pyrimidine ring), 3265 (>N-H of -CONH-). 1H-NMR (DMSO-d6 δ ppm): 0.98 (s, -CH3), 1.43 (m,-CH2), 2.17 (s, -CH3), 2.15 (s, -CH3), 3.11 (t, -CH2), 5.37 (s, -CH), 7.09-7.21(m, Ar-H), 9.25 (s, -NH), 9.76 (s, -NH), 9.99 (s, -NH). 13C-NMR (100 MHz, DMSO-d6 δ ppm): 174.1, 163.6, 162.8, 158.2, 151.2, 140.2, 139.7, 136.7, 128.0, 126.4, 106.2, 58.9, 38.9, 21.9, 21.1, 17.4, 13.5. m/z: 481.06 M+ calculated, 480.7 found. Elemental Analysis: C20H21Cl2N5OS2, C, 49.79; H, 4.39; Cl, 14.70; N, 14.52; O, 3.32; S, 13.29.

[3]N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-4-(4-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5c)

FT-IR (KBr, cm-1): 722 (>C-Cl), 1215 (>C-N of pyrimidine ring), 1250 ((>C-O-C stretching),1345 ((>C=S stretching), 1529 (>C=N of pyrimidine ring), 1640 (>C=O stretching in -CONH- group), 2983 (>C-H of methyl group), 3022 (>C-H stretching of the pyrimidine ring), 3260 (>N-H of -CONH-). 1H-NMR (DMSO-d6 ppm): 1.05 (s, -CH3), 1.36 (m,-CH2), 2.21 (s, -CH3), 3.18 (t, -CH2), 3.85 (s, -OCH3), 5.45 (s, -CH), 6.71-7.22 (m, Ar-H), 9.27 (s, -NH), 9.83 (s, -NH), 9.90 (s, -NH).13C-NMR (100 MHz, DMSO-d6 δ ppm):173.1, 163.7, 162.4, 159.5, 158.6, 150.3, 139.5, 134.2, 124.3, 115.1, 107.0, 58.9, 55.9, 38.2, 21.7, 17.1, 13.9. Elemental Analysis: C, 48.19; H, 4.25; Cl, 14.22; N, 14.05; O, 6.42; S, 12.86. Chemical Formula: C20H21Cl2N5O2S2

[4] 4-(4-cyanophenyl)-N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5d)

FT-IR (KBr, cm-1): 722 (>C-Cl), 1215 (>C-N of pyrimidine ring), 1250 ((>C-O-C stretching),1345 ((>C=S stretching), 1529 (>C=N of pyrimidine ring), 1640 (>C=O stretching in -CONH- group), 2983 (>C-H of methyl group), 3022 (>C-H stretching of the pyrimidine ring), 3260 (>N-H of -CONH-). **1H-NMR** (DMSO-d6 ppm): 1.05 (s, -CH3), 1.36 (m,-CH2), 2.21 (s, -CH3), 3.18 (t, -CH2), 3.85 (s, -OCH3), 5.45 (s, -CH), 6.71-7.22 (m, Ar-H), 9.27 (s, -NH),

9.83 (s, -NH), 9.90 (s, -NH) .**^{13}C-NMR** (100 MHz, DMSO-d_6 δ ppm): 173.1, 163.7, 162.4, 159.5, 158.6, 150.3, 139.5, 134.2, 124.3, 115.1, 107.0, 58.9, 55.9, 38.2, 21.7, 17.1, 13.9. Elemental Analysis: C, 48.68; H, 3.68; Cl, 14.37; N, 17.03; O, 3.24; S, 12.99. Chemical Formula: $C_{20}H_{18}Cl_2N_6OS_2$

[5] N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-6-methyl-4-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5e)

FT-IR (KBr, cm-1): 715 (>C-Cl), 1221 (>C-N of pyrimidine ring), 1357 ((>C=S stretching), 1529 (>C=N of pyrimidine ring), 1644 (>C=O stretching in -CONH- group), 2986 (>C-H of methyl group), 2268 (-CN streching), 3023 (>C-H stretching of the pyrimidine ring), 3277 (>N-H of -CONH-). 1H-NMR (DMSO-d6 ppm): 1.03 (s, -CH3), 1.39 (m,-CH2), 2.23 (s, -CH3), 3.08 (t, -CH2), 5.42 (s, -CH), 7.45-7.78(m, Ar-H), 9.27 (s, -NH), 9.84 (s, -NH), 9.98 (s, -NH). 13C-NMR (100 MHz, DMSO-d6 δ ppm): 174.1, 163.8, 162.7, 159.5, 151.1, 147.8, 140.1, 132.5, 127.2, 118.2, 111.1, 106.8, 58.2, 38.3, 21.2, 17.5, 13.2. Elemental Analysis: C, 44.45; H, 3.53; Cl, 13.81; N, 16.37; O, 9.35; S, 12.49. Chemical Formula: C19H18Cl2FN5OS2

[6] 4-(4-bromophenyl)-N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5f)

FT-IR (KBr, cm-1): 680 (>C-Br stretching),730 (>C-Cl), 1230 (>C-N of pyrimidine ring), 1367 ((>C=S stretching), 1533 (>C=N of pyrimidine ring), 1644 (>C=O stretching in CONH-group), 2972 (>C-H of methyl group), 3033 (>C-H stretching of the pyrimidine ring), 3280 (>N-H of -CONH). 1H-NMR (DMSO-d6 ppm): 1.07 (s, -CH3), 1.40 (m,-CH2), 2.11 (s, -CH3), 3.08 (t, -CH2), 5.38 (s, -CH), 7.15-7.80(m, Ar-H), 9.27 (s, -NH), 9.84 (s, -NH), 9.94 (s, -NH), 13C-NMR (100 MHz, DMSO-d6 δ ppm):174.7, 163.4, 162.8, 159.4, 150.8, 142.4, 139.9, 131.4, 129.3, 121.4, 106.5, 58.7, 38.3, 21.6, 17.6, 13.4. Elemental Analysis: C, 41.70; H, 3.32; Br, 14.60; Cl, 12.95; N, 12.80; O, 2.92; S, 11.72. Chemical Formula: C19H18BrCl2N5OS2

[7] 4-(4-chlorophenyl)-N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5g)

FT-IR (KBr, cm^{-1}): 731 (>C-Cl), 1234 (>C-N of pyrimidine ring), 1334 ((>C=S stretching), 1540 (>C=N of pyrimidine ring), 1660 (>C=O stretching in -CONH- group), 2985 (>C-H of methyl group), 3040 (>C-H stretching of the pyrimidine ring), 3252 (>N-H of -CONH-). **1H-NMR** (DMSO-d6 ppm):1.06 (s, -CH_3), 1.46 (m,-CH_2), 2.11 (s, -CH_3), 3.15 (t, -CH_2), 5.50 (s, -

CH), 7.21-7.42(m, Ar-H), 9.23 (s, -NH), 9.88 (s, -NH), 9.98 (s, -NH).**^{13}C-NMR** (100 MHz, DMSO-d_6 δ ppm): 174.1, 163.2, 162.6, 159.2, 150.0, 141.9, 132.6, 139.7, 128.5, 126.5, 106.4, 58.9, 38.9, 21.3, 17.4, 13.8. Elemental Analysis: C, 45.38; H, 3.61; Cl, 21.15; N, 13.93; O, 3.18; S, 12.75. Chemical Formula: $C_{19}H_{18}Cl_3N_5OS_2$

[8] N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5h)

FT-IR (KBr, cm^{-1}): 739 (>C-Cl), 1243 (>C-N of pyrimidine ring), 1253 ((>C-O-C stretching),1333 ((>C=S stretching), 1538 (>C=N of pyrimidine ring), 1655 (>C=O stretching in -CONH- group), 2982 (>C-H of methyl group), 3043 (>C-H stretching of the pyrimidine ring), 3252 (>N-H of -CONH-), 3390 (-OH stretching). **1H-NMR** (DMSO-d6 ppm):1.01 (s, -CH_3), 1.41 (m,-CH_2), 2.12 (s, -CH_3), 3.14 (t, -CH_2), 3.72 (s, -OCH_3), 5.45 (s, -CH), 6.90-7.21(m, Ar-H), 9.26 (s, -NH), 9.85 (s, -NH), 9.92 (s, -NH), 9.98 (s, -NH).**^{13}C-NMR** (100 MHz, DMSO-d_6 δ ppm):174.5, 163.7, 162.4, 159.3, 147.3, 146.7, 150.3, 139.9, 136.5, 118.7, 115.9, 112.4, 106.8, 58.4, 56.8, 38.5, 21.6, 17.9, 13.4. Elemental Analysis: C, 46.70; H, 4.11; Cl, 13.78; N, 13.61; O, 9.33; S, 12.46. Chemical Formula: $C_{20}H_{21}Cl_2N_5O_3S_2$

[9] N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5i)

FT-IR (KBr, cm^{-1}): 739 (>C-Cl), 1243 (>C-N of pyrimidine ring), 1253 ((>C-O-C stretching),1333 ((>C=S stretching), 1538 (>C=N of pyrimidine ring), 1655 (>C=O stretching in -CONH- group), 2982 (>C-H of methyl group), 3043 (>C-H stretching of the pyrimidine ring), 3252 (>N-H of -CONH-), 3390 (-OH stretching). **1H-NMR** (DMSO-d6 ppm):1.01 (s, CH_3), 1.41 (m,-CH_2), 2.12 (s, -CH_3), 3.14 (t, -CH_2), 3.72 (s, -OCH_3), 5.45 (s, -CH), 6.90-7.21(m, Ar-H), 9.26 (s, -NH), 9.85 (s, -NH), 9.92 (s, -NH), 9.98 (s, -NH).**^{13}C-NMR** (100 MHz, DMSO-d_6 δ ppm):174.5, 163.7, 162.4, 159.3, 147.3, 146.7, 150.3, 139.9, 136.5, 118.7, 115.9, 112.4, 106.8, 58.4, 56.8, 38.5, 21.6, 17.9, 13.4. Elemental Analysis: C, 46.70; H, 4.11; Cl, 13.78; N, 13.61; O, 9.33; S, 12.46. Chemical Formula: $C_{20}H_{21}Cl_2N_5O_3S_2$

[10] N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-4-(4-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxamide (5j)

FT-IR (KBr, cm^{-1}): 730 (>C-Cl), 1232 (>C-N of pyrimidine ring), 1367 ((>C=S stretching), 1544 (>C=N of pyrimidine ring), 1635 (>C=O stretching in -CONH- group), 2967 (>C-H of methyl group), 3033 (>C-H stretching of the pyrimidine ring), 3280 (>N-H of -CONH-), 3401 (-OH stretching). **1H-NMR** (DMSO-d6 ppm):1.04 (s, -CH_3), 1.45 (m,-CH_2), 2.18 (s, -CH_3), 3.08 (t, -CH_2), 5.49 (s, -CH), 6.75-7.05(m, Ar-H), 9.05 (s, -OH) 9.24 (s, -NH), 9.89 (s, -NH),

9.95 (s, -NH). **^{13}C-NMR** (100 MHz, DMSO-d_6 δ ppm):174.1, 163.2, 162.2, 159.2, 156.8, 150.8, 139.8, 135.4, 126.4, 115.3, 106.4, 58.9, 38.9, 21.4, 17.5, 13.6. Elemental Analysis: C, 47.11; H, 3.95; Cl, 14.64; N, 14.46; O, 6.61; S, 13.24. Chemical Formula: $C_{19}H_{19}Cl_2N_5O_2S_2$

ANTIMICROBIAL STUDIES:

The synthesized compounds **5a–5j** were screened for their in vitro antibacterial activity against two Gram-positive and two Gram-negative bacterial strains using the serial dilution method [23]. For comparison, **Norfloxacin, Ampicillin, and Ciprofloxacin** were employed as antibacterial reference drugs, while **Nystatin and Griseofulvin** were used as antifungal standards. The minimum inhibitory concentration (MIC) values are summarized in **Table 1.**

Compound **5a** (phenyl unsubstituted derivative) and **5b (methyl group** at the 4-position of the phenyl ring) exhibited moderate antimicrobial activity. Introduction of a **para-amino group (5c)** significantly enhanced activity, showing good antibacterial potency against both Gram-positive (S. aureus, S. pyogenes) and Gram-negative (E. coli, P. aeruginosa) strains, in addition to improved antifungal efficacy against C. albicans, A. niger, and A. clavatus.

Compound **5d,** bearing a **hydroxyl group** at the para-position, demonstrated excellent showing good antibacterial potency against both Gram-positive (S. aureus, S. pyogenes) and Gram-negative (E. coli, P. aeruginosa) strains, in addition to excellent antifungal efficacy against C. albicans, A. niger, and A. clavatus. The **para-methoxy derivative (5e)** was moderately active against S. aureus and P. aeruginosa, with additional moderate activity against C. albicans. The **fluoro-substituted analogue (5f)**, an electron-withdrawing substituent, enhanced antimicrobial activity substantially, showing marked antibacterial effects against both Gram-positive and Gram-negative bacteria, together with notable antifungal activity against C. albicans, A. niger, and A. clavatus.

Compound **5g**, containing a **chloro substituent**, exhibited moderate antibacterial activity against S. aureus and S. pyogenes, along with moderate antifungal action against A. niger. **The bromo analogue (5h)**, shows marked antibacterial effects against S. aureus and P. aeruginosa, together with good antifungal activity against C. albicans. The **nitro derivative (5i)** showed good inhibition of S. aureus and shows moderate antifungal activity against A. niger. Finally, the **cyano-substituted compound (5j)** exhibited good antibacterial activity against S. aureus, moderate activity against E. coli, and moderate antifungal activity against A. clavatus.

Table 1: Antimicrobial activity of compounds 5a to 5j

Compounds	Minimum Bactericidal Concentration (µg/ml)				Minimum Fungicidal Concentration (µg/ml)		
	Gram positive organisms		Gram negative organisms				
	S. aureus	*S. pyogenes*	*E. coli*	*P. aeruginosa*	*C. albicans*	*A. niger*	*A. clavatus*
5a (R = -H)	500	500	500	500	500	500	500
5b (R = -CH_3)	500	500	500	500	500	500	500
5c (R = -NH_2)	250	250	350	200	250	200	150
5d (R = -OH)	200	150	200	250	250	200	150
5e (R = -OCH_3)	200	500	500	300	500	250	500
5f (R = -F)	150	100	200	150	200	100	150
5g (R = -Cl)	200	250	500	500	500	250	500
5h (R = Br)	200	500	500	250	250	500	500
5i (R = -NO_2)	250	500	500	250	500	250	500
5j (R = -CN)	250	500	250	500	500	500	250
Norfloxacin	50	50	50	50	-	-	-
Ciprofloxacin	50	50	50	50	-	-	-
Ampicillin	50	50	50	50	-	-	-
Nystatin-B	-	-	-	-	100	100	100
Gresiofulvin	-	-	-	-	100	100	100

CONCLUSION:

A **series of ten novel compounds (5a–5j)** was synthesized through a multicomponent reaction involving *N-(4,6-dichloro-2-(propylthio)pyrimidin-5-yl)-3-oxobutanamide*, thiourea, and a variety of aldehydes. The structures of the synthesized compounds were confirmed by **FT-IR, ^{1}H-NMR, ^{13}C-NMR, and elemental analysis**. All derivatives were subsequently screened for their antibacterial and antifungal properties. Among them, **compound 5d**, incorporating a **para-hydroxyl group** on the phenyl ring, exhibited remarkable antibacterial activity against both **Gram-positive bacteria (*S. aureus, S. pyogenes*)** and **Gram-negative strains (*E. coli, P. aeruginosa*)**. It also displayed enhanced antifungal activity against ***C. albicans, A. niger,* and *A. clavatus***. Likewise, **compound 5f**, featuring a **para-fluoro substituent**, emerged as the most potent antibacterial agent of the series, showing broad-spectrum inhibition against both Gram-positive and Gram-negative bacteria, while also demonstrating strong antifungal activity against the same fungal strains. Overall, the synthesized compounds exhibited **good to moderate antimicrobial activity**, with some derivatives being selectively active against particular strains, while others showed dual

antibacterial and antifungal potential. Furthermore, the **cytotoxicity and antimalarial activity** of the synthesized series were also evaluated to explore their therapeutic relevance.

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