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Recent advances in the synthesis and biological activity studies of pyridine and pyrimidine derivatives: A review

Piridin ve pirimidin türevlerinin sentezi ve biyolojik aktivite çalişmalarindaki son gelişmeler: Bir inceleme

Gönül Bükülmez[1], Rahmi Kasımoğulları[1]*

[1]Department of Chemistry, Faculty of Arts and Sciences, Kütahya Dumlupınar University, Kütahya, Türkiye.
gonul.bukulmez@dpu.edu.tr, rahmi.kasimogullari@dpu.edu.tr

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Abstract

Pyridine and pyrimidine derivatives are aromatic heterocyclic compounds containing one or more nitrogen atoms and have a wide range of applications in modern drug design and development. Their ability to interact at the molecular level, pharmacophore properties, and bioavailability potential make them highly suitable candidates for various therapeutic targets. These derivatives, which can exhibit pharmacological effects such as antibacterial, antifungal, antiviral, anticancer, and anti-inflammatory, play a critical role in the development of molecules with multiple mechanisms of action. Recent studies show that these heterocyclic skeletons can be optimized by chemical modifications to increase their selectivity and efficacy against biological targets. This review discusses innovative methods for the synthesis of pyridine and pyrimidine derivatives, structural diversity strategies, and biological activities of these compounds in vitro and in vivo. Furthermore, recent scientific advances on the mechanisms of action of these compounds in biological systems are discussed, and perspectives that will contribute to future drug discovery efforts are put forward.

Keywords: Pyridine, Pyrimidine, Heterocyclic, Drugs, Biological Activity

Öz

Piridin ve pirimidin türevleri, bir veya daha fazla azot atomu içeren aromatik heterosiklik bileşiklerdir ve modern ilaç tasarımı ve geliştirilmesinde geniş bir uygulama alanına sahiptir. Moleküler düzeyde etkileşime girme yetenekleri, farmakofor özellikleri ve biyoyararlanım potansiyelleri, onları çeşitli terapötik hedefler için oldukça uygun adaylar haline getirmektedir. Antibakteriyel, antifungal, antiviral, antikanser ve anti-inflamatuar gibi farmakolojik etkiler gösterebilen bu türevler, çoklu etki mekanizmalarına sahip moleküllerin geliştirilmesinde kritik bir rol oynamaktadır. Son çalışmalar, bu heterosiklik iskeletlerin biyolojik hedeflere karşı seçiciliklerini ve etkinliklerini artırmak için kimyasal modifikasyonlarla optimize edilebileceğini göstermektedir. Bu derlemede, piridin ve pirimidin türevlerinin sentezi için yenilikçi yöntemler, yapısal çeşitlilik stratejileri ve bu bileşiklerin in vitro ve in vivo biyolojik aktiviteleri tartışılmaktadır. Ayrıca, bu bileşiklerin biyolojik sistemlerdeki etki mekanizmalarına ilişkin son bilimsel gelişmeler tartışılmakta ve gelecekteki ilaç keşif çabalarına katkıda bulunacak perspektifler ortaya konmaktadır.

Anahtar kelimeler: Piridin, Pirimidin, Heterosiklik, İlaçlar, Biyolojik Aktivite

1 Introduction

Heterocyclic compounds are involved in many drug molecules and are used in different therapeutic areas such as antifungal [1-4], antiviral [5-7], antidepressant [8-10], anticancer [11, 12], and anti-inflammatory agents [13, 14]. The biological activity of these structures has made them molecules that play a key role in drug design. That is, in both organic and medicinal chemistry, heterocyclic compounds constitute an important research area for the discovery of new and effective treatment methods [15-19]. In this context, another research area of interest in medicinal chemistry is the design and synthesis of metal complexes with pyridine and pyrimidine structures [20-23]. In particular, metal complexes containing Schiff bases have been reported to exhibit remarkable thermochromic and photochromic properties [24]. These properties make these complexes valuable in various applications such as imaging systems [25], organic light emitting diodes [26], photonic/electronic devices [27], and solar filters [28]. Moreover, the coordination of metals with different biological ligands plays an important role in understanding biological processes and opens new horizons in explaining the biochemical functions of biometals (29).

Pyridine has a six-membered ring structure consisting of one nitrogen and five carbon atoms and is an important heterocyclic compound in organic chemistry (Figure 1).

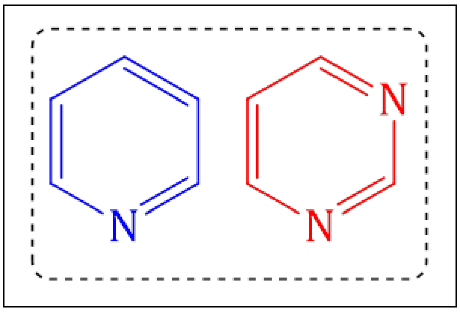


Figure 1. Basic ring structures of pyridine and pyrimidine.

The presence of the nitrogen atom in the ring has a marked effect on the chemical and biological properties of pyridine [30]. Pyridine is a widely used building block, especially in drugs with various biological activities such as antimicrobial

*Corresponding author/Yazışılan Yazar

[31-44], antitumor [45-49], antiviral [50-52], antituberculosis [53, 54], and anti-Alzheimer's [55, 56]. Pyrimidine exhibits a similar structure to pyridine, but has two nitrogen atoms in the first and third positions of its six-membered ring [57]. This difference makes pyrimidine have more biologically specific functions. Pyrimidine derivatives are considered one of the basic building blocks of genetic material, as they are located in DNA and RNA bases (uracil, thymine, and cytosine) [58, 59]. They also form the basic structure of many drugs with anticancer [60-66], antimicrobial [67-70], antiviral [71, 72], and anticonvulsant [73] properties. Both ring systems are widely used in drug discovery. Thus, the fact that pyridine and pyrimidine derivatives offer such a broad spectrum of biological activity has made them indispensable structures in pharmaceutical research and the development of new treatment methods [74].

Although many studies in the literature have separately examined the specific biological activities or synthesis methods of these compounds, studies that comprehensively evaluate both their recent synthesis strategies and their versatile biological activities together are limited. In order to address this shortcoming, in our article, both the current synthesis methods and the biological activities of these compounds, such as anticancer, antibacterial, antiviral, and neurotropic, have been systematically reviewed. Thus, our study aims not only to compile the available information in the literature but also to encourage further in-depth exploration of the biological and pharmaceutical potential of nitrogen-containing heterocyclic compounds.

2 Synthesis and biological activity studies of pyridine and pyrimidine derivatives

2.1. Anticancer Activity Studies

In 2020, Jian *et al.* synthesized 26 novel pyrazolo[3,4-b]pyridine-linked compounds **1** combretastatin A-4 analogs that exhibited antiproliferative and tubulin polymerization inhibitory activities (Figure 2). The most active analog, compound **2**, arrests HeLa cells in a dose-dependent manner, indicating the potential for developing potent tubulin inhibitors as anticancer agents (Figure 3). The molecular docking study revealed that this compound likely occupied the colchicine binding site at the α/β-tubulin interface, using similar binding modes as CA-4 [75].

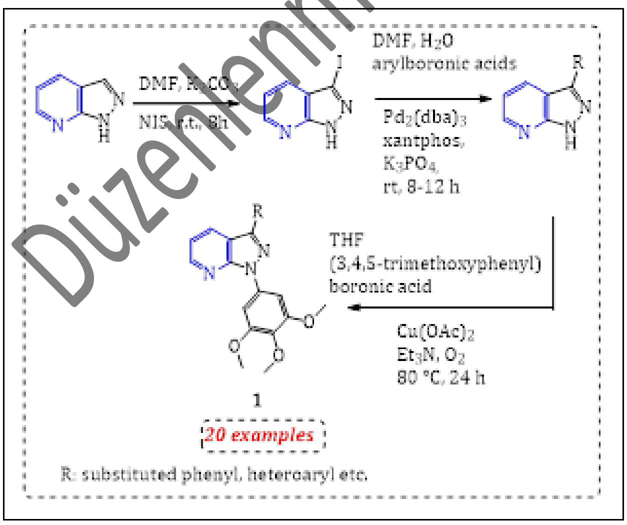


Figure 2. Synthesis of compound **1**.

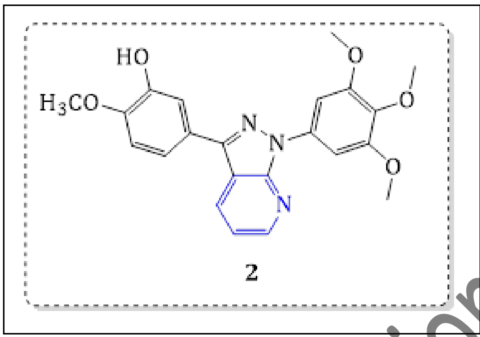


Figure 3. Compound **2**.

(IC_{50}±SD: 18.08±1.48 μM)

The study by Hatti *et al.* 2024 focused on the synthesis of 1,3,4-oxadiazole derivatives linked to pyridine and substituted aryl groups. In the first step, nicotinic acid **3** was refluxed with ethanol and a catalytic amount of H_2SO_4 for 6 h to obtain ethyl pyridine-3-carboxylate **4**. The obtained ester was refluxed with a mixture of ethanol and hydrazine hydrate for 6 h to synthesize pyridine-3-carbohydrazide derivative **5**. In the final step, compound 5 was converted into 2,5-disubstituted 1,3,4-oxadiazole derivatives **6** by cyclocondensation with various aromatic carboxylic acids in the presence of polyphosphoric acid (PPA) at 90°C for 4 hours (Figure 4). The anticancer activities of the oxadiazole derivatives against HeLa, MDA-MB-231, MCF-7, and A549 cell lines were investigated using doxorubicin as a standard drug, and the MTT reduction assay protocol (Table 1). It is very important that these derivatives did not show any cytotoxicity on HEK-293 kidney cell lines. In particular, the compound with a cinnamyl ring was found to exhibit better activity against HeLa and MCF-7 cell lines [76].

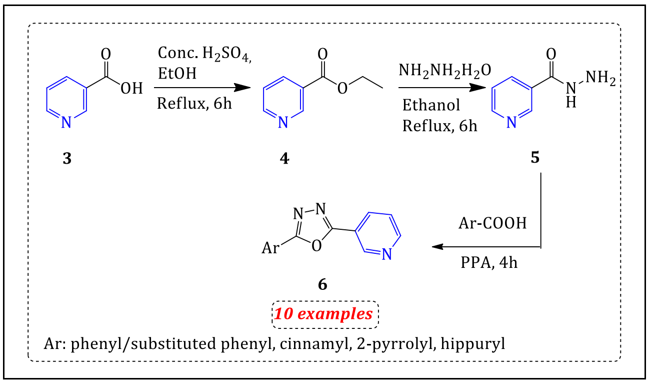


Figure 4. Synthesis of compound 6.

In 2023, Jami *et al.* synthesized a new series of **7** amide derivatives of isoxazole-imidazo[1,2-*a*]pyridine derivatives (Figure 5). In order to evaluate their anticancer potential, the effects of these derivatives on prostate cancer cell lines (PC3 and DU-145), lung cancer cell line (A549), and breast cancer cell line (MCF-7) were studied by MTT assay. The *in vitro* anticancer activity of these compounds was compared with that of the clinical drug candidate etoposide. As a result of the study, five compounds exhibited stronger anticancer activity compared to the positive control (Table 2) [77]. These findings suggest that these compounds in particular could be potential drug candidates in cancer treatment.

Table 1. *In vitro* cytotoxicity of the compound showing anticancer activity with IC_{50} in µM and the drug doxorubicin.

Compound	Ar	MDA-MB-231	A549	HeLa	MCF-7	HEK 293
	cinnamyl	-	8.9±0.06	1.8±0.3	1.3±0.11	97±0.8
Doxorubicin	-	*0.36 ±0.14*	*0.47 ±0.4*	*0.98 ±0.14*	*0.89 ±0.26*	-

Table 2. *In vitro* cytotoxicity of five compounds showing potent anticancer activity with IC_{50} in µM and the drug etoposide.

Compound	R	PC3	A549	MCF-7	DU-145
	3,4,5-trimethoxy	0.01±0.009	0.11±0.066	0.14±0.074	0.51±0.096
	3,5-dimethoxy	0.83±0.093	0.75±0.081	0.56±0.098	0.89±0.055
	4-methoxy	1.37±0.46	1.44±0.52	2.01±0.86	1.93±2.03
	4-methyl	2.47±1.73	2.11±1.64	2.09±1.40	2.61±1.55
	4-(dimethylamino)	2.70±1.62	1.99±0.75	1.39±0.66	3.55±2.22
Etoposide	-	*2.39±1.56*	*3.08 ± 0.135*	*2.11 ± 0.024*	*1.97 ± 0.45*

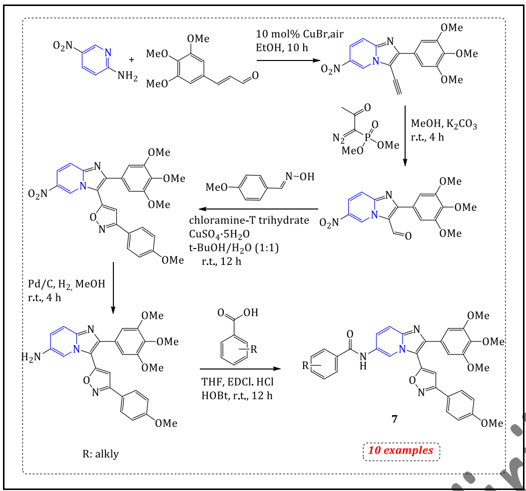


Figure 5. Synthesis of compound **7**.

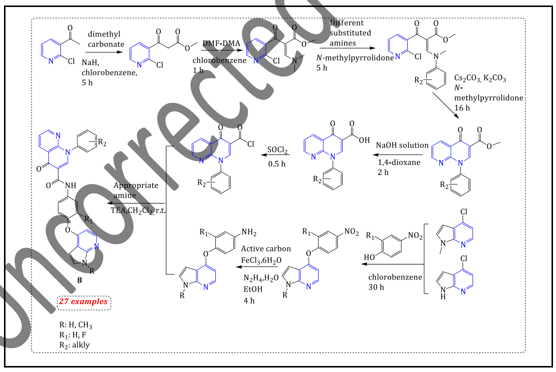


Figure 6. Synthesis of compound **8**.

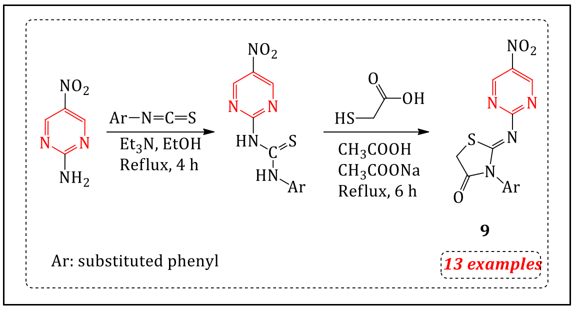


Figure 7. Synthesis of compound **9**.

The study on novel pyrrole-pyridine benzamide derivatives **8** synthesized by Zhang *et al.* in 2022 represents an important step forward, especially in cancer research (Figure 6). The cytotoxic activities of 27 synthesized compounds were tested against non-small cell lung cancer (A549), cervical cancer (HeLa), and breast cancer (MCF-7) cells. Cabozantinib anticancer drug was taken as a positive control in the tests performed using the MTT method. According to the results obtained, the compound containing bromophenyl ring showed better antitumor activity in the rate of inhibition of tumor growth compared to Cabozantinib (Table 3). This finding is promising for the development of potential new drug candidates for the treatment of cancer [78].

The study carried out by Khan *et al.* in 2023 focused on the synthesis of pyrimidine-based thiazolidinone derivatives **9**. This synthesis was carried out using stepwise processes (Figure 7). The anti-urease and anticancer activities of the obtained compounds were investigated in the presence of standard drugs thiourea, and tetrandrineb. The four compounds tested in the study showed excellent results for both activity profiles (Table 4). These findings are considered an important development in terms of potential therapeutic applications of the related compounds [79].

The study by Wang *et al.* in 2021 focused on 2,4-diamino pyrimidine (DAPY) derivatives **10-11** and investigated their potential as focal adhesion kinase (FAK) inhibitors (Figure 8). FAK is an enzyme overexpressed especially in tumor cells, and plays an important role in cancer cell survival, metastasis, and angiogenesis. Therefore, inhibiting FAK is considered a promising approach for cancer therapy. Most of the DAPY derivatives synthesized in the study effectively suppressed the enzymatic activities of FAK *in vitro*. In particular, compounds 2-Cl, and 2-methoxy bonded to the ring showed potent antiproliferative activity against FAK-overexpressing pancreatic cancer cell lines PANC-1, and BxPC-3. These compounds not only slowed down the growth of cancer cells but also suppressed their ability to form colonies, migrate, and invade in a dose-dependent manner. A flow cytometry assay showed that these compounds induced apoptosis in PANC-1 cells and inhibited cell division by arresting the cell cycle in the G2/M phase. These results suggest that 2-Cl and 2-methoxy bonded compounds to the ring are potent FAK inhibitors with both antitumor, and anti-angiogenesis potential (Table 5) [80].

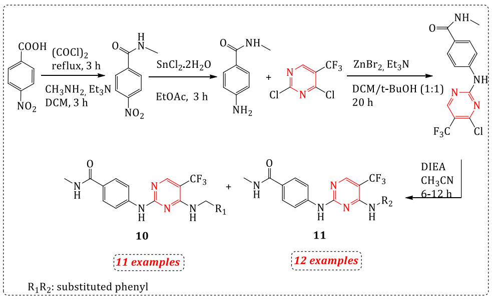


Figure 8. Synthesis of compound **10** and compound **11**.

In a study conducted by Reddy *et al.* in 2024, pyridine, and triazole-containing pyrimidine derivatives **12** were synthesized, and their *in vitro* anticancer activities against various human cancer cell lines were evaluated using the MTT method. MCF-7 (breast cancer), A549 (lung cancer), Colo-205 (colon cancer), and A2780 (ovarian cancer) cell lines were used in the study (Figure 9). The IC_{50} values obtained revealed that the compounds showed good to moderate anticancer activity compared to etoposide. In particular, six derivatives exhibited stronger activity than the others, of which the compound 3,4,5-$(OCH_3)_3$ linked to the ring is the most remarkable and showed promising anticancer activity. (Table 6) [81].

Table 3. Compound showing potent anticancer activity and IC_{50} values of Cabozantinib in µM.

Compound	R	R_1	R_2	A549	HeLa	MCF-7
	H	F	4-Br	1.06 ± 0.04	10.87 ± 2.15	0.11 ± 0.02
Cabozantinib		-	-	*0.33 ± 0.05*	*79.06 ± 0.39*	*30.87 ± 0.23*

Table 4. IC_{50} values of compounds and standard drugs with anti-urease (µM ± SEM) and anticancer (mM ± SEM) potential.

Compound	Ar	Anti-urease	Anticancer
-	4-CF_3-C_6H_4	2.30 ± 0.30	3.20 ± 0.50
-	3-CF_3-C_6H_4	3.10 ± 0.20	6.20 ± 0.10
-	4-F-2-OH-C_6H_4	3.20 ± 0.20	3.80 ± 0.30
-	3-Cl-4-F-C_6H_4	4.20 ± 0.20	5.10 ± 0.30
Thiourea	-	*8.20 ± 0.20*	-
Tetrandrineb	-	-	*12.30 ± 0.10*

Table 5. Kinase inhibitory activities and antiproliferative activities of compounds with potent antiproliferative activity and defactinib used as standard against different human cell lines.

		Enzymatic activity (IC_{50}, nM)		Antiproliferative activity (IC_{50}/µM)						
		Cancer cells								
Compound	**R_1/R_2**	**FAK**	**VRGFR2**	**PANC-1**	**BxPC-3**	**MCF-7**	**MDA-MB-231**	**HepG2**	**A549**	**HCT-15**
10	2-Cl-C_6H_4	2.75	146.8	0.98	0.55	1.47	0.76	0.71	2.72	0.79
11	2-OMe-C_6H_4	1.87	291.8	0.11	0.15	0.25	0.35	0.14	0.65	0.12
Defactinib	-	*1.16*	*273.2*	*3.48*	*3.25*	*5.81*	*3.75*	*3.69*	*4.09*	*4.36*

		Antiproliferative activity (IC_{50}/µM)		
		Normal cells		
Compound	**R_1/R_2**	**HUVEC**	**HEK293**	**L02**
10	2-Cl-C_6H_4	2.29	4.92	15.14
11	2-OMe-C_6H_4	0.18	16.17	>20
Defactinib	-	*3.24*	*4.07*	*4.66*

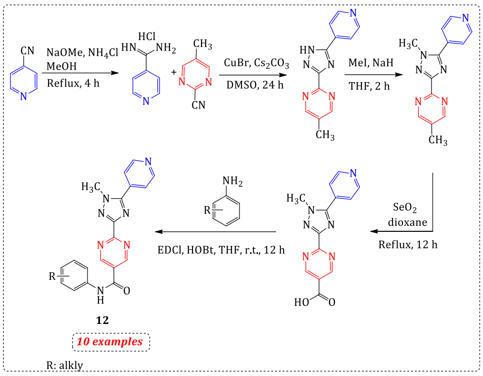


Figure 9. Synthesis of compound **12**.

2.2. Neurotropic Activity Studies

The work of Dashyan *et al.* in 2024 involved the synthesis of novel compounds **13-14** with a wide range of biological activities, such as neuropeptide antagonists, anticancer, antiulcer, antiarthritic, and antidiabetic effects. Ethyl 4-phenyl-2-thioxo-1,2-dihydropyridine-3-carboxylate derivatives were used in the synthesis of these compounds (Figure 10). Eight of the twelve synthesized compounds showed potent anticonvulsant activity through antagonism with pentylenetetrazole. This indicates that the compounds are potential candidates for the treatment of neurological disorders such as epilepsy. Furthermore, these compounds also exhibited anxiolytic effects, activating behaviors, and sedative properties, meaning that they could also be treatment options for such disorders. In particular, a fourfold increase in olfactory cell studies compared to diazepam was observed, further reinforcing the potential of these compounds for neurological treatment [82].

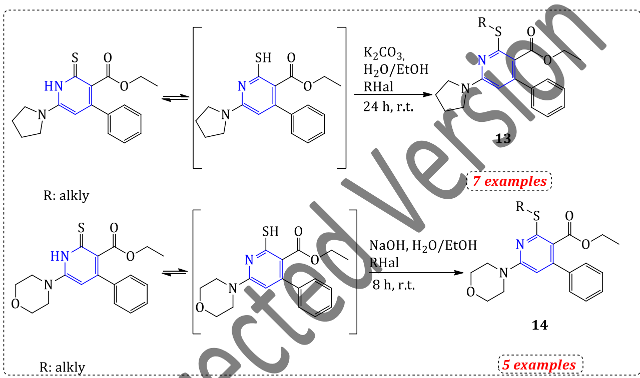


Figure 10. Synthesis of compound **13** and compound **14**.

2.3. Antimicrobial Activity Studies

The study by Desai *et al.* in 2021 aimed to develop new pyridine-containing compounds **15** as potential antimicrobial agents (Figure 11). These compounds were evaluated for both antibacterial and antifungal activities (Table 7). In particular, 3-OH and 4-F-linked compounds were found to exhibit good activity against *S. aureus* and *Escherichia coli* bacteria, respectively. It was also reported that the 2,4-dichloro-linked compound showed superior activity against *Pseudomonas aeruginosa* compared to the standard drugs ampicillin and chloramphenicol. This compound was also found to be highly effective against *Streptococci pyogenes*. In the study, it was emphasized that derivatives with electron-donating groups (2-OH, 3-OH, 4-CH_3, and 4-OH-3-OCH_3) showed both antibacterial and antifungal activity. In contrast, derivatives bearing electron-withdrawing groups (4-F and 2,4-dichloro) showed a marked increase in antibacterial activity. In terms of antifungal activities, 4-CH_3 and 4-OH-3-OCH_3-linked compounds exhibited significant activities against various fungal strains. It was reported that 4-CH_3-linked compounds showed significant antifungal activity against *Aspergillus niger*, and 4-OH-3-OCH_3-linked compounds exhibited excellent activity against *Candida albicans* and *Aspergillus clavatus* fungi. These results suggest that novel pyridine-containing compounds have potential as antimicrobial agents and may be effective against fungal infections [83].

Table 6. IC_{50} values in µM of compounds with strong anticancer activity and Etoposide used as standard.

Compound	R	MCF-7	A549	Colo-205	A2780
-	3,4,5-$(OCH_3)_3$	0.1 ± 0.075	0.26 ± 0.037	0.48 ± 0.048	0.13 ± 0.023
-	3,5-$(OCH_3)_2$	0.86 ± 0.064	0.94 ± 0.082	1.49 ± 0.66	1.22 ± 0.54
-	4-OCH_3	1.55 ± 0.37	1.61 ± 0.41	1.67 ± 0.48	1.95 ± 0.76
-	4-CH_3	2.09 ± 0.82	2.10 ± 1.05	2.34 ± 1.12	2.44 ± 1.27
-	4-$N(CH_3)_2$	2.76 ± 1.55	2.38 ± 1.21	2.88 ± 1.89	3.17 ± 2.76
-	3,5-$(CH_3)_2$	3.16 ± 2.49	2.66 ± 1.44	2.81 ± 1.52	2.56 ± 1.33
Etoposide	-	*2.11 ± 0.024*	*3.08 ± 0.135*	*0.13 ± 0.017*	*1.31 ± 0.27*

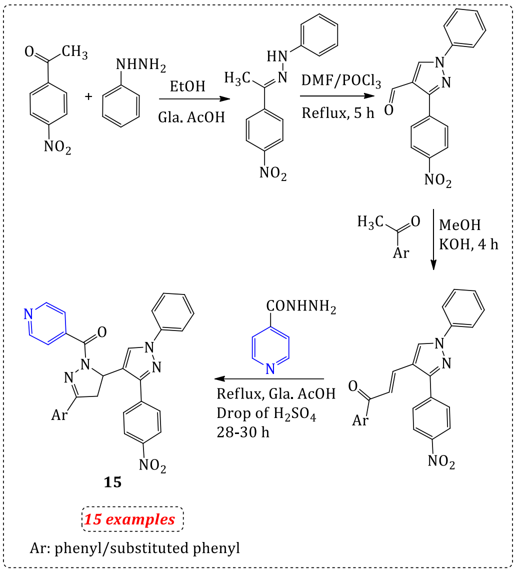


Figure 11. Synthesis of compound **15**.

The study by Borthakur *et al.* in 2020 focused on the synthesis of 1,3-thiazolopyrimidine derivatives **18** using 4-phenylthiazol-2-amine **16** and arylidinemalononitrile **17** (Figure 12). The antifungal activities of the synthesized compounds were carried out by testing them against *Rhizoctonia solani* and *Drechslera orazae*, two fungal pathogens causing diseases in rice crops. The results showed that four compounds exhibited mild to moderate antifungal activity (Table 8). This suggests that these compounds could be developed as a potential agricultural antifungal if further tested with other agriculturally important fungi. The study reveals that new antifungal agents can make an important contribution for disease control in agriculture [84].

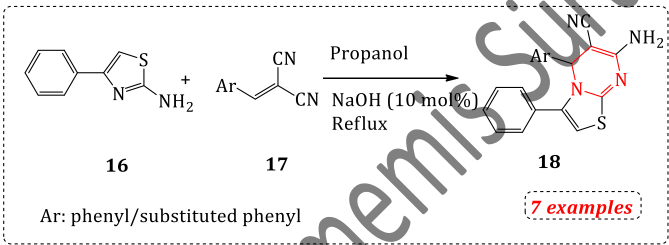


Figure 12. Synthesis of compound **18**.

In a study conducted by Hari *et al.* in 2022, 16 pyrimidine derivatives **19** were synthesized, and the antibacterial activity of these compounds was evaluated (Figure 13). Some of the synthesized compounds showed strong inhibition against bacteria such as *Xanthomonas campestris pv. Campestris, Pseudomonas fluorescens, and Bacillus subtilis*, while other compounds were moderately effective (Table 9). Such studies can be an important step towards the development of new antibacterial agents. Further research on the structural properties and antibacterial mechanisms of the target molecules will help to better understand the potential of these compounds [85].

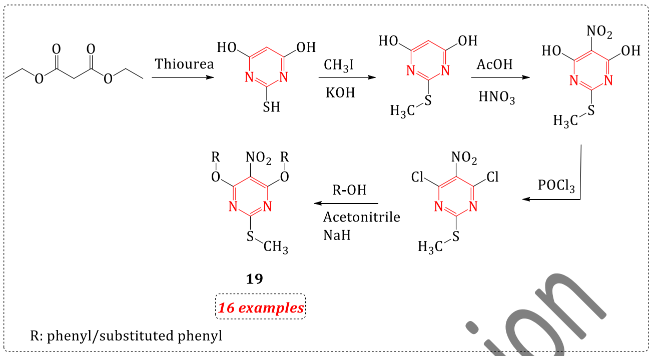


Figure 13. Synthesis of compound **19**.

In 2024, Elsayed *et al.* utilized the chalcone derivative **20**, obtained from 4-bromoacetophenone and 3,4-dimethoxybenzaldehyde, as the starting material for the synthesis of pyridine **21** and thienopyridine **22-23** compounds in their studies on the development of new antimicrobial agents. In the study, thienopyridine derivative was obtained from the reaction of chalcone with 2-cyanothioacetamide, and this intermediate product was converted into various pyridine and thienopyridine derivatives by one- or two-step reactions with 2-chloro-*N*-arylacetamide derivatives, *α*-haloketones, methyl iodide, and chloroacetonitrile (Figure 14). All synthesized compounds were evaluated against *E. coli, B. mycoides, and C. albicans*, and two compounds showed strong antimicrobial activity (Table 10). The findings suggest that these derivatives have antimicrobial potential and that the relationship between their structural properties and biological activities is important [86].

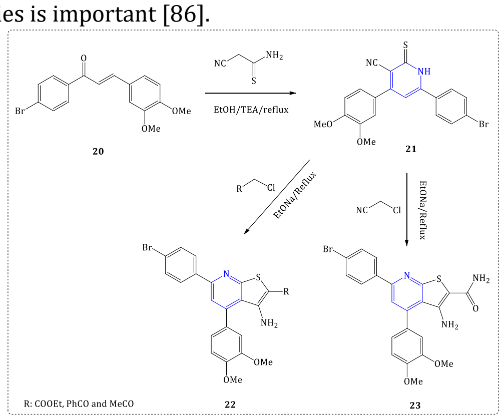


Figure 14. Synthesis of compound **20**, **21** , **22**, and **23** compound.

3 Pyridine and Pyrimidine Derivative Drugs

In recent years, nitrogen-containing fused heterocyclic compounds have attracted great interest in the field of drug discovery. In particular, pyridine and pyrimidine derivatives have become important building blocks in drug discovery, exhibiting a variety of pharmacological properties such as antiviral, antibacterial, antimicrobial and anticancer activities [87, 88]. Such a wide range of biological activity of these compounds is based on the strong interactions of the nitrogen atom in their chemical structure with biological systems. Nitrogen-containing heterocyclic compounds can interact with biological targets by forming hydrogen bonds with biomolecules or by altering electron density. These interactions make them effective against biological agents such as viruses, bacteria and cancer cells. Therefore, pyridine and pyrimidine derivatives stand out as potential drug candidates for the treatment of various diseases and play a critical role in drug development processes [89-92]. The pharmacological potentials of pyridine and pyrimidine-containing drugs, which prove their broad efficacy, and the structure of marketed drugs such as minoxidil, divaplon, indiplon, trimethoprim, ocinaplon, etc. are shown below (Table 11).

Table 7. Screening results in µg/mL for compounds showing potent antibacterial and antifungal activity and drugs used as standards.

		Minimum bactericidal concentrations (MBC)				**Minimum fungicidal concentrations (MFC)**		
Compound	**R**	***E. c.***	***P. a.***	***S. a.***	***S. p.***	***C. a.***	***A. n.***	***A. c.***
-	2-OH	250	500	100	125	500	50	>1000
-	3-OH	100	500	50	500	100	>1000	>1000
-	4-CH_3	100	500	250	250	>1000	12.5	>1000
-	4-F	100	200	250	250	200	1000	500
-	2,4-$(Cl)_2$	250	12.5	500	25	250	500	500
-	4-OH-3-OCH_3	100	500	125	500	12.5	>1000	12.5
Ampicillin	-	*100*	*100*	*250*	*100*	-	-	-
Chloramphenicol	-	*50*	*50*	*50*	*50*	-	-	-
Nystatin	-	-	-	-	-	*100*	*100*	*100*
Griseofulvin	-	-	-	-	-	*500*	*100*	*100*

Abbreviation: *A. c., Aspergillus clavatus; A. n., Aspergillus niger; C.a., Candida albicans; E. c., Escherichia coli; P. a., Pseudomonas aeruginosa; S. a., Staphylococcus aureus; S. p., Streptococcus pyogenes.*

Table 8. Results of inhibition percentages of compounds with antifungal activity and carbendazim used as standard.

		***Rhizoctonian solani* Concentration**		***Drechslea orazae* Concentration**	
Compound	**Ar**	**A.I. (50 ppm)**	**A.I. (100 ppm)**	**A.I. (50 ppm)**	**A.I. (100 ppm)**
-	4-Cl-C_6H_4	48.86	64.10	51.09	57.76
-	4-OH-3-OCH_3-C_6H_3	37.87	65.88	43.25	55.78
-	4-$N(CH_3)_2$- C_6H_4	34.77	54.55	54.75	70.45
-	4-OCH_3- C_6H_4	46.75	52.76	46.54	67.95
Carbendazim	-	*96.67*	*98.56*	*95.45*	*98.26*

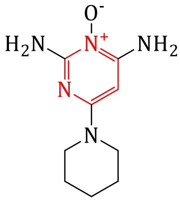
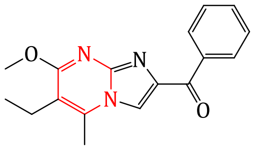
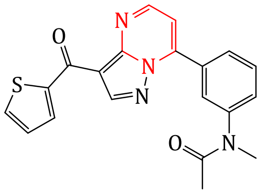
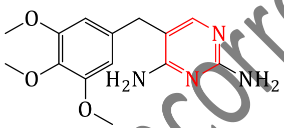
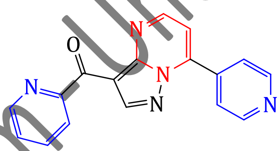
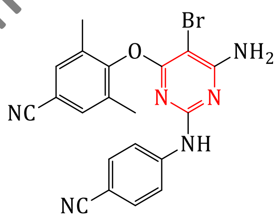
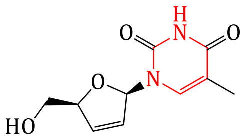
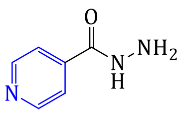
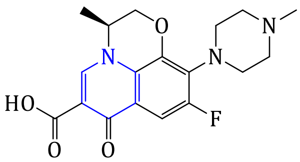
Table 9. *In vitro* effects of compounds with potent antimicrobial activity and chloramphenicol used as a standard.

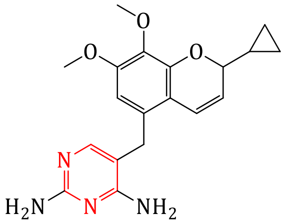
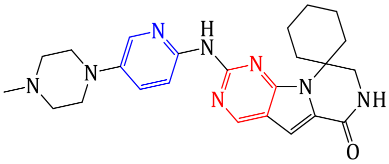
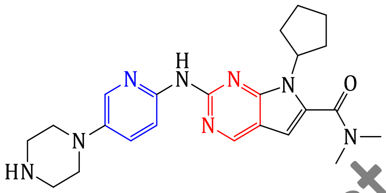
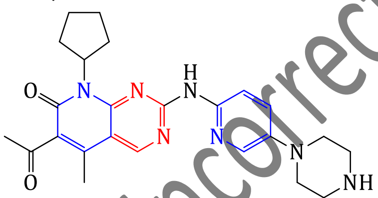
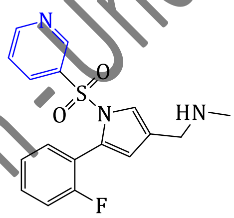
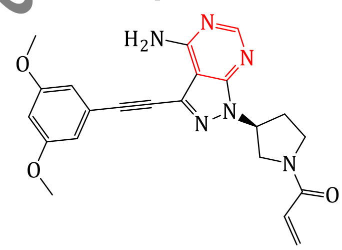
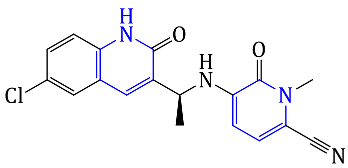
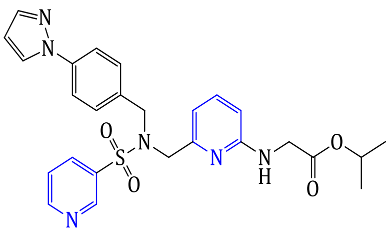
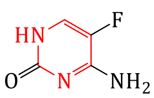
		%Inhibition Compared to Positive Control		
Compound	**R**	***Xanthomonas campestris pv. Campestris***	***Pseudomonas fluorescens***	***Bacillus subtilis***
-	4-Br-C_6H_4	63.90	70.61	51.02
-	3,5-$(CH_3)_2$-C_6H_3	65.76	71.33	51.39
-	4-Cl-C_6H_4	67.12	69.89	57.49
-	2-NH_2-C_6H_4	67.46	73.12	56.56
-	4-OCH_3-C_6H_4	66.78	70.97	58.41
Chloramphenicol	-	*100*	*100*	*100*

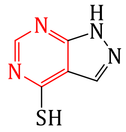
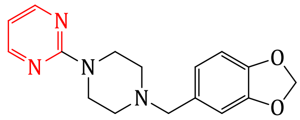
Table 10. Antimicrobial activity evaluation of compounds by agar diffusion and MIC values.

		Inhibition zone (mm)			**MIC value (mg/mL)**		
Compound	**R**	***E. coli***	***B. mycoides***	***C. albicans***	***E. coli***	***B. mycoides***	***C. albicans***
22	COOEt	32	33	31	0.0195	>0.0048	>0.0048
23	-	28	28	29	> 0.0048	0.0098	0.039
Ampicillin 10 µg	-	*20*	*12*	*14*	-	-	-
Gentamicin 10 µg		*12*	*11*	*12*	-	-	-
Tobramycin 10 µg	-	*13*	*10*	*12*	-	-	-

Table 11. Marketed drugs containing pyridines and pyrimidines.

S. No	Drug	Structure	Treatment	Ref.
1	Minoxidil		Vasodilator	[93]
2	Divaplon		Anticonvulsant and anxiolytic	[94]
3	Indiplon		Sedative-hypnotic	[95]
4	Trimethoprim		Antibiotic	[96]
5	Ocinaplon		Anxiolytic	[97]
6	Etravirine		Antiviral	[98]
7	Stavudine		Anti-HIV	[99]
8	Isoniazid		Antituberculosis	[100]
9	Levofloxacin		Anti-allergic	[101]

10	Iclaprim		Antibiotic	[102]
11	Trilaciclib		Small-cell lung cancer	[103]
12	Ribociclib		Breast cancer	[104]
13	Palbociclib		Advanced cancer	[105]
14	Vonoprazan		Gastroesophageal reflux and peptic ulcer	[106]
15	Futibatinib		Non-small cell lung cancer and breast cancer	[107]
16	Olutasidenib		Acute myeloid leukaemia	[108]
17	Omidenepag		Glaucoma and ocular hypertension	[109]
18	Flucytosine		Antifungal	[110]

19	Tisopurine		Disorders associated with hyperuricemia	[111]
21	Piribedil		Parkinsonism	[112]

4 Conclusions

This review systematically brings together the recent synthetic strategies and reported biological activities of pyridine- and pyrimidine-based heterocycles. By outlining both the diversity of synthetic methodologies and the wide spectrum of pharmacological evaluations, we provide a comprehensive perspective that allows researchers to better link chemical design with biological potential. The survey of literature reveals not only the versatility of these scaffolds but also the recurring emphasis on their anticancer, antimicrobial, and neurotropic properties, which highlights promising directions for drug discovery. While our work does not aim to cover mechanistic details exhaustively, its contribution lies in integrating chemical and biological knowledge into a single framework, thus serving as a useful reference point for medicinal chemists. We believe that this synthesis of information can facilitate a more rational approach to the exploration of nitrogen-containing heterocycles and stimulate further innovation in the field.

5 Author contribution statements

Author 1 contributed to the conception of the idea, literature review, writing, and editing of the article, and Author 2 contributed to the literature review and editing of the article.

6 Ethics committee approval and conflict of interest statement

“The prepared article does not require approval from the ethics committee”.

“The article was written with no conflict of interest with any individual or organization”.

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