Synthesis and Spectroscopic Characterization of Pyrazolone Based Pyrimidines from 2-Chloro-7h-Pyrrolo-[2, 3-D] Pyrimidine

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ABSTRACT

Aromatic heteroatom bearing cyclic compound such as pyrimidine, benzimidazole, benzoxazole etc. Triazoles is the heterocyclic compounds having five membered rings with three nitrogen atoms in it. Chemistry of heterocyclic compounds plays an important role in our daily lives. Pyrimidines are common heterocyclic aromatic moiety resemble to benzene and pyridine having two N atoms at 1 and 3 positions of the six membered rings. Pyrimidines are biologically very significant heterocycles and shows by far the most prominent of the diazine class with uracil and thymine being constituents of ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) and with cytosine.

The present study shows synthesis of various pyrimidine by reaction of N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) acetamide with 2-Chloro-7H-pyrrolo[2,3-d] pyrimidine followed by reflux under ethanol using various aromatic aldehyde in the presence of alkali. All the synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, IR, MASS spectroscopic techniques.

Keywords: Pyrimidine, Chalcone, Spectroscopy, Aldehydes, 2-Chloro-7H-pyrrolo[2,3-d] pyrimidine.

INTRODUCTION

Chalcones represent an important class of open-chain flavonoids characterized by the presence of an α, β-unsaturated carbonyl system connecting two aromatic rings through the general structure 1,3-diphenyl-2-propen-1-one. Their simple framework and high synthetic accessibility make them versatile intermediates in organic and medicinal chemistry. Chalcones exhibit a wide range of pharmacological activities, including antimicrobial, anticancer, anti-inflammatory, antioxidant, and antimalarial properties, which are largely attributed to the electrophilic nature of the enone moiety that enables Michael addition with various biological nucleophiles. The classical Claisen–Schmidt condensation between appropriately substituted acetophenones and benzaldehydes remains the most widely employed method for chalcone synthesis due to its operational simplicity, high yields, and tolerance of diverse functional groups **[1,2]**. Furthermore, structural modifications on chalcone scaffolds have facilitated the development of hybrid pharmacophores and have provided promising leads in drug discovery.

Pyrimidines, six-membered heterocycles containing two nitrogen atoms at positions 1 and 3, constitute a fundamental structural motif in numerous natural and synthetic bioactive molecules. Naturally occurring pyrimidine bases cytosine, thymine, and uracil—are essential components of nucleic acids. Synthetic pyrimidine derivatives have gained equal prominence due to their broad spectrum of biological activities, including antiviral, anticancer, antibacterial, antihypertensive, and anti-inflammatory effects **[3]**. A wide variety of synthetic strategies have been developed for pyrimidine construction, with the Biginelli reaction, cyclocondensation of β-

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dicarbonyl compounds with amidines or urea derivatives, and multicomponent reactions standing out as efficient approaches. Recent advances in catalysis such as transition-metal catalysis, microwave-assisted synthesis, and green synthetic methodologies have further enhanced the efficiency, selectivity, and environmental compatibility of pyrimidine synthesis **[4, 5]**. The integration of chalcone scaffolds with pyrimidine pharmacophores has emerged as a promising strategy to generate novel heterocyclic hybrids with synergistic biological properties. Such hybrid molecules often combine the electrophilic Michael acceptor functionality of chalcones with the heteroaromatic framework of pyrimidines, potentially enhancing target specificity and bioactivity. Consequently, the synthesis of chalcone–pyrimidine hybrids has become an increasingly active area of research aimed at discovering new therapeutic agents with improved potency and reduced toxicity.

Pyrimidines constitute one of the most significant classes of nitrogen-containing heterocycles in pharmaceutical chemistry. Their prominence stems from their presence in essential biomolecules cytosine, thymine, and uracil which form the structural basis of nucleic acids and are crucial for cellular replication and genetic information transfer. Because of this central biological role, synthetic pyrimidine derivatives can interact selectively with nucleic acid metabolism, enzymes, and receptors, making them highly valuable scaffolds in drug discovery.

One of the greatest pharmaceutical contributions of pyrimidines lies in anticancer therapy. Several clinically used anticancer agents, such as 5-fluorouracil (5-FU), capecitabine, and pemetrexed, are pyrimidine-based antimetabolites that inhibit thymidylate synthase or interfere with DNA/RNA synthesis. These agents exploit the structural similarity of pyrimidine analogues to native nucleobases, enabling them to disrupt tumor cell proliferation **[6]**. Modifications to the pyrimidine ring have also yielded potent kinase inhibitors and small-molecule targeted therapies.

Pyrimidines also hold a central place in antiviral therapy. Many nucleoside and nucleotide analogues used to treat viral infections derive from pyrimidine frameworks. Drugs such as zidovudine (AZT), lamivudine (3TC), sofosbuvir, and brivudine act by mimicking natural pyrimidine nucleosides, thereby inhibiting viral polymerases and terminating viral genome replication **[7]**. The success of such compounds demonstrates the adaptability of the pyrimidine ring in designing broad-spectrum antiviral agents.

In addition to anticancer and antiviral applications, pyrimidine derivatives have demonstrated a wide spectrum of other pharmacological activities, including antibacterial, anti-inflammatory, antimalarial, antihypertensive, and CNS-active properties **[8]**. For example, certain dihydropyrimidines obtained through the Biginelli reaction exhibit calcium-channel-blocking effects similar to those of clinically used antihypertensive drugs such as nifedipine. Similarly, pyrimidine-based dihydrofolate reductase inhibitors have shown potent antibacterial action, while fused pyrimidine heterocycles (e.g., thienopyrimidines, quinazolines) have led to the development of kinase inhibitors widely used in cancer treatment.

Overall, the pyrimidine ring serves as a highly versatile platform capable of diverse chemical modifications that enhance molecular recognition, bioavailability, and target specificity. Its established role in approved therapeutics and ongoing relevance in medicinal chemistry research underscore its enduring pharmaceutical importance.

Present paper describes the synthesis of various pyrimidine derivative by reaction between N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) acetamide and 2-Chloro-7H-pyrrolo[2,3-d] pyrimidine in the presence of sodium hydroxide under ethanol solvent followed by reaction with various aromatic aldehyde.

METHODS AND MATERIALS

Chemicals and Reagents

All reagents were used of laboratory grade and used without further purification. Various aldehydes, N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) acetamide, 2-Chloro-7H-pyrrolo[2,3-d] pyrimidine, Guanidine, NaOH and ethanol were used as received from Merck, Mumbai, India.

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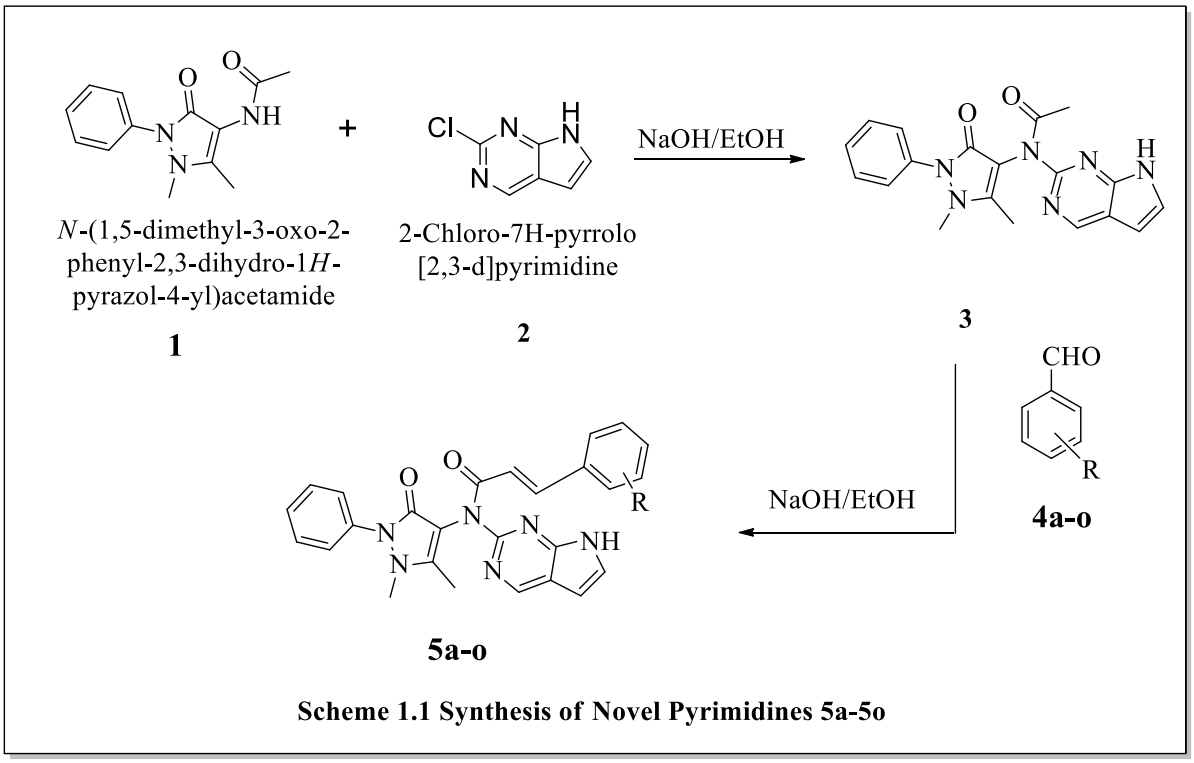
Experimental

Bruker Avance-400 instrument was used for Proton NMR study and 100MHZ frequency instrument was used for ^{13}C NMR. Parts per million unit was used to expressed chemical shift value. ABB Bomem Inc. FT-IR 3000 Spectrophotometer was used for Infrared Spectral study. Data obtained was expressed in cm^{-1} unit. Shimadzu LCMS-2010 was used for MASS spectral analysis. Perkin Elmer-2400 Series II CHNS/O Elemental Analyzer was used for Composition measurement.

Method of Synthesis

Reaction Scheme



Scheme 1.1 Synthesis of Novel Pyrimidines 5a-5o

Synthesis of various Chalcones 5a-5o

To a solution of N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)acetamide compound contain heterocycle along with acetyl group 1 (0.01 mol) is taken in absolute ethanol (40 ml), add 2% NaOH and 2-Chloro-7H-pyrrolo[2,3-d]pyrimidine 2 (0.01 mol) and refluxed for 30 minutes to obtained product 3 then add aromatic aldehyde 4a-o (0.01 mol) and further refluxed the mixture for 4-5hr, cooled and poured into ice cold water. The solid thus obtained was filtered and give wash of distilled water and further crystallization is done using ethanol. Products obtained called chalcones 5a-5o (**Table 1.1**).

Table 1 Data showing synthesis of Pyrimidines 5a-5o

Sr. No.	Compounds Code	R	Reaction Time (hr)	% Yield[b]	Melting Point (°C)
1	**5a**	-H	4.5	81	226
2	**5b**	2-OH	5.5	75	234
3	**5c**	3-OH	5.0	78	242
4	**5d**	4-OH	5.5	75	235
5	**5e**	2-Cl	4	86	219

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6	**5f**	3-Cl	4.5	82	226
7	**5g**	4-Cl	4	88	224
8	**5h**	2-Br	4	85	231
9	**5i**	3-Br	4.5	80	248
10	**5j**	4-Br	4	86	246
11	**5k**	2-NO_2	4	83	233
12	**5l**	3-NO_2	4.5	82	212
13	**5m**	4-NO_2	4	85	239
14	**5n**	2-OCH_3	5.5	73	244
15	**5o**	4-OCH_3	5.5	74	241

[a]Reaction is monitored by TLC, [b]Isolated yield

RESULT AND DISCUSSION

From the Table 1 show that the various pyrimidines synthesized by reaction between N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) acetamide and 2-Chloro-7H-pyrrolo[2,3-d] pyrimidine in the presence of sodium hydroxide under ethanol solvent followed by reaction with various aromatic aldehyde. From table-1, it clearly indicates that the compounds possessing electron withdrawing group are synthesized in shorter reaction time as compared to compounds bearing electron releasing group. Compounds 5j-5l bearing electron withdrawing were synthesized in 4-4.5hr whereas compounds **5b-5d**, **5n** and **5o** bearing electron donating group were synthesized in 5-5.5hr.

Optimization of Reaction:

Table 2 Effect of different amount of catalyst on synthesis of chalcones

Entry	**% of NaOH Sol in Ethanol.**	**Time[a] (Hours)**	**Yields[b] (%)**
1	1	4.5	76
2	2	4.5	81
3	3	4.5	79
4	4	4.5	79
5	5	4.5	76

To a solution of N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)acetamide compound contain heterocycle along with acetyl group **1** (0.01 mol) is taken in absolute ethanol (40 ml), add Cyanuric chloride **2** (0.01 mol) and various concentration of NaOH and refluxed for 30 minutes to obtained product **3** then add benzaldehyde **4a** (0.01 mol) and further refluxed the mixture for 3.5hr, cooled and poured into ice cold water. The solid thus obtained was filtered and give wash of distilled water and further crystallization is done using ethanol. Products obtained called chalcones **5a-5o.** Data obtained are shown in the **Table**

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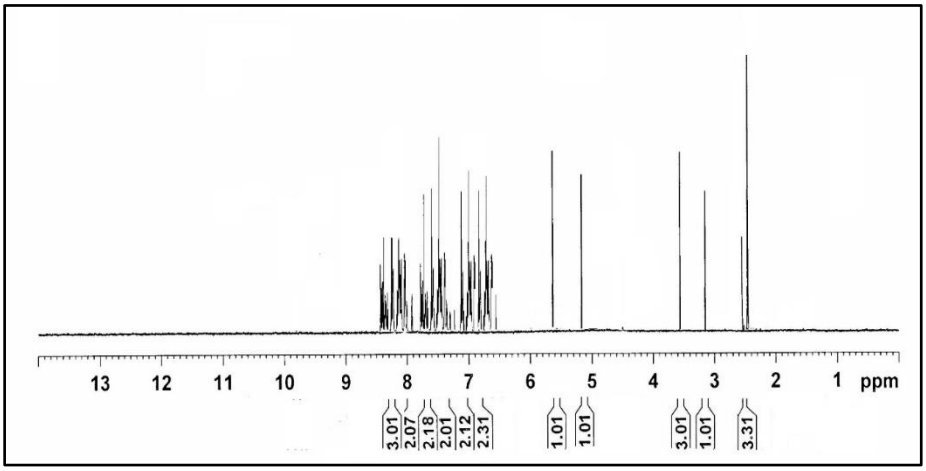
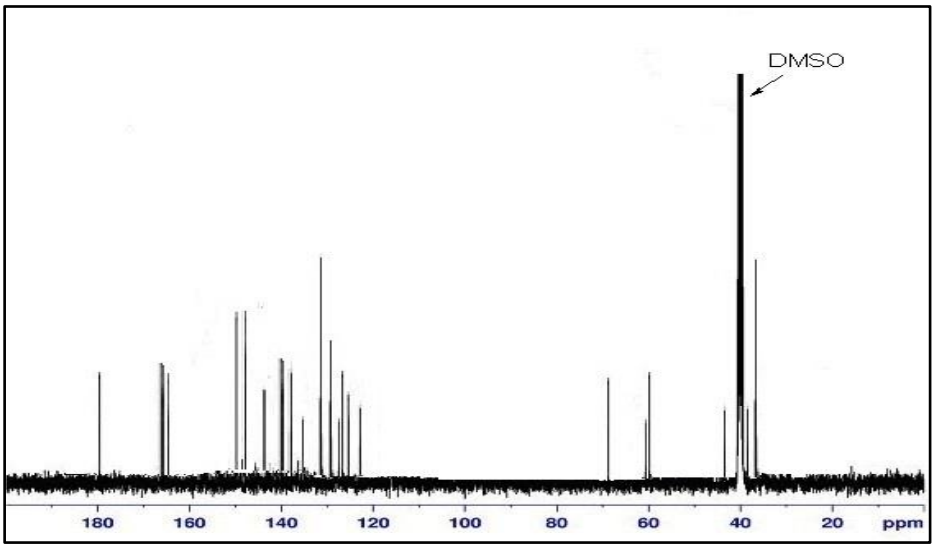
Characterization

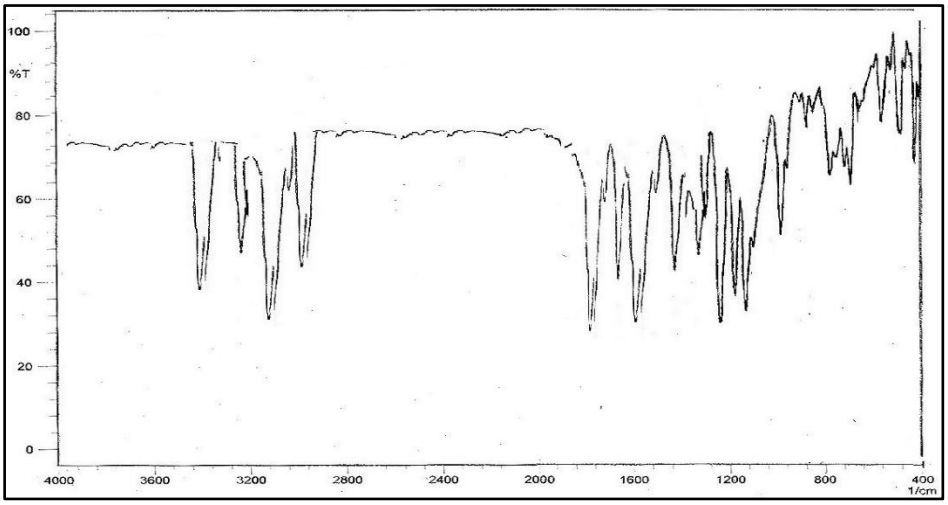
Compound **5a** of the series is taken as the representative compound. In the ^{1}HNMR spectrum the characteristic signals due to each protons and functional groups with protons are well described on the basis of shielding and deshielding effects. The signal due to aromatic proton of compound was observed in more downfield region at chemical shift value around 6.5 to 8.5ppm. ^{1}H NMR, ^{13}C NMR, IR, MASS spectroscopic data of **5a** compound shown below.



^{1}H NMR Spectra of Compound 5a



^{13}C NMR Spectra of Compound 5a



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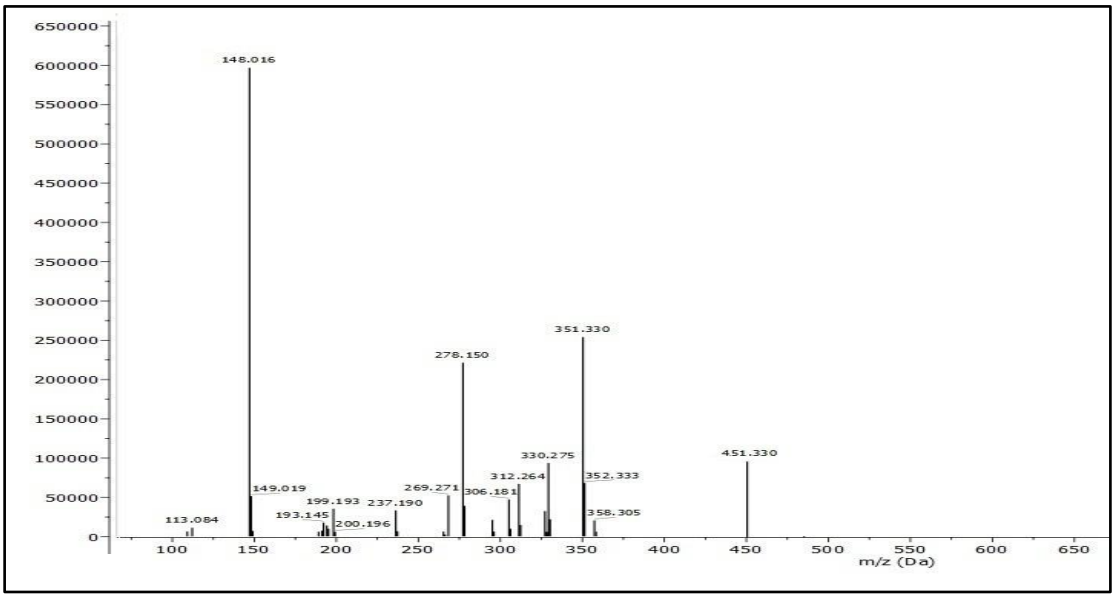
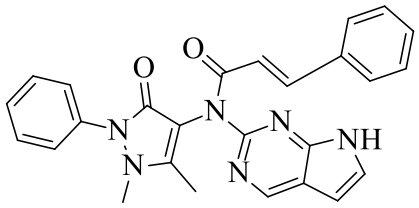
IR Spectra of Compound 5a



MASS Spectra of Compound 5a

Compound code: 5a	
Molecular formula:	$C_{26}H_{22}N_6O_2$
	
M. P. (°C):	226
^{1}HNMR (400 MHz, $CDCl_3$) δ ppm:	2.5 (3H, -CH_3, s), 3.2 (1H, s, N-H), 3.5 (3H, -CH_3, s), 5.1 (1H, -CH, d), 5.8 (1H, -CH, d), 6.5-8.5 (13, Ar-H of Phenyl ring).
^{13}CNMR (100 MHz, $CDCl_3$) δ ppm:	38.3, 45.3, 62.2, 68.3, 124.4, 126.8, 127.5, 128.2, 129.2, 130.1, 131.4, 134.5, 139.7, 139.6, 139.8, 140.3, 142.0, 150.8, 151.0, 150.9, 153.9, 154.2, 155.2, 180.5.
IR cm^{-1} (KBr):	3330 (N-H strtching), 3120-3015 (Ar C-H), 2995-2920 (C-H aliphatic), 1671 (C=O), 1664 (C=O), 1622 (C=C), 1595 (C=C), 1554 (C=C), 1536 (C=N), 1330 (C-N), 835 (monosubstituted phenyl ring).
Mass (M+1):	451.3
Elemental analysis:	Calculated (%): C, 69.32; H, 4.92; N, 18.66 Found (%) : C, 69.30; H, 4.95; N, 18.60

CONCLUSION

In conclusion, the highly functionalized pyrimidines were synthesized from readily available starting materials. We have synthesized library of pyrimidines compound possesses reactive functional group. All compounds are characterized by spectroscopic techniques.

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REFERENCES

1. Prasad, Y. R., Reddy, C. S., & Sreenivasulu, R. (2021). Chemistry and biological significance of chalcones: A review. Journal of Chemical and Pharmaceutical Research, 13(2), 1–15.
2. Singh, P., Anand, A., & Kumar, V. (2014). Recent developments in biological activities of chalcones: A mini review. European Journal of Medicinal Chemistry, 85, 758–777.
3. Kumar, A., & Rao, M. (2018). Advances in the chemistry and pharmacology of pyrimidines. European Journal of Medicinal Chemistry, 157, 335–367.
4. Gomha, S. M., Abdallah, A. E., Abdelmoniem, A. M., & Hassaneen, H. M. (2022). Recent advances in pyrimidine synthesis via multicomponent reactions. Molecules, 27(3), 865.
5. Zhang, W., Li, J., & Chen, X. (2020). Efficient strategies for pyrimidine synthesis: From classical methods to modern catalysis. RSC Advances, 10, 159–173.
6. Longley, D. B., Harkin, D. P., & Johnston, P. G. (2003). 5-Fluorouracil: Mechanisms of action and clinical strategies. Nature Reviews Cancer, 3, 330–338.
7. De Clercq, E., & Li, G. (2016). Approved antiviral drugs over the past 50 years. Clinical Microbiology Reviews, 29 (3), 695–747.
8. Kumar, A., & Rao, M. (2018). Advances in the chemistry and pharmacology of pyrimidines. European Journal of Medicinal Chemistry, 157, 335–367.