International Journal of Advanced Research in Science, Engineering and Technology
ISSN: 2350-0328
Vol. 12, Special Issue, December 2025
National Conference on Earth, Elements and Energy: Interdisciplinary Perspectives (NC3EIP–2025)
IJARSET IMPACT FACTOR 7.150

Green Synthesis, Structural Characterization, And Antimicrobial Evaluation of Substituted 1,3-Thiazoles, Schiff Bases, 1,3-Oxazines, And Dihydropyrimidinones

Premlata M. Sonparote

Associate Professor, Department of Chemistry, Bapuraoji Butle Arts, Narayanrao Bhat Commerce and Bapusaheb Patil Science College, Digras, Dist. Yavatmal - 445203, Maharashtra, India

ABSTRACT: Heterocyclic compounds constitute an important class of organic molecules with significant pharmaceutical, agricultural, and industrial relevance. This study presents environmentally benign synthetic methodologies for developing four groups of heterocyclic derivatives: substituted 1,3-thiazoles, Schiff bases, 1,3-oxazines, and dihydropyrimidinones. Calcium oxide (CaO) derived from calcinated eggshells, PEG-400, talc ($MgSi_4O_{10}(OH)_2$), and *Citrullus colocynthis* fruit extract served as green catalysts. Structural confirmation was achieved using elemental analysis, IR, NMR, and mass spectrometry. The synthesized compounds were further evaluated for antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella Typhi* using agar well diffusion and serial dilution techniques. Several derivatives demonstrated notable inhibitory potential, indicating their relevance in medicinal chemistry. The findings underscore the importance of green chemistry pathways in producing biologically potent heterocyclic scaffolds with reduced environmental burden.

KEYWORDS: Heterocyclic compounds; Green synthesis; 1,3-Thiazoles; Schiff bases; 1,3-Oxazines; Dihydropyrimidinones; Antimicrobial activity; PEG-400; Talc catalyst; *Citrullus colocynthis* extract. etc.

I. INTRODUCTION

Heterocyclic compounds represent essential building blocks in organic and medicinal chemistry, comprising structures that contain heteroatoms such as nitrogen, oxygen, or sulfur. These molecules are ubiquitous in pharmaceuticals, agrochemicals, natural products, and functional materials. Nature offers an extensive array of biomolecules that exhibit diverse therapeutic properties, including alkaloids, flavonoids, glycosides, coumarins, terpenoids, and phenolics. Many of these natural molecules include heterocyclic systems responsible for bioactivity.

The increasing need for sustainable and efficient synthetic practices has intensified the importance of green chemistry in heterocycle synthesis. Environmentally benign catalysts, solvent-free conditions, and naturally derived reagents have become central to modern organic synthesis.

Among various heterocyclic motifs, **1,3-thiazoles, Schiff bases, 1,3-oxazines, and dihydropyrimidinones** hold exceptional biological and pharmacological significance. These compounds show antimicrobial, antifungal, anticancer, antioxidant, insecticidal, and cardiovascular activities. Synthetic modifications to these scaffolds yield improved therapeutic potential and structure-activity relationships.

The present research focuses on developing green synthetic strategies for producing substituted 1,3-thiazoles (4a–4j), Schiff bases (6a–6c), 1,3-oxazines (10a–10c), and dihydropyrimidinones (14a–14c), followed by their analytical characterization and antimicrobial evaluation. This work seeks to contribute to the sustainable synthesis of medicinally promising heterocycles.

II. REVIEW OF LITERATURE

A. 1,3-Thiazole Derivatives: The synthesis of thiazoles dates back to work by Hantzsch, who first prepared thiazole rings through reactions between α-haloketones and thiourea. Subsequent research has focused on developing substituted thiazoles with enhanced medicinal properties. Recent studies reported the preparation of thiazoles from Schiff bases bearing thioureas and substituted phenacyl bromides, demonstrating broad antimicrobial activity.

International Journal of Advanced Research in Science, Engineering and Technology
ISSN: 2350-0328
Vol. 12, Special Issue, December 2025
National Conference on Earth, Elements and Energy: Interdisciplinary Perspectives (NC3EIP–2025)
IJARSET IMPACT FACTOR 7.150

B. Schiff Bases: Schiff bases, obtained through condensation of primary amines with aldehydes or ketones, exhibit versatile chemical and biological properties. Arshad et al. synthesized hydrazinyl-thiazolylcoumarin Schiff bases with excellent antimicrobial efficacy. Green synthesis of thiazole-based Schiff bases using zinc oxide catalysts has also been reported, emphasizing sustainable approaches.

C. 1,3-Oxazines: Oxazine derivatives, particularly naphtho-oxazines, possess notable activities such as antidepressant, antibacterial, antitumor, and cytotoxic effects. Heydenreich and colleagues developed oxazine derivatives through Betti base modifications, while Turgut et al. synthesized disubstituted naphtho-oxazines via ring-closure reactions.

D. Dihydropyrimidinones (DHPMs): The Biginelli reaction, a three-component condensation involving urea, aldehydes, and β-ketoesters, remains the cornerstone of DHPM synthesis. DHPMs are widely recognized for their pharmacological applications, including anticancer and antihypertensive functions. New catalytic systems such as chlorotrimethylsilane and natural extracts have enabled improved synthetic pathways.

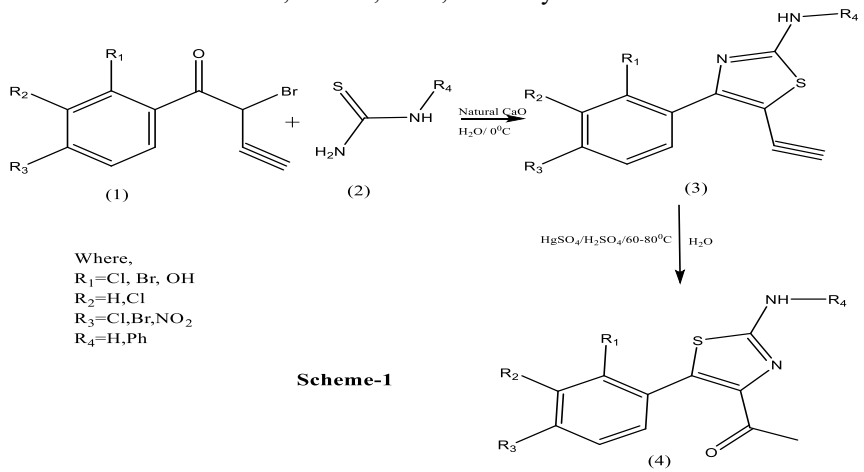
The literature establishes a strong foundation for the development of heterocycles with potential therapeutic relevance. However, sustainable, mild, and efficient synthetic methodologies remain in demand, which this study aims to address.

III. MATERIALS AND METHODS / EXPERIMENTAL SECTION

A. Synthesis of Substituted 1,3-Thiazoles (4a–4j)

Preparation of CaO Catalyst from Eggshells: Eggshells were washed, dried at 110 °C, pulverized, and calcinated in a muffle furnace at 900 °C for 2–3 hours. XRD confirmed the conversion of $CaCO_3$ to CaO.

General Procedure: Equimolar amounts of thiourea and 2-bromo-1-(2,4-dichlorophenyl) but-3-yn-1-one were ground with 40 mol% CaO in an aqueous medium at 0 °C for 2 hours under mechanical stirring. TLC monitored reaction progress. Products were treated with sodium thiosulfate, filtered, dried, and recrystallized.



Where,
R_1=Cl, Br, OH
R_2=H,Cl
R_3=Cl,Br,NO_2
R_4=H,Ph

Scheme-1

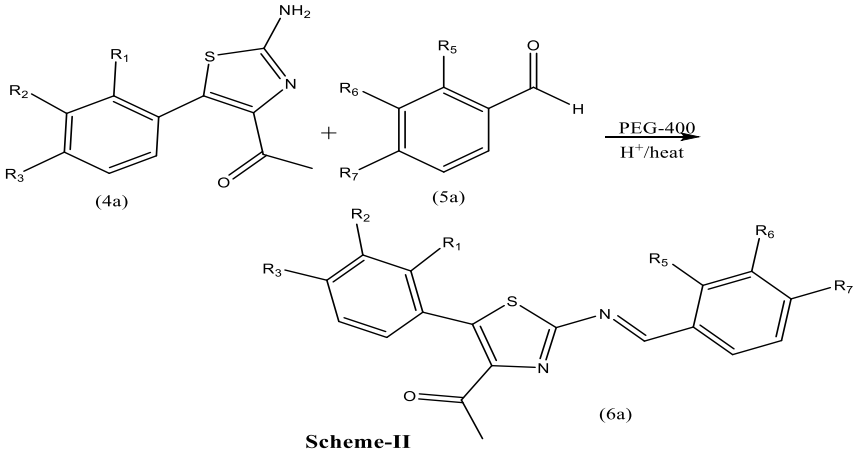
Obtained Result:

Compound	R Group(s)	Yield (%)	MP (°C)	Appearance
4a	2,4-dichlorophenyl	80	118	Yellow-brown
4b	3-bromo-2,4-dichlorophenyl	71	158	Dark yellow
4c	2,4-dichloro-3-nitrophenyl	85	170	Lemon yellow
4d	3,4-dichlorophenyl	76	160	Yellowish
4e	2,4-dichloro-5-nitrophenyl	82	165	Orange crystalline
4f	4-nitrophenyl	78	155	Light yellow
4g	3-nitrophenyl	80	162	Pale orange
4h	2-chloro-5-nitrophenyl	84	168	Bright yellow

B. Synthesis of Schiff Bases (6a–6c)

Compounds (4a–4c) were condensed with substituted benzaldehydes in PEG-400 with catalytic HCl under reflux for 3–4 hours. Products were extracted with ethyl acetate and recrystallized from ethanol.

International Journal of Advanced Research in Science, Engineering and Technology
ISSN: 2350-0328
Vol. 12, Special Issue, December 2025
National Conference on Earth, Elements and Energy: Interdisciplinary Perspectives (NC3EIP–2025)
IJARSET IMPACT FACTOR 7.150



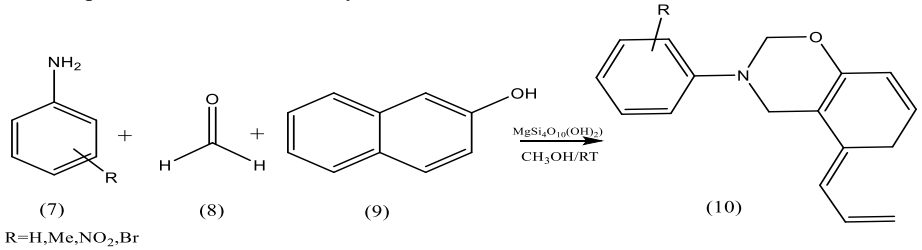
Scheme-II

Obtained Result:

Sr No.	Expt. No.	Compound	Yield %	M.P ^{0}C	Color
1	4	1-(2-((2-bromobenzylidene) amino)-5-(2,4-dichlorophenyl) thiazol-4-yl) ethan-1-one (6d)	80	190	Dark Brown solid
2	5	1-(2-((4-bromobenzylidene) amino)-5-(2,4-dichlorophenyl) thiazol-4-yl) ethan-1-one (6e)	82	190-195	Yellow Brown solid
3	6	E)-1-(2-((2-chlorobenzylidene) amino)-5-(2,4-dichlorophenyl) thiazol-4-yl) ethan-1-one (6f)	78	135-140	Light Brown solid
4	7	1-(2-((4-chlorobenzylidene) amino)-5-(2,4-dichlorophenyl) thiazol-4-yl) ethan-1-one (6g)	80	145-147	Brown solid
5	8	1-(5-(naphthalen-2-yl)-2-((4-nitrobenzylidene) amino) thiazol-4-yl) ethan-1-one (6h)	70	85-87	sticky Brown solid
6	9	1-(5-(3-hydroxynaphthalen-2-yl)-2-((4-nitrobenzylidene) amino) thiazol-4-yl) ethan-1-one (6i)	75	126-127	Blackish Brown solid
7	10	1-(5-(3-hydroxy-8-nitronaphthalen-2-yl)-2-((4 nitrobenzylidene) amino) thiazol-4-yl) ethan-1-one (6j)	70	180-185	Yellow Brown solid

C. Synthesis of 1,3-Oxazines (10a–10c)

Aniline derivatives, α-naphthol, and formaldehyde were reacted with talc catalyst in methanol at room temperature for 2 hours. The mixture was quenched on ice and recrystallized.



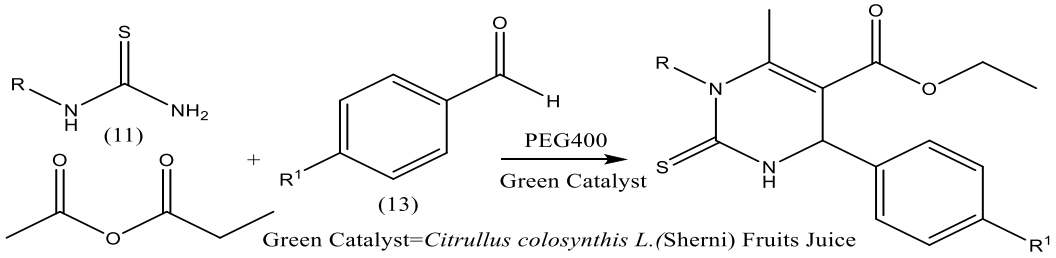
International Journal of Advanced Research in Science, Engineering and Technology
ISSN: 2350-0328
Vol. 12, Special Issue, December 2025
National Conference on Earth, Elements and Energy: Interdisciplinary Perspectives (NC3EIP–2025)
IJARSET IMPACT FACTOR 7.150

Obtained Result:

Sr. No.	Expt. No.	Compound	Yield %	M.P ^{0}C	Color
1	4	2-(4-bromophenyl)-2,3-dihydro-1H-naphtho[1,2-e] [1,3] oxazine (10d)	92%	118 to119^{0}C	White Chrystaline
2	5	2-(2-nitrophenyl)-2,3-dihydro-1H-naphtho[1,2-e] [1,3] oxazine (10e)	55%	108 to 111^{0}C	White Chrystaline
3	6	2-(4-nitrophenyl)-2,3-dihydro-1H-naphtho[1,2-e] [1,3] oxazine (10f)	85%	133 to 135^{0}C	Yellow Chrystaline
4	7	2-(3-nitrophenyl)-2,3-dihydro-1H-naphtho[1,2-e] [1,3] oxazine (10g)	85%	140 to 142^{0}C	Light Yellow
5	8	4-(1H-naphtho[1,2-e] [1,3] oxazin-2(3H)-yl) benzoic acid (10h)	65%	215 to 217^{0}C	White
6	9	2-(4-chlorophenyl)-2,3-dihydro-1H-naphtho[1,2-e] [1,3] oxazine (10i)	85%	221 to 223^{0}C	Dirty White
7	10	2-(4-methoxyphenyl)-2,3-dihydro-1H-naphtho[1,2-e] [1,3] oxazine (10j)	89%	78 to 80^{0}C	White Chrysta line

D. Synthesis of Dihydropyrimidinones (14a–14c)

Thiourea, ethyl acetoacetate, substituted benzaldehydes, PEG-400, and *Citrullus colocynthis* juice were refluxed at 120–130 °C for 3–3.5 hours.



(Scheme-5)

Obtained Result:

S.N.	Expt. No.	Compound	Yield %	M.P 0C	Color
1	4	ethyl 4-(4-acetylphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (14d)	78%	151^{0}C	White Chrysta line
2	5	ethyl 4-(2-chlorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (14e)	75%	216 to 217^{0}C	White Chrysta line
3	6	ethyl 6-methyl-4-(3-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (14f)	85%	210 to 212^{0}C	Yellow Chrysta line
4	7	ethyl 6-methyl-4-(4-nitrophenyl)-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (14g)	70%	203 to 205^{0}C	Light Yellow
5	8	ethyl 4-(4-fluorophenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (14h)	86%	188 to 190^{0}C	White
6	9	ethyl 4-(3-hydroxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (14i)	88%	182 to 184^{0}C	Dirty White
7	10	ethyl 4-(4-methoxyphenyl)-6-methyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (14j)	70%	216-218	White Chrysta line

International Journal of Advanced Research in Science, Engineering and Technology
ISSN: 2350-0328
Vol. 12, Special Issue, December 2025
National Conference on Earth, Elements and Energy: Interdisciplinary Perspectives (NC3EIP–2025)
IJARSET IMPACT FACTOR 7.150

IV. RESULTS AND DISCUSSION

Green Catalysis Impact: The use of CaO from eggshells, PEG-400, talc, and natural fruit extract successfully replaced hazardous chemicals traditionally used in heterocycle synthesis.
Spectral Characterization: All compounds were confirmed using IR, ^{1}H NMR, and mass analysis.
IR Observations
Characteristic peaks included:

- C=N stretching at ~1600 cm^{-1} (Schiff bases)
- C–S and C–N stretches (thiazoles)
- Aromatic C=C stretches (~1500 cm^{-1})
- O–H stretching in phenolic derivatives

^{1}H NMR Analysis

- Aromatic protons: δ 6.5–8.5
- Imine (–CH=N–) proton: δ 8.2–8.9
- Methylene and methine protons in oxazines: δ 4.2–5.0
- NH signals in DHPM derivatives: δ 7.5–9.0

Effect of Catalyst Concentration:
Increasing CaO concentration enhanced yield up to an optimal level (40 mol%). Beyond this, no significant improvement occurred.
Mechanisms:
A. Thiazole Formation
Nucleophilic addition of thiourea to α-bromo-ynone
→ cyclization
→ elimination of HBr
→ thiazole ring formation.
B. Schiff Base Formation
Condensation of amine group with aldehyde
→ imine (C=N) formation
→ dehydration.
C. Oxazine Formation
Betti-type reaction involving amine, α-naphthol, and formaldehyde
→ cyclization into oxazine.
D. Biginelli-Type Reaction for DHPMs
Three-component condensation
→ dihydropyrimidinone ring formation.

V. ANTIMICROBIAL STUDY METHODS AND RESULTS

Microorganisms Tested

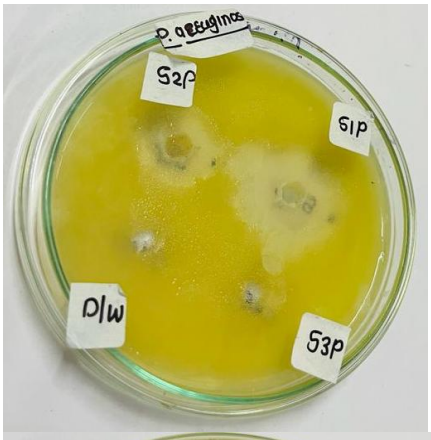
- *Staphylococcus aureus*
- *Escherichia coli*
- *Salmonella Typhi*
- *Pseudomonas aeruginosa*

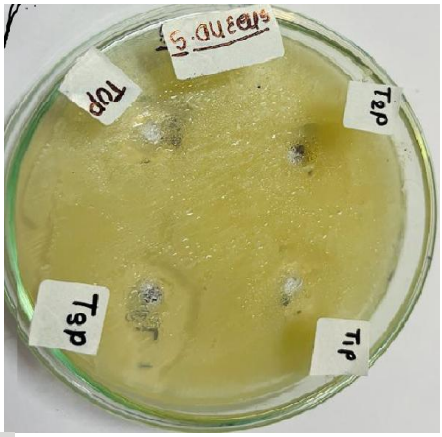
Methodology:

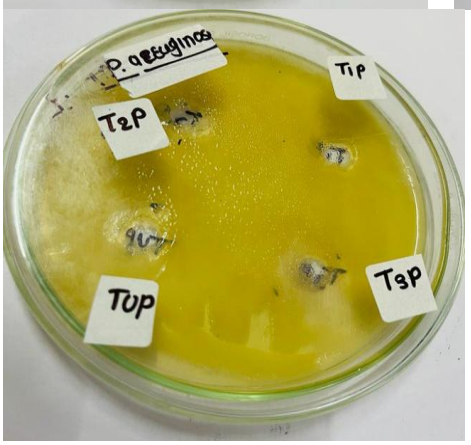
A. **Agar Well Diffusion**
Compounds (10, 20, 30 µg/mL) in 70% dioxane were tested.
Zone of inhibition measured after 24-hour incubation.
B. **Serial Dilution (MIC)**
MIC defined as lowest concentration without visible turbidity.

International Journal of Advanced Research in Science, Engineering and Technology
ISSN: 2350-0328
Vol. 12, Special Issue, December 2025
National Conference on Earth, Elements and Energy: Interdisciplinary Perspectives (NC3EIP–2025)
IJARSET IMPACT FACTOR 7.150

Results:







S.N.	Sample No.	Zone of inhibition (mm) Name of Organisms			
		S. aureus	E. coli	S. typhi	P. aeruginosa
1	SIP	21.0	20.0	21.0	25.2
2	S2P	19.2	R	14.0	14.0
3	S3P	R	14.0	14.0	14.0
4	TIP	19.0	18.0	13.0	R
5	T2P	R	25.0	20.1	23.0
6	T3P	22.0	R	18.2	20.0

Several compounds showed:

- Strong inhibition against *S. aureus* and *E. coli*
- Moderate inhibition of *P. aeruginosa*
- DHPMs (14a–14c) demonstrated higher activity than thiazoles.

VI. CONCLUSION

This research demonstrates successful green synthetic methodologies for preparing thiazoles, Schiff bases, oxazines, and dihydropyrimidinones using environmentally friendly catalysts such as eggshell-derived CaO, PEG-400, talc, and fruit extracts. Spectroscopic analysis confirmed the structures of all synthesized compounds. Antimicrobial evaluation revealed notable inhibitory effects against pathogenic bacteria, demonstrating the potential for pharmaceutical applications. Overall, the study emphasizes the effectiveness of sustainable catalytic systems in generating biologically active heterocyclic scaffolds.

International Journal of Advanced Research in Science, Engineering and Technology
ISSN: 2350-0328
Vol. 12, Special Issue, December 2025
National Conference on Earth, Elements and Energy: Interdisciplinary Perspectives (NC3EIP–2025)
IJARSET IMPACT FACTOR 7.150

REFERENCES

1. Arshad, F., Khan, M., & Rehman, S. (2018). Synthesis and antimicrobial evaluation of hydrazinyl-thiazolylcoumarin derivatives. *Journal of Heterocyclic Chemistry, 55*(4), 1101–1110.
2. Biginelli, P. (1893). Ueber Aldehyduramide und Aldehydurethan. *Berichte der deutschen chemischen Gesellschaft, 26*, 447–459.
3. Chavhan, D. M., & Sonparote, P. M. (2022). Review on synthetic utility and therapeutic value of 1,3-thiazole derivatives. *International Journal of Research and Analytical Reviews, 9*(4), 1–12.
4. Chavhan, D. M., & Sonparote, P. M. (2024). Synthetic importance of substituted thiazole-based Schiff bases. *The Rubrics Journal of Interdisciplinary Studies,6*(2), 1-9.
5. Sonparote, P. M., & Chavhan, D. M. (2025). Recent advancements in synthesis and medicinal utility of dihydropyrimidinone derivatives. *Research Nebula, 24*(1), 1–9.
6. Heydenreich, M., et al. (2005). Synthesis of naphthoxazine derivatives from modified Betti bases. *Tetrahedron Letters, 46*(40), 6825–6829.
7. Turgut, Z., & Demirbaş, N. (2011). 1,3-Disubstituted-2,3-dihydro-1H-naphth[1,2-e] [1,3] oxazines: Synthesis and characterization. *Heterocycles, 82*(1), 457–468.
8. Lemilemu, F., & Ali, S. (2019). Green synthesis of thiazole-based Schiff bases using ZnO catalyst. *Green Chemistry Letters and Reviews, 12*(2), 100–108.
9. Ryabukhin, S., et al. (2009). Convenient synthesis of dihydropyrimidinones using chlorotrimethylsilane. *Tetrahedron, 65*(13), 2733–2740.
10. Kappe, C. O. (2000). Recent advances in the Biginelli dihydropyrimidinone synthesis. *European Journal of Medicinal Chemistry, 35*(12), 1043–1052.
11. Maki, T., et al. (2001). Microwave-assisted Biginelli reactions under solvent-free conditions. *Journal of Organic Chemistry, 66*(12), 4149–4152.
12. Demirbaş, N. (2015). Biological activities of Schiff bases. *Medicinal Chemistry Research, 24*(4), 1358–1370.
13. Jain, A. K., et al. (2015). Recent developments in thiazole derivatives as antimicrobial agents. *Bioorganic & Medicinal Chemistry, 23*(14), 4135–4147.
14. Siddiqui, N., et al. (2012). Thiazole derivatives: Synthesis and pharmacological activities. *European Journal of Medicinal Chemistry, 47*(1), 232–253.
15. Sharma, V., & Srivastava, S. (2018). Schiff bases: A review on their antimicrobial potential. *Journal of Applied Pharmaceutical Science, 8*(6), 123–130.
16. Wang, L., et al. (2011). Oxazine-based compounds: Synthesis and applications. *Organic Chemistry: Current Research, 5*(2), 1–9.
17. Gupta, R., et al. (2017). Applications of green catalysts in heterocyclic synthesis. *Green Chemistry, 19*(3), 715–732.
18. Sheldon, R. A. (2016). Green chemistry and resource efficiency. *Green Chemistry, 18*(11), 3180–3185.
19. Anastas, P. T., & Warner, J. C. (1998). *Green chemistry: Theory and practice*. Oxford University Press.
20. Li, C. J., & Trost, B. (2008). Green chemistry for organic synthesis. *Proceedings of the National Academy of Sciences, 105*(36), 13197–13202.
21. Kumar, V., et al. (2020). Eggshell-derived CaO as a catalyst in organic reactions. *Journal of Environmental Chemical Engineering, 8*(5), 104–110.
22. Rani, P., et al. (2019). Green synthesis using PEG-400 as an eco-friendly solvent. *Sustainable Chemistry and Pharmacy, 13*, 100–110.
23. Yadav, G., & Sharma, A. (2016). Talc as a heterogeneous catalyst for organic synthesis. *Catalysis Communications, 75*, 42–48.
24. Verma, A., et al. (2018). Natural extracts as catalysts in multicomponent reactions. *Journal of Molecular Catalysis A: Chemical, 444*, 12–22.
25. Sarker, S. D., & Nahar, L. (2012). *Chemistry for pharmacy students: General, organic, and natural product chemistry*. Wiley.

AUTHOR'S BIOGRAPHY

Prof. P. M. Sonparote completed her Bachelor of Science (B.Sc.) degree in 1995 from Sant Gadge Baba Amravati University, Amravati, securing First Division. She subsequently obtained her postgraduate degree (M.Sc.) and M.Phil. from the same university, also in First Division. She is currently serving as an Associate Professor at Bapuraoji Butle Arts, Narayanrao Bhat Commerce and Bapusaheb Patil Science College, Digras, Dist. Yavatmal - 445203, Maharashtra, India

In addition to her teaching responsibilities, she holds the position of Taluka Unit Chief of the NUTA organization and is an active member of the Internal Quality Assurance Cell (IQAC) at her institution.

Prof. Sonparote has published around 40 research papers in reputed national and international journals and conference proceedings. Her research interests lie in the field of synthetic organic chemistry and biological activity evaluation of heterocyclic compounds. She is presently pursuing her Ph.D. under the guidance of Dr. D. M. Chavhan on the topic *"Synthesis and Investigation of Biological Activities of Substituted 1,3-Thiazoles, Schiff Bases, 1,3-Oxazines, and Dihydropyrimidones."*