International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 16(4): July-August 2026

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Science

Review Article……!!!

Received: 23-04-2026; Revised: 26-06-2026; Accepted: 10-07-2026

DESIGN, GREEN MICROWAVE-ASSISTED SYNTHESIS AND BIOLOGICAL EVALUATION OF NOVEL HETEROCYCLIC CHALCONE–OXIME HYBRID DERIVATIVES

Atish Pajgade, Prachi Kanawade

Shantiniketan College of Pharmacy, Dhotre, Tal. Parner, Dist. Ahilyanagar, Maharashtra, India.

Keywords:

Chalconeoxim hybrids; Heterocyclic compounds; Green chemistry; Microwave-assisted synthesis; Molecular hybridization; Structureactivity relationship (SAR); Anticancer activity; Enzyme inhibition.

For Correspondence:

Atish Pajgade

Shantiniketan College of Pharmacy, Dhotre, Tal. Parner, Dist. Ahilyanagar, Maharashtra, India

E-mail:

atishpajgade080@gmail.com

ABSTRACT

The heterocyclic chalcone-oxime hybrid derivatives have become one of the promising structures in the contemporary medicinal chemistry due to their structural diversity and wide range of biological activities. A combination of the alpha, beta-unsaturated carbonyl skeleton of chalcones with the hydrogen-bonding oxime group and biologically active heterocyclic crossover intermediates is an example of a rational hybridization strategy to increase the pharmacological potential. The approach to molecular design is intended to enhance target affinity and selectivity, and physicochemical characteristics and overcome the drawbacks of mono-pharmacophoric systems. The past years have seen a growing interest in environmentally friendly synthetic methodology. Green microwave-assisted organic synthesis has been of great concern as an effective substitute to conventional heating techniques. The heating is very fast and even at microwave irradiation leading to less reaction time, higher yields, less energy use and less solvent. Green chemistry principles coupled with the use of microwave-assisted methods provide a viable and ecologically-friendly method of achieving chalcone-oxime hybrids. These hybrids have shown promising anticancer, antimicrobial, anti-inflammatory, antioxidant and enzyme inhibitory properties as evidenced by their biological evaluations. The structure-activity relationship studies involve the impact of substituent patterns, heterocyclic incorporation and oxime modification on biological performance. Also, molecular docking and in silico studies offer mechanistic data and justify rational optimization programs. This review is a holistic summary of the latest developments in the design, green microwave-assisted synthesis, and biological assessment of the new heterocyclic chalcone-oxime hybrid derivatives, besides outlining the current difficulties and future research focus of the new rapidly developing avenue.

Introduction

Significance of Heterocyclic Compounds in Drug Discovery.

Heterocyclic compounds form one of the most crucial types of organic compounds in medicinal chemistry. The substitution of carbon by exotic elements including nitrogen, oxygen, and sulfur in cyclic structures plays a major role in the distribution of electronics, polarity, hydrogen-binding ability and the general pharmacokinetic characteristics. Heterocyclic rings are also an essential aspect of drug discovery today since a large percentage of clinically approved drugs include at least one heterocyclic ring [1].

Heterocyclic scaffolds offer structural variety and allow exquisite regulation of biological action by substitution styles. Their hydrogen bonding and π–π stacking properties to the enzymes, receptors, and nucleic acids make them the perfect pharmacophores in the design of anticancer, antimicrobial, anti-inflammatory, and antiviral agents. In turn, the design of new heterocyclic hybrids is an encouraging approach towards the identification of effective therapeutic candidates [2].

Chalcone Scaffold as a Privileged Pharmacophore.

The chemically defined 1,3-diaryl-2-propen-1-ones are the open-chain flavonoids that contain an 1, 2-unsaturated carbonyl system. This conjugated enone backbone is important in biological reactions especially by Michael addition reactions with nucleophilic residues of biological targets [3].

The chalcone derivatives have a wide range of pharmacological effects such as anticancer, antimicrobial, anti-inflammatory, antioxidant and antimalarial activity. Systematic exploration of structure-activity Relationships (SAR) is achieved by systematic structural modification of either aromatic ring. Chalcones have been regarded as the so-called privilege scaffolds in the medical field because of its synthetic accessibility, structural flexibility, and broad biological potential [4].

Oxime Functionality in Medicinal Chemistry

In oximes, the functional group -C=NOH is present and the oximes are usually the product of reacting ketones/aldehydes with hydroxylamine. Oxime moiety has been known to increase the hydrogen bonding ability, increase metabolic stability and alter lipophilicity [5].

To minimize the adverse effects, oxime derivatives have been investigated to have anticancer, antimicrobial, and enzyme inhibitory properties in medicinal chemistry. The oxime capability has also been utilized as a general synthetic starting material to be cyclized further to heterocyclic. Notably, the oxime group can be incorporated to enhance the pharmacological characteristics affecting the molecular conformation and affinity of the target [6].

Rationale for Chalcone–Oxime Hybridization

Molecular hybridization is a proven method of drug designing wherein two or more pharmacophoric units are spliced into one molecular structure to improve the biological activity and selectivity. The chalcones and oxime functionalities merge together to combine the electrophilic alpha, beta-unsaturated carbonyl framework of chalcones with the hydrogen bonding and stability improving properties of oximes.

Such hybridization is expected to:

- Enhance target binding interactions
- Improve pharmacokinetic properties
- Reduce resistance development
- Provide multi-target activity

Moreover, heterocyclic rings can be included in chalcone-oxime hybrids which could be additional structural modifications to enhance biological effectiveness through structural diversity and specificity to the receptor [7].

Aim and Scope of the Review

The current review seeks to fully compile the more recent developments in designing, green microwave-assisted synthesizing and biological testing of novel heterocyclic chalcone-oxime hybrid derivatives. The focus is made on synthetic methodologies that are environmental friendly especially microwave-assisted technology in accordance with green chemistry [8].

The trends in structure-activity relationship, comparative analysis of traditional and green synthetic systems, and therapeutic potential of such hybrids in different diseases models, are also addressed in this review. Through the critical review of existing literature, the review aims to determine the gaps in research and

prospects of future studies in this promising medicinal chemistry field [9].

Molecular Design Strategy of Chalcone–Oxime Hybrids

The rationality of the chalcone-oxime hybrids design lies in the intuitive integration of several pharmacophoric building blocks into one molecular platform to produce a greater biological functionality. The incorporation of electrophilic 0,1-unsaturated carbonyl chalcone system coupled with hydrogen-bonding oxime functionality and other heterocyclic functionalities can be adopted to produce structurally diversified compounds, which have better target affinity and selectivity and pharmacokinetic attributes. Its design strategy is mainly based on pharmacophore hybridization, systematic structural modification and structure-activity relationship (SAR)-guided optimization [10].

Pharmacophore Hybridization Concept

The pharmacophore hybridization technique is long-established in medicinal chemistry and entails the combination of two or more bioactive scaffolds into one hybrid molecule to realize synergistic or multi-target effects. Within the chalcone-oxime systems, the chalcone moiety provides a reactive 2, 4-unsaturated carbonyl system with the ability to react with nucleophilic residues of biological macromolecules and the oxime group adds extra hydrogen-bond acceptor and donor properties .

This combination is expected to enhance molecular recognition through:

- Improved hydrogen bonding interactions
- Increased π–π stacking with aromatic residues
- Enhanced binding stability through conformational rigidity
- Potential dual or multi-target activity

Moreover, substitution of heterocyclic rings, including pyrazole, isoxazole, thiazole, pyridine, or indole in the chalcone -oxime structure can give further electronic modulation and receptor selectivity. The limitations of single molecules such as the reduced potency or the drug resistance can be potentially overcome using such hybrid systems [11].

Structural Modifications and Design Considerations

It is the structural adjustment in various positions of the aromatic rings and the heterocyclic core that have a significant impact on the biological performance of chalconeoxime hybrids. The design aspects to be taken into account are:

(i) Substituent Effects on Aromatic Rings: Electron-withdrawing groups (e.g., -Cl, -NO 2, -CF 3) and electron-donating groups (e.g., -OH, -OCH 3, -CH 3) have a notable impact on the electronic density, lipophilicity, and reactivity of the alpha, beta-unsaturated carbonyl system. These changes affect the target binding and the biological potency.

(ii)Position of Substitution (Ortho, Meta, Para): The arrangement of substituents on aromatic rings changes the steric hindrance and molecular conformation and the receptor interaction and activity profiles.

(iii) Nature of Heterocyclic Moiety: Addition of nitrogen-, oxygen-, or sulfur-based heterocycles increases the level of polarity and capacity to form hydrogen bonds. Heterocyclic rings can also add other pharmacological properties, and this will help increase the selectivity.

(iv) Oxime Configuration (E/Z Isomerism): The oxime derivatives can be in the form of E or Z isomer, and they may have a different biological activity because of the differences in conformational states and affinity of binding

(v) Lipophilicity and Drug-Likeness: Physicochemical parameters, including LogP, molecular weight, and hydrogen-bonding capacity should be optimized to have desirable ADME (Absorption, Distribution, Metabolism, and Excretion) properties.

All these structural variables are collectively tuned together to attain improved potency and reduced toxicity[12].

Anticipated Structure-Activity Link (SAR) Intuitions.

The initial SAR findings obtained on reported chalcone and oxime derivatives indicate that biological activity is firmly linked to electronic and steric properties of substituents. Generally:

lectron-withdrawing groups in general tend to increase anticancer and antimicrobial efforts by raising the electrophilicity of the enone system.

Electron-donating groups could enhance the anti-inflammatory and antioxidant activity.The addition of heterocyclic rings often increases the enzyme inhibitors activity and molecular stability.

The oxime oxidation of carbonyl could make it more hydrogen bonding and metabolically stable.

Besides, conjugation length and planarity of the molecule are also important factors contributing to the ease of π- π stacking with biological targets. Systematic optimization of chalcone-oxime hybrids towards particular therapeutic use is possible by use of rational modification based on SAR trends.

In general, chalcone-oxime hybrids molecular design approach combines the theory of hybrid pharmacophore, specific structural alteration, and SAR-based optimization to create effective and greener therapeutic agents [13].

Green MWA-Assisted Synthetic Techniques.

The advancement of heterocyclic chalconeoxime hybrids using methodologies that are environmentally friendly has attracted a lot of attention in the recent years. The concept of green microwave-assisted synthesis incorporates both the concepts of green chemistry and microwave irradiation efficiency, and provides a high-yielding, quick, and environmentally friendly method of preparing biologically active molecules. This strategy does not only lower reaction time and solvent-consumption, but also increases selectivity and energy-efficiency [14].

Fundamentals of Green Chemistry in Organic Synthesis

Green chemistry focuses on designing chemical processes that will produce minimal environmental impact and increase safety. This applies in organic synthesis through the use of less hazardous solvents, less energy use, less waste, and better atom economy.

In the case of chalcone-oxime hybrids, there is the green synthetic strategy of:

Use of solvent free or ethanol or water.

- Minimization of reagents that are hazardous.
- Short reaction times
- Recyclable or weak catalysts.
- Greater yield and purity of the products.

Traditional refluxing processes as well as high volumes of solvents commonly result in increased use of energy and waste production. Contrarily, green microwave-assisted methods are far much better on sustainability and lasted synthetic efficiency [15].

Principles of Microwave-Assisted Organic Synthesis (MAOS)

The principle of the microwave-assisted organic synthesis is based on dielectric heating in which directly the polar molecules in the reaction mixture interact with the microwave energy. The advantage of the microwave irradiation over the conventional method of heating is that the heating is rapid and uniform in all parts of the item instead of relying on external heating.

The main mechanisms include:

- Polarization of polar molecules into dipolar molecules.
- The conduction by ions which results in effective energy transfer.

Major advantages of MAOS are:

- Radical decrease in reaction time (minutes, as opposed to hours)
- Higher yields
- Better selectivity
- Less side-product development.
- Lower energy consumption

All these benefits render microwave-assisted synthesis very amenable to the principles of green chemistry [16].

General Synthetic Route for Chalcone–Oxime Hybrids

Synthesis Chalconeoxime hybrids are usually synthesized in two steps:

Step 1: Chalcone Formation

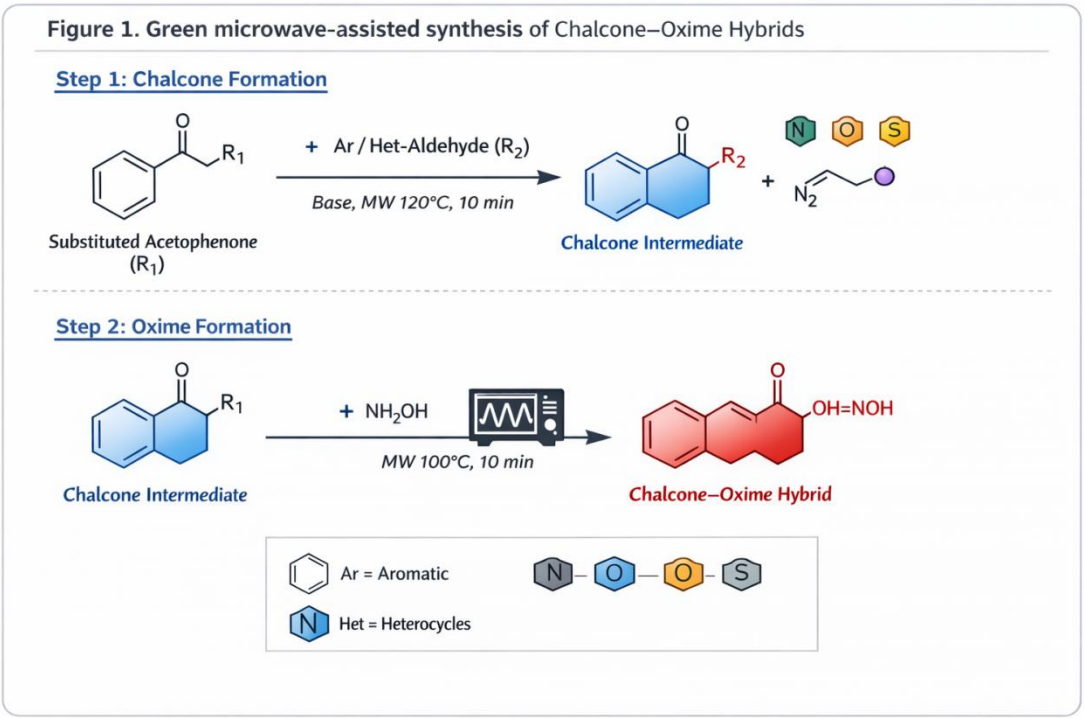
Under basic conditions, the acetophenones are substituted with aromatic or heterocyclic aldehydes to form substituted acetophenones that react with them in Claisen-Schmidt condensation. The reaction is done under the influence of microwave irradiation and the α, beta unsaturated ketone intermediate is obtained within a few minutes.

Step 2: Oxime Formation

The chalcone obtained is reacted with hydroxylamine hydrochloride in order to change the carbonyl group to the oxime (–C=NOH). This transformation can be accelerated using microwave irradiation and

this enhances yield and decreases the reaction time.

Heterocyclic rings are also included to increase the structural diversity and the potential biological activity [17].



The parameters that are optimized are: Solvent, Catalyst, Temperature.

Optimization is critical to the level of efficiency:

- Solvent: Polar solvents like ethanol increase the rate and absorption of microwave.

N: Mild bases (NaOH, KOH) or solid catalysts that are environmental friendly are desired.

- Temperature/Power: It has controlled microwave power (a medium range of temperatures) which inhibits decomposition.
- Reaction Time: It is usually decreased by some several hours down to 5-20 minutes.

An adequate optimization guarantees high atom economy and a low environmental impact [18].

Comparison with Traditional methodology.

Green microwave assisted synthesis has the following advantages compared to its traditional methods of reflux:

Much reduced reaction time.

- Higher product yields
- Less solvent expenditure.
- Lower energy requirements
- More environmentally friendly conditions.

In general, the green microwave-assisted synthesis is an effective, sustainable, and contemporary method towards the production of new heterocyclic chalcone-oxime hybrids with a high biological potential [19].

Biological Analysis of ChalconeOxime Hybrids.

The nature of the 1, 2-unsaturated carbonyl system, oxime-based groups, and heterocyclic moieties in Chalcone-oxime hybrid derivatives leads to a wide pharmacological profile of the latter. The hybrid structure improves the interaction of the molecules with the biological targets due to hydrogen-bonding, π- π stacking, and hydrophobic interactions. Their therapeutic potential has been shown to be promising by various in vitro and computational research [20].

Anticancer Activity

Chalcone-based compounds are known for their ability to inhibit cancer cell proliferation, induce apoptosis, and interfere with microtubule assembly. The electrophilic α,β-unsaturated carbonyl group plays a key role in interacting with nucleophilic residues of cancer-related proteins.Theoxime group incorporation

increases hydrogen bonding ability and it can potentially increase metabolic stability. A series of hybrids of chalconeoxime have demonstrated cytotoxic efficacy against cancer cell lines (e.g. breast, lung and colon cancer model) with activity in the micromolar range. Halogen and nitro substituents tend to increase anticancer activity, whereas incorporation of heterocycle increases specificity [21].

Antimicrobial Activity

The chalcone-oxime hybrids have also been shown to have antibacterial and antifungal activities against Gram-positive and Gram-negative microorganisms. Conjugated enone system helps in disrupting microbial enzymes and cellular processes whereas the oxime group increases interactions of binding. It has been argued that electron-withdrawing substituents enhance antimicrobial properties through making lipophilic and increasing membrane penetration. The resistance could also be minimized by the hybrid character of such molecules, which targets more than one pathway of the microbes [22].

Anti-inflammatory and Antioxidant Potential

The anti-inflammatory effect of the chalcone derivatives is known to be due to the inhibition of the inflammatory mediators, e.g., the COX enzymes. Phenolic groups and conjugated systems are also present and promote antioxidant potential through free radical scavenging. The oxime moiety can further help to increase the interaction with inflammatory targets and stabilize reactive oxygen species in chalcone-oxime hybrids. Antioxidants having an electron-donating group are usually exhibited as more active compounds [23].

Enzyme Inhibition Studies

Several chalcone–oxime hybrids have been evaluated as enzyme inhibitors, including acetylcholinesterase, tyrosinase, and α-glucosidase inhibitors. The oxime functionality enables additional hydrogen bonding within enzyme active sites, while the aromatic rings participate in hydrophobic and π–π interactionsThese enzyme inhibition properties expand the therapeutic relevance of chalcone–oxime hybrids to neurodegenerative, metabolic, and inflammatory disorders [24.

Molecular Docking and In Silico Assessment.

Investigations of molecular docking can give a clue about binding modes and patterns of chalconeoxime hybrids with their target proteins. Hydrogen bonding is usually very strong as seen in docking analyses of the oxime group and the hydrophobic interactions between aromatic rings [25].

ADME prediction in silico suggests that a large number of derivatives meet drug-likeness criteria, which makes them lead compounds. Computational studies are therefore used to supplement experimental results and aid in rational optimization. Altogether, it could be stated that chalcone-oxime hybrids have multifunctional biological properties, which make them one of the possible therapeutic candidates. More in vivo and clinical research is needed before their pharmacological importance can be fully determined [26].

Table 1. Summary of Biological Activities of Chalcone–Oxime Hybrids

Compound Type / Key Substitution	Biological Activity	Target / Cell Line	Observed Effect	SAR Insight
Halogen-substituted hybrids (Cl, Br)	Anticancer	MCF-7, A549	Low micromolar IC_{50}	Electron-withdrawing groups enhance cytotoxicity
Nitro-substituted derivatives	Antimicrobial	S. aureus, E. coli	Strong inhibition	Increased electrophilicity improves activity
Methoxy / Hydroxy substituted	Antioxidant	DPPH assay	Good radical scavenging	Electron-donating groups improve antioxidant potential
Heterocyclic (Pyrazole-linked)	Enzyme inhibition	AChE / COX	Moderate–strong inhibition	Heterocycle improves binding affinity
Oxime-modified derivatives	Anticancer / Enzyme inhibition	Various models	Enhanced activity vs parent chalcone	Oxime improves hydrogen bonding interactions

Structure-Activity Relationship (SAR) Analysis.

The analysis of Structure-Activity Relationship (SAR) is an important part of the phenomena of structural changes on the biological activity of chalcone-oxime hybrids. Changes in substituents, incorporation of heterocycles and functional group changes have a great influence on electronic allocation, lipophilicity, steric and molecular interactions with biological targets. These parameters can be systematically analyzed and optimally optimized through therapeutic potential [27].

Influence of Substituents

Hydroxyl groups on the aromatic rings of the chalcone-oxime hybrids have a strong effect on the biological activity. The nature as well as position (ortho, meta, para) of substituents also affect changes in potency. Electron-withdrawing groups (–Cl, –Br, –NO 2, - CF 3) tend to augment anticancer and antimicrobial action by raising the electrophilicity of the alpha, beta - unsaturated carbonyl system, leading to an augmented interaction with nucleophilic residues in biological targets [28].

Electron-donating groups (–OH, -OCH3, -CH3) also have the potential to enhance antioxidant and anti-inflammatory activities because of the increase of the radical scavenging capacity and the hydrogen bonding capacity. Halogen replacement are common to make lipophilic and more prone to penetrating membranes and better bioactivity.The position of substitution has the influence on steric hindrance and molecular planarity that influences the binding affinity and selectivity. Altogether, a combination of electronic and steric properties is a key to attaining high levels of biological performances [29].

Function of Heterocyclic Moieties.

Substitution of the chalconeoxime base with heterocyclic rings including pyrazole, isoxazole, thiazole, pyridine or indole is also an important advancement in biologic activity. The heterocycles add other heteroatoms (N, O, S), which enhance hydrogen bonding inter-relationships and polarity.

The heterocyclic moieties are present to:

- Greater specificity of the target.
- Increased affinity of enzyme binding.
- Better pharmacokinetic characteristics.
- Increased structural diversity.

Heterocycles that contain nitrogen frequently raise anticancer and enzyme inhibitory medicine as they have the ability to engage with catalytic residues in active locations of proteins. Therefore, heterocyclic incorporation is one of the major strategies towards optimization of chalcone -oxime hybrids [30].

Effect of Oxime Functional Group.

The oxime (– C=NOH) functional group is the key to the regulation of the biological activity. The oxime form of the carbonyl group promotes the ability of hydrogen bonds to be donors or acceptors and promotes the interaction with biological macromolecules.

Oxime group makes contributions to:

Hydrogen bonding results in better binding stability.

- Increased metabolism stability.
- Conformational modulation of molecules.
- Selectivity may be improved.

Also, oximes can be E/Z isomers and variations in structure can modify biological activity because of changes in conformation caused by changes in the interaction of different receptors.

All together, the effects of substituent variation, heterocyclic incorporation, and the oxime modification were combined, from which useful outcomes were derived in the field of rational drug design. These SAR trends are important to gain an idea on how to come up with powerful and selective chalcone-oxime hybrid derivatives [31].

Comparison Analysis: Conventional and Green Microwave Techniques.

Chalcone-oxime hybrids could be synthesized by traditional heating methods or by more contemporary methods based on the use of the microwave. Both techniques are compared to show that there is a drastic difference in the efficiency and environmental effects, and the sustainability of each method. The traditional synthetic methods typically imply the use of long-term heating in organic solvents at a boiled state. Transfers of heat takes place by conduction and convection leading to a gradual rise in temperature. These approaches are time-consuming, usually take many hours, and demand a lot of energy coupled with thermal

degradation or the formation of side-products [32].

However, green microwave-assisted synthesis is based on dielectric heating where microwave energy gets directly in contact with polar molecules in the reaction mixture. This gives high speed and homogeneous internal heating which drastically increases the reaction rate. MW irradiation combined with the concept of green chemistry increases efficiency in the process without necessarily straining the environment [33].

Key Comparative Parameters

Reaction Time:

Traditional processes in most cases need 4-12 hours to form the chalcone along with conversion of the oxime. Microwave-assisted synthesis is able to shorten this time range to 5-20 minutes, and this is a tremendous boost to the synthesis process [34]

Energy Consumption:

The alternative conventional methods demand the use of protracted heating, which increases energy demand. The use of microwave irradiation has the benefit of consuming relatively low energy based on the fact that the reaction time is often short and the heat transfer is effective [35].

Solvent Usage:

Conventional procedures tend to use a lot of organic solvents. Green microwaves methods prefer solvent systems that are minimal, ethanol, water or solvent free conditions thus decreasing hazardous waste [36].

Product Yield and Purity:

Reactions carried out with the aid of microwaves are often more productive and selective. High heating rate reduces side reactions and increases reproducibility[37].

Environmental Impact:

The production of green microwaves is consistent with the implementation of sustainability development because it reduces the rate of waste production, minimizes the exposure to toxic substances, and enhances atom economy [38].

Overall Assessment

Although traditional approaches are still easy and highly available, they are inefficient and unsustainable environment-wise. The green microwave-assisted fabrication has better benefits in terms of reaction rate, yield, and energy consumption, and environmental protection. Thus, to prepare the heterocyclic chalcone-oxime hybrid derivatives, it is more recent that microwave-based green methodologies would be more sustainable, modern and attractive to industry as compared to the conventional ways of preparing them [39].

Difficulties and Gaps in Research.

Although, heterocyclic chalconeoxime hybrids are promising pharmacologically with high potential and the benefits of green microwave-assisted synthesis, there are still a number of challenges and gaps in research that need to be resolved in order to translate them into widely-used clinical and industrial applications [40].

Limited In Vivo and Clinical Studies

Majority of the published works on chalcone-oxime hybrids are limited to in vitro biological experiments. Despite the fact that most of the derivatives show intensive performance in cell-based assays, there are few in vivo studies that support the therapeutic effect and safety of these derivatives. Lack of expedition of preclinical and clinical data inhibits the development of these compounds to drug development [41].

Insufficient Toxicological Profiling

Many of the synthesized derivatives do not have comprehensive toxicity studies, such as acute, sub-chronic and long-term toxicity studies. Knowledge of possible cytotoxicity against normal cells and the determination of the indices of selectivity are also important to be safe and minimize undesirable effects [42].

Mechanistic Understanding

Although anticancer, antimicrobial and enzyme inhibitory acts have been reported, mechanistic studies are not thoroughly covered. It requires a clear description of the molecular targets and the signaling pathways that are involved in order to facilitate rational drug design and optimization [43].

Scalability and Industrial Have an application.

In spite of the fact that microwave-assisted synthesis is competent on a laboratory scale, there are still problems in scaling up of microwave reactions in industrial production. Homogeneity of energy and optimization in the design of the reactor are crucial issues with regard to large-scale implementation [44].

Limited Venture into Structural Diversity.

The vast majority of research is done on a limited set of substituents and heterocyclic systems. More powerful and selective derivatives might be discovered through further research on the range of heterocycles, new patterns of substitution, and novel architectures [45].

Need for Advanced Computational Integration

Though molecular docking studies are widely presented, it is premature to state that the application of advanced computational methods, including molecular dynamics simulations, QSAR modelings, and AI-assisted drug design, is underreported in the given area.On the whole, the scientific conclusions to be drawn in order to fill these research gaps with the help of thorough biological assessment, mechanistic, scalable green synthesis, and improved computational strategy will enable the enhancement of the translational potential of chalcone and oxime hybrid derivatives significantly [46].

Future Perspectives

Heterocyclic chalconeoxime hybrid derivatives are a potential category of multifunctional therapeutic candidates with structural diversity and high biological potential. The work in this area should be developed in the future by incorporating rational drug design, newer green synthetic techniques where the entire biological validation should be included to increase the use of the work in a translational manner. The process of increasing structural diversity with the help of systematic alteration of heterocyclic scaffolds and substituent patterns can be regarded as one of the directions. New heterocycles and hybrid architectures can be studied and result in compounds with enhanced potency, selectivity and pharmacokinetics. There should also be more focus on optimization of physicochemical properties so as to achieve desirable absorption, distribution, metabolism, and excretion (ADME) properties [47].

Quantitative structureactivity relationship (QSAR) modeling, molecular dynamics simulations, and artificial intelligence-based drug design are considered advanced computational techniques that can be used to considerably shorten the process of lead optimization. The combination of in silico and experimental validation will allow finding promising candidates more efficiently. Synthetically, the scalable, continuous-flow microwave systems can be further developed to help increase the industrial viability. Integrating of microwave irradiation with more environmentally friendly catalysts, solvent free environment and recycling materials will enhance sustainability and economic feasibility [48].

Furthermore, there is a need to do comprehensive in vivo experiments and elaborate mechanistic experiments to confirm therapeutic potentials. Clinical translation will be important because of the evaluation of toxicity profiles, pharmacodynamics, and pharmacokinetics. All in all, the interplay between green chemistry, hybrid pharmacophore design and contemporary computational tools creates an excellent foundation on which the future development of chalconeoxime hybrids as next-generation therapeutic agents could be built. Further interdisciplinary studies will play a major role in unlocking their entire medicinal potential [49].

Conclusion

Multifunctional compounds Multifunctional heterocyclic chalcone-oxime hybrids have become the new promising type of compounds in the area of medicinal chemistry. The combination of chalcone scaffold, the oxime functionality, and the heterocyclic moieties should be strategically combined to offer a rational platform to improve the biological activity, selectivity, and structural diversity. The α, beta unsaturated carbonyl system adds to important molecular interactions, and the oxime functional group increases the potential of hydrogen bonding and it also has the possibility to increase pharmacokinetic stability.

The development of the green microwave-assisted synthetic methodologies is an important step toward the preparation of these hybrids. Microwave-assisted methods of heating, compared to conventional heating methods, possess reduced reaction time, improved yields, less energy usage, and reduced environmental impact. These green strategies are consistent with the current green chemistry concepts and contribute to the development of drugs in an environment-friendly manner.

The biological analysis shows that chalcone-oxime hybrids have various pharmacological properties, such as anticancer, antimicrobial, antidermal, antioxidant, and antiflammatory effects, as well as enzyme inhibitory. The analysis of structure-activity relationship reveals that substituent effects, incorporation in the heterocyclic form, as well as oxime modification is essential to maximize the therapeutic potential.

Although these results are encouraging, they still have to be further in vivo validated by providing additional toxicity, profiling, and mechanistic research to propel these compounds into clinical use. All in all, the future of chalcone-oxime hybrids as a promising candidate of a future drug discovery and development can be seen in the merging of hybrid pharmacophore design, green synthetic methods, and rational biological analysis.

References

1. Kalaria PN, Karad SC, Raval DK. A review on diverse heterocyclic compounds as the privileged scaffolds in antimalarial drug discovery. European journal of medicinal chemistry. 2018 Oct 5;158:917-36.
2. Kolb HC, Finn MG, Sharpless KB. Click chemistry: diverse chemical function from a few good reactions. Angewandtechemie international edition. 2001 Jun 1;40(11):2004-21.
3. Kolb HC, Finn MG, Sharpless KB. Click chemistry: diverse chemical function from a few good reactions. Angewandtechemie international edition. 2001 Jun 1;40(11):2004-21.
4. Kolb HC, Finn MG, Sharpless KB. Click chemistry: diverse chemical function from a few good reactions. Angewandtechemie international edition. 2001 Jun 1;40(11):2004-21.
5. Chandran N, Bose K, Thekkantavida AC, Thomas RR, Anirudhan K, Bindra S, Sura S, Hasan HA, Kumar S, Rangarajan TM, Al-Sehemi AG. Oxime derivatives: a valid pharmacophore in medicinal chemistry. ChemistrySelect. 2024 Jul 18;9(27):e202401726.
6. Chandran N, Bose K, Thekkantavida AC, Thomas RR, Anirudhan K, Bindra S, Sura S, Hasan HA, Kumar S, Rangarajan TM, Al-Sehemi AG. Oxime derivatives: a valid pharmacophore in medicinal chemistry. ChemistrySelect. 2024 Jul 18;9(27):e202401726.
7. Ibrahim TS, Almalki AJ, Moustafa AH, Allam RM, Abuo-Rahma GE, El Subbagh HI, Mohamed MF. Novel 1, 2, 4-oxadiazole-chalcone/oxime hybrids as potential antibacterial DNA gyrase inhibitors: design, synthesis, ADMET prediction and molecular docking study. Bioorganic Chemistry. 2021 Jun 1;111:104885.
8. Ibrahim TS, Almalki AJ, Moustafa AH, Allam RM, Abuo-Rahma GE, El Subbagh HI, Mohamed MF. Novel 1, 2, 4-oxadiazole-chalcone/oxime hybrids as potential antibacterial DNA gyrase inhibitors: design, synthesis, ADMET prediction and molecular docking study. Bioorganic Chemistry. 2021 Jun 1;111:104885.
9. Ibrahim TS, Almalki AJ, Moustafa AH, Allam RM, Abuo-Rahma GE, El Subbagh HI, Mohamed MF. Novel 1, 2, 4-oxadiazole-chalcone/oxime hybrids as potential antibacterial DNA gyrase inhibitors: design, synthesis, ADMET prediction and molecular docking study. Bioorganic Chemistry. 2021 Jun 1;111:104885.
10. Alshazly O, Abdel-Aziz M, Abuo-Rahma GE, Mohamed MF. Novel pyrazole–oxadiazole–chalcone/oxime hybrids as dual EGFR/VEGFR-2 inhibitors with promising anticancer potential: a comprehensive cytotoxicity evaluation, mechanistic insights and SAR analysis. Molecular Diversity. 2026 Jan 21:1-33.
11. Frühbeis H, Klein R, Wallmeier H. Computer-Assisted Molecular Design (CAMD)—An Overview. Angewandte Chemie International Edition in English. 1987 May;26(5):403-18.
12. Streeten P. Structural adjustment: A survey of the issues and options. World Development. 1987 Dec 1;15(12):1469-82.
13. Lester C, Reis A, Laufersweiler M, Wu S, Blackburn K. Structure activity relationship (SAR) toxicological assessments: The role of expert judgment. Regulatory Toxicology and Pharmacology. 2018 Feb 1;92:390-406.
14. Fan BQ, He XW, Chen HH, Zhang WM, Tang W. US-guided microwave ablation for primary hyperparathyroidism: a safety and efficacy study. European Radiology. 2019 Oct 1;29(10):5607-16.
15. Sharma M, Sharma M. Fundamental and principles of green synthesis. InAdvances in Green Synthesis: Avenues and Sustainability 2021 May 19 (pp. 257-265). Cham: Springer International Publishing.
16. Rodríguez AM, Prieto P, de la Hoz A, Díaz-Ortiz Á, Martín DR, García JI. Influence of polarity and activation energy in microwave–assisted organic synthesis (MAOS). ChemistryOpen. 2015 Jun;4(3):308-17.
17. Hu D, Zhang N, Zhou Q, Zhou Y, Gong C, Zhang Y, Xue W. Synthesis and biological activities of novel chalcone derivatives containing pyrazoleoxime ethers. Fitoterapia. 2023 Apr 1;166:105458.

18. Rajadhyaksha RA, Karwa SL. Solvent effects in catalytic hydrogenation. Chemical engineering science. 1986 Jan 1;41(7):1765-70.
19. Pereira T, Kennedy JV, Potgieter J. A comparison of traditional manufacturing vs additive manufacturing, the best method for the job. Procedia manufacturing. 2019 Jan 1;30:11-8.
20. El-Sherief HA, Abuo-Rahma GE, Shoman ME, Beshr EA, Abdel-baky RM. Design and synthesis of new coumarin–chalcone/NO hybrids of potential biological activity. Medicinal Chemistry Research. 2017 Dec;26(12):3077-90.
21. Farghaly TA, Masaret GS, Muhammad ZA, Harras MF. Discovery of thiazole-based-chalcones and 4-hetarylthiazoles as potent anticancer agents: Synthesis, docking study and anticancer activity. Bioorganic chemistry. 2020 May 1;98:103761.
22. El-Sherief HA, Abuo-Rahma GE, Shoman ME, Beshr EA, Abdel-baky RM. Design and synthesis of new coumarin–chalcone/NO hybrids of potential biological activity. Medicinal Chemistry Research. 2017 Dec;26(12):3077-90.
23. Cabral B, Siqueira EM, Bitencourt MA, Lima MC, Lima AK, Ortmann CF, Chaves VC, Fernandes-Pedrosa MF, Rocha HA, Scortecci KC, Reginatto FH. Phytochemical study and anti-inflammatory and antioxidant potential of Spondiasmombin leaves. RevistaBrasileira de Farmacognosia. 2016 Jun;26(3):304-11.
24. Nidhar M, Sonker P, Sharma VP, Kumar S, Tewari AK. Design, synthesis and in-silico & in vitro enzymatic inhibition assays of pyrazole-chalcone derivatives as dual inhibitors of α-amylase & DPP-4 enzyme. Chemical Papers. 2022 Mar;76(3):1707-20.
25. Ibrahim TS, Almalki AJ, Moustafa AH, Allam RM, Abuo-Rahma GE, El Subbagh HI, Mohamed MF. Novel 1, 2, 4-oxadiazole-chalcone/oxime hybrids as potential antibacterial DNA gyrase inhibitors: design, synthesis, ADMET prediction and molecular docking study. Bioorganic Chemistry. 2021 Jun 1;111:104885.
26. Pradeepkiran JA, Sainath SB, Shrikanya KV. In silico validation and ADMET analysis for the best lead molecules. InBrucellamelitensis 2021 Jan 1 (pp. 133-176). Academic Press.
27. Alshazly O, Abdel-Aziz M, Abuo-Rahma GE, Mohamed MF. Novel pyrazole–oxadiazole–chalcone/oxime hybrids as dual EGFR/VEGFR-2 inhibitors with promising anticancer potential: a comprehensive cytotoxicity evaluation, mechanistic insights and SAR analysis. Molecular Diversity. 2026 Jan 21:1-33.
28. Ibrahim TS, Almalki AJ, Moustafa AH, Allam RM, Abuo-Rahma GE, El Subbagh HI, Mohamed MF. Novel 1, 2, 4-oxadiazole-chalcone/oxime hybrids as potential antibacterial DNA gyrase inhibitors: design, synthesis, ADMET prediction and molecular docking study. Bioorganic Chemistry. 2021 Jun 1;111:104885.
29. An J, Zhang Z, Jin A, Tan M, Jiang S, Li Y. Organic Functional Groups and Their Substitution Sites in Natural Flavonoids: A Review on Their Contributions to Antioxidant, Anti-Inflammatory, and Analgesic Capabilities. Food science & nutrition. 2025 May;13(5):e70191.
30. Padmapriya M, Hakkimane SS, Gaonkar SL. Synthetic approaches, emerging applications, and challenges of indole-based five-membered heterocycles in medicinal chemistry. Discover Applied Sciences. 2025 Mar 7;7(3):208.
31. Chandran N, Bose K, Thekkantavida AC, Thomas RR, Anirudhan K, Bindra S, Sura S, Hasan HA, Kumar S, Rangarajan TM, Al-Sehemi AG. Oxime derivatives: a valid pharmacophore in medicinal chemistry. ChemistrySelect. 2024 Jul 18;9(27):e202401726.
32. Ruiz-Ojeda LM, Peñas FJ. Comparison study of conventional hot-water and microwave blanching on quality of green beans. Innovative Food Science & Emerging Technologies. 2013 Oct 1;20:191-7.
33. Mishra RK, Yadav A, Mishra V, Mishra SN, Singh DS, Verma DK. Fundamental theory of electromagnetic spectrum, dielectric and magnetic properties, molecular rotation, and the green chemistry of microwave heating equipment. Green Chemical synthesis with microwaves and ultrasound. 2024 Mar 28:21-67.
34. Mazumder R, Ichudaule N, Ghosh A, Deb S, Ghosh R. Significance of chalcone scaffolds in medicinal chemistry. Topics in Current Chemistry. 2024 Jun 27;382(3):22.
35. Sorrell S. Reducing energy demand: A review of issues, challenges and approaches. Renewable and Sustainable Energy Reviews. 2015 Jul 1;47:74-82.
36. Cseri L, Razali M, Pogany P, Szekely G. Organic solvents in sustainable synthesis and engineering. InGreen chemistry 2018 Jan 1 (pp. 513-553.
37. Horikoshi S, Schiffmann RF, Fukushima J, Serpone N. Microwave chemical and materials processing. Microwave Chemical and Materials Processing. 2018;1:33-45.
38. Gallego-Schmid A, Mendoza JM, Azapagic A. Environmental assessment of microwaves and the effect of European energy efficiency and waste management legislation. Science of the Total Environment. 2018 Mar 15;618:487-99.
39. Fischer-Kreer D, Brettel M. Accentuate the positive? Sustainable entrepreneurs' framing of

positive and negative impacts. Journal of Cleaner Production. 2022 Nov 20;376:134319.
40. Almas I, Malik A, Rasool N, Kanwal A, Khalid T, Nawaz H. Microwave-assisted protocol towards synthesis of heterocyclic molecules: a comparative analysis with conventional synthetic methodologies (years 2019–2023): a review. Molecular Diversity. 2025 Jun;29(3):2717-63.
41. Ibrahim TS, Almalki AJ, Moustafa AH, Allam RM, Abuo-Rahma GE, El Subbagh HI, Mohamed MF. Novel 1, 2, 4-oxadiazole-chalcone/oxime hybrids as potential antibacterial DNA gyrase inhibitors: design, synthesis, ADMET prediction and molecular docking study. Bioorganic Chemistry. 2021 Jun 1;111:104885.
42. Shakya A, Chaudhary SK, Bhat HR, Ghosh SK. Acute and sub-chronic toxicity studies of Benincasahispida (Thunb.) cogniaux fruit extract in rodents. Regulatory Toxicology and Pharmacology. 2020 Dec 1;118:104785.
43. Ahmed KB, Raman T, Veerappan A. Future prospects of antibacterial metal nanoparticles as enzyme inhibitor. Materials Science and Engineering: C. 2016 Nov 1;68:939-47.
44. Asase RV, Okechukwu QN, Ivantsova MN. Biofuels: present and future. Environment, Development and Sustainability. 2025 Sep;27(9):22847-75.
45. Kalaria PN, Karad SC, Raval DK. A review on diverse heterocyclic compounds as the privileged scaffolds in antimalarial drug discovery. European journal of medicinal chemistry. 2018 Oct 5;158:917-36.
46. Yuriev E, Agostino M, Ramsland PA. Challenges and advances in computational docking: 2009 in review. Journal of Molecular Recognition. 2011 Mar;24(2):149-64.
47. Alshazly O, Abdel-Aziz M, Abuo-Rahma GE, Mohamed MF. Novel pyrazole–oxadiazole–chalcone/oxime hybrids as dual EGFR/VEGFR-2 inhibitors with promising anticancer potential: a comprehensive cytotoxicity evaluation, mechanistic insights and SAR analysis. Molecular Diversity. 2026 Jan 21:1-33.
48. Anjaneyulu B, Goswami S, Banik P, Chauhan V, Raghav N, Chinmay. Revolution of artificial intelligence in computational chemistry breakthroughs. Chemistry Africa. 2024 Aug;7(6):3443-59.
49. Golay J, Introna M. Mechanism of action of therapeutic monoclonal antibodies: promises and pitfalls of in vitro and in vivo assays. Archives of biochemistry and biophysics. 2012 Oct 15;526(2):146-53.

HOW TO CITE THIS ARTICLE

Atish Pajgade, Prachi Kanawade: Design, green microwave-assisted synthesis and biological evaluation of novel heterocyclic chalcone–oxime hybrid derivatives. International Journal of Institutional Pharmacy and Life Sciences, Vol 16[4] July-August 2026 : 01-19.