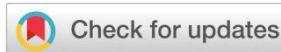
Available online on 15.10.2026 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Copyright © 2026 The Author(s): This is an open-access article distributed under the terms of the CC BY-NC 4.0 which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited



Open Access Full Text Article

Review Article

A Review on the Synthesis, Characterization and Evaluation of Benzimidazole Derivatives for Antimicrobial and Antioxidant Activities

Dharmendra Sahu¹, Rahul Dev¹, Ruchi Gupta¹, Niharika Sahu², Rupesh Sahu³, Shiv Kumar Bhardwaj^{3*}

¹ Gracious College of Pharmacy, Village-Belbhatta, Abhanpur, Raipur-493661, Chhattisgarh, India

² Columbia College of Pharmacy, Columbia Professional University, Tekari, Near Vidhansabha Road, Raipur-493111, Chhattisgarh, India

³ Columbia Institute of Pharmacy, Columbia Professional University, Tekari, Near Vidhansabha Road, Raipur-493111, Chhattisgarh, India

Article Info:



Article History:

Received 13 July 2026
Reviewed 27 Aug 2026
Accepted 20 Sep 2026
Published 15 Oct 2026

Cite this article as:

Sahu D, Dev R, Gupta R, Sahu N, Sahu R, Bhardwaj SK, A Review on the Synthesis, Characterization and Evaluation of Benzimidazole Derivatives for Antimicrobial and Antioxidant Activities, Journal of Drug Delivery and Therapeutics. 2026; 16(10):129-140 DOI: <https://doi.org/10.22270/jddt.v16i10.8051>

For Correspondence:

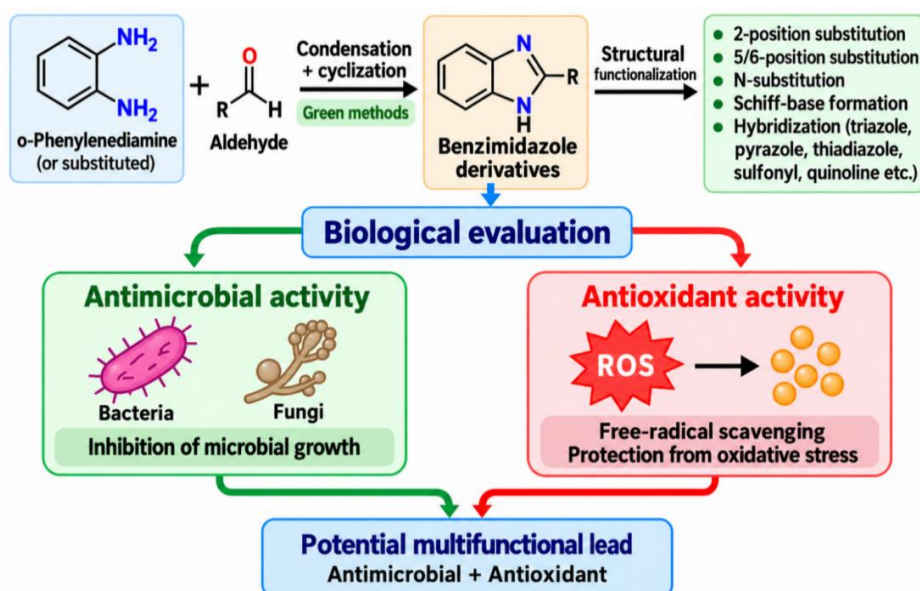
Shiv Kumar Bhardwaj, Assistant Professor, Dept. of Pharmacology, Columbia Institute of Pharmacy, Columbia Professional University, Vill-Tekari, Near Vidhansabha, Raipur-493111, Chhattisgarh, India.

Abstract

Benzimidazole is a privileged nitrogen-containing fused heterocyclic scaffold that has attracted considerable interest in medicinal and pharmaceutical chemistry because of its structural versatility, favorable physicochemical properties and broad biological profile. The benzimidazole nucleus comprises a benzene ring fused with an imidazole ring containing two nitrogen atoms, providing multiple sites for structural modification and interaction with biological targets. This review summarizes recent advances in the synthesis, characterization, antimicrobial evaluation and antioxidant potential of benzimidazole derivatives, with particular emphasis on structure-activity relationships (SAR). Classical synthetic approaches mainly involve the condensation of *o*-phenylenediamine with aldehydes, carboxylic acids and related carbonyl compounds, whereas modern methodologies increasingly employ microwave irradiation, solvent-free conditions, recyclable catalysts, nano-catalysts, photocatalysis, mechanochemistry and other green-chemistry strategies. Structural characterization is commonly performed using Fourier-transform infrared spectroscopy (FTIR), ¹H and ¹³C nuclear magnetic resonance (NMR), mass spectrometry, elemental analysis, ultraviolet-visible spectroscopy and, where appropriate, single-crystal X-ray diffraction. Benzimidazole derivatives demonstrate promising antibacterial and antifungal activities against diverse pathogens. Their antioxidant potential is commonly evaluated using DPPH, ABTS, FRAP and lipid-peroxidation assays. Overall, benzimidazole provides a versatile platform for developing multifunctional antimicrobial and antioxidant agents, although standardized biological protocols, mechanistic validation, selectivity assessment, pharmacokinetic studies and *in vivo* investigations remain necessary for successful therapeutic translation.

Keywords: Benzimidazole; Heterocyclic chemistry; Antimicrobial activity; Antioxidant activity; Structure-activity relationship

Graphical Abstract



Highlights

- ✓ Benzimidazole is a privileged nitrogen-containing heterocyclic scaffold with broad medicinal and pharmacological applications.
- ✓ Condensation of *o*-phenylenediamine with aldehydes is a key synthetic route for 2-substituted benzimidazole derivatives.
- ✓ Structural modification at the 2-, 5/6- and N-positions enables optimization of antimicrobial and antioxidant activities.
- ✓ Benzimidazole derivatives exhibit promising antibacterial, antifungal and free-radical-scavenging activities.
- ✓ Green synthesis, nano-catalysis, hybrid pharmacophores, molecular docking and ADME studies offer promising directions for future benzimidazole research.

1. Introduction

Heterocyclic compounds constitute one of the most important classes of molecules in medicinal chemistry because incorporation of heteroatoms into aromatic and partially saturated ring systems can substantially modify molecular recognition, physicochemical properties, metabolic behavior and biological activity.¹ Among nitrogen-containing heterocycles, benzimidazole has emerged as an important privileged scaffold for pharmaceutical research.² It consists of a benzene ring fused to an imidazole ring and contains two nitrogen atoms capable of participating in hydrogen bonding, protonation/deprotonation and other molecular interactions.³ The versatility of the benzimidazole nucleus arises from the possibility of introducing different substituents around the fused heterocyclic system. Modification at the 2-position, 5/6-positions and nitrogen atom can alter lipophilicity, electronic distribution, steric characteristics, solubility and biological target interactions.⁴ Consequently, numerous benzimidazole derivatives have been investigated as antimicrobial, antifungal, antiviral, anticancer, anti-inflammatory, antiulcer, anthelmintic, antitubercular and antioxidant agents.⁵ Several benzimidazole-containing compounds have achieved practical pharmaceutical or agrochemical importance. The scaffold is also present in established antifungal agents such as benomyl, carbendazim, fuberidazole and thiabendazole, demonstrating the relevance of this chemical framework to antimicrobial research.⁶ **Figure 1** Structural modification of the benzimidazole scaffold at the C-2, 5/6- and N-positions provides opportunities to modulate biological target interactions, pharmacokinetic/pharmacodynamic (PK/PD) properties and lipophilicity.

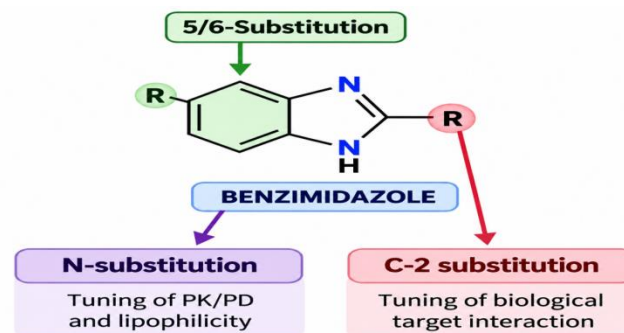


Figure 1. Benzimidazole scaffold and major sites of structural modification

(Substitution at the 2-, 5/6- and N-positions modulates target interactions, PK/PD properties, and lipophilicity).

1.1 Medicinal-chemistry significance of benzimidazole

Benzimidazole derivatives have attracted attention because their fused aromatic system provides rigidity while the nitrogen atoms permit diverse intermolecular interactions. The scaffold can participate in hydrogen bonding and π -related interactions and can be incorporated into hybrid molecules containing additional pharmacophores.⁷ The medicinal relevance of benzimidazole is also reflected by the continuous development of new derivatives. Recent reviews emphasize the importance of substitutions at the 2- and 5/6-positions and the incorporation of additional pharmacophores for improving antimicrobial potency and selectivity.⁸

2. Synthesis of benzimidazole derivatives

The synthesis of benzimidazoles has been extensively investigated because the heterocycle can be generated through several convergent synthetic approaches. Classical strategies commonly begin with *o*-phenylenediamine derivatives and introduce the carbon atom required for formation of the imidazole ring through aldehydes, carboxylic acids, esters, nitriles or related substrates.

2.1 Condensation with aldehydes

The condensation of *o*-phenylenediamine with aldehydes is among the most frequently employed methods for producing 2-substituted benzimidazoles. Initially, condensation produces an imine or related intermediate, followed by intramolecular cyclization and oxidation to afford the aromatic benzimidazole system.⁹ Various oxidizing agents, catalysts and reaction conditions have been developed to improve yield and selectivity.¹⁰ **Figure 2** The synthesis of 2-substituted benzimidazole derivatives commonly involves the condensation of *o*-phenylenediamine with aldehydes, followed by cyclization to form the benzimidazole ring.

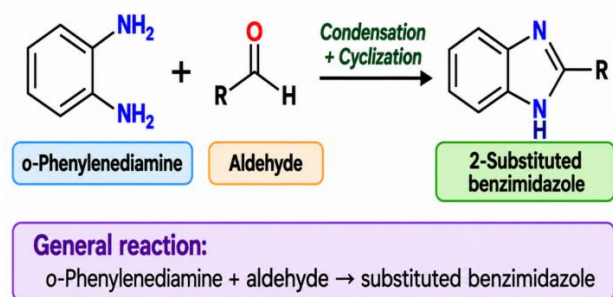


Figure 2. General synthetic route for 2-substituted benzimidazoles

(Condensation and cyclization of *o*-phenylenediamine with an aldehyde affords 2-substituted benzimidazole derivatives).

2.2 Condensation with carboxylic acids and derivatives

Carboxylic acids and their derivatives can also serve as carbon sources for construction of the benzimidazole

ring. Depending on the substrate and reaction conditions, cyclodehydration can generate 2-substituted or more highly functionalized products. Such approaches are useful when incorporation of specific substituents is required.¹¹

2.3 Green synthetic approaches

Recent advances in synthetic chemistry have increasingly focused on minimizing solvent consumption, reaction time, energy requirements, and hazardous waste. Various green strategies have been explored for benzimidazole synthesis, including solvent-free reactions, microwave- and ultrasound-assisted synthesis, recyclable and nano-catalysts, photocatalytic and metal-free catalysis, aqueous reaction media and mechanochemical synthesis. Among these, microwave-assisted, solvent-free, mechanochemical and recyclable catalytic approaches have emerged as particularly promising strategies for achieving more sustainable and efficient benzimidazole synthesis.¹²

Table 1. Major synthetic approaches for benzimidazole derivatives

Synthetic approach	Typical starting materials	Major advantage	Important consideration	Ref.
Aldehyde condensation	<i>o</i> -Phenylenediamine + aldehyde	Simple and versatile	Oxidation/cyclization required	¹³
Carboxylic acid route	<i>o</i> -Phenylenediamine + acid	Direct access to 2-substituted products	Often requires stronger conditions	¹⁴
Microwave-assisted synthesis	Diamine + carbonyl substrate	Short reaction time	Requires controlled microwave conditions	¹⁵
Solvent-free synthesis	Diamine + aldehyde/acid	Reduced solvent waste	Mixing and heat transfer may affect scale-up	¹⁶
Nano-catalytic synthesis	Diamine + carbonyl compound	High catalytic efficiency	Catalyst recovery and characterization	¹⁷
Aqueous synthesis	Diamine + aldehyde	Environmentally favorable	Substrate solubility can be limiting	¹⁸
Photocatalytic synthesis	Diamine + suitable precursor	Mild and sustainable conditions	Photochemical optimization required	¹⁹
Mechanochemical synthesis	Solid reactants	Minimal solvent requirement	Scale-up and uniform milling require optimization	²⁰

3. Characterization of benzimidazole derivatives

Reliable structural characterization is essential because biological activity depends directly on molecular identity, substitution pattern, purity and stereochemical/tautomeric state where relevant.

3.1 FTIR spectroscopy

FTIR spectroscopy provides rapid evidence for functional-group transformations. Characteristic absorptions associated with N–H, C=N, aromatic C=C, C–

N and substituted functional groups can support formation of the benzimidazole nucleus.²¹

3.2 ¹H NMR spectroscopy

¹H NMR spectroscopy is particularly useful for confirming aromatic proton environments, N–H protons, methyl/methylene substituents, substituent-specific signals and the disappearance of the aldehyde proton. The disappearance of characteristic starting-material signals, together with the emergence of appropriate benzimidazole resonances, provides supporting evidence for cyclization and formation of the benzimidazole ring.²²

3.3 ^{13}C NMR spectroscopy

^{13}C NMR provides information regarding the carbon skeleton and is useful for confirming the heteroaromatic C=N-containing environment and substituted aromatic carbons.

3.4 Mass spectrometry

ESI-MS, HRMS or related techniques can establish molecular mass and assist in confirming the proposed

molecular formula. Representative studies have used IR, ^1H NMR and ESI-MS for structural elucidation of substituted benzimidazoles.²³

3.5 Elemental analysis

CHN analysis provides an additional method for verifying the elemental composition and purity of synthesized compounds.²⁴

Table 2. Characterization techniques commonly applied to benzimidazole derivatives

Technique	Major information obtained	Typical application	Ref
FTIR	Functional groups and bond vibrations	Confirmation of C=N, N-H, aromatic and substituent groups	25
^1H NMR	Proton environments	Structural assignment and substitution pattern	26
^{13}C NMR	Carbon environments	Confirmation of heteroaromatic carbon framework	27
HRMS/ESI-MS	Accurate molecular mass	Molecular formula confirmation	28
UV-Vis	Electronic transitions	Conjugation and chromophore assessment	29
Elemental analysis	C/H/N composition	Purity and molecular-formula support	30
X-ray crystallography	Three-dimensional structure	Definitive structural confirmation where crystals are available	31
DFT calculations	Optimized molecular/electronic properties	Complementary structural and mechanistic interpretation	32

4. Antimicrobial activity of benzimidazole derivatives

Antimicrobial resistance has increased the need for new chemical entities with alternative or complementary mechanisms of action. Benzimidazole provides a flexible framework for developing antibacterial and antifungal molecules because modifications around the heterocycle can influence target binding, membrane permeability and cellular accumulation.³³ Recent reviews covering 2018–2024 identify substantial progress in antimicrobial benzimidazole chemistry, including derivatives directed against resistant bacterial and fungal organisms.³⁴

4.1 Antibacterial activity

Benzimidazole derivatives have been extensively investigated against both Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus*, methicillin-resistant *S. aureus* (MRSA), *Streptococcus* spp., *Enterococcus faecalis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*.³⁵ Notably, N,2,6-trisubstituted benzimidazole derivatives have exhibited MIC values of 4–16 $\mu\text{g/mL}$ against selected MSSA and MRSA strains, highlighting the importance of systematic structural modification for improving antibacterial potency.³⁶ In addition, optimized benzimidazole-based compounds have demonstrated MIC values as low as 0.125 $\mu\text{g/mL}$ against specific *E. coli* mutant strains, further supporting

the potential of the benzimidazole scaffold as a promising framework for the development of novel antibacterial agents.³⁷

4.2 Antifungal activity

Benzimidazole derivatives have demonstrated considerable antifungal potential against clinically important fungal pathogens, particularly *Candida*, *Aspergillus* and *Fusarium* species.³⁸ Their antifungal activity is associated with interference in fungal cellular processes, including ergosterol biosynthesis and membrane integrity. Benzimidazole-1,2,4-triazole derivatives have shown promising activity against *Candida* species, with selected compounds exhibiting MIC values of approximately 0.97 $\mu\text{g/mL}$ against *Candida glabrata*.³⁹ Molecular docking studies have suggested favorable interactions with 14 α -demethylase (CYP51), a key enzyme involved in fungal ergosterol biosynthesis.⁴⁰ Furthermore, recent benzimidazole-sulfonate derivatives have exhibited pronounced activity against *Candida albicans*, associated with intracellular ROS accumulation and disruption of ergosterol-associated membrane integrity. These findings highlight benzimidazole as a promising scaffold for the development of novel antifungal agents.⁴¹

5. Evaluation of antimicrobial activity

Antimicrobial evaluation should use standardized methods and appropriate positive and negative controls.

Table 3. Major methods for antimicrobial evaluation

Method	Parameter obtained	Major application	Ref.
Agar well/disk diffusion	Inhibition-zone diameter	Preliminary screening	42
Broth microdilution	MIC	Quantitative antimicrobial potency	43
MBC determination	Minimum bactericidal concentration	Bactericidal assessment	44
MFC determination	Minimum fungicidal concentration	Fungicidal assessment	45
Time-kill assay	Change in viable population over time	Kinetic mechanism	46
Checkerboard assay	FIC/FICI	Combination/synergy studies	47
SEM/TEM	Cellular morphology	Mechanistic evidence	48
ROS assay	Intracellular ROS	Oxidative mechanism	49
Membrane integrity assay	Membrane damage	Mechanistic evaluation	50
Molecular docking	Ligand–target interaction	Target hypothesis generation	51

6. Mechanisms Associated with Antimicrobial Activity

The precise mechanism depends on the substitution pattern and molecular target. Potential mechanisms include:

6.1 DNA and topoisomerase-related mechanisms

Bacterial DNA gyrase and topoisomerase IV are validated antibacterial targets. Benzimidazole-containing inhibitors have been developed that interact with these enzymes, demonstrating the potential of the scaffold for targeting bacterial DNA topology.⁵²

6.2 Fungal ergosterol-related mechanisms

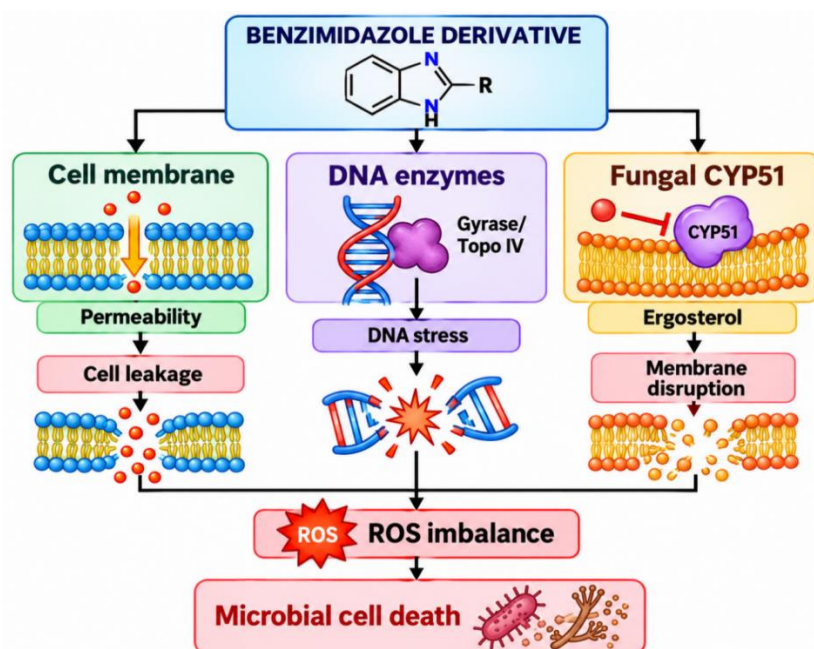
Some benzimidazole derivatives interfere with fungal membrane biology. In recent work, benzimidazole derivatives produced ROS accumulation and showed evidence of ergosterol-associated membrane targeting.⁵³

6.3 Membrane disruption

Increasing lipophilicity can improve interaction with microbial membranes, although excessive lipophilicity may adversely affect solubility and selectivity. Recent fluoro-substituted benzimidazoles were associated with morphological changes in *S. aureus* and *K. pneumoniae*, supporting membrane-associated effects.⁵⁴

6.4 Enzyme inhibition

The benzimidazole ring can interact with enzymes through hydrogen bonding, π - π interactions and hydrophobic contacts. Hybridization with other pharmacophores may enhance target recognition.⁵⁵ **Figure 3** Benzimidazole derivatives may exert antimicrobial effects through multiple mechanisms, including disruption of cell-membrane integrity, inhibition of bacterial DNA enzymes and interference with fungal CYP51-mediated ergosterol biosynthesis, ultimately contributing to ROS imbalance and microbial cell death.

**Figure 3.** Proposed biological mechanisms of antimicrobial action

7. Structure-Activity Relationship of Benzimidazole Derivatives

The biological performance of benzimidazole derivatives depends strongly on substitution pattern. The 2-position is particularly important because it permits attachment of aromatic, heteroaromatic, alkyl,

carbonyl, hydrazone and other pharmacophoric groups. Functionalization at the 5/6 positions can further modify electronic and physicochemical properties.⁵⁶ Recent antimicrobial SAR studies have emphasized the importance of 2- and 5/6-substitution, hybrid pharmacophores and modulation of lipophilicity.⁵⁷

Table 4. Important structural features influencing biological activity

Structural feature	Expected influence	Potential biological consequence	Ref.
2-Aryl substitution	Increases aromatic/hydrophobic interactions	Can improve antimicrobial potency	58
Electron-withdrawing groups	Modify electron density and lipophilicity	May enhance target interaction	59
Halogen substitution	Alters lipophilicity and metabolic stability	Often favorable for antimicrobial activity	60
Hydroxyl group	H-bonding and radical scavenging	May enhance antioxidant activity	61
Methoxy group	Alters electronic and lipophilic character	Can influence target binding	62
N-alkylation	Changes ionization and lipophilicity	Can improve membrane interaction	63
Heterocyclic hybridization	Adds complementary pharmacophoric interactions	Potential synergistic activity	64
Hydrazone/Schiff base	Adds H-bond donor/acceptor features	May improve biological interactions	65
Excessive lipophilicity	Can reduce aqueous solubility	May decrease bioavailability/selectivity	66
Multiple H-bonding groups	Improve polar interactions	May increase target affinity but reduce permeability	67

8. Antioxidant activity of benzimidazole derivatives

Oxidative stress results from an imbalance between reactive oxygen/nitrogen species and endogenous antioxidant defenses. Excessive production of reactive species can damage lipids, proteins and nucleic acids. Consequently, compounds capable of scavenging free radicals or inhibiting oxidative damage are of interest in medicinal chemistry. Benzimidazole derivatives containing suitable electron-donating groups can exhibit radical-scavenging activity. The antioxidant behavior is highly dependent on substitution pattern and the ability of the molecule to donate hydrogen/electrons and stabilize the resulting radical.⁶⁸

8.1 DPPH radical-scavenging assay

The 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay is one of the most frequently used methods for preliminary antioxidant screening. A decrease in DPPH absorbance following reaction with the test compound reflects radical-scavenging capacity. A representative study of substituted benzimidazoles reported significant DPPH activity for selected derivatives, with one compound

showing an IC₅₀ of 16.73 µg/mL compared with 14.44 µg/mL for BHT under the reported conditions.⁶⁹

8.2 ABTS assay

The ABTS assay evaluates the ability of a compound to reduce the ABTS radical cation. It complements DPPH because differences in radical chemistry and assay environment can reveal antioxidant properties that may not be apparent from a single assay.⁷⁰

8.3 FRAP assay

The ferric-reducing antioxidant power (FRAP) assay measures the reducing ability of a compound. It is useful as a complementary assay because antioxidant activity is not exclusively dependent on direct radical scavenging.⁷¹

8.4 Lipid-peroxidation inhibition

Lipid-peroxidation assays provide additional biological relevance by evaluating whether a compound can inhibit oxidative damage to lipid substrates. Benzimidazole derivatives have been investigated using lipid-peroxidation models, including biological tissue homogenates.⁷²

Table 5. Antioxidant evaluation of benzimidazole derivatives

Assay	Principle	Main endpoint	Interpretation	Ref.
DPPH	Reduction of stable free radical	% inhibition / IC ₅₀	Direct radical-scavenging potential	⁷³
ABTS	Scavenging of ABTS•+	Trolox-equivalent activity / IC ₅₀	Broad radical-scavenging activity	⁷⁴
FRAP	Reduction of Fe ³⁺	FRAP value	Reducing capacity	⁷⁵
Lipid peroxidation	Inhibition of oxidative lipid damage	TBARS/MDA-related endpoint	Protection against lipid oxidation	⁷⁶
Superoxide scavenging	Reduction of superoxide-related signal	% inhibition / IC ₅₀	Reactive oxygen species scavenging	⁷⁷
ORAC	Inhibition of oxidation induced by peroxy radicals	Area under curve	Chain-breaking antioxidant capacity	⁷⁸

9. Relationship between antimicrobial and antioxidant properties

The combination of antimicrobial and antioxidant properties makes some benzimidazole derivatives particularly interesting as multifunctional candidates. However, these activities should not automatically be considered mechanistically identical. In some antimicrobial systems, increased ROS generation contributes to microbial killing. Conversely, antioxidant compounds can reduce radical-mediated damage in host tissues. Thus, the desired biological effect may depend on where and how ROS modulation occurs. This distinction is important when designing multifunctional molecules:

Antimicrobial action⁷⁹

Controlled/pro-microbial ROS generation → microbial oxidative damage → microbial death

Antioxidant action

Antimicrobial activity associated with intracellular ROS accumulation may contribute to microbial killing, whereas radical scavenging and reduction of oxidative damage can protect host biomolecules. Recent benzimidazole studies have reported antimicrobial activity associated with intracellular ROS accumulation, while separate derivatives containing phenolic groups have demonstrated significant radical-scavenging antioxidant activity, highlighting the potential of benzimidazole derivatives as multifunctional agents.⁸⁰

10. Recent Trends in benzimidazole-based antimicrobial and antioxidant research

Contemporary benzimidazole research is moving beyond simple synthesis and endpoint biological screening toward integrated medicinal-chemistry optimization. Important trends include:

10.1 Hybrid pharmacophores

Benzimidazole is increasingly combined with diverse pharmacophores, including triazoles, pyrazoles, thiadiazoles, quinolines, sulphonamides, sulfones, hydrazones, amides, and Schiff bases, to generate

structurally diverse hybrid molecules. Such molecular hybridization is intended to integrate complementary pharmacophoric features and biological interactions within a single molecular framework, potentially improving target affinity, selectivity, and overall biological activity.⁸¹

10.2 Green chemistry

Solvent-free, microwave, ultrasound, mechanochemical, photocatalytic and recyclable catalytic approaches can reduce environmental burden and improve synthetic efficiency.⁸²

10.3 Computational drug design

Molecular docking, molecular dynamics (MD) simulations, density functional theory (DFT), and ADME prediction are increasingly employed to predict target binding, identify key molecular interactions, elucidate structure–activity relationships (SAR), prioritize promising compounds, estimate physicochemical and pharmacokinetic properties, and reduce unnecessary experimental synthesis. However, molecular docking should be regarded as supportive rather than definitive evidence of biological activity and its predictions should be validated through appropriate experimental studies.⁸³

10.4 Resistance-oriented design

Recent studies increasingly examine benzimidazole derivatives against resistant bacterial strains and investigate combination strategies. This represents an important direction because antimicrobial resistance cannot be adequately addressed by simply increasing the potency of existing mechanisms.⁸⁴

11. Future perspectives

The future development of benzimidazole derivatives should move toward a more integrated and evidence-based drug-discovery strategy.

11.1 Rational SAR optimization

Systematic modification of the 2-, 5/6- and N-positions should be used to establish quantitative relationships

between molecular structure and antimicrobial/antioxidant activity.

11.2 Standardized biological evaluation

Future studies should preferably report minimum inhibitory concentration (MIC) values rather than relying solely on inhibition-zone data, together with minimum bactericidal/fungicidal concentrations (MBC/MFC), time-kill kinetics, cytotoxicity and selectivity indices, activity against resistant clinical isolates, appropriate reference drugs and mechanistic assays. Such standardized evaluation would facilitate more reliable comparison of antimicrobial efficacy across different studies.

11.3 Mechanism validation

Molecular docking alone should not be considered sufficient to establish a mechanism. Future work should combine docking with biochemical target assays, genetic studies, resistance mapping, membrane studies, ROS analysis and cellular imaging.

11.4 Antioxidant validation

DPPH or ABTS activity should be complemented by cellular antioxidant models, lipid-peroxidation assays and evaluation of oxidative biomarkers. This is necessary because strong chemical radical-scavenging activity does not necessarily translate into biological antioxidant efficacy.

11.5 Green and scalable synthesis

Future synthetic protocols should prioritize: high yield + low toxicity + low solvent consumption + recyclable catalyst + reduced energy consumption + scalability. Recent literature demonstrates increasing interest in solvent-free, microwave, mechanochemical and catalytic approaches.

11.6 AI/ML-assisted design

Machine-learning approaches could integrate molecular descriptors, substituent characteristics, MIC values, antioxidant IC₅₀ values, ADME properties and toxicity data to prioritize new derivatives before synthesis.

11.7 *In vivo* translation

A major gap in the current literature is the transition from *in vitro* activity → cellular efficacy → *in vivo* efficacy → pharmacokinetics → safety. Future benzimidazole candidates should be evaluated systematically across this translational pathway.

12. Conclusion

Benzimidazole represents a highly versatile and pharmacologically important heterocyclic scaffold for the development of antimicrobial and antioxidant agents. Its fused aromatic-imidazole architecture provides a favorable platform for structural modification, while substitution at the 2-, 5/6- and N-positions enables substantial modulation of physicochemical and biological properties. Conventional condensation of *o*-phenylenediamine with aldehydes remains an important synthetic strategy, whereas green approaches involving microwave irradiation, solvent-

free conditions, aqueous media, nano-catalysts, photocatalysis and recyclable catalysts are expanding the synthetic toolbox. Reliable characterization using FTIR, ¹H/¹³C NMR, mass spectrometry and elemental analysis is fundamental for establishing molecular identity. Biological investigations demonstrate that benzimidazole derivatives can possess meaningful antibacterial and antifungal activities, while selected hydroxylated and appropriately substituted derivatives exhibit antioxidant effects in DPPH, ABTS, FRAP and lipid-peroxidation models. The available evidence further indicates that antimicrobial potency is strongly influenced by substitution pattern, lipophilicity, electronic properties, molecular hybridization and target-specific interactions. Recent research has progressed toward resistant pathogens, hybrid pharmacophores, molecular docking, mechanistic studies and green synthesis. Nevertheless, important limitations remain, particularly inconsistent biological protocols, limited mechanistic validation, insufficient toxicity and selectivity data, and inadequate translation from *in vitro* activity to *in vivo* efficacy. Future research should therefore integrate green synthesis + systematic SAR + standardized antimicrobial testing + mechanistic validation + antioxidant/cellular studies + ADME/toxicity assessment + computational drug design. Such an integrated strategy could facilitate the identification of safer and more effective benzimidazole-based multifunctional leads for antimicrobial and oxidative-stress-related therapeutic applications.

Abbreviations

ABTS: 2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)
ADME: Absorption, Distribution, Metabolism and Excretion
AI: Artificial Intelligence
DFT: Density Functional Theory
DNA: Deoxyribonucleic Acid
DPPH: 2,2-Diphenyl-1-picrylhydrazyl
ESI-MS: Electrospray Ionization Mass Spectrometry
FIC: Fractional Inhibitory Concentration
FICI: Fractional Inhibitory Concentration Index
FRAP: Ferric-Reducing Antioxidant Power
FTIR: Fourier-Transform Infrared Spectroscopy
HRMS: High-Resolution Mass Spectrometry
IC₅₀: Half-Maximal Inhibitory Concentration
MBC: Minimum Bactericidal Concentration
MFC: Minimum Fungicidal Concentration
MIC: Minimum Inhibitory Concentration
ML: Machine Learning
MRSA: Methicillin-Resistant *Staphylococcus aureus*
MSSA: Methicillin-Susceptible *Staphylococcus aureus*
NMR: Nuclear Magnetic Resonance
ORAC: Oxygen Radical Absorbance Capacity
PK/PD: Pharmacokinetics/Pharmacodynamics
ROS: Reactive Oxygen Species
SAR: Structure-Activity Relationship
SEM: Scanning Electron Microscopy
TBARS: Thiobarbituric Acid-Reactive Substances
TEM: Transmission Electron Microscopy
UV-Vis: Ultraviolet-Visible Spectroscopy

Ethics approval and consent to participate: Ethical clearance and informed consent were not required, since this manuscript presents a narrative review based solely on previously published literature and involved no primary research involving humans or animals.

Clinical Trial No: Clinical trial registration was not applicable, as this work is a narrative review of published literature and does not involve clinical trials.

Consent for publication: Clinical trial registration was not applicable, as this manuscript is a narrative review based exclusively on previously published literature and does not involve any clinical trial.

Availability of data and material: Data availability was not applicable, as this manuscript is a narrative review of previously published literature and does not involve any original datasets.

Funding: The authors declare that no specific funding was received from governmental, commercial, or non-profit organizations for the preparation of this review.

Declaration of competing interest: The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

Acknowledgements: The authors gratefully acknowledge the Principals of Columbia Institute of Pharmacy, Columbia

Professional University, Raipur, Chhattisgarh, India, and Gracious College of Pharmacy, Village

Belbhata, Abhanpur, Raipur, Chhattisgarh, India, for their encouragement, institutional support, and

provision of essential infrastructure and library resources for the completion of this review.

Authorship contribution statement:

Dharmendra Sahu: Conceptualization, methodology and critical review of the manuscript.

Rahul Dev: Writing-original draft, review and editing, and critical revision of the manuscript.

Ruchi Gupta: Writing-review and editing.

Niharika Sahu: Visualization, schematic design, graphical abstract development, and figure illustration.

Rupesh Sahu: Literature review, data collection and curation, validation, and manuscript evaluation.

Shiv Kumar Bhardwaj: Writing, methodology, visualization and final manuscript editing.

References:

- Ertl P, Altmann E, Wilcken R. Ring systems in medicinal chemistry: A cheminformatics analysis of ring popularity in drug discovery over time. *Eur J Med Chem.* 2025;300:118178. <https://doi.org/10.1016/j.ejmech.2025.118178> PMID:40992171
- Kumar R, Marianesan AB, Pathak S. Benzimidazole as a Privileged Scaffold in Drug Design and Discovery. *Curr Top Med Chem.* 2024;24(17):1504-1528. <https://doi.org/10.2174/0115680266314704240522112439> PMID:38818908
- Chu Y, Zhang P, Zhu Y, Ma P, Ma C. Functional group effects on thermal stability and initial decomposition behavior of nitrogen-rich fused heterocyclic energetic materials: a DFT study. *Struct Chem.* Published online July 13, 2026. <https://doi.org/10.1007/s11224-026-02838-x>
- Tarek A, Jaballah MY, Elrazaz EZ, Samir N. The recent advances in benzimidazole-based antimicrobials and antitubercular agents. *Futur J Pharm Sci.* 2025;11(1):109. <https://doi.org/10.1186/s43094-025-00867-7>
- Sundharaj V, Vijayakumar V, Sarveswari S. A review on biologically important benzimidazole derivatives. *Results Chem.* 2026;21:103042. <https://doi.org/10.1016/j.rechem.2026.103042>
- Lian Z, Zhou J. Recent advances in toxicity and determination methods of benzimidazole fungicides (carbendazim and thiabendazole) in plant-derived foods: a review since 2015. *Microchemical Journal.* 2025;219:116271. <https://doi.org/10.1016/j.microc.2025.116271>
- Irfan A, Arshad M, Al-Hussain SA, et al. Recent advances in the synthetic transformation of benzimidazole scaffolds as privileged pharmacophores for cancer chemotherapy (2020-present). *Journal of Saudi Chemical Society.* 2026;30(1):6. <https://doi.org/10.1007/s44442-025-00051-9>
- Omar MA, Temirak A, Abdelraof M, et al. Design and synthesis of benzimidazole-based derivatives with antimicrobial activity: mechanistic insights into ROS-mediated oxidative damage, hemolytic assessment, and molecular docking studies. *Bioorg Chem.* 2026;174:109736. <https://doi.org/10.1016/j.bioorg.2026.109736> PMID:41831427
- Sundharaj V, Mohanraj S, Sarveswari S, Vijayakumar V. Catalyst-Assisted Synthesis of Benzimidazole Derivatives: Recent Advances and Mechanistic Insights. *Top Curr Chem.* 2026;384(1):5. <https://doi.org/10.1007/s41061-025-00535-7> PMID:41484321
- Keri RS, Adimule V, Kendrekar P, Sasidhar BS. The Nano-Based Catalyst for the Synthesis of Benzimidazoles. *Top Catal.* 2025;68(13):1449-1469. <https://doi.org/10.1007/s11244-022-01562-0>
- Karhale S, Kadam A. Cellulose-based surface-modified heterogeneously feasible novel solid acid catalyst to access bioactive heterocycles. *Research on Chemical Intermediates.* 2024;50(1):31-48. <https://doi.org/10.1007/s11164-023-05171-8>
- Vločskó RB, Mishra M, Stoica AI, Gustin L, Török B. Catalyst-free synthesis of substituted benzimidazoles and benzothiazoles in a sustainable solvent. *Tetrahedron Green Chem.* 2024;3:100035. <https://doi.org/10.1016/j.tgchem.2023.100035>
- Saini P, Kumar K, Saini S, et al. Nanostructured Materials for Visible-Light-Driven Organic Synthesis: A New Catalytic Solution for a Sustainable World. In: 2025:143-180. https://doi.org/10.1007/978-981-96-8229-4_6 PMID:PMC11762537
- Rashid Mohd, Kasana S, Nigam V, et al. Ball-mill-assisted mechanochemical approaches for heterocyclic compound synthesis (2015-2024). *Mol Divers.* 2026;30(1):3-40. <https://doi.org/10.1007/s11030-025-11176-9> PMID:40208427
- Mthembu S, Malevu T, Cele Z, Jonnalagadda S, Gumbi B, Maddila S. A green microwave-assisted synthetic approach of covalent organic frameworks for use in the treatment of saline water. *Inorg Chem Commun.* 2025;178:114494. <https://doi.org/10.1016/j.inoche.2025.114494>
- Monga J, Ghosh NS, Rani I, et al. Unlocking the Pharmacological Potential of Benzimidazole Derivatives: A Pathway to Drug Development. *Curr Top Med Chem.* 2024;24(5):437-485. <https://doi.org/10.2174/0115680266283641240109080047> PMID:38311918
- Agrwal A, Rai P, Kumar V. Recent Developments in Heterogeneous Nano Catalyst for Green Synthesis: A Review. *Top Catal.* 2025;68(18-19):2213-2231. <https://doi.org/10.1007/s11244-025-02118-8>
- Badbedast M, Abdolmaleki A, Khalili D. Synthesis of benzazoles via oxidative cyclization using Fe3O4@PDA/CuCl2 as a green

- nanocatalyst. Research on Chemical Intermediates. 2024;50(2):639-650. <https://doi.org/10.1007/s11164-023-05195-0>
19. Parmar B, Bhandari D, Agrawal S, et al. Temperature-tuned synthesis of g-C₃N₄ for efficient visible light driven nitro-Mannich reactions. J Photochem Photobiol. 2026;33:100288. <https://doi.org/10.1016/j.jpap.2026.100288>
20. Alamiery A. Standardized protocols and applications in mechanochemical synthesis for organic and inorganic materials. Discover Chemistry. 2026;3(1):65. <https://doi.org/10.1007/s44371-026-00526-7>
21. Liu X, Zhou Y, Rajalakshmi K, et al. Functionalization of Halo-Hydroxy Benzimidazole onto SiO₂ Nanoparticles: Catalytic, Photophysical, and Biological Investigations for Sustainable Applications. Silicon. 2025;17(17):4059-4070. <https://doi.org/10.1007/s12633-025-03449-7>
22. Chauhan M, Gupta S, Paliwal S, Nain S. Synthesis, Characterization and Biological Evaluation of Novel Benzimidazole Derivatives against *Candida albicans*. Pharm Chem J. 2024;57(12):1934-1940. <https://doi.org/10.1007/s11094-024-03099-w>
23. Jadhav SK, Devraye SM, Deshmukh RR, Chaitanya GK, Zangade SB. Ultrasound assisted green synthesis, spectral study, crystal structure, Hirshfeld surface analysis, molecular docking and in-vitro cytotoxicity, antimicrobial and antioxidant activity of halohydroxy substituted benzimidazole and benzothiazole Schiff bases. J Mol Struct. 2026;1370:146474. <https://doi.org/10.1016/j.molstruc.2026.146474>
24. Usri SNK, Jamain Z, Makmud MZH. Synthesis and molecular elucidation of new hexasubstituted cyclotriphosphazene derivatives: Determination on flame retardancy, thermal behavior and dielectric properties. J Mol Struct. 2025;1328:141349. <https://doi.org/10.1016/j.molstruc.2025.141349>
25. Banu H V, Arulnangai R, Karthi G B, Thabassoom H A, Thirugnanasambandham K, Ganesamoorthy R. Synthesis, characterization, DFT, HOMO-LUMO, MEP analysis, and in-silico docking studies of piperidine derivatives. Journal of the Indian Chemical Society. 2025;102(5):101679. <https://doi.org/10.1016/j.jics.2025.101679>
26. Mohnish M, Ramavath V, Ghule VD, Sarangapani R. Computation of ¹H NMR chemical shifts: structural assessment of energetic materials. J Mol Model. 2025;31(9):230. <https://doi.org/10.1007/s00894-025-06448-y> PMID:40762858
27. Zhu S, Zou Y, Zhang X, et al. Thiazole and thiophene based heterocyclic tailored TiO₂ nanocomposite for anti-pancreatic cancer activity against PANC-1 pancreatic cells and its unravelling photodegradation dynamics. Colloids Surf B Biointerfaces. 2026;266:115814. <https://doi.org/10.1016/j.colsurfb.2026.115814> PMID:42150516
28. Patel N V, Patel PR, Kamdar NR. One-pot CAN-catalyzed synthesis of indole-substituted pyrimido-fused naphthyridine and thiazole-based derivatives from diverse amines: Cytotoxicity against breast cancer cell line. Tetrahedron. 2026;196:135278. <https://doi.org/10.1016/j.tet.2026.135278>
29. Akash MSH, Rehman K. Comprehensive Insights into UV-VIS Spectrophotometry. In: Essentials of Pharmaceutical Analysis. Springer Nature Singapore; 2025:95-160. https://doi.org/10.1007/978-981-96-5996-8_3
30. Harisankar S, Pragadeshwar Babu MV, Srinivasan S, Vinu R. Hydrothermal liquefaction of diverse plastics using water and seawater. Chemical Engineering Journal. 2024;501:157365. <https://doi.org/10.1016/j.cej.2024.157365>
31. Xiao J. Structural Insights from X-Ray Crystallography. In: 2024:103-118. https://doi.org/10.1007/978-981-10-1941-8_6
32. Dahham Abed M, M. Saeed Younus Tahhan O, Muhsin Mohammed Youns Pto A, Kebiroğlu MH, Bulut N. Halogen-dependent electronic regulation of reactivity and acetylcholinesterase recognition in halomethyl acetates: a predictive DFT-docking framework. J Comput Aided Mol Des. 2026;40(1):117. <https://doi.org/10.1007/s10822-026-00828-z> PMID:42126661 PMCID:PMC13171781
33. G AC, Kumari J, Kishan J, et al. 2-Substituted and 1,2-disubstituted benzimidazole derivatives: Synthesis and identification of potential antibacterial agents. J Mol Struct. 2025;1333:141693. <https://doi.org/10.1016/j.molstruc.2025.141693>
34. Gori C, Katariya D, Akbari A, Naliapara Y. Benzimidazole: An Overview of Synthesis, Properties, and Diverse Biological Applications in Medicinal Chemistry. Reviews and Advances in Chemistry. 2025;15(4):466-487. <https://doi.org/10.1134/S2634827625600331>
35. Natarajan R, Kumar P, Subramani A, et al. A Critical Review on Therapeutic Potential of Benzimidazole Derivatives: A Privileged Scaffold. Med Chem (Los Angeles). 2024;20(3):311-351. <https://doi.org/10.2174/0115734064253813231025093707> PMID:37946342
36. Saha S, Singh M, Thapliyal N, Ahamad S, Bhat SA, Jakhmola V. Imidazole Scaffolds against *Staphylococcus aureus* and MRSA: a medicinal chemistry review. Mol Divers. Published online May 11, 2026. <https://doi.org/10.1007/s11030-026-11580-9>
37. Shao WB, Zhou X, Yang S, Zhou Y. Targets for bacterial resistance: recent advances in small-molecule FtsZ inhibitors. Future Med Chem. 2026;18(9):1133-1152. <https://doi.org/10.1080/17568919.2026.2642580> PMID:41870231 PMCID:PMC13154970
38. Negm E, Mosaad AM, El-Taweel F, Sofan M. Sustainable Dyeing, thermodynamic Investigation, and antimicrobial finishing of Nylon-6 fabrics using novel Benzimidazole-Based azo dyes in supercritical carbon dioxide. Journal of Industrial and Engineering Chemistry. Published online August 2026. <https://doi.org/10.1016/j.jiec.2026.07.040>
39. Tu J, Sheng C. Triazole antifungal drug-fluconazole. In: Medicinal Chemistry and Drug Development. Elsevier; 2025:449-464. <https://doi.org/10.1016/B978-0-443-27402-2.00017-6> PMID:39289330
40. Ünver H, Bağcı ER, Gül ÜD, Kapavarapu R, AY EN, Acar Çevik U. Design, synthesis, in vitro, and in silico studies of benzimidazolium derivatives as potent antimicrobial agents. J Mol Struct. 2025;1345:143119. <https://doi.org/10.1016/j.molstruc.2025.143119>
41. Omar MA, Temirak A, Abdelraof M, et al. Design and synthesis of benzimidazole-based derivatives with antimicrobial activity: mechanistic insights into ROS-mediated oxidative damage, hemolytic assessment, and molecular docking studies. Bioorg Chem. 2026;174:109736. <https://doi.org/10.1016/j.bioorg.2026.109736> PMID:41831427
42. Boy S, Ardahanlı H, Gören K, Manap S, Yüksek H. Novel triazole derivative Mannich bases as potential therapeutic agents: synthesis, in-vitro and in-silico studies. J Mol Struct. 2026;1375:146893. <https://doi.org/10.1016/j.molstruc.2026.146893>
43. Liu T, Wang ZJ, Shi YZ, et al. Curcusinol from the fruit of *Carex baccans* with antibacterial activity against multidrug-resistant strains. J Ethnopharmacol. 2024;318:116892. <https://doi.org/10.1016/j.jep.2023.116892> PMID:37460030
44. Farokhnasab O, Moghadam A, Eslamifar Z, Moghadam AH. Fabrication and characterization of chitosan-based bionanocomposite coating reinforced with TiO₂ nanoparticles and carbon quantum dots for enhanced antimicrobial efficacy. Int J Biol Macromol. 2025;296:139648. <https://doi.org/10.1016/j.ijbiomac.2025.139648> PMID:39798761
45. Tópor A, Veras FF, Cacciatore FA, Silveira RD, da Silva Malheiros P, Welke JE. Carvacrol nanocapsules as a new antifungal strategy: Characterization and evaluation against fungi important for grape quality and to control the synthesis of ochratoxins. Int J Food Microbiol. 2024;416:110659. <https://doi.org/10.1016/j.ijfoodmicro.2024.110659> PMID:38461732
46. Li Y, Chen J, Zhang W, Li J, Pu Y. Making Mycobacterium tuberculosis Killable: Operational Survival Phenotyping Beyond the Persister Metaphor. Cell Insight. Published online September 2026:100358. <https://doi.org/10.1016/j.cellin.2026.100358>

47. Kurmi A, Singh AP, Gautam Y, et al. Gallic Acid Derived 1, 2-Diarylindole as a Potential Synergistic Antifungal Agent against *Candida* Strains. *Curr Top Med Chem.* 2025;25(9):999-1015. <https://doi.org/10.2174/0115680266278892240102045630> PMID:38549526
48. Li X, Zhou Q, Chen Y, Huang Y, Yang W. Strength-ductility synergy of additive manufactured non-equiatomic FCC-based CoCrFeNi2Mox high entropy alloys: Intrinsic cellular structure and σ phase modulation strategy. *Materials Science and Engineering: A.* 2025;945:149021. <https://doi.org/10.1016/j.msea.2025.149021>
49. Li F, Mao Z, Du Y, et al. Mesoporous MOFs with ROS scavenging capacity for the alleviation of inflammation through inhibiting stimulator of interferon genes to promote diabetic wound healing. *J Nanobiotechnology.* 2024;22(1):246. <https://doi.org/10.1186/s12951-024-02423-6> PMID:38735970 PMCID:PMC11089722
50. Wang W, Chen Y, Fang J, Zhang F, Qu G, Cai Z. Toxicity of substituted p-phenylenediamine antioxidants and their derived novel quinones on aquatic bacterium: Acute effects and mechanistic insights. *J Hazard Mater.* 2024;469:133900. <https://doi.org/10.1016/j.jhazmat.2024.133900> PMID:38442600
51. Abbaoui Z, Khibech O, Oulous A, et al. In silico and in vitro evaluation of N-heterocyclic derivatives as antimicrobials: ADMET analysis, SAR, and molecular docking. *In Silico Pharmacol.* 2025;13(3):163. <https://doi.org/10.1007/s40203-025-00445-y> PMID:41163692 PMCID:PMC12559536
52. Marinescu M. Benzimidazole-Quinoline Hybrids: Synthesis and Antimicrobial Properties. *Pharmaceuticals.* 2026;19(1):180. <https://doi.org/10.3390/ph19010180> PMID:41599778 PMCID:PMC12845349
53. Wang J, Zuo L, Lu Z, et al. Clotrimazole disrupts ergosterol biosynthesis and cell membrane integrity via targeting sterol 14 α -demethylases to suppress virulence of *Magnaporthe oryzae*. *Int J Biol Macromol.* 2026;335:148998. <https://doi.org/10.1016/j.ijbiomac.2025.148998> PMID:41232888
54. Hagar FF, Abbas SH, Atef E, Abdelhamid D, Abdel-Aziz M. Benzimidazole scaffold as a potent anticancer agent with different mechanisms of action (2016-2023). *Mol Divers.* 2025;29(2):1821-1849. <https://doi.org/10.1007/s11030-024-10907-8> PMID:39031290 PMCID:PMC11909089
55. Poyraz S, Yildirim M, Ersatir M. Recent pharmacological insights about imidazole hybrids: a comprehensive review. *Medicinal Chemistry Research.* 2024;33(6):839-868. <https://doi.org/10.1007/s00044-024-03230-2>
56. Lee CH, Oh JI, Park HD, et al. Pharmacological characterization of LB50016, N-(4-amino)butyl 3-phenylpyrrolidine derivative, as a new 5-HT1A receptor agonist. *Arch Pharm Res.* 1999;22(2):157-164. <https://doi.org/10.1007/BF02976540> PMID:10230506
57. Nawareg NA, Mostafa AS, El-Messery SM, Nasr MNA. New benzimidazole based hybrids: Synthesis, molecular modeling study and anticancer evaluation as TopoII inhibitors. *Bioorg Chem.* 2022;127:106038. <https://doi.org/10.1016/j.bioorg.2022.106038> PMID:35870412
58. da Silva Santos I, Magalhaes LO, Marra RKF, et al. Natural and Synthetic Coumarins as Potential Drug Candidates against SARS-CoV-2/COVID-19. *Curr Med Chem.* 2025;32(3):539-562. <https://doi.org/10.2174/0109298673285609231220111556> PMID:38243979
59. Deshmukh HS, Adole VA, Mali SN, Jagdale BS. Design, synthesis, biological evaluation, and computational insights of 2-(Aryl)benzo[d]imidazo[2,1-b]thiazole-7-sulfonamide derivatives as potent antitubercular and antibacterial agents. *BMC Chem.* 2025;19(1):126. <https://doi.org/10.1186/s13065-025-01405-5> PMID:40361163 PMCID:PMC12076927
60. Ghorab MM, Aboul-Magd DS, Soliman AM. Novel 2-oxoethylthio-sulfonamide derivatives targeting pyocyanin/staphyloxanthin producing-pathogens: Antibiofilm, DHPS inhibition and gamma radiation effects. *Bioorg Chem.* 2025;167:109228. <https://doi.org/10.1016/j.bioorg.2025.109228> PMID:41240624
61. Sharanya J, Purushothaman A, Janardanan D, Koley K. Theoretical exploration of the antioxidant activity of honokiol and magnolol. *Comput Theor Chem.* 2024;1232:114460. <https://doi.org/10.1016/j.comptc.2023.114460>
62. Sulistianingrum R, Suryadi H, Hayun H. New structure development of chalcone to discover potent antibacterial agents: A systematic review. *J Mol Struct.* 2026;1352:144353. <https://doi.org/10.1016/j.jmolstruc.2025.144353>
63. Biswas A, Bhalani D V., Bhojani G, et al. Poly(vinylidene fluoride)/partially alkylated poly(vinyl imidazole) interpolymer ultrafiltration membranes with intrinsic anti-biofouling and antifouling property for the removal of bacteria. *J Hazard Mater.* 2022;438:129538. <https://doi.org/10.1016/j.jhazmat.2022.129538> PMID:35999742
64. Priya TS, Swain S, Rao BV, et al. Exploring the anticancer potential of β -amyrin: Scalable process for isolation, semi synthesis, and molecular docking studies. *Bioorg Med Chem.* 2025;130:118388. <https://doi.org/10.1016/j.bmc.2025.118388> PMID:40957263
65. Dağ AK, Köse A, Comlekcioglu U, Sirajuddin M, Köse M. New hydralazine-based Allyl derivatives: Crystal structures and in vitro/in silico DNA-binding studies. *J Mol Struct.* 2026;1368:146317. <https://doi.org/10.1016/j.jmolstruc.2026.146317>
66. Gavisiddaiah M, Goswami SK, Somanna M, et al. Insights into the potential role of sEH inhibition in the prevention and progression of neurological disorders. *Endocrine and Metabolic Science.* 2025;19:100277. <https://doi.org/10.1016/j.endmts.2025.100277>
67. Kaur N, Gupta S, Pal J, Bansal Y, Bansal G. Design of BBB permeable BACE-1 inhibitor as potential drug candidate for Alzheimer disease: 2D-QSAR, molecular docking, ADMET, molecular dynamics, MMGBSA. *Comput Biol Chem.* 2025;116:108371. <https://doi.org/10.1016/j.compbiolchem.2025.108371> PMID:39954613
68. Lumov N, Anichina K, Vuchev D, et al. Synthesis of 2-aryl substituted benzimidazoles as bifunctional agents combining antiparasitic activity with radical-scavenging properties against *Trichinella* infection. *Curr Res Biotechnol.* 2026;11:100383. <https://doi.org/10.1016/j.crbiot.2026.100383>
69. Almansour AI, Arumugam N, Soliman SM, et al. Eco-friendly synthesis, structural elucidation, computational investigation and in vitro antioxidant activity of a new N-tosylated benzimidazole derivative. *J Mol Struct.* 2024;1296:136825. <https://doi.org/10.1016/j.jmolstruc.2023.136825>
70. Adardour M, Drioua S, Ait Lahcen M, et al. Deciphering the cytotoxic and antioxidant potential of 3,5-disubstituted isoxazole-linked benzimidazolone derivatives. *J Mol Struct.* 2025;1320:139683. <https://doi.org/10.1016/j.jmolstruc.2024.139683>
71. Donoso-Bustamante V, Osorio E, Arias-Santé MF, et al. Antioxidant activity of sinapic acid anilides: DPPH, ABTS, FRAP, electrochemical and theoretical analysis. *LWT.* 2025;222:117656. <https://doi.org/10.1016/j.lwt.2025.117656>
72. El-Saidy SA, El-Feki AS, El-Khodary GM, Hassan AAA, Elgendy DI, Gawaan YM. A potential therapeutic effect of sea cucumber *Holothuria polii* extract during the intestinal phase of experimental trichinellosis. *Journal of Parasitic Diseases.* 2025;49(1):224-241. <https://doi.org/10.1007/s12639-024-01737-4> PMID:39975624 PMCID:PMC11832982
73. Aljerf L, Maad AH, Rasool S, Alajlani M. Harnessing the antioxidant and cytoprotective power of *Aitchisonia rosea*: phytochemical insights and mechanistic validation. *BMC Plant Biol.* 2025;25(1):1116. <https://doi.org/10.1186/s12870-025-07084-7> PMID:40846912 PMCID:PMC12372252
74. Zorlu A, Elmastaş M, Soy M, et al. *Mentha* genotypes as rich sources of eriocitrin and rosmarinic acid: phenolic profiling, antioxidant capacity, and implications for a sustainable bioeconomy. *Journal of Food Measurement and Characterization.* 2026;20(4):5948-5963. <https://doi.org/10.1007/s11694-026-04044-z>

75. Yapıcı İ, Gülçin İ. Evaluation of antioxidant and antiproliferative activities of shogaol and its modulatory effects on key metabolic enzymes. *Discover Food*. 2026;6(1):186. <https://doi.org/10.1007/s44187-026-00892-2>
76. Wang J, Jiang B, Lin X, et al. Genistein ameliorates glucose-induced β -amyloid toxicity, oxidative stress, and aging in the *C. elegans* model of Alzheimer's disease. *Free Radic Biol Med*. 2026;242:167-187. <https://doi.org/10.1016/j.freeradbiomed.2025.10.263> PMID:41130542
77. Nacer SN, Lanez E, Harkati D, et al. Synthesis, characterisation and antioxidant activity of novel ferrocenyl acetylaniline regioisomers: Electrochemical, spectrophotometric and computational study. *J Organomet Chem*. 2026;1057:124202. <https://doi.org/10.1016/j.jorganchem.2026.124202>
78. Suhag R, Ferrentino G, Morozova K, Zatelli D, Scampicchio M, Amorati R. Antioxidant efficiency and oxidizability of mayonnaise by oximetry and isothermal calorimetry. *Food Chem*. 2024;433:137274. <https://doi.org/10.1016/j.foodchem.2023.137274> PMID:37666126
79. Zheng P, Liu J, Gao B, Yi J, Al-Farraj S, Sillanpää M. Active and molecular biological mechanisms of *Escherichia coli* death caused by CuCeO_x: Synergy of ROS-mediated oxidative stress and cuproptosis-associated metabolic collapse. *J Environ Chem Eng*. 2025;13(6):120472. <https://doi.org/10.1016/j.jece.2025.120472>
80. Mali S, Vatagude SD, Horitani M, Gurubasavaraj PM. Recent advances in Copper(II) Schiff base complexes: A comparative review of ligand core influence on biomedical applications. *J Mol Struct*. 2026;1360:145599. <https://doi.org/10.1016/j.molstruc.2026.145599>
81. Patil SM, Nikalje P, Gavande N, Asgaonkar KD, Rathod V. An Insight into the Structure-activity Relationship of Benzimidazole and Pyrazole Derivatives as Anticancer Agents. *Curr Top Med Chem*. 2025;25(4):350-377. <https://doi.org/10.2174/0115680266343336241021080438> PMID:39484762
82. Shi Y, Zhang W xian. Mechanochemistry in hazardous wastes treatment: A review. *J Environ Chem Eng*. 2025;13(4):117223. <https://doi.org/10.1016/j.jece.2025.117223>
83. Tandel P, Makwana BB, Patel AB. Development of coumarin-benzimidazole conjugates via Pd/Cu-catalyzed coupling for mycobacterial inhibition supported by molecular docking, ADME prediction, and molecular dynamics simulations. *Research on Chemical Intermediates*. Published online August 10, 2026. <https://doi.org/10.1007/s11164-026-06081-1>
84. Zhang Y, Qin L, Li R, et al. A potential benzimidazole-derived compound, NSC348884, combats carbapenem-resistant gram-negative bacteria. *Biochem Pharmacol*. 2026;249:117910. <https://doi.org/10.1016/j.bcp.2026.117910> PMID:41861964