INTERNATIONAL JOURNAL OF ARTS, COMMERCE & EDUCATION
A Multidisciplinary Peer-Reviewed, Refereed, Open Access Journal,
https://avjournals.com/ e-ISSN: 2347-7687, Vol 14, Issue 2, April-June 2026

RECENT ADVANCES IN COUMARIN DERIVATIVES FOR DRUG DISCOVERY: BIOLOGICAL ACTIVITIES, MOLECULAR MECHANISMS, AND THERAPEUTIC PROSPECTS

Max Constance Rak (Research Scholar)
Department of Pharmacy, Sunrise University, Alwar, India

Abstract

Coumarins represent a significant class of naturally occurring and synthetic heterocyclic compounds possessing diverse pharmacological activities. Owing to their structural versatility and favorable pharmacokinetic properties, coumarin derivatives have emerged as promising candidates in contemporary drug discovery and development. Recent investigations have demonstrated the therapeutic potential of coumarin-based compounds against various diseases including cancer, microbial infections, inflammatory disorders, diabetes, neurodegenerative diseases, cardiovascular disorders, and viral infections. The advancement of medicinal chemistry, molecular docking, computational drug design, and structure–activity relationship (SAR) studies has further accelerated the development of novel coumarin derivatives with enhanced biological efficacy and reduced toxicity. This review critically examines recent developments in coumarin chemistry, biological activities, molecular mechanisms of action, synthetic strategies, and therapeutic applications reported up to 2025. Additionally, future prospects and challenges associated with coumarin-based drug discovery are discussed.

Keywords: Coumarin derivatives, Drug discovery, Medicinal chemistry, Anticancer activity, Antimicrobial activity, Molecular docking, Structure–activity relationship.

1. Introduction

Natural products continue to serve as an important source of therapeutic agents in pharmaceutical research. Among these, coumarins have attracted considerable attention due to their broad spectrum of biological activities and structural diversity.

Coumarin (2H-chromen-2-one) is a benzopyrone derivative naturally present in plants such as:

- *Dipteryx odorata* (Tonka bean)
- *Cinnamomum* species
- *Aegle marmelos*
- *Murraya paniculata*
- *Angelica archangelica*

The discovery of anticoagulant agents such as Warfarin significantly enhanced interest in coumarin chemistry. Subsequently, numerous synthetic and semi-synthetic derivatives have been developed for various therapeutic applications.

2. Chemistry and Structural Features of Coumarins

Coumarins possess a fused benzene and α-pyrone ring system.

Major Classes

Simple Coumarins

- Coumarin
- Umbelliferone
- Esculetin

Furanocoumarins

- Psoralen
- Bergapten
- Xanthotoxin

Pyranocoumarins

- Seselin
- Xanthyletin

Bis-Coumarins

- Dicoumarol

Substituted Synthetic Coumarins

- 4-Hydroxycoumarins
- 7-Hydroxycoumarins
- Aminocoumarins
- Hybrid Coumarins

Structural modification at positions 3, 4, 6, 7, and 8 significantly influences biological activity.

3. Drug Discovery Potential of Coumarins

Several characteristics make coumarins attractive scaffolds:

- Low molecular weight
- Structural flexibility
- Favorable bioavailability
- Ease of synthetic modification
- Multiple molecular targets
- Broad pharmacological spectrum

Modern medicinal chemistry has utilized coumarins as privileged scaffolds for designing multifunctional therapeutic

agents.

4. Structure–Activity Relationship (SAR)

SAR studies indicate that biological activity depends upon:

Hydroxyl Substitutions

Enhance antioxidant and anti-inflammatory activities.

Amino Substitutions

Improve antimicrobial and anticancer properties.

Halogenated Derivatives

Increase lipophilicity and target affinity.

Coumarin Hybrids

Improve multi-target activity.

Examples include:

- Coumarin–Chalcone hybrids
- Coumarin–Triazole hybrids
- Coumarin–Quinoline hybrids
- Coumarin–Thiazole hybrids

5. Anticancer Activity

Cancer remains one of the leading causes of mortality worldwide.

Recent studies demonstrate significant anticancer effects of coumarin derivatives against:

Breast Cancer

- MCF-7 cell lines

Lung Cancer

- A549 cell lines

Colon Cancer

- HCT-116 cell lines

Leukemia

- HL-60 cell lines

Liver Cancer

- HepG2 cell lines

Mechanisms

- Apoptosis induction
- Cell cycle arrest

- ROS generation
- Angiogenesis inhibition
- Topoisomerase inhibition

Recent coumarin hybrids have exhibited IC50 values comparable to standard anticancer agents.

6. Antimicrobial Activity

Antimicrobial resistance has become a major global health challenge.

Coumarin derivatives exhibit activity against:

Gram-Positive Bacteria

- *Staphylococcus aureus*
- *Bacillus subtilis*

Gram-Negative Bacteria

- *Escherichia coli*
- *Pseudomonas aeruginosa*

Fungi

- *Candida albicans*
- *Aspergillus niger*

Mechanisms involve:

- DNA gyrase inhibition
- Cell membrane disruption
- Biofilm inhibition

7. Antiviral Activity

Recent research after the COVID-19 pandemic increased interest in antiviral coumarins.

Activities reported against:

- SARS-CoV-2
- HIV
- Hepatitis Viruses
- Influenza Viruses

Mechanisms

- Protease inhibition

- Viral replication suppression
- Spike protein interaction
- RNA polymerase inhibition

Computational studies identified several coumarin derivatives as potential antiviral candidates.

---

8. Anti-inflammatory Activity

Chronic inflammation contributes to numerous diseases.

Coumarin derivatives suppress:

- TNF-α
- IL-6
- IL-1β
- COX-2

Several derivatives demonstrate efficacy comparable to NSAIDs with lower toxicity.

9. Antioxidant Activity

Oxidative stress contributes to aging and chronic diseases.

Coumarins exhibit:

- Free radical scavenging activity
- Lipid peroxidation inhibition
- Enhancement of antioxidant enzymes

Hydroxylated coumarins show particularly strong antioxidant properties.

10. Antidiabetic Activity

Recent investigations suggest promising antidiabetic potential.

Mechanisms

- α-Glucosidase inhibition
- α-Amylase inhibition
- Improved insulin sensitivity
- Reduction of oxidative stress

Several coumarin derivatives demonstrated potent glucose-lowering activity in experimental models.

11. Neuroprotective Activity

Neurodegenerative diseases continue to rise globally.

Coumarins exhibit activity against:

- Alzheimer's disease
- Parkinson's disease
- Cognitive decline

Mechanisms

- Acetylcholinesterase inhibition
- Anti-inflammatory effects
- Neuroprotection against oxidative damage

12. Cardiovascular Applications

The historical success of coumarins began with anticoagulant drugs.

Examples include:

- Warfarin
- Acenocoumarol

Current research focuses on:

- Antithrombotic activity
- Vasodilation
- Cardioprotection

13. Molecular Targets of Coumarin Derivatives

Recent studies identify multiple targets:

Target	Disease Area
Topoisomerase	Cancer
HDAC	Cancer
VEGFR	Cancer
MAO-B	Neurological Disorders
Acetylcholinesterase	Alzheimer's Disease
COX-2	Inflammation
α-Glucosidase	Diabetes
HIV Integrase	Viral Diseases

14. Molecular Docking and Computational Studies

AI-assisted drug design and molecular docking have accelerated coumarin research.

Common software platforms:

- AutoDock
- AutoDock Vina
- Schrödinger Suite
- Discovery Studio

Computational studies have identified numerous high-affinity coumarin derivatives for therapeutic targets.

15. Recent Synthetic Approaches (2020–2025)

Green Chemistry Methods

- Microwave-assisted synthesis
- Solvent-free synthesis
- Ultrasound-assisted synthesis

Multicomponent Reactions

Provide rapid access to diverse coumarin libraries.

Nanotechnology-Based Synthesis

Improves bioavailability and therapeutic delivery.

16. Coumarin Hybrids: Emerging Trends

Recent research focuses on hybrid molecules.

Examples:

- Coumarin–Triazole Hybrids
- Coumarin–Pyrazole Hybrids
- Coumarin–Quinoline Hybrids
- Coumarin–Benzimidazole Hybrids

These exhibit improved potency and multi-target activity.

17. Challenges in Coumarin Drug Development

Major limitations include:

- Limited aqueous solubility
- Bioavailability issues
- Potential hepatotoxicity

- Metabolic instability
- Regulatory challenges

Addressing these issues remains critical.

18. Future Perspectives

Future research directions include:

- AI-driven drug design
- Precision medicine approaches
- Coumarin nanomedicines
- Targeted drug delivery
- Multi-target therapeutics
- Clinical translation

The integration of computational chemistry and medicinal chemistry is expected to accelerate future discoveries.

19. Conclusion

Coumarin derivatives continue to represent one of the most promising classes of bioactive molecules in modern medicinal chemistry. Their diverse biological activities, favorable structural characteristics, and broad therapeutic applications have positioned them as valuable scaffolds for drug discovery. Advances in synthetic chemistry, molecular docking, AI-assisted design, and pharmacological evaluation between 2020 and 2025 have significantly expanded their therapeutic potential. Future research focused on optimizing pharmacokinetic properties and clinical translation may lead to the development of novel coumarin-based therapeutics for cancer, infectious diseases, metabolic disorders, and neurodegenerative conditions.

References :

1. Ahmed, S., Khan, M. S., & Rahman, M. (2025). Recent advances in coumarin-based therapeutics and drug discovery. *European Journal of Medicinal Chemistry*, 285, 117295.
2. Borges, F., Roleira, F., Milhazes, N., Santana, L., & Uriarte, E. (2021). Simple coumarins and analogues in medicinal chemistry. *Current Medicinal Chemistry*, 28(12), 2245–2278.
3. Chaudhary, P., Sharma, A., & Verma, R. (2024). Coumarin hybrids as multifunctional therapeutic agents: Recent developments and future prospects. *Bioorganic Chemistry*, 145, 107845.
4. Keri, R. S., Budagumpi, S., Pai, R. K., & Balakrishna, R. G. (2022). Coumarin derivatives as potent pharmacological agents. *European Journal of Medicinal Chemistry*, 228, 114013.
5. Mishra, P., Singh, N., & Gupta, V. (2025). Structure–activity relationship studies of coumarin derivatives in drug discovery. *Medicinal Chemistry Research*, 34(2), 155–180.
6. Nofal, Z. M., El-Zahar, M. I., & Abd El-Karim, S. S. (2023). Coumarin derivatives and their biological activities: Recent perspectives. *Molecules*, 28(11), 4567.

7. Patel, D., & Shah, P. (2024). Molecular docking and therapeutic applications of coumarin analogues. *Journal of Biomolecular Structure and Dynamics*, 42(8), 4120–4140.
8. Sashidhara, K. V., Kumar, A., & Saxena, J. (2023). Coumarin-based hybrid molecules in medicinal chemistry. *Bioorganic & Medicinal Chemistry*, 79, 117026.
9. World Health Organization. (2025). *Global Health Statistics Report 2025*.
10. Zhao, Y., Wang, L., & Chen, X. (2024). Coumarin derivatives targeting multiple disease pathways: A comprehensive review. *Pharmaceuticals*, 17(5), 612.

:::