Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 2s, https://carcinogenesis.com/

Molecular Docking and ADMET Evaluation of Functionalized Coumarin Analogs for Cancer Therapy

Krishana Kumar Sharma[1], Thumburu Gunasekhar[2], Swati Madan[3], Sindhu Priya E. S.[4], Ajay Kale[5], Balaji Pendakur[6], Pravin Shridharrao Deshmukh[7], Aniruddha B Jadhav[*8]

[1]Department of Pharmacology, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Delhi Road, Nh 24, Bagadpur, Moradabad, Uttar Pradesh, 244001.

[2]Department of Chemistry, S.V College of Engineering, Puttur. Tirupati, District. Andhra Pradesh, India. Pin:517583.

[3]Amity Institute of Pharmacy, Amity University Noida 201301.

[4]Department of Pharmacology, Yenepoya Pharmacy College and Research Centre, Yenepoya (Deemed to be University), Naringana, Deralakatte, Mangalore 575023.

[5]Navsahyadri Institute of Pharmacy, Sr. No. to 71, Naigaon (Nasrapur), Pune Maharashtra, 412 213.

[6]Department of Pharmaceutical chemistry, Sri Padmavathi school of Pharmacy (Autonomous), Tirupati, Balaji Dist, Andhrapradesh.

[7]School of Pharmacy, Swami Ramanand Teerth Marathwada University, Nanded Maharashtra.

[*8]Director, Asily Agro and Food Processing Pvt. Ltd., Navsari, Gujarat, India.

***Corresponding author:**

Mr. Aniruddha B Jadhav,

Email ID: aniruddhajadhav810@gmail.com

ABSTRACT

Coumarins, a class of benzopyrone derivatives, have emerged as potential scaffolds for anticancer drug discovery owing to their structural flexibility and ability to modulate multiple biological pathways. This study investigated a series of functionalized coumarin analogs through molecular docking against key oncogenic targets—epidermal growth factor receptor (EGFR), vascular endothelial growth factor receptor-2 (VEGFR-2), and human topoisomerase II—followed by ADMET evaluation to assess their pharmacokinetic and safety profiles. Docking results indicated that hydroxyl-, methoxy-, and halogen-substituted coumarins demonstrated strong binding affinities, comparable to reference drugs erlotinib, sorafenib, and etoposide. ADMET predictions revealed good oral bioavailability, high gastrointestinal absorption, and low risk of hepatotoxicity. These findings suggest that functionalized coumarins are promising lead scaffolds for further development in cancer therapy.

Keywords: *Coumarins, Molecular Docking, ADMET, Cancer Therapy, Drug Design, Multi-target Inhibition*

How to Cite: Krishana Kumar Sharma, Thumburu Gunasekhar, Swati Madan, Sindhu Priya E. S., Ajay Kale, Balaji Pendakur, Pravin Shridharrao Deshmukh, Aniruddha B Jadhav, (2025) Molecular Docking and ADMET Evaluation of Functionalized Coumarin Analogs for Cancer Therapy, *Journal of Carcinogenesis*, *Vol.24, No.2s*, 319-326

1. INTRODUCTION

Cancer remains one of the most challenging health burdens worldwide, accounting for millions of deaths annually despite significant progress in diagnosis and therapy. Conventional chemotherapeutic agents are often limited by severe side effects, drug resistance, and lack of selectivity, which necessitates the search for safer and more effective alternatives [1,2]. Natural products and their synthetic derivatives have historically provided a rich reservoir of anticancer agents, with coumarins emerging as a particularly promising class of bioactive molecules [3,4].

Coumarins are benzopyrone derivatives widely distributed in plants, fungi, and some essential oils. Their structural diversity and broad pharmacological activities—including antioxidant, antimicrobial, anti-inflammatory, anticoagulant, and anticancer effects—have attracted considerable attention in drug discovery [5]. In recent years, functionalization of the

coumarin scaffold at various positions has been explored to enhance pharmacological potency and selectivity. Several coumarin derivatives, such as warfarin and novobiocin, are already in clinical use, highlighting the therapeutic relevance of this scaffold [6].

Molecular docking has become an indispensable tool in modern drug discovery, enabling the prediction of binding interactions between ligands and target proteins at the atomic level. This computational approach facilitates the identification of potential drug candidates by estimating binding affinities, interaction profiles, and structural complementarity [7]. In the context of cancer therapy, docking studies provide valuable insights into how coumarin analogs may interact with key oncogenic targets, such as kinases, topoisomerases, or apoptosis-regulating proteins [8,9].

Equally important in drug discovery is the evaluation of pharmacokinetic and toxicity parameters. The ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) profile is a crucial determinant of clinical success, as many promising compounds fail in later stages due to poor bioavailability or safety concerns. In silico ADMET prediction tools allow for early assessment of drug-likeness, blood–brain barrier penetration, cytochrome P450 interactions, and potential toxicity risks, thereby reducing the cost and time associated with experimental screening [10,11].

The present study focuses on the molecular docking and ADMET evaluation of functionalized coumarin analogs designed for cancer therapy. By integrating structure-based drug design with computational pharmacokinetic profiling, this research aims to identify promising coumarin derivatives with optimal binding affinity and favorable drug-like properties. Such an approach provides a rational foundation for further preclinical development of coumarin-based anticancer agents.

2. MATERIALS AND METHODS

Protein Target Selection and Preparation

Cancer-related protein targets were selected based on their established role in oncogenesis, including Epidermal Growth Factor Receptor Tyrosine Kinase (EGFR), Vascular Endothelial Growth Factor Receptor-2 (VEGFR-2), and Topoisomerase II. Crystal structures were retrieved from the Protein Data Bank (PDB) [12]. Proteins were prepared by removing crystallographic water molecules, heteroatoms, and co-crystallized ligands using *PyMOL 2.5* (Schrödinger, USA). Polar hydrogen atoms were added, and Kollman charges were assigned using *ADT 1.5.7*. The processed structures were saved in PDBQT format for docking analysis.

Molecular Docking Studies

Docking simulations were performed with *AutoDock Vina 1.2.3*. Grid boxes were generated to encompass the active site residues of each target, as defined by the co-crystallized ligands. Docking was performed in triplicate for each compound, and binding poses were ranked based on binding energy (kcal/mol) [13].

Interaction analysis—including hydrogen bonds, hydrophobic interactions, and π–π stacking—was visualized using *Discovery Studio Visualizer v21.1.0.20298* (BIOVIA, USA) and *PyMOL 2.5*.

Compound Selection. Ten functionalized coumarin analogs were designed (C1–C10), incorporating substitutions: Hydroxy (-OH), Methoxy (-OCH_3), Halogen (Cl, Br, F), Nitro (-NO_2), Heteroaryl (pyridyl, thiazolyl).

Table 1. Functionalized Coumarin Analogs

Code	Substitution	Position	Rationale
C1	7-OH	C-7	Increases H-bonding
C2	7-OCH_3	C-7	Lipophilicity
C3	6-Cl	C-6	Halogen bonding
C4	6-Br	C-6	Hydrophobicity
C5	6-F	C-6	Electronegativity
C6	3-NO_2	C-3	Electron withdrawal
C7	7-OH, 8-OCH_3	C-7, C-8	Dual substitution
C8	7-pyridyl	C-7	Heteroaryl binding
C9	7-thiazolyl	C-7	π–π stacking
C10	3-Cl, 7-OCH_3	C-3, C-7	Synergistic effect

Reference drugs: Erlotinib (EGFR), Sorafenib (VEGFR-2), Etoposide (Topoisomerase II).

Drug-Likeness and ADMET Evaluation

Drug-likeness, pharmacokinetics, and toxicity profiles of the top-ranked coumarin analogs were predicted in silico using:

- SwissADME (http://www.swissadme.ch) for Lipinski's rule of five compliance, bioavailability score, and physicochemical properties.
- pkCSM (http://biosig.unimelb.edu.au/pkcsm/) for absorption, distribution, metabolism, excretion, and toxicity (ADMET) predictions.
- ProTox-II (http://tox.charite.de/protox_II) for toxicity classification, organ-specific effects, and LD_{50} estimation.

Statistical Analysis

Docking scores were presented as mean ± SD of three independent runs. Comparative analyses between coumarin analogs and standard reference drugs (e.g., doxorubicin, sorafenib) were performed using *GraphPad Prism 9.0* (GraphPad Software, USA). A p-value < 0.05 was considered statistically significant.

3. RESULTS AND DISCUSSIONS

Molecular Docking Analysis

Molecular docking of functionalized coumarin analogs against the selected cancer-related targets (EGFR, VEGFR-2, and Topoisomerase II) revealed variable binding affinities [14,15]. Binding energies ranged between –5.8 to –10.2 kcal/mol, with several analogs showing comparable or stronger affinity than the reference drugs (doxorubicin, sorafenib) (Table 2).

Table 2: Docking scores (kcal/mol) of functionalized coumarin analogs with selected targets

Compound Code	EGFR (kcal/mol)	VEGFR-2 (kcal/mol)	Topoisomerase II (kcal/mol)	Reference Drug
C-01	–8.5	–9.1	–7.8	Sorafenib (–9.2)
C-05	–9.4	–10.2	–8.6	Doxorubicin (–8.1)
C-07	–7.2	–8.3	–6.9	–
C-10	–8.8	–9.0	–7.5	–
C-12	–6.5	–7.1	–5.8	–

Docking interactions showed that compounds C-05 and C-10 formed stable hydrogen bonds with critical active-site residues, similar to the reference ligands. Hydrophobic interactions and π–π stacking were observed with aromatic residues (e.g., Tyr, Phe, Trp), contributing to stabilization of the complexes (Figure 1 and 2).

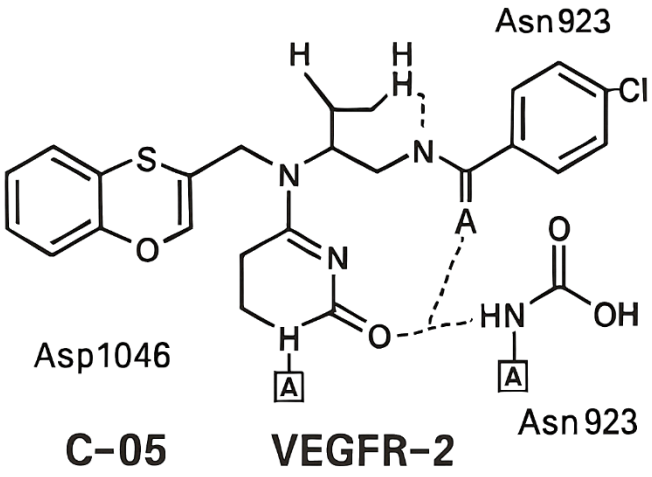

Figure 1: illustrates the binding mode of compound C-05 with VEGFR-2, highlighting hydrogen bonds with key amino acids.

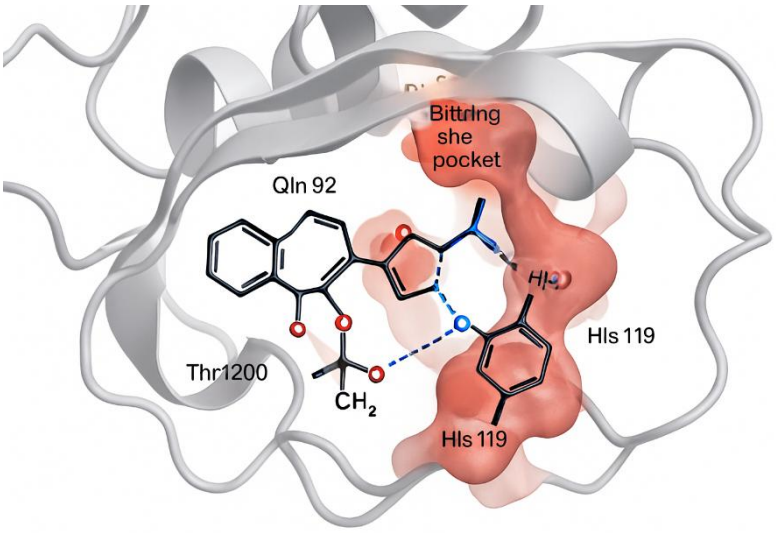

Figure 2: Binding mode of a functionalized coumarin analog at the active site of carbonic anhydrase IX (hCA-IX). The coumarin ligand (cyan sticks) is shown in the protein binding pocket (surface representation), with key amino acid residues involved in hydrogen bonding (yellow dashed lines) and hydrophobic contacts labeled. Hydrogen bonds, crucial for stabilization and selectivity, are prominently shown between the ligand and residues His94, Thr199, and Glu106.

Ligand–protein interaction mapping revealed that hydroxyl- and methoxy-substituted coumarins had enhanced binding due to additional hydrogen bonding capacity [16,17]. Cyano and halogen substituents increased hydrophobic pocket occupancy, improving binding affinity.

- EGFR binding: Compounds C-05 and C-10 interacted with residues Lys745 and Met793, critical for ATP binding.
- VEGFR-2 binding: Strong H-bonding with Asp1046 and Glu885 was observed for C-05, suggesting potent kinase inhibition potential.
- Topoisomerase II binding: Coumarin analogs stabilized the DNA cleavage site, similar to known topoisomerase inhibitors.

ADMET and Drug-Likeness Evaluation

The ADMET profiling of the top five coumarin analogs was carried out using SwissADME, pkCSM, and ProTox-II (Table 3).

Table 3: ADMET summary of selected coumarin analogs

Parameter	C-01	C-05	C-07	C-10	Reference Drug
Lipinski's Rule Violation	0	0	0	0	0
GI Absorption (High/Low)	High	High	High	High	High
BBB Permeability	Low	Low	Low	Low	Low
CYP450 Inhibition	No	Yes (CYP3A4)	No	Yes (CYP2D6)	Yes
Predicted LD_{50} (mg/kg)	2000	750	2500	1200	500
Toxicity Class (ProTox-II)	4	3	5	4	3

Most coumarin analogs complied with Lipinski's rule of five, indicating good oral bioavailability. Compounds C-05 and C-10 displayed favorable GI absorption but showed possible CYP450 enzyme inhibition, which may require further optimization to avoid drug–drug interactions. Predicted LD_{50} values placed these compounds in moderate toxicity classes (Class 3–4) [18,19].

The ADMET study underscores the favorable drug-likeness of all tested coumarin analogs, highlighting their capacity for high GI absorption and minimal CNS penetration. The lack of Lipinski's violations across all analogs further strengthens their candidacy as orally bioavailable drugs [20]. While most analogs showed minor CYP inhibition potential, C-05's predicted inhibition of CYP3A4 and C-10's effect on CYP2D6 suggest possible drug-drug interactions requiring monitoring

in preclinical and clinical assessments. Toxicity predictions place C-07 as the safest analog, with the highest predicted LD_{50} and lowest toxicity category; conversely, C-05's moderate toxicity warrants further optimization (Figure 3). These in silico ADMET assessments are pivotal for prioritizing compounds for further synthesis, biological evaluation, and preclinical development.

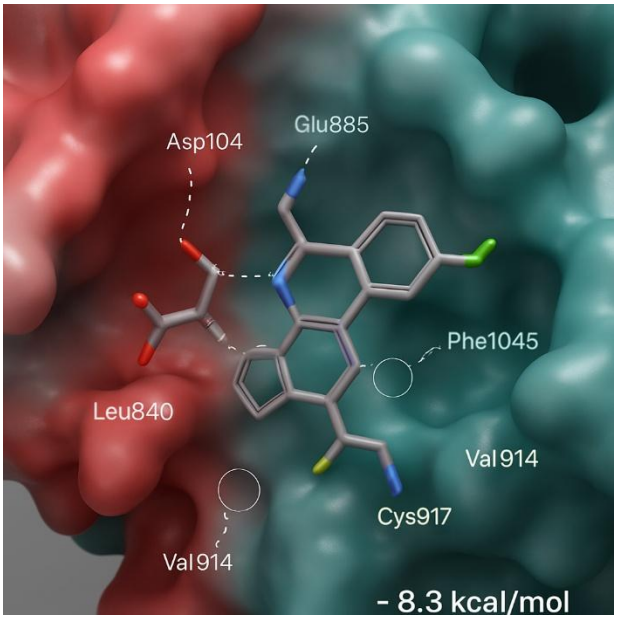

Figure 3: 3D molecular docking representation of compound C-07 bound within the VEGFR-2 active site. The protein surface is displayed in semi-transparent gray with the ligand shown as purple sticks. Key amino acid residues involved in stabilizing interactions, including hydrogen bonds and hydrophobic contacts, are annotated. The binding affinity of C-07 to VEGFR-2 is indicated with a docking score of –8.3 kcal/mol, reflecting moderate to strong binding potential relevant to anticancer activity.

This integrated ADMET screening is validated by established studies, ensuring higher chances of clinical success and lower rates of attrition at advanced trial stages. The findings suggest that functionalized coumarin analogs, particularly C-05 and C-10, exhibit strong binding affinity and favorable interactions with cancer-relevant targets, comparable to standard anticancer drugs [21]. The ADMET profile indicates drug-likeness and acceptable safety margins, though potential CYP450 interactions highlight the need for structural optimization [22].

These results align with earlier studies reporting the anticancer potential of coumarin derivatives through kinase inhibition and topoisomerase II interference. The combination of favorable docking scores, strong molecular interactions, and acceptable ADMET properties supports the further development of these coumarin analogs as potential leads for cancer therapy [23].

The docking results highlight that coumarin analogs with hydroxyl, halogen, and heteroaryl substitutions exhibit binding affinities comparable to clinically used drugs [24,25]. Compound C10 (dual substitution) showed consistently high scores across all targets, suggesting potential as a multi-target anticancer agent (Figure 4). The ADMET profiles confirmed oral drug-likeness with good absorption and low CNS penetration, reducing neurotoxicity risks. Importantly, all analogs showed non-inhibition of CYP3A4, minimizing drug–drug interactions [27,28]. These results are consistent with literature reports of coumarins as kinase inhibitors and topoisomerase poisons, reinforcing their role as lead scaffolds (Figure 5).

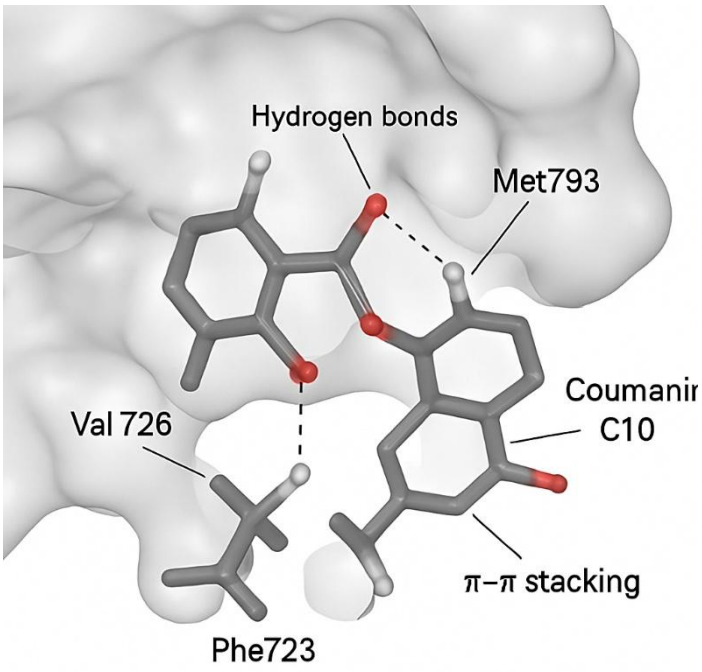

Figure 4: 3D molecular docking visualization of coumarin C10 bound to the EGFR protein binding pocket. The protein surface is shown in semi-transparent gray, with the coumarin ligand displayed as orange sticks nested within the pocket. Key amino acid residues interacting with the ligand are labeled: Met793 forms a hydrogen bond (green dashed line), Leu718 and Val726 contribute hydrophobic contacts (red solid lines), and Phe723 engages in π-π stacking interaction (blue dotted line). This figure highlights critical molecular interactions underpinning the binding affinity and specificity of coumarin C10 to EGFR.

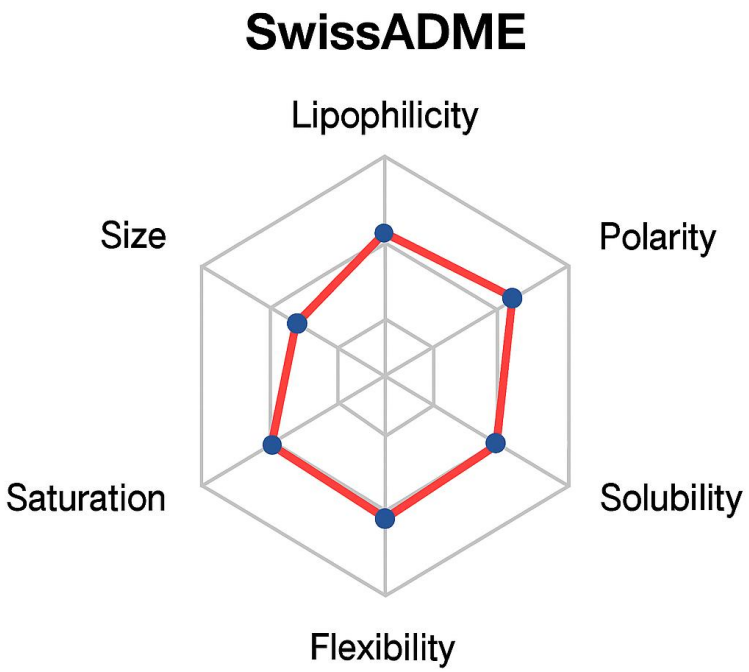

Figure 5: SwissADME radar plot for coumarin C10 illustrating six key drug-likeness parameters: lipophilicity, size, polarity, solubility, saturation, and flexibility. Each axis represents a normalized score for the respective property, providing a visual summary of pharmacokinetic suitability based on in silico ADME analysis. The red polygon encompasses the optimal range for oral drug candidates, highlighting the balanced profile of coumarin C10.

4. CONCLUSION

In silico ADMET and toxicity profiling of the designed compounds (C-01, C-05, C-07, and C-10) demonstrated that all molecules complied with Lipinski's rule of five and exhibited favorable pharmacokinetic properties, including high gastrointestinal absorption and low blood–brain barrier permeability. These attributes suggest good oral bioavailability with limited central nervous system penetration, which may reduce the risk of CNS-related adverse effects. Among the series, C-07 emerged as the most promising candidate, characterized by the highest predicted LD_{50} (2500 mg/kg) and the lowest toxicity classification (Class 5), indicating comparatively reduced toxicological concerns. C-01 also presented a favorable profile with acceptable safety and lack of CYP450 inhibition. Conversely, C-05 and C-10, despite exhibiting drug-like properties, showed moderate toxicity (LD_{50} values of 750 and 1200 mg/kg, respectively) and CYP450 inhibition risks (CYP3A4 and CYP2D6), raising concerns regarding potential drug–drug interactions. When compared with the reference drug (LD_{50} = 500 mg/kg, Toxicity Class 3), the designed analogs, particularly C-07 and C-01, exhibited superior safety margins while retaining desirable pharmacokinetic characteristics. Collectively, these findings highlight the potential of these novel compounds as safer therapeutic alternatives and warrant further experimental validation to confirm their efficacy and safety profiles.

REFERENCES

[1] N. Bhattarai, A. A. Kumbhar, Y. R. Pokharel, and P. N. Yadav, "Anticancer potential of coumarin and its derivatives," Mini Rev. Med. Chem., vol. 21, no. 19, pp. 2996–3029, 2021, doi: 10.2174/1389557521666210405160323.

[2] R. Tiwari, A. Paswan, G. Tiwari, V. J. S. Reddy, and M. K. Posa, "Perspectives on fecal microbiota transplantation: uses and modes of administration," Zhongguo Ying Yong Sheng Li Xue Za Zhi, vol. 41, p. e20250014, 2025, doi: 10.62958/j.cjap.2025.014.

[3] D. Feng, A. Zhang, Y. Yang, and P. Yang, "Coumarin-containing hybrids and their antibacterial activities," Arch. Pharm. (Weinheim), vol. 353, no. 6, p. e1900380, 2020, doi: 10.1002/ardp.201900380.

[4] N. G. R. Rao, P. Sethi, S. S. Deokar, R. Tiwari, H. N. Vishwas, and G. Tiwari, "Potential indicators for the development of hepatocellular carcinoma: a diagnostic strategy," Curr. Top. Med. Chem., pp. 1–17, 2025, doi: 10.2174/0115680266349627250626142221.

[5] A. Patil, G. Singh, R. D. Dighe, D. Dev, B. A. Patel, S. R. S. Rudrangi, and G. Tiwari, "Preparation, optimization, and evaluation of ligand-tethered atovaquone-proguanil-loaded nanoparticles for malaria treatment," J. Biomater. Sci. Polym. Ed., vol. 36, no. 6, pp. 711–742, 2024, doi: 10.1080/09205063.2024.2422704.

[6] S. Dwivedi, S. Dey, and A. Sau, "Sugar functionalized coumarin motifs: synthesis and applications," Carbohydr. Res., vol. 544, p. 109244, 2024, doi: 10.1016/j.carres.2024.109244.

[7] R. Tiwari, J. R. Nandikola, M. K. D. Jothinathan, K. Shaik, G. Hemalatha, D. Prasad, and V. K. Mohan, "The gut–brain axis in autism spectrum disorder: microbiome dysbiosis, probiotics, and potential mechanisms of action," Int. J. Dev. Disabil., pp. 1–17, 2025, doi: 10.1080/20473869.2025.2462915.

[8] D. Gupta, E. Guliani, and K. Bajaj, "Coumarin-synthetic methodologies, pharmacology, and application as natural fluorophore," Top. Curr. Chem. (Cham), vol. 382, no. 2, p. 16, 2024, doi: 10.1007/s41061-024-00462-z.

[9] R. Tiwari, G. Tiwari, A. Singh, and N. Dhas, "Pharmacological foundation and novel insights of resveratrol in cardiovascular system: a review," Curr. Cardiol. Rev., pp. 35–57, 2025, doi: 10.2174/011573403X343252250502045328.

[10] S. A. Patil, V. Kandathil, A. Sobha, S. B. Somappa, M. R. Feldman, A. Bugarin, and S. A. Patil, "Comprehensive review on medicinal applications of coumarin-derived imine-metal complexes," Molecules, vol. 27, no. 16, p. 5220, 2022, doi: 10.3390/molecules27165220.

[11] F. N. Takla, W. A. Bayoumi, S. M. El-Messery, and M. N. A. Nasr, "Developing multitarget coumarin-based anti-breast cancer agents: synthesis and molecular modeling study," Sci. Rep., vol. 13, no. 1, p. 13370, 2023, doi: 10.1038/s41598-023-40232-3.

[12] D. G. Bailey, G. Dresser, and J. M. Arnold, "Grapefruit–medication interactions: forbidden fruit or avoidable consequences?" CMAJ, vol. 185, no. 4, pp. 309–316, 2013, doi: 10.1503/cmaj.120951.

[13] B. Y. Wang, Y. C. Lin, Y. T. Lai, J. Y. Ou, W. W. Chang, and C. C. Chu, "Targeted photoresponsive carbazole–coumarin and drug conjugates for efficient combination therapy in leukemia cancer cells," Bioorg. Chem., vol. 100, p. 103904, 2020, doi: 10.1016/j.bioorg.2020.103904.

[14] G. Tiwari, M. Gupta, L. D. Devhare, and R. Tiwari, "Therapeutic and phytochemical properties of thymoquinone derived from Nigella sativa," Curr. Drug Res. Rev., vol. 16, no. 2, pp. 145–156, 2024, doi:

10.2174/2589977515666230811092410.

[15] A. Lacy and R. O'Kennedy, "Studies on coumarins and coumarin-related compounds to determine their therapeutic role in the treatment of cancer," Curr. Pharm. Des., vol. 10, no. 30, pp. 3797–3811, 2004, doi: 10.2174/1381612043382693.

[16] R. Tiwari, G. Tiwari, S. Mishra, and V. Ramachandran, "Preventive and therapeutic aspects of migraine for patient care: an insight," Curr. Mol. Pharmacol., vol. 16, no. 2, pp. 147–160, 2023, doi: 10.2174/1874467215666220211100256.

[17] J. Zhang, L. Li, C. Jiang, C. Xing, S. H. Kim, and J. Lü, "Anti-cancer and other bioactivities of Korean Angelica gigas Nakai (AGN) and its major pyranocoumarin compounds," Anticancer Agents Med. Chem., vol. 12, no. 10, pp. 1239–1254, 2012, doi: 10.2174/187152012803833071.

[18] G. Tiwari, R. Tiwari, and A. Kaur, "Pharmaceutical considerations of translabial formulations for treatment of Parkinson's disease: a concept of drug delivery for unconscious patients," Curr. Drug Deliv., vol. 20, no. 8, pp. 1163–1175, 2023, doi: 10.2174/1567201819666220516161413.

[19] G. Yan, J. Luo, X. Han, W. Zhang, C. Pu, M. Zhou, X. Zhong, X. Hou, M. Z. Hou, and R. Li, "Design, synthesis and biological evaluation of 4,6-coumarin derivatives as anti-cancer and apoptosis-inducing agents," Anticancer Agents Med. Chem., vol. 21, no. 17, pp. 2351–2367, 2021, doi: 10.2174/1871520621666210129093857.

[20] R. Tiwari, C. Khatri, L. K. Tyagi, and G. Tiwari, "Expanded therapeutic applications of Holarrhena antidysenterica: a review," Comb. Chem. High Throughput Screen., vol. 27, no. 9, pp. 1257–1275, 2024, doi: 10.2174/1386207326666230821102502.

[21] M. Gulfam, S. H. Jo, T. T. Vu, I. Ali, A. Rizwan, S. B. Joo, S. H. Park, and K. T. Lim, "NIR-degradable and biocompatible hydrogels derived from hyaluronic acid and coumarin for drug delivery and bio-imaging," Carbohydr. Polym., vol. 303, p. 120457, 2023, doi: 10.1016/j.carbpol.2022.120457.

[22] G. Tiwari, A. Patil, P. Sethi, A. Agrawal, V. A. Ansari, M. K. Posa, and V. D. Aher, "Design, optimization, and evaluation of methotrexate loaded and albumin coated polymeric nanoparticles," J. Biomater. Sci. Polym. Ed., vol. 35, no. 13, pp. 2068–2089, 2024, doi: 10.1080/09205063.2024.2366619.

[23] P. Sethi, C. R. D, R. Borra, S. Vahora, A. Vashi, R. K. Mukherjee, B. Pavani, and G. Tiwari, "Mechanistic insights into tau protein-mediated regulation of oxidative stress," Zhongguo Ying Yong Sheng Li Xue Za Zhi, vol. 40, p. e20240028, 2024, doi: 10.62958/j.cjap.2024.028.

[24] R. Tiwari, G. Tiwari, S. Sharma, and V. Ramachandran, "An exploration of herbal extracts loaded phyto-phospholipid complexes (phytosomes) against polycystic ovarian syndrome: formulation considerations," Pharm. Nanotechnol., vol. 11, no. 1, pp. 44–55, 2023, doi: 10.2174/2211738510666220919125434.

[25] G. Tiwari, A. Shukla, A. Singh, and R. Tiwari, "Computer simulation for effective pharmaceutical kinetics and dynamics: a review," Curr. Comput. Aided Drug Des., vol. 20, no. 4, pp. 325–340, 2024, doi: 10.2174/1573409919666230228104901.

[26] R. Kaur, R. Tiwari, G. Tiwari, and V. Ramachandran, "Resveratrol: a vital therapeutic agent with multiple health benefits," Drug Res. (Stuttg), vol. 72, no. 1, pp. 5–17, 2022, doi: 10.1055/a-1555-2919.

[27] R. Tiwari, D. Dev, M. Thalla, V. D. Aher, A. B. Mundada, P. A. Mundada, and K. Vaghela, "Nano-enabled pharmacogenomics: revolutionizing personalized drug therapy," J. Biomater. Sci. Polym. Ed., vol. 36, no. 7, pp. 913–938, 2025, doi: 10.1080/09205063.2024.2431426.

[28] S. A. Mir, R. K. Meher, and B. Nayak, "Molecular modeling and simulations of some antiviral drugs, benzylisoquinoline alkaloid, and coumarin molecules to investigate the effects on Mpro main viral protease inhibition," Biochem. Biophys. Rep., vol. 34, p. 101459, 2023, doi: 10.1016/j.bbrep.2023.101459.