RESEARCH PAPER

Coumarin And Its Multifaceted Pharmacological Activities: A Comprehensive Update

Sonia yadav[1], Sumita Kumari[2*], Sushma Maratha[3], Kavita Attri[3], Navgeet Kaur[4], Sunny Antil[5]

[1]School of Medical and Allied Sciences, K. R. Mangalam University, Gurugram, Haryana-122103, Orcid Id: 0000-0001-9645-8005 Email: pharmasonia@gmail.com

[2*]P M College of Pharmacy, Kami, Sonipat, Haryana-131001, Orcid Id: 0000-0002-1972-5349 Email: sumitabajia87@gmail.com

[3]SGT College of Pharmacy, SGT University, Gurugram, Haryana-122505, Orcid Id: 0000-0002-5221-8373 Email: 1102sushma@gmail.com

[3]SGT College of Pharmacy, SGT University, Gurugram, Haryana-122505, Orcid Id: 0000-0002-6164-506X Email: Kavita.attri@sgtuniversity.org

[4]Sri Sukhmani Institute of Pharmacy, Derabassi, Mohali-140507, Orcid Id: 0000-0001-5942-9774 Email: Navgeet.pharmacy@sddgpi.com

[5]Assistant Professor, South Point College of Pharmacy, Murthal, Haryana, india, Orcid Id: 0009-0009-9894-0271 Email: sunnyantil0123@gmail.com

***Corresponding author;** Sumita Kumari
P M College of Pharmacy, Kami Sumitabajia87@gmail.com

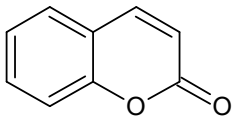
ABSTRACT

Coumarins, a class of aromatic lactones, and their synthesized derivatives exhibit diverse pharmacological activities, making them significant in drug development. Coumarin is a key heterocycle and its analogs are extracted from plants, animals, and microbes. Recent studies emphasize that modifications to the coumarin ring enhance efficacy, and potency, and reduce toxicity. This review provides an updated perspective on coumarin's pharmacological actions, such as antibacterial, antifungal, antineoplastic, antioxidant, anti-inflammatory, analgesic, PDE inhibitor, antitumor features. Furthermore, recent advancements in coumarin derivatives' synthesis and their mechanistic insights are discussed. This paper covers a variety of one pot coumarin derivative synthesis techniques as well as well-known name reactions. In this paper, we primarily covered conventional name reaction-mediated coumarin synthesis, detailed innovative synthetic approaches for accessing coumarin heterocycles, and demonstrated fresh intriguing uses that have been published in recent years. This article describes the physiological actions and chemical structures of coumarins.

Keywords: coumarin, antibacterial, antifungal, anticancer, antioxidant, anti-inflammatory, analgesic, PDE inhibitor
How to cite this article: Yadav S, Kumari S, Maratha S, Attri K, Kaur N, Antil S. Coumarin And Its Multifaceted Pharmacological Activities: A Comprehensive Update. Int J Drug Deliv Technol. 2026;16(70s): 836-847. DOI: 10.25258/ijddt.16.70s.86

INTRODUCTION

Coumarins are 2H-1-benzopyran-2-one (I), belongs to (benzopyrone class) aromatic lactones.[1]



I

The greatest class of 1-benzopyran derivatives is coumarins. Most naturally occurring coumarins contain a carbon-7 hydroxycoumarin; umbelliferon (7-hydroxycoumarin) appears to be the structural and biogenetic parent of the 2H-chromen-2-one with higher oxygenation level.[2-6] Coumarins possess wide variety of physiologically active substances found in plants, many of which have long been utilized in conventional medicine for ages. Due to its pleasant aroma, , coumarin has been utilised in perfumes since 1882, when it was first isolated from coumarone. In 1868, it was first synthesized.[7,8] Several derivatives of coumarin have been shown to be widely distributed in plant kingdom. Several extraction techniques such as supercritical fluid extraction, maceration under sonication, and infusion can be used to extract coumarins from plants.[9,10] As we know, plant extraction is laborious and lengthy procedure therefore for separation process an advanced instrument is required to obtain product with purity. Coumarins can be synthesized in number of ways including Knoevenagel condensation[11], Pechmann reaction[12,13], Claisen rearrangement[14], Perkin[15], Wittig, Reformatsky[16] and catalytic cyclization reactions[17] etc. Coumarins are well-known aromatic lactones with the IUPAC name 2H-1-benzopyran-2-one. They are widely distributed in nature and contain different plant based bioactive compounds, lot of them utilized in conventional medicine. Coumarin exhibited numerous

pharmacological actions, generally with less toxicity and also have enhanced remarkable interest due to effective benefits on health of human being. Recent developments have focused on the extraction and synthetic methodologies to obtain more potent coumarin derivatives. Modern methods of extraction including ultrasound-assisted extraction, supercritical fluid extraction, and green synthesis approaches have been explored for enhanced yield and purity.[18]

SOURCES OF COUMARIN

Various families like Ruteceae, Apiaceae, Fabaceae, Asteraceae, Calophyllaceae, Apocynaceae and much more provide sources for coumarins. Coumarins are obtained from different plant parts, like leaves, flowers and seeds. In general, coumarin concentration are higher in fruit and flowers than in leaves, stem bark, seeds and roots. An outline of coumarin affiliates classes, source parts, their isolation techniques provided in Table 1.

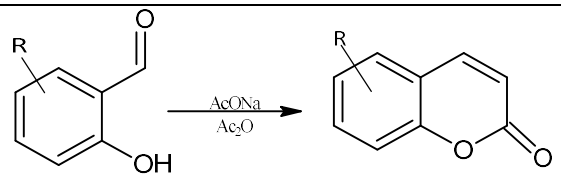
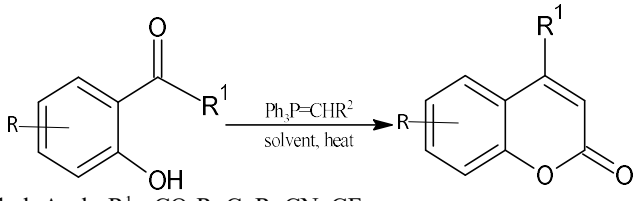
Table 1. Plant derived coumarins with class and isolation technique

Sr. No.	Sources	Part of source	Isolation method	Coumarin number and type	Reference
1.	Angelica dahurica	Roots (air-dried)	Reflux	Furanocoumarins (23 compounds)	19
2.	Bombax ceiba	Dried flowers	Ultrasound assisted extraction	Simple coumarins (24 compounds)	20
3.	Calophyllum brasilliense	Leaves (air-dried)	Percolation	Simple coumarins (3 compounds)	21
4.	Citrus species	Peels	Percolation	Simple and furanocoumarins (6 componds)	22
5.	Citrus grandis	Dried fruits	Reflux	Simple and furanocoumarins (17 compounds)	23
6.	Murraya paniculate	Leaves & stem (air-dried)	Extraction	Simple coumarins (19 compounds)	24
7.	Paxillus involutus	Dried fruit	Soxhlet	Furanocoumarins (4 compounds)	25
8.	Ailanthus altissima	Root barks (air-dried)	Reflux	Simple coumarin (14 compounds)	26

SYNTHESIS OF COUMARIN DERIVATIVES

Coumarins can be synthesized through well-established name reaction methods, including the Pechmann reaction, Knoevenagel condensation, Perkin reaction, Witting reaction, Claisen reaction, Michael reaction, Baylis-Hillman reaction, and Reformatsky reaction. Recent advances like microwave-assisted synthesis, ultrasound mediated synthesis, solvent-free synthesis metal catalyzed electrophilic cyclization, metal free radical cyclization and green catalytic methodologies have improved reaction efficiency and yield. Synthetic reactions shown in tables 2 and 3.

Table 2: Name reactions for synthesis of coumarin

Sr. no	Name of reaction	Schematic reaction	Reference
1.	Perkin reaction		15
2.	Witting reaction	 R= H, alkyl, Aryl; R^1= CO_2R, CoR, CN, CF_3	16

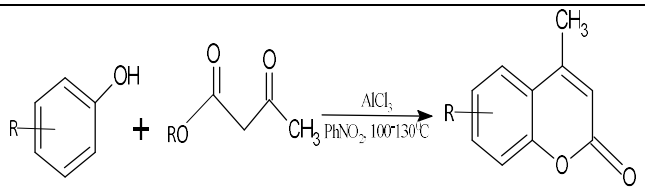
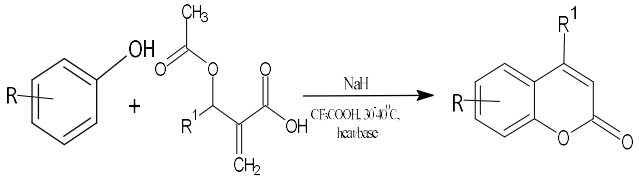
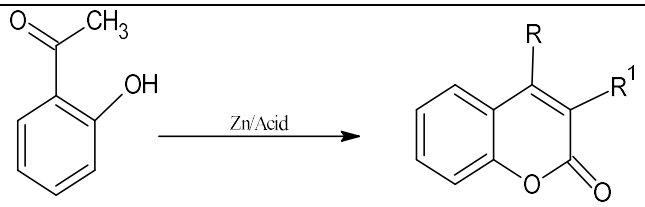
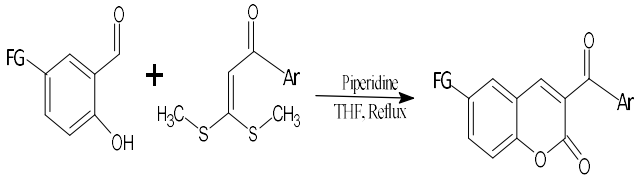
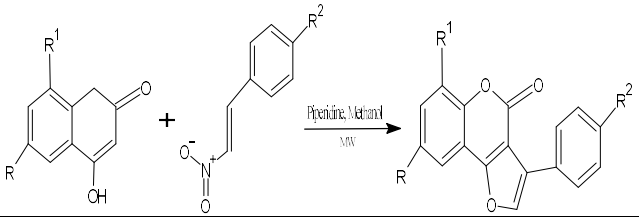
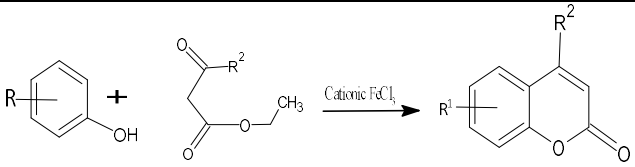
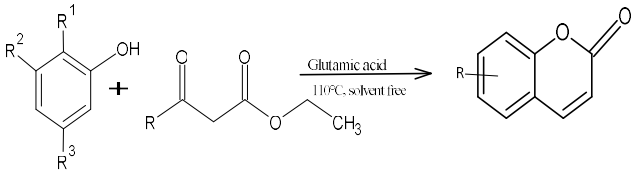
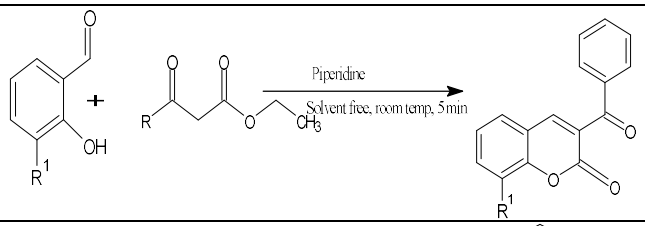
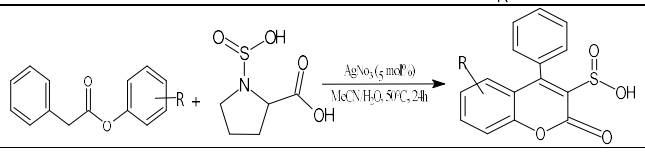
3.	Pechmann reaction	 R= Me, Et	14
4.	Claisen reaction	 R= Me, Et ; R^1= $CHBrCOOC_2H_5$	14
5.	Reformatsky reaction	 R= Me, Et ; R^1= $CHBrCOOC_2H_5$	16
6.	Michael addition reaction		14

Table 3: New synthetic approaches for coumarins

Sr. no	Name of reaction	Schematic reaction	Reference
1.	Microwave assisted synthesis		27,28
2.	Ultrasound helped synthesis	 R^1= OH, OCH_3; R^2=Me, Propyl	29
3.	Solvent free synthesis	 R^1= H; R^2=OH; R^3=H; R=Ph, Me	30

4.	Metal free radical cyclization		31
5.	Metal mediated radical cyclisation		17,32

VARIOUS ACTIVITIES REPORTED FOR COUMARIN DERIVATIVES

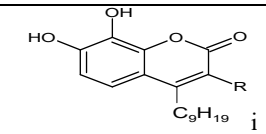
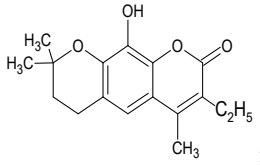
Anti-cancer Activity: A class of naturally occurring substances known as coumarins has been shown to have anticancer potential. Coumarins block several signaling pathways that are essential for cell division. For instance, they can inhibit the PI3K/mTOR pathway, which often harms cancer cells and reduces their growth and viability.[33] Many research has been done on coumarin's anti-tumorigenic effects which shown in table 4.

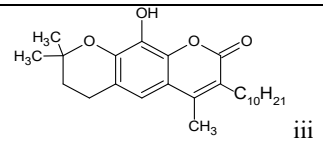
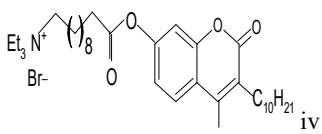
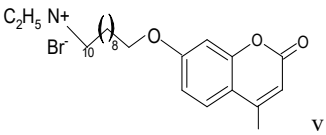
Table 4: Coumarin against cancers

Type of cancer	In vitro/In vivo	Cell lines	Source	Mechanism	Reference
Breast cancer	In vivo	SKBR 3 cells	Coumarin	Cell death caused by increased p21 protein and cell cycle arrest at G0/G1	34
Breast cancer	In vitro	MCF 7	Coumarin	Cytotoxic action showed against MCF 7 cells with IC50 values 1.24 to 8.68μM	35
Prostate cancer	In vivo	PC-3 cell lines	Coumarin	Coumarin has a significant inhibitory effect on 15-LOX-1	36
Colon cancer	In vitro	HT-29 cell lines	Coumarin	PI3K/mTOR/Akt and AMPK/mTOR signaling in HT-29 cells	37
Lung cancer	In vitro	A549 and A2170 cell lines	Coumarin	Inhibiting EMT-associated migration in 549 cells and reversing EMT in 1L-1-βstimulated a549 cells	38
Gastric cancer	In vivo	MGC-803 and HCG-27 cells	Coumarin	Tumor growth in MGC-803 xenograft models and suppression of MAPK signaling	39

Abha and colleagues published synthesis and also assessed ability of different coumarin derivatives for cell proliferation inhibition of SK-OV-3 (ovary cancer), MDAMB or MCF-7 (breast cancer), HT-29 (colon cancer) cells. Synthesized derivatives were coumarin carboxamide, 4-aminocoumarin, pyranocoumarin, 3-alkyl-4-methylcoumarins, quaternary ammonium coumarins, and amino derivatives of coumarins.[33] Compounds given in table 5 inhibited the proliferation of different cancer cells.

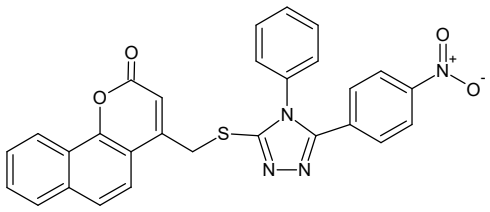
Table 5: Assessed by Abha et al

Compound	Structure	Cells	% inhibition
C- 3-Alkyl substituted analogs of 4-methylcoumarins (i) and C- 3-Alkyl substituted analogs of pyranocoumarins (ii)	 i  ii	MDA-MB 468 and SK-OV- 3	53-74% at 50μM concentration

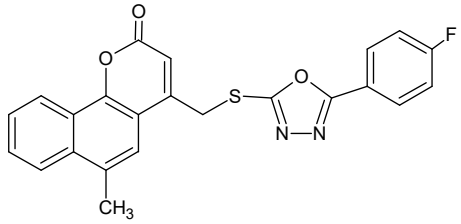
3-decyl substituted pyranocoumarin (iii) and triethyl substituted quaternary ammonium coumarin derivative (iv)	 iii  iv	HT-29 and SK-OV-3	63-72% at 50μM concentration
C-3 decyl substituted quaternary ammonium coumarin derivative v	 v	Src kinase inhibition	78% at IC50 21. 6μM

Amongst all the compounds studied, compound **v** showed the greatest Src kinase inhibition.[40]

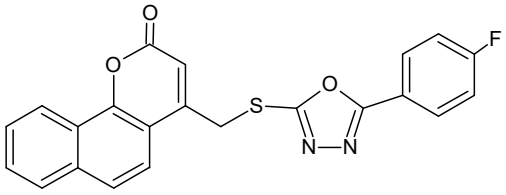
Shaimaa et al synthesized novel coumarin compounds with methylene thio-linker. At National cancer Institute, Cairo, Egypt various compounds were physiologically tested against hepatic cancer (HepPG-2) and breast cancer cell lines using 5-fluorouracil as reference. Against MCF-7 and HepPG-2 cell lines, compounds II, III, IV, V, VI and VII shown potent activity. Compound 13a was the most active with IC50 values of 5.5 mg/ml and 6.9 mg/ml respectively. The mode of binding of designed compounds with protein 1KE9 was studied using docking.[41]



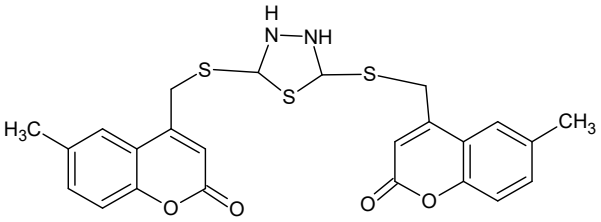
II



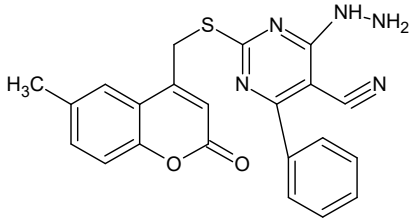
III



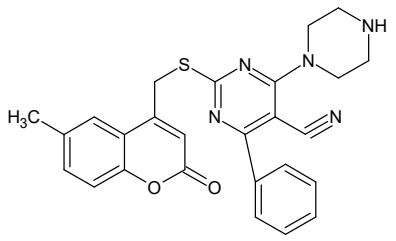
IV



V

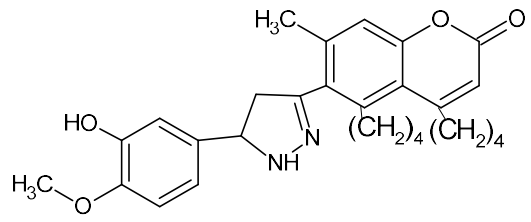


VI



VII

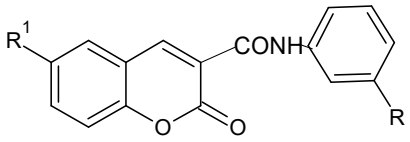
Yana et al employed a multistep procedure to synthesize a series of 6-pyrazolinylcoumarins using Claisen-Schmidt condensation, Fries rearrangement reactions. Recent studies indicate that coumarin derivatives exhibit strong anticancer potential. Novel 6-pyrazolinylcoumarins (compound VIII) with greatest antimitotic activity have been synthesized and evaluated in NCI-60 cell lines, demonstrating significant inhibition against leukemia and breast cancer cell lines[42] Additionally, molecular docking studies have provided details into their mechanism, suggesting their role in apoptosis induction and kinase inhibition.



VIII

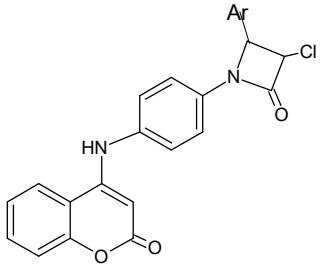
Antimicrobial activity

Multidrug resistant (MDR) bacterial infections are global concern that raise mortality rates due to the ineffectiveness of available treatments for bacterial infections. Several attempts have been made during the last ten years to find broad-spectrum antibacterials. The coumarin moiety proved to be a suitable scaffold for the development of potential antimicrobial medicines.[43]
Alok et al produced different substituted coumarin & Schiff base through condensation reactions between (R) phenyl malonanilic acid and different substituted salicylaldehydes by using pyridine as catalyst at maintained temperature. Physical properties, elemental analysis and spectrographic identification like IR, NMR etc were used to characterize newly synthesized compound IX. Additionally, their antibacterial potential was tested against S. aureus and E. coli micro-organism.[44]



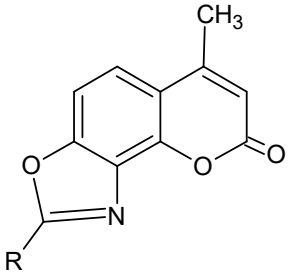
IX

Divyesh et al synthesized novel azetidinones (X) in the presence of triethyl amine by using cyclo-condensation of different coumarin Schiff bases with chloro acetyl chloride. Further 4-chloro-3, 4', 3', 4"-tercoumarin were obtained on reacting 4-hydroxy coumarin with $POCl_3$. Then 4-[(4-aminophenyl)amino]-2*H*-chromen-2-one produced with *p*-phenylene diamine and finally different coumarin schiff bases were obtained by condensation of 4-[(4-aminophenyl)amino]-2*H*-chromen-2-one with different aldehydes. IR, ^{1}H NMR, ^{13}C NMR and element analysis done for structure elucidation and also tested for antimicrobial using broth dilution method.[45]



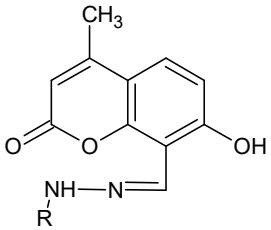
X

Swayam et al prepared 13 novel coumarin affiliates (XI) and characterization done by spectroscopy like IR and 1H NMR. By using cup plate method, these novel affiliates were analyzed for antibacterial potential towards E. coli and S. aureus. Amoxicillin selected as reference. In recent study found that all novel obtained compounds (1-13) specifically ($P<0.001$) shown bacterial inhibition in comparison to control group.[46]

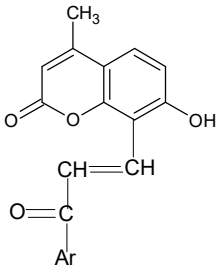


XI

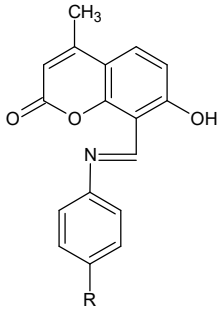
From 7-hydroxy-4-methyl coumarin, Shokhan and Ammar et al created a novel class of coumarin derivatives by inserting the formyl group at 8th carbon through Duff reaction. These derivatives include hydrazone (XII), chalcones (XIII), Schif bases (XIV, XV) and hydrazinyl thiazole (XVI). Structure elucidation of newly synthesized derivatives was verified using the analytical and spectroscopic data, such as FT-IR, 13C-NMR, and mass spectroscopy. The preliminary screening for antibacterial activity of all newly synthesized coumarin affiliates was done by using method broth dilution against *S. epidermidis* and *S. hemolyticus* and *E. coli* and *K. pneumoniae*.[47]



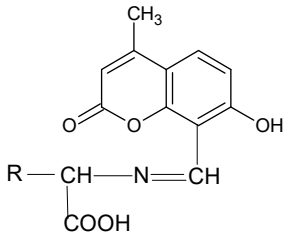
XII



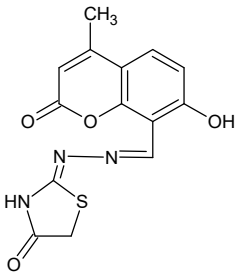
XIII



XIV

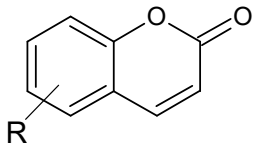


XV



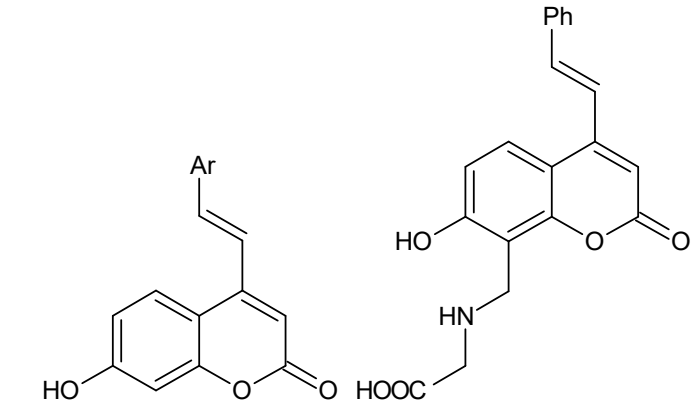
XVI

Vahid & Farhad prepared coumarin affiliates (XVII) through solvent free reaction Pechmann condensation using FeF_3 (catalyst) in one pot synthesis of ethyl acetoacetate with phenol using microwave irradiation. Systematic characterization of obtained compounds done by elemental analysis, InfraRed, Mass and Nuclear Magnetic Resonance spectral studies. By using disk diffusion method, obtained compounds tested for antibacterial efficacy against S. aureus and E. coli with various concentrations. In comparison to reference drug, penicillin all obtained compounds showed greater potential against both bacteria. Newly synthesized coumarin-Schiff base derivatives have shown promising antibacterial potential against multidrug-resistant *S. aureus* and *E. coli*. Moreover, coumarin derivatives conjugated with metal nanoparticles have demonstrated enhanced antifungal properties against *Candida albicans* and *Aspergillus niger*.[48]

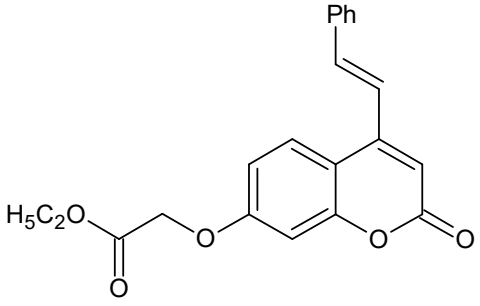


XVII

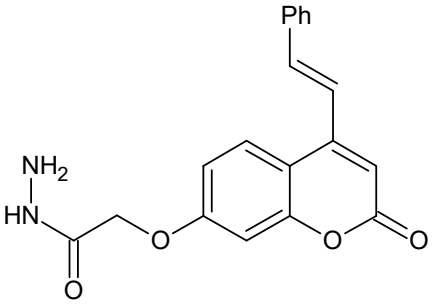
Fattah et al, synthesized various coumarin derivatives of 7-hydroxy-4-methylcoumarin (XVIII-XXII) through Pechmann condensation based on number of reactions. Synthesized deriatives were exhibited for antimicrobial potential against *Bacillus Subtilis*, *Serratia marcenses* and *Trichoderma Sp*.[49,50]



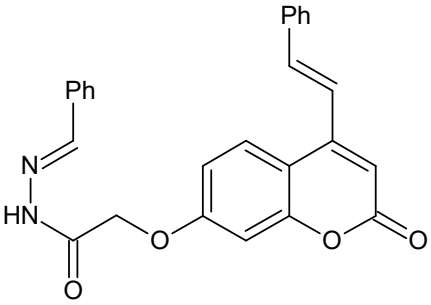
XVIII **XIX**



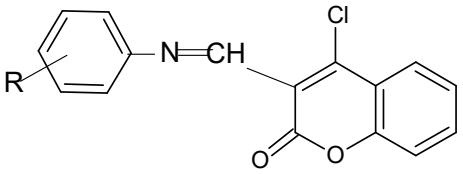
XX



XXI

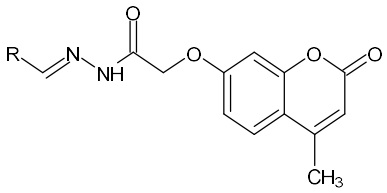


XXII



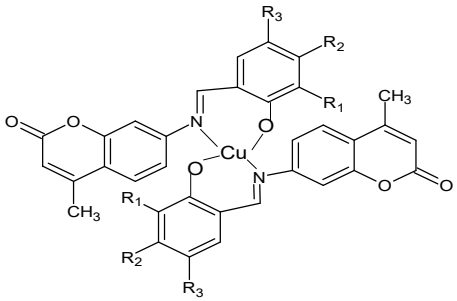
XXIII

Tamaya et al synthesized new Schiff bases through condensation of aromatic aldehydes (hetero/aryl) with different amines under conventional conditions and characterized by IR, 1HNMR and LC-MS spectral methods. Synthesized derivatives have been evaluated for antimicrobial potential. Compounds XXIV exhibited substantial activity against Staphylococcus and Pseudomonas species but not effective towards Klebsiella species.[51]

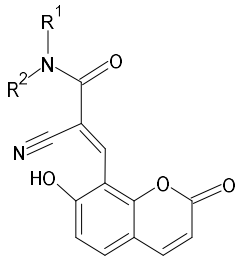


XXIV

Condensing 7-amino-4-methyl-coumarin and several salicylaldehyde (substituted), Bernadetta et al created new compounds that produced various schiff bases with good yields. Cu complexes were produced when ligands reacted with copper (II) acetate (XXV), and X-ray crystallography was used to describe some of these complexes. Synthesized ligands alongwith metal complexes were evaluated for anti-Candida potential. Several of synthesized ligands and complexes (XXVI) showed potential anti-Candida activity compared to Ketoconazole and Amphotericin B.[52,53]

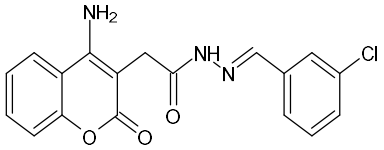


XXV



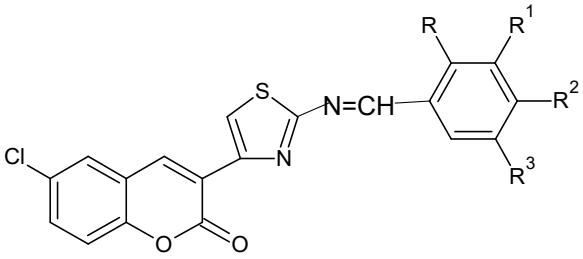
XXVI

Yadav S. et al synthesized, characterized and evaluated ten derivatives of 4-aminocoumarins. These derivatives showed effective antimicrobial profile against bacterial strains both gram positive and negative. Compound XXVII found the most effective for all microbial strains by using zone inhibition assay method.[54]



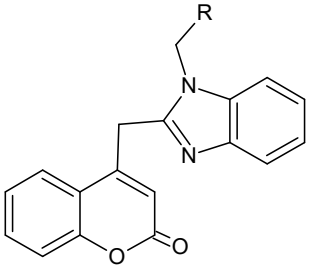
Analgesic & Antinflammatory Activity

Hamid S. J. et al synthesized aminothiazolylchlorocoumarin schiff bases (XXVIII) by reaction betwaeen aromatic aldehydes substituted and 2'-amino-4'-(6-chloro-3-coumarinyl)thiazole. Characterization of obtained compounds done by spectroscopical analysis and antiinflammatory as well as analgesic potential also evaluated. It was clear from the study that electron withdrawing substituents substituted on aromatic ring significantly increases analgesic activity whereas a electron donating group like methyl suppressed the activity. However, the schiff bases of aliphatic aldehydes such as formaldehye and acetaldehyde showed reduced activity.[55]



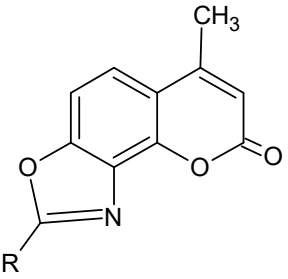
XXVIII

A series of novel chromen-2-one derivatives (XXIX)designed with formaldehyde and various secondary amines using Mannich condensation reaction by Kalyani et al. Derivatives were tested for anti-inflammatory potentials. Compounds with 50 mg/kg as compared to 20mg/kg dose level reported greater anti-inflammatory potential.[56]



XXIX

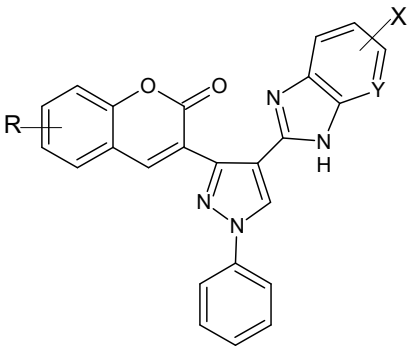
Sharma et al prepared 13 novel coumarin affiliates (XXX) are and analyzed them by Infrared and Nuclear Magnetic Resonance spectroscopy. Anti-inflammatory and antibacterial activity was examined for the newly generated coumarin derivatives using carrageenan induced rat paw edema model and cup plate method for S. aureus and E. coli. Compound (XXX) showed in figure effectively reduced rat paw edema induced by carrageenan in 10mg/kg oral dose. Coumarin based Mannich bases have been found to be effective anti-inflammatory drugs in recent drugs. Some coumarin derivatives have shown comparable activity to standard NSAIDs.[57]



XXX

PDE Inhibitors

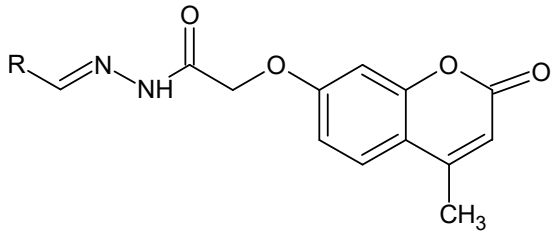
Kumbar et al designed coumarins (XXXI) appended to benzimidazole through pyrazole and synthesized using microwave irradiation. In human spermatozoa, these substances were examined for their indirect inhibition of phosphodiesterase (PDE) through motility pattern. Coumarin derivatives have also been explored as phosphodiesterase (PDE) inhibitors, demonstrating potential in treating cardiovascular diseases and erectile dysfunction. Antioxidant studies reveal that hydroxycoumarins act as free radical scavengers, contributing to their protective role in oxidative stress-related disorders.[58]



XXXI

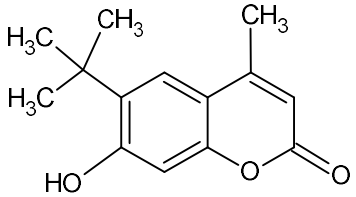
Antioxidant Activity

Taymaa et al synthesized new Schiff bases (XXXII) under conventional conditions with different aromatic amines and aromatic aldehydes by condensation and characterization done by using IR, 1HNMR and Liquid Chromatography-Mass Spectroscopy spectral methods. Synthesized compounds have been screened for the free radical scavenging activity (antioxidant activity) by evaluating their binding with free radical DPPH and from results it was found that all prepared derivatives have demonstrated positive antioxidant activities.[51]



XXXII

Compound XXXIII, which demonstrated the highest scavenging action, was assessed for its primary antioxidant capacity by Popova and coworkers. Hydroxy and tert-butyl groups at positions 7 and 8 respectively were discovered to be essential for both primary and secondary antioxidant action in aqueous and lipid medium. DFT calculations were also done. Li and collaborators synthesised chitosan derivatives bearing coumarin nucleus and investigated that coumarin moiety enhances strongly antioxidant properties of chitosan derivatives by inhibition of lipid peroxidation.[59,60]



XXXIII

RECENT DEVELOPMENTS AND FUTURE PERSPECTIVES

Advancements in computational drug design and QSAR modeling have enabled the discovery of novel coumarin affiliates with enhanced pharmacological properties. The integration of green chemistry principles in their synthesis further underscores their potential in sustainable drug development.[61] In future, emphasis should be on clinical trials to establish their efficacy and safety in humans.

DISCUSSSION

Coumarin compounds have been extensively explored for their role in pharmaceutical industry. Due to their therapeutic qualities, they have been shown to be extremely useful as antibacterial, antifungal, anticancer, antioxidant, antiinflammatory, analgesic, PDE inhibitor, antitumor etc. This review focusd on how many researchers have synthesised and examined their physiochemical & structural characteristics using QSAR, IR, NMR, Mass spectral analysis and other methods.

CONCLUSION

Coumarin and its derivatives continue to be promising candidates in drug discovery because of their broad and great spectrum of pharmacological actions. Recent developments in synthetic strategies and mechanistic

studies have further solidified their therapeutic potential. Continued exploration of novel derivatives and their clinical applications will pave the way for new treatments in various diseases.

FUNDING
Not funded by any means.

AUTHORS CONTRIBUTION
SK: Contribution to conceptualization, initial drafting. SY: Assisted in data validation. SM: Supervised the study design and finalized the manuscript. KA: Reviewed, edited and refined the work. NK:&SSA: finalized the manuscript. All authors approved the final version and agreed to accountability for the work.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

ACKNOWLEDGEMENT
The authors sincerely acknowledge the financial support received from the Department of Scientific and Industrial Research (DSIR), Government of India, under Project No. 15398/Note-18/Head(A2K+/DSIR), and the Anusandhan National Research Foundation (ANRF), Government of India, under Project No. ANRF/283/2026-2027, through the conference grant. The author is grateful for their support in facilitating the presentation/publication of this work.

REFERENCES
1. Matos MJ, Santana L, Uriarte E, Abreu OA, Molina E, Yordi EG. Coumarins- An Important Class of Phytochemicals. Isolation, Characterization and Role in Human Health. IntechOpen. 2015;113-140. DOI: 10.5772/59982.
2. Jain PK, Joshi H. Coumarin: Chemical and pharmacological profile. Journal of Applied Pharmaceutical Science. 2012; 2(6):236-240. DOI: 10.7324/ JAPS.2012.2643.
3. Santana L, Uriarte E, Roleira F, Milhazes N, Borges F. Furocoumarins in medicinal chemistry. Synthesis, natural occurrence and biological activity. Current Medicinal Chemistry. 2012; 11(24):3239-3261. DOI: 10.2174/ 0929867043363721.
4. Bhatnagar A, Sharma PK, Kumar N, Dhudhe RA. Review on recent advances in coumarin derivatives with their multidisciplinary actions. Der Pharmacia Lettre. 2010;2(4):297-306.
5. Khursheed A, Jain V. Medicinal research progress of natural coumarin and its derivatives. The Natural Products Journal. 2021;11(5): 648-662.
6. Sandhu S, Bansal Y, Silakari O, Bansal G. Coumarin hybrids as novel therapeutic agents. Bioorganic Medicinal Chemistry. 2014;22(15):3806-3814. DOI: 10.1016/j.bmc.2014.05.032
7. Ismael R N, Mustafa Y F, Al-Qazaz H K. Coumarin-based products: Their biodiversity and pharmacology. Iraqi Journal of Pharmacy. 2022;18(2): 162-179.
8. Kumari S, Sharma A, Yadav S. Pharmacological Potential of Coumarin-Based Derivatives: (A Comprehensive Brief Review). Orient. J. Chem. 2023; 39(3), 568-576.
9. Annunziata F, Pinna C, Dallavalle S, Tamborini L, Pinto A. An Overview of Coumarin as a Versatile and Readily Accessible Scaffold with Broad-Ranging Biological Activities. Int J Mol Sci. 2020;21(13):4618.
10. Gupta R, Sharma V, Mehta A. Advanced Extraction Techniques for Bioactive Coumarins. Journal of Natural Product Research. 2023;45(7): 1204-1216.
11. Vekariya R H, Patel H D. Recent Advances in the Synthesis of Coumarin Derivatives via Knoevenagel Condensation: A Review. Synth. Commun. 2014; 44: 2756.
12. Loncaric M, Sokac DG, Jokic S, Molnar M. Recent advances in the synthesis of coumarin derivatives from different starting materials. Biomolecules. 2020;10(1):1-36. DOI: 10.3390/biom10010151
13. Zambare AS, Kalam Khan FA, Zambare SP, Shinde SD, Sangshetti JN. Recent advances in the synthesis of coumarin derivatives via Pechmann condensation. Current Organic Chemistry. 2015;20(7):798-828. DOI: 10.2174/ 1385272820666151026224227
14. Mustafa YF. Classical approaches and their creative advances in the synthesis of coumarins: A brief review. Journal of Medicinal Chemistry. 2021; 4(6):612-625. DOI: 10.26655/ JMCHEMSCI.2021.6.10.
15. Rabbani GA. Concise introduction of Perkin reaction. Organic Chemistry: Current Research. 2018;07(02):7-10. DOI: 10.4172/2161-0401.1000191.
16. Balu S Navale, Mrunali R Vaidya, Rameshwar S Shinde. Recent methods for the synthesis of coumarin derivatives using different strategies. International Journal of Current Science. 2023;13(4): 337-346.
17. Kanyiva KS, Hamada D, Makino S, Takano H, Shibata T. α-Amino acid sulfonamides as versatile sulfonylation reagents: Silver-catalyzed synthesis of coumarins and oxindoles by radical cyclization. European Journal of Organic Chemistry. 2018;2018(43):5905-5909. DOI: 10.1002/ejoc.201800901.
18. Wang L, Zhou Y, Li H. Green Synthesis of Coumarins: A Sustainable Approach. Green Chemistry Letters and Reviews. 2023;16(3): 505-517.
19. Bai Y, Li D, Zhou T, Qin N, Li Z, Yu Z, et al. Coumarins from the roots of Angelica dahurica with antioxidant and antiproliferative activities. J Funct Foods. 2016; 20:453–62
20. Joshi KR, Devkota HP, Yahara S. Chemical Analysis of Flowers of Bombax ceiba from Nepal. Nat Prod Commun. 2013;8(5):583–4.

21. Rodríguez-Hernández KD, Martínez I, Agredano-Moreno LT, Jimenez-Garcia LF, Reyes-Chilpa R, Espinoza B. Coumarins isolated from Calophyllum brasiliense produce ultrastructural alterations and affect in vitro infectivity of Trypanosoma cruzi. Phytomedicine. 2019; 61:152827.
22. Ramirez-Pelayo C, Martinez-Quiñones J, Gil J, Durango D. Coumarins from the peel of citrus grown in Colombia: composition, elicitation and antifungal activity. Heliyon. 2019;5(6):01937.
23. Tian D, Wang F, Duan M, Cao L, Zhang Y, Yao X, et al. Coumarin Analogues from the Citrus grandis (L.) Osbeck and Their Hepatoprotective Activity. J Agric Food Chem. 2019;67(7):1937–47.
24. Liang H, Cao N, Zeng K, Zhao M, Tu P, Jiang Y. Coumarin and spirocyclopentenone derivatives from the leaves and stems of Murraya paniculata (L.) Jack. Phytochemistry. 2020; 172:112258.
25. Zhang JX, Lv JH, Zhao LQ, Shui XX, Zhang J, Wang LA. Coumarin-pi, a new antioxidant coumarin derivative from Paxillus involutus. Nat Prod Res. 2020;34(9):1246–9.
26. Wang J, Huang S, Li C, Ding W, She Z, Li C. A New Coumarin Produced by Mixed Fermentation of Two Marine Fungi. Chem Nat Compd. 2015;51(2):239–41.
27. Kaneria AR, Giri RR, Bhila VG, Prajapati HJ, Brahmbhatt DI. Microwave assisted synthesis and biological activity of 3-Aryl-Furo[3,2-c] Coumarins. Arabian Journal of Chemistry. 2017;10: S1100-S1104. DOI: 10.1016/j. arabjc.2013.01.017.
28. Mangasuli SN, Hosamani KM, Satapute P, Joshi SD. Synthesis, molecular docking studies and biological evaluation of potent coumarin Carbonodithioate hybrids via microwave irradiation. Chemical Data Collection. 2018;15(16):115-125. DOI: 10.1016/j. cdc.2018.04.001
29. Kaur N. Ultrasound-assisted green synthesis of five-membered O- and S Heterocycles. Synthetic Communication. 2018;48(14):1715-1738. DOI: 10.1080/ 00397911.2018.1460671
30. Sabetpoor S, Hatamjafari F. Synthesis of coumarin derivatives using glutamic acid under solvent-free conditions. Oriental Journal of Chemistry. 2014;30(2):863-865. DOI: 10.13005/ojc/300265
31. Wu X, Jia M, Huang M, Kim JK, Zhao Z, Liu J, et al. A visible-light induced “on-off” one-pot synthesis of 3 arylacetylene coumarins with AIE Properties. Organic and Biomolecular Chemistry. 2020;18(17):3346-3353. DOI: 10.1039/d0ob00479k
32. Fu W, Sun Y, Li X. Silver-catalyzed monofluoromethylation of alkynoates with sodium monofluoroalkanesulfinate (CH2FSO2Na) to Access 3 monofluoromethylated coumarins. Synthetic Communication. 2020;50(3): 388-398. DOI: 10.1080/ 00397911.2019.1697452.
33. Salem MA, Marzouk MI, El-Kazak AM. Synthesis and Characterization of Some New Coumarins with in Vitro Antitumor and Antioxidant Activity and High Protective Effects against DNA Damage. Molecules. 2016;21(2):249. doi: 10.3390/molecules21020249
34. Kupeli A, Genc B, Karpuz E, Sobarzo S, Capasso R. Coumarins and Coumarin- Related Compounds in Pharmacotherapy of Cancer. Cancers. 2020;12(7): 1959.
35. Ahmed EY, Latif NA, El- Mansy MF, Elserwy WS, Abdelhafez OM. VEGFR- 2 Inhibiting Effect and Molecular Modeling of Newly Synthesized Coumarin Derivatives as Anti- Breast Cancer Agents. Bioorganic & Medicinal Chemistry. 2020;28(5): 115328.
36. Maleki F, Sadeghian H, Bahrami AR, Goftari SN, Matin MM. Investigating the Anti- Tumor and Apoptosis- Inducing Effects of Coumarin Derivatives as Potent 15- Lipoxygenase Inhibitors on PC- 3 Prostate Cancer Cells. Anti- Cancer Agents in Medicinal Chemistry. 2023; 15: 1722–1730.
37. Hoveizi E, Hushmandi K. Comparison of Effects of P- Coumaric Acid and Coumarin on Colorectal Cancer Cell Line by Inducing Apoptosis and Autophagy. Avicenna Journal of Phytomedicine. 2024;14(4): 470.
38. De Araujo RSA, Carmo JD, De Omena SL. Coumarin Derivatives Exert Anti- Lung Cancer Activity by Inhibition of Epithelial–Mesenchymal Transition and Migration in A549 Cells. Pharmaceuticals. 2022;15(1): 104.
39. Song J, Guan YF, Liu WB, et al. Discovery of Novel Coumarin- Indole Derivatives as Tubulin Polymerization Inhib.itors with Potent Anti-Gastric Cancer Activities. European Journal of Medicinal Chemistry. 2022;238: 114467.
40. Kathuria A, Jalal S, Tiwari R, Shirazi AN, Gupta S, Kumar S, et al. Substituted Coumarin Derivatives: Synthesis and Evaluation of Antiproliferative and Src Kinase Inhibitory Activities. Chemistry Biology Interface. 2011; 1(2):279-296.
41. Morsy SA, Farahat AA, Nasr MNA, Tantawy AS. Synthesis, Molecular Modeling and Anticancer Activity of New Coumarin Containing Compounds. Saudi Pharmaceutical Journal. 2017; 25: 873-883. https://doi.org/10.1016/j.jsps.2017.02.003
42. Garazd Y, Garazd M, Lesyk R. Synthesis and evaluation of anticancer activity of 6-pyrazolinylcoumarin derivatives. Saudi Pharmaceutical Journal. 2017;25(2):214-223. doi: 10.1016/j.jsps.2016.05.005.
43. Douglas EJA, Marshall B, Alghamadi A, Joseph EA, Duggan S, Vittorio S, et al. Improved Antibacterial Activity of 1,3,4-Oxadiazole-Based Compounds That Restrict *Staphylococcus*

Aureus Growth Independent of LtaS Function. Europe PMC. 2023; 9(11):2141-2159.

44. Rawat A, Bhaskar AV. Recent advances on anticancer activity of coumarin derivatives. European Journal of Medicinal Chemistry Reports. 2022;5: 100038, https://doi.org/10.1016/j.ejmcr.2022.100038.
45. Singh R, Kumar A. PGPR Isolates from the Rhizosphere of Vegetable Crop Momordica charantia: Characterization and Application as Biofertilizer. International Journal of Current Microbiology Applied Science. 2017;6: 1789-1802. https://doi.org/10.20546/ijcmas.2017.603.205
46. Metwally NH, Elgemeie GH, Fahmy FG. Green synthesis: Antimicrobial activity of novel benzothiazole-bearing coumarin derivatives and their fluorescence properties. Egyptian Journal of Chemistry. 2022;65(2):679-686. DOI: 10.21608/ EJCHEM.2021.91887.4365
47. Patel R, Kumar S, Rao V. Schiff Base Coumarins Against Drug-Resistant Bacteria. International Journal of Antimicrobial Agents. 2024;63(2): 105317.
48. Kumar N, Desai P, Sharma M. Coumarin-Nanoparticle Conjugates for Antifungal Applications. Materials Science & Engineering. 2023;150: 113487.
49. Singh AD, Kumar S, Saini S, Prabha H. Asian Pacific Journal of Health Sciences. 2017; 4(4):84-93.
50. Yadav S, Kumar N, Bhalla V. Synthesis and evaluation of novel 4-anilinocoumarin derivatives as potential antimicrobial agents. J Appl Pharm Sci. 2022;12(5): 196-204.doi:10.7324/ JAPS.2022.120518
51. Nesaragi AR, Kamble RR, Dixit S, Kodasi B, Hoolageri SR, Bayannavar PK, et al. Green synthesis of therapeutically active 1,3,4-oxadiazoles as antioxidants, selective COX-2 inhibitors and their in-silico studies. Bioorg Med Chem Lett. 2021; 1(43):128112. doi: 10.1016/j.bmcl.2021.128112.
52. Duddu VR, Sidde L, Kasoju A, Chakka G. Design, synthesis, characterization of coumarin derivatives and its pharmacological evaluation. Solovyov Studies. 2023;71(8): 107-125.
53. Darla MM, Krishna BS, Rao UM, Reddy NB, Reddy CS. Synthesis and bio-evaluation of novel 7-hydroxy coumarin derivatives via Knoevenagel reaction. Research on Chemical Intermediates. 2015;41(2): 1258-1276.
54. Yadav S, Kumar N. Synthesis and Evaluation of Novel 4-hydroxycoumarin Derivatives as Potential anti-microbial Agents. Oriental Journal of Chemistry. 2021, 37(5): 1132-1138.
55. Hamid SJ, Salih T. Design, Synthesis, and Anti-Inflammatory Activity of Some Coumarin Schiff Base Derivatives: In silico and in vitro Study. Drug Design, Development and Therapy. 2022;16: 2275–2288. https://doi.org/10.2147/DDDT.S364746
56. G Kalyani, B Srinivas, KV Sastry, K Vijaya. Synthesis of Novel Cinnoline fused Mannich Bases: Pharmacological Evaluation of Anti-bacterial, Analgesic and Anti-inflammatory activities. International Journal of Pharmaceutical and Clinical Research. 2017; 9(7): 515-520.
57. Sharma D, Kapoor P, Singh A. Mannich Base Derivatives of Coumarins as Anti-inflammatory Agents. Bioorganic Chemistry. 2023;132: 105215.
58. Ghosh, S, Banerjee T, Roy P. Phosphodiesterase Inhibitory Potential of Coumarins. Journal of Pharmacological Sciences. 2024;155(1): 45-56.
59. Popova SA, Shevchenko OG, Chukicheva IY, Kutchin AV. Synthesis and Biological Evaluation of Novel Coumarins with tert-Butyl and Terpene Substituents. Chem. Biodivers. 2019;16 doi: 10.1002/cbdv.201800317.
60. Li Q, Wei L, Zhang J, Gu G, Guo Z. Significantly enhanced antioxidant activity of chitosan through chemical modification with coumarins. Polym. Chem. 2019; 10:1480–1488. doi: 10.1039/C8PY01790E.
61. Zhang J, Wei L, Feng Y. Computational Approaches in Coumarin Drug Design. Current Medicinal Chemistry. 2024;31(4): 785-798.