10.37021/ijper.v7i1.01

REVIEW ARTICLE

Exploring the Efficacy of Metal Complexes of Coumarin Derivative: Open New Avenues for Discovery of Noval Therapeutic Agents

Reema Sinha*, Pankaj Kumar, Karishma

ABSTRACT

Coumarins are fused six-membered oxygen-containing benzoheterocyclic compounds consisting of an α-pyrone and a benzene ring. Coumarins and their derivatives exhibit a range of biological activities, including antiallergic, insecticidal, antifungal, antiviral, and antibacterial effects. Hydroxycoumarins, as typical phenolic compounds, act as potent metal chelators and free radical scavengers. The metal complexes of coumarins have attracted significant attention from synthetic chemists, medicinal scientists, and pharmacists due to their broad biological applications. These coumarin-derived metal complexes demonstrate various therapeutic properties, such as antibacterial, antifungal, anticancer, antioxidant, anthelmintic, pesticidal, and nematocidal activities. This review highlights recent synthetic methodologies and the known bioactivities of coumarin–metal complexes, emphasizing their potential as promising scaffolds for the development of novel therapeutic agents.

Keywords: Coumarin, Metal complex, Antibacterial, Antifungal

How to cite this article: Sinha R, Kumar P, Karishma. Exploring the Efficacy of Metal Complexes of Coumarin Derivative: Open New Avenues for Discovery of Noval Therapeutic Agents. Int. J. Pharm. Edu. Res. 2025;7(1):1-7.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Coumarins (2H-chromen-2-ones), oxygen-containing benzo-fused heterocycles, represent one of the most important classes of compounds in medicinal chemistry due to their diverse pharmacological activities (Figure 1). Metal ions play a crucial role in various biological processes (35). Our study focuses on coumarin-based metal complexes, which have shown promise as antibacterial, antifungal, antitubercular and antioxidant agents (12) .The ligands and their corresponding metal complexes have been screened for antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa, Bacillus cereus, and Staphylococcus aureus,* as well as for antifungal activity against *Candida albicans and Aspergillus flavus.* Metal ions play essential roles at the molecular level in biological systems. The formation of metal chelates increases the lipophilicity of the drug, enhancing its permeability and bioavailability, thereby improving its pharmacological efficacy(4)(5) Moreover, interactions between metal ions and antibiotics may enhance the antimicrobial activity compared to free ligands (30). The exploration of coumarin derivatives represents a promising direction for the developent of new therapeutic agents with improved efficacy and reduced side effects (5). These investigations significantly advance medicinal chemistry by contributing novel compounds that can potentially meet currently unmet medical needs and improve human health (1)(3).

Coumarin synthesis via various name reaction

several named reactions have been reported for the synthesis of coumarin derivatives, including the Perkin reaction, Pechmann reaction, Claisen rearrangement, Knoevenagel reaction, Kostanecki-Robinson coupling reaction, Reformatsky reaction, Heck-lactonization reaction, and the Baylis–Hillman reaction. These syntheses are often carried out in the presence of either metal-free or metal-based homogeneous and

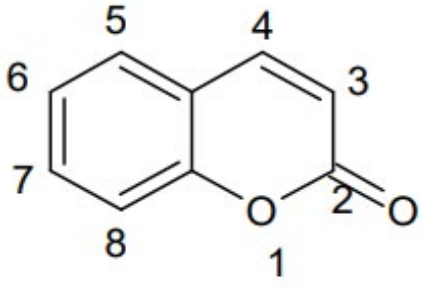


Fig. 1: Structure of coumarin

Ram-Eesh Institute of Vocational & Technical Education Greater Noida.**Corresponding Author**

Reema Sinha, Ram-Eesh Institute of Vocational & Technical Education Greater Noida., E-mail: sinhareema2@gmail.com

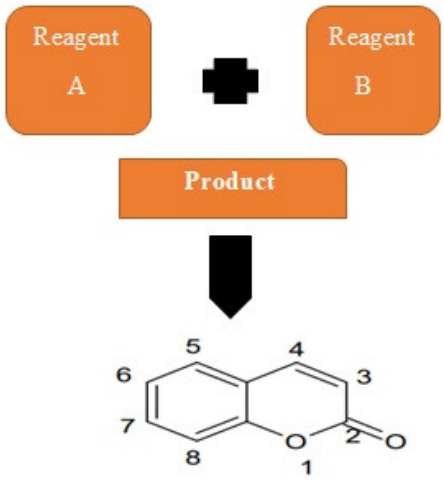
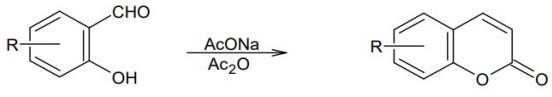


Fig 2: Structure of Coumarin

heterogeneous catalytic systems. The following sections summarize these key reactions used to construct coumarin motifs (2) (Figure 2).

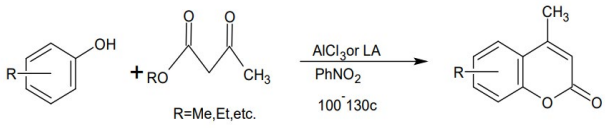
Perkin Reaction

The Perkin reaction is a classical method for the synthesis of coumarins. It involves the condensation of salicylaldehyde with acetic anhydride under basic conditions. The reaction forms an α, β-unsaturated aromatic acid intermediate, which undergoes intramolecular cyclization in the presence of sodium acetate to yield substituted coumarins (2).



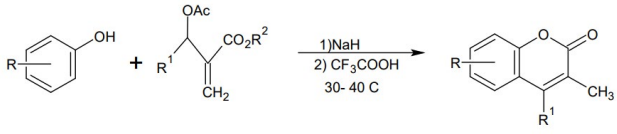
Pechmann Reaction

The Pechmann reaction involves the synthesis of coumarins via the acid-catalyzed condensation of phenols (e.g., carbolic acid) with β-keto esters containing an α-carbonyl group. This process typically proceeds through esterification or transesterification, followed by electrophilic substitution and intramolecular cyclization to form the coumarin ring system(2).



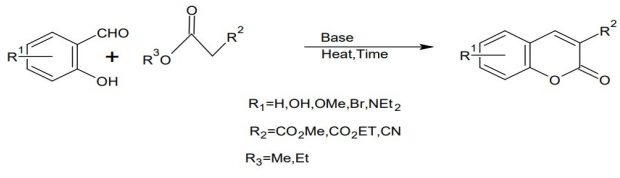
Claisen Rearrangement

The Claisen rearrangement is employed in the synthesis of 3,4-substituted coumarins. This reaction involves the rearrangement of allyl aryl ethers (such as phenol and protected allyl alcohol) in the presence of trifluoroacetic acid (TFA) under moderately basic conditions and mild heating. The process yields 3,4-substituted coumarins in good yields (2).



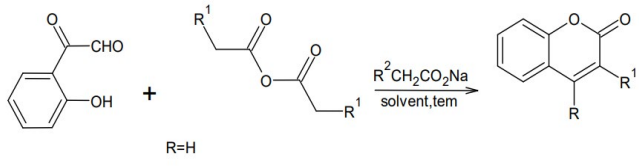
Knoevenagel reaction

Knoevenagel reaction utilized for the synthesis of 3-substituted coumarin derivative. The reaction of 2-hydroxy benzaldehydes with coupling partner containing an active methylene group in the presence of the base under heating conditions and produced coumarin product in good yield. Various reports for the synthesis of Knoevenagel reaction in the presence of ultrasound solvent-free conditions (2).



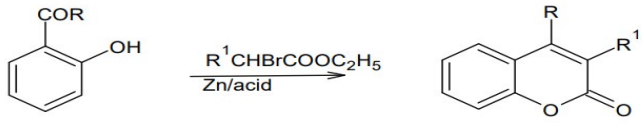
Kostanecki-Robinson coupling reaction

Kostanecki-Robinson coupling reaction utilized for the synthesis of coumarin derivative. The reaction of aliphatic anhydride and aryl ketone with a substitution of the hydroxyl group which gives the desired product as coumarin with good yield (2).



Reformatsky reaction

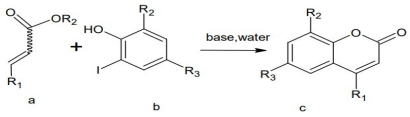
The Reformatsky reaction of aldehydes or ketones with α-halo esters in presence of a zinc to form β-hydroxy-esters and converts 3,4-disubstituted coumarins from α, β-unsaturated ester (2).



Heck-lactonization reaction

The Heck-Lactonization reaction utilized for the synthesis of coumarin analogues in presence of Pd catalysis. Different reaction conditions using aqueous water and organic

solvent. Even with 10 mol% of the PdCl2 or Pd (OAc)2-catalyst used for enoate reacted with iodo compound to produce coumarin in good yields under conditions A and B with water. The condition C was indicating low chemical yield and the proposed catalytic cycle (2).



Condition A:10mol%of pd($OAc)_2$,H_2O,3Equiv Et_3N,80 C

Condition B: 10 mol%of $pdcl_2$,H_2O,3Equiv Et_3N,80 C

Condition A:10mol%of pd($OAc)_2$,in the presence or absence of 20 mol %PPh_3,acetone,euiv $AgNO_3$,reflux

Various methodologies for coumarin synthesis

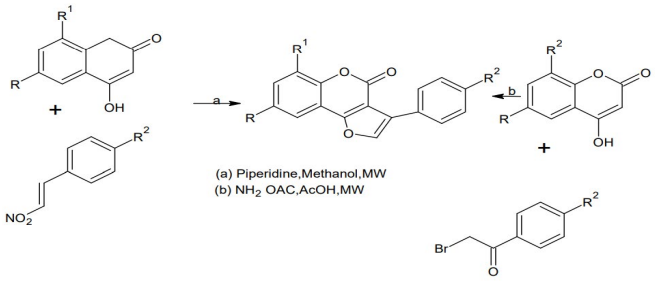
several innovative and eco-friendly methodologies have been developed for the synthesis of coumarin derivatives. These include

- Microwave-assisted synthesis
- Ultrasound-mediated synthesis
- Solvent-free synthesis
- Homogeneous catalytic reactions
- Heterogeneous catalytic reactions

Microwave-Assisted Synthesis

Microwave-assisted synthesis has emerged as a powerful tool in modern organic synthesis, especially in drug discovery, due to its advantages such as higher product yields, reduced reaction times, and improved reproducibility (2). This technique offers a flexible platform for chemical transformations and allows reactions that may not proceed efficiently under conventional heating.

Microwave irradiation accelerates chemical reactions and often produces higher yields in a matter of minutes compared to hours with traditional methods(22). For example, Brahmbatt and co-workers reported the microwave-assisted synthesis of 3-aryl-furo[3,2-c] coumarins, achieving good yields within just 2–4 minutes (16)(17).



Ultrasound mediated synthesis

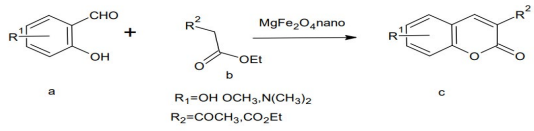
Ultrasound irradiation has become an important green technique in synthetic organic chemistry. Acoustic cavitation—the rapid formation, growth, and collapse of microbubbles creates localized hot spots of high temperature and pressure that accelerate reactions. Key advantages include:

Very short reaction times compared with conventional heating

Simple experimental setups that often operate under solvent-free or mild condition

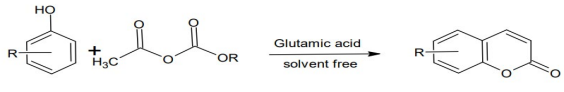
High yields and improved selectivity for many coumarin derivatives

For example, ultrasound-assisted coupling of substrate A (e.g., a phenol bearing R^1 = OH, OCH_3, or $N(CH_3)_2$) with substrate B (bearing $R^2 = COCH_3$ or CO_2Et) at 45 °C under solvent-free conditions rapidly affords the desired coumarin product C through cavitation-induced activation (2).



Solvent-free synthesis

Large volumes of hazardous and volatile organic solvents are used in conventional chemical reactions. Green chemistry aims to replace toxic reaction solvents with safer alternatives. Many researchers have reported the synthesis of coumarin under solvent-free conditions. Sabetpoor et al. (2014) reported the synthesis of simple coumarin analogs under solvent-free conditions using glutamic acid as a catalyst. The reaction was carried out between phenol and keto-ester reactants, and excellent yields were obtained (2).

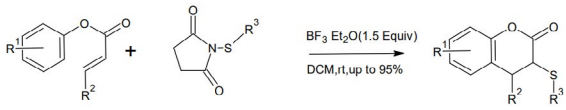


Homogeneous catalytic reaction

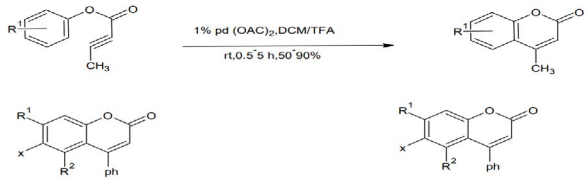
Chang et al. (2014) proposed a metal-free approach to synthesize 3-sulfenylated coumarins through the cyclization of aryl alkynoates and N-sulfanylsuccinimides in the presence of BF3•Et2O as a Lewis acid (2).

Heterogeneous catalytic reaction

Heterogeneous catalysis plays a vital role in converting petroleum and natural gas into cleaner, more efficient



fuels. Yuzo Fujiwara et al. (2000) reported a novel method for synthesizing coumarins and quinolinones via intermolecular hydroarylation. Different aryl alkynoates and alkynanilides were quickly converted to the required coumarin derivatives at 25–27°C using Pd(OAc)2 as a catalyst in a mixture of TFA and DCM solvents (2).



Preparation of coumarins catalysed by PtCl4.

In 2004, Chuan and coworkers reported a gold(III)-mediated intermolecular hydroarylation reaction of aryl alkynoates in the presence of 5 mol% AuCl3 and AgOTf. Higher temperatures (up to 70°C) were required in some cases. Catalysis by Pd(II), Pt(II), Pt(IV), and Ru(II) has also been described (2).

Metal Complex

Metal complexes of coumarin derivatives have garnered significant attention due to their enhanced biological activities compared to parent coumarin ligands (Fig -3) (4) (5). These complexes are formed by coordinating coumarin derivatives with metal ions, resulting in compounds that exhibit broad-spectrum biological properties, including anticancer, antibacterial, antioxidant, and enzyme-mimicking activities (15). The chelation property of these compounds increases the lipophilicity of the drug, improving its permeability and enhancing drug action (7)(14). Although coumarin itself can be toxic to the liver and kidneys, its biological activity significantly increases upon binding with metal ions, often with reduced toxicity (6)(43). Coumarins are a class of compounds that combine a broad spectrum of biological activities with excellent chelating properties, making them suitable candidates for the synthesis of novel complexes. Many reviews on transition metal coumarin complexes with biological activity have been published over the previous decade (Balcıoğlu et al.,2020; Balewski et al., 2021; Patil et al., 2022). The present review aims to inform the reader on the latest developments of metal complex of Schiff base of Coumerin which is new approach (3).Cu(II) , Zn (II),Co (III) are used for metal complex as these metals have shown good activity.

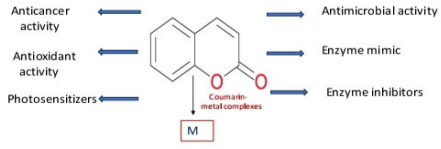


Figure.3: Biological properties of coumarin-metal complexes

Metal coordination tends to improve biological activity. This would be in agreement Overtone's concept of cell permeability - the cellular membrane tends to favor the passage of hydrophobic molecules. Chelation theory suggests partial sharing of the positive charge of the transition metal ion with the donor groups, combined with π-delocalization within the chelate ring. As a result, lipophilicity and, hence, membrane permeation and biological activity tend to increase. As demonstrated by (Mujahid et al., 2023), there are additional factors at play - if biological activity is realized by the metal ion its particular coordination mode determines whether it is (3).

MEDICINAL APPLICATION OF COUMARIN METAL COMPLEX

- Coumarin complexes with antimicrobial activity.
- Coumarin complexes with anticancer activity.
- Coumarin complexes as photodynamic and photochemotherapeutic agents.
- Coumarin complexes as enzyme inhibitors

Antimicrobial activity

With the rise of resistance to commonly used antibiotics, there is a need for novel therapeutic agents and drugs. The therapeutic options for many bacteria strains are still limited and the research aimed at discovering new antimicrobial drugs with metal complexes.Valuable information regarding antimicrobial metal complexes of coumarins can be found in recently published papers (12) (30)

Aldovic and coworkers synthesized several coumarin-derived ligands and coordinated with Pd(II) (Avdović et al., 2019). Compounds manifested moderate to low antimicrobial activity. Ligand and its corresponding compound manifested minimal inhibitory concentration

(MIC) of 125 μg/mL and 62.5 μg/mL respectively toward *Aspergillus flavus* ATCC, comparable value to the standard fluconazole with MIC = 62.5 μg/mL. The same compounds had MICs of 62.5 μg/mL when tested against *Bacillus subtilis* IP 5832 and *Bacillus cereus*, compared to less than 2.0 μg/mL exhibited by the standard substance doxycycline. Generally, coordination of the ligands with Pd(II) tended to increase antibacterial activity. (8)

In 2019, *Belkhir-Talbi et al*. described copper (II) and zinc(II) complexes of 3-(2- hydroxybenzoyl)-2H-chromen-2-one as effective agents against Gram-positive bacteria strain: *Staphylococcus aureus* (ATCC 25923) *(Belkhir-Talbi et al., 2019).* It was found that both complexes exhibited moderate antibacterial activity and diameters of inhibition zones (range of 14–17 mm) in comparison to reference second-generation cephamycin group antibiotic - cefoxitin (diameter of inhibition zone: 20 mm). Furthermore, complexes showed a higher activity comparison to the free ligand. ADMET and drug-likeness profile of these compounds confirmed their non-toxic and non-carcinogenic properties. (1)

Huang and coworkers synthesized a coumarin-bearing ligand and together with a series of ancillary ligands, coordinated with Ru(II). The ancillary ligands were 2,2′-bipyridine and 2,2′-bipyridine disubstituted at positions 4 and 4′ with methyl methoxy, and tert-butyl substituents. The novel complexes were tested against gram negative E. coli and P. aeruginosa and found to be inactive. Compound manifested antibacterial activity against gram-negative S. aureus (MIC = 1.56 μg/mL). Further studies showed could interact with phospholipids in the bacterial membrane, generating reactive oxygen species, consequently impairing membrane integrity. (3)(28)

Anticancer Activity

Coumarin-metal complexes have shown significant potential in cancer therapy. For instance complexes with metals like copper and platinum exhibit strong antiproliferative effects against cancer cell lines, including cervical and breast cancer. These complexes can induce DNA damage and inhibit tumor-associated inflammation, effective in targeting cancer cells while minimizing harm to normal tissues. (1)(3) The ability of these complexes to interact with DNA suggests a mechanism that could be exploited for novel anticancer drug development. (4)(10)

Antioxidant activity

The antioxidant capabilities of coumarin-metal complexes are particularly valuable in combating oxidative stress-related diseases. These complexes can effectively scavenge reactive oxygen species (ROS), which are implicated in cancer, neurodegenerative diseases, and other pathologies. By protecting normal cells from oxidative damage while targeting tumor cells, these compounds hold promise for therapeutic strategies in hematologic cancers. (1)(13)

Enzyme Inhibition

Coumarin-metal complexes exhibit enzyme-inhibiting properties, can be harnessed for therapeutic purposes. For example, they inhibitors of cyclooxygenase enzymes involved in inflammation and pain pathways, offering a approach to managing conditions like arthritis and other inflammatory diseases. (1)

Photodynamic Therapy

Coumarin-metal complexes are increasingly being investigated for use in photodynamic therapy (PDT). The unique fluorescent properties of coumarins make them suitable as photosensitizers when coordinated with transition metals. (45) These complexes can generate reactive oxygen species upon light activation, leading to targeted destruction of cancer cells. Recent studies have focused on optimizing these complexes for enhanced photodynamic activity.

Antioxidant Properties

Recent research highlights that coumarin-metal complexes possess superior antioxidant capabilities. The metal ions can modify the radical-scavenging properties of the coumarin ligands, allowing these complexes to effectively neutralize reactive oxygen species (ROS) associated with various diseases, including cancer and neurodegenerative disorders. This modification not only protects normal cells but also selectively targets tumor cells.

CONCLUSION

The integration of metal ions into coumarin derivatives improve biological activity and avenues for the creation of novel therapeutic agents with improved efficacy against various diseases .The Authors may concluded that their ability to modify safety profile and enhance therapeutic efficacy which makes them attractive candidates for further investigation. Future studies are expected to focus on elucidating structure-activity relationships and exploring new synthetic pathways to optimize their biological activities. The integration of metal ions into coumarin derivatives not only augments their biological functions but also opens avenues for discovery of novel therapeutic agents with improved efficacy against various diseases and reduce the toxicity. Future studies

are expected to focus on elucidating structure-activity relationships and exploring new synthetic pathways to optimize their biological activity. The ongoing research into coumarin-metal complexes underscores their potential therapeutic agents with enhanced biological activities. The combination of coumarins with various metal ions not only improves their pharmacological profiles but also opens new avenues for treatment strategies in pharmacology and infectious diseases. Continued exploration of these compounds is yield innovative solutions in drug development and therapeutic applications. The integration of metal ions into coumarin derivatives improve biological activity and avenues for the creation of novel therapeutic agents with improved efficacy against various diseases.

REFERENCES

1. Lončarić M, Gašo-Sokač D, Jokić S, Molnar M. Recent advances in the synthesis of coumarin derivatives from different starting materials. Biomolecules. 2020 Jan 16;10(1):151.
2. Ye FF, Gao JR, Sheng WJ, Jia JH. One-pot synthesis of coumarin derivatives. Dyes and Pigments. 2008 Jan 1;77(3):556-8.
3. Balewski Ł, Szulta S, Jalińska A, Kornicka A. A mini-review: Recent advances in coumarin-metal complexes with biological properties. Frontiers in Chemistry. 2021 Dec 1;9:781779.
4. Todorov LT, Kostova IP. Coumarin-transition metal complexes with biological activity: current trends and perspectives. Frontiers in Chemistry. 2024 Feb 12;12:1342772.
5. Rehman SU, Chohan ZH, Gulnaz F, Supuran CT. In-vitro antibacterial, antifungal and cytotoxic activities of some coumarins and their metal complexes. Journal of Enzyme Inhibition and Medicinal Chemistry. 2005 Jan 1;20(4):333-40
6. Sahoo SS, Shukla S, Nandy S, Sahoo HB. Synthesis of novel coumarin derivatives and its biological evaluations. Eur. J. Exp. Biol. 2012;2(4):899-908
7. Carneiro A, Matos MJ, Uriarte E, Santana L. Trending topics on coumarin and its derivatives in 2020. Molecules. 2021 Jan 19;26(2):501
8. Rehman SU, Chohan ZH, Gulnaz F, Supuran CT. In-vitro antibacterial, antifungal and cytotoxic activities of some coumarins and their metal complexes. Journal of Enzyme Inhibition and Medicinal Chemistry. 2005 Jan 1;20(4):333-40.
9. Patil SA, Kandathil V, Sobha A, Somappa SB, Feldman MR, Bugarin A, Patil SA. Comprehensive review on medicinal applications of coumarin-derived imine–metal complexes. Molecules. 2022 Aug 16;27(16):5220.
10. Koley M, Han J, Soloshonok VA, Mojumder S, Javahershenas R, Makarem A. Latest developments in coumarin-based anticancer agents: mechanism of action and structure–activity relationship studies. RSC medicinal Chemistry. 2024;15(1):1054. biological evaluations. Eur. J. Exp. Biol. 2012;2(4):899-908.
11. Xia YL, Wang JJ, Li SY, Liu Y, Gonzalez FJ, Wang P, Ge GB. Synthesis and structure-activity relationship of coumarins as potent Mcl-1 inhibitors for cancer treatment. Bioorganic & medicinal chemistry. 2021 Jan 1;29:115851.
12. Cheke RS, Patel HM, Patil VM, Ansari IA, Ambhore JP, Shinde SD, Kadri A, Snoussi M, Adnan M, Kharkar PS, Pasupuleti VR. Molecular insights into coumarin analogues as antimicrobial agents: Recent developments in drug discovery. Antibiotics. 2022 Apr 24;11(5):566.
13. Hariprasath K, Deepthi B, Babu IS, Venkatesh P, Sharfudeen S, Soumya V. Metal complexes in drug research-a review. Journal of Chemical and Pharmaceutical Research. 2010;2(4):496-9.
14. Todorov LT, Kostova IP. Coumarin-transition metal complexes with biological activity: current trends and perspectives. Frontiers in Chemistry. 2024 Feb 12;12:1342772.
15. Satyanarayana VS, Sreevani P, Sivakumar A, Vijayakumar V. Synthesis and antimicrobial activity of new Schiff bases containing coumarin moiety and their spectral characterization. Arkivoc. 2008 Jan 1;17:221-33..
16. Kapadiya K, Dholaria P. Microwave and conventional study of coumarin-oxadiazole adducts and their anti-microbial evaluation. Folia Medica. 2021 Feb 28;63(1):105-12.
17. Das R, Mehta D, Bhardawaj H. An overview on microwave mediated synthesis. Int J Res Dev Pharm Life Sci. 2012;1(2):32-9.
18. Lončarić M, Gašo-Sokač D, Jokić S, Molnar M. Recent advances in the synthesis of coumarin derivatives from different starting materials. Biomolecules. 2020 Jan 16;10(1):151.
19. Stepanenko I, Babak MV, Spengler G, Hammerstad M, PopovicBijelic A, Shova S, Büchel GE, Darvasiova D, Rapta P, Arion VB. Coumarin-Based Triapine Derivatives and Their Copper (II) Complexes: Synthesis, Cytotoxicity and mR2 RNR Inhibition Activity. Biomolecules. 2021 Jun 9;11(6):862.
20. Sahoo J, Paidesetty SK. Antimicrobial activity of novel synthesized coumarin based transitional metal complexes. Journal of Taibah University Medical Sciences. 2017 Apr
21. 1;12(2):115-24.
22. Grazul M, Budzisz E. Biological activity of metal ions complexes of chromones, coumarins and flavones. Coordination chemistry reviews. 2009 Nov 1;253(21-22):2588-98.
23. Rehman SU, Chohan ZH, Gulnaz F, Supuran CT. In-vitro antibacterial, antifungal and cytotoxic activities of some coumarins and their metal complexes. Journal of Enzyme Inhibition and Medicinal Chemistry. 2005 Jan 1;20(4):333-40.
24. Alghool S. Metal complexes of azo coumarin derivative: synthesis, spectroscopic, thermal, and antimicrobial studies. Journal of Coordination Chemistry. 2010 Sep 20;63(18):3322-33.
25. Alghool S. Metal complexes of azo coumarin derivative: synthesis, spectroscopic, thermal, and antimicrobial studies. Journal of Coordination Chemistry. 2010 Sep 20;63(18):3322-33.
26. Sahoo J, Paidesetty SK. Antimicrobial activity of novel synthesized coumarin based transitional metal complexes. Journal of Taibah University Medical Sciences. 2017 Apr
27. 1;12(2):115-24.
28. Karaliota A, Kretsi O, Tzougraki C. Synthesis and characterization of a binuclear coumarin-3-carboxylate copper (II) complex. Journal of Inorganic Biochemistry. 2001 Mar 1;84(1-2):33-7.
29. Giriraj K, Mohamed Kasim MS, Balasubramaniam K, Thangavel SK, Venkatesan J, Suresh S, Shanmugam P, Karri C. Various coordination modes of new coumarin Schiff bases toward Cobalt (III) ion: synthesis, spectral characterization, in vitro cytotoxic activity, and investigation of apoptosis. Applied Organometallic Chemistry. 2022 Mar;36(3):e6536.
30. Creaven BS, Egan DA, Kavanagh K, McCann M, Noble A, Thati B, Walsh M. Synthesis, characterization and antimicrobial activity of a series of substituted coumarin-3carboxylatosilver (I) complexes. Inorganica Chimica Acta. 2006 Sep 1;359(12):3976-84.
31. Hankare PP, Naravane SR, Bhuse VM, Delekar SD, Jagtap AH.

Synthesis and characterization of Mn (II), Co (II), Ni (II), Cu (II) and Zn (II) azo coumarin complexes.
32. Manidhar DM, Kesharwani RK, Reddy NB, Reddy CS, Misra K. Designing, synthesis, and characterization of some novel coumarin derivatives as probable anticancer drugs. Medicinal Chemistry Research. 2013 Sep;22:4146-57.
33. Kostova I, Momekov G. New cerium (III) complexes of coumarins–synthesis, characterization and cytotoxicity evaluation. European journal of medicinal chemistry. 2008 Jan 1;43(1):178-88.
34. Kostova I, Momekov G. New cerium (III) complexes of coumarins–synthesis, characterization and cytotoxicity evaluation. European journal of medicinal chemistry. 2008 Jan 1;43(1):178-88.
35. Mruthyunjayaswamy, Bennikallu Hire Mathada. "Synthesis, spectroscopic characterization, electrochemistry and biological activity evaluation of some metal (II) complexes with ONO donor ligands containing indole and coumarin moieties." Journal of Saudi Chemical Society 21 (2017): S202-S218.
36. Creaven, Bernadette S., et al. "Copper (II) complexes of coumarin-derived Schiff bases and their anti-Candida activity." Journal of inorganic biochemistry 103.9 (2009): 1196-1203.
37. Refat, Moamen S., et al. "Bivalent transition metal complexes of coumarin-3-yl thiosemicarbazone derivatives: Spectroscopic, antibacterial activity and thermogravimetric studies." Journal of Molecular Structure 920.1-3 (2009): 149-162.
38. Mosa AI, Emara AA, Yousef JM, Saddiq AA. Novel transition metal complexes of 4-hydroxy-coumarin-3thiocarbohydrazone: Pharmacodynamic of Co (III) on rats and antimicrobial activity. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2011 Oct 15;81(1):35-43.
39. Thati B, Noble A, Rowan R, Creaven BS, Walsh M, McCann M, Egan D, Kavanagh K. Mechanism of action of coumarin and silver (I)–coumarin complexes against the pathogenic yeast Candida albicans. Toxicology in vitro. 2007 Aug 1;21(5):801-8.
40. 38. Elhusseiny AF, Aazam ES, Al-Amri HM. Synthesis of new microbial pesticide metal complexes derived from coumarinimine ligand. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2014 Jul 15;128:852-63.
41. Sunitha N, Raj CI, Kumari BS. Synthesis, spectral studies, biological evaluation and molecular docking studies of metal complexes from coumarin derivative. Journal of Molecular Structure. 2023 Aug 5;1285:135443.
42. Budzisz E, Małecka M, Lorenz IP, Mayer P, Kwiecień RA, Paneth P, Krajewska U, Rózalski M. Synthesis, cytotoxic effect, and structure− activity relationship of Pd (II) complexes with coumarin derivatives. Inorganic Chemistry. 2006 Nov 27;45(24):9688-95.
43. Pereira TM, Franco DP, Vitorio F, Kummerle AE. Coumarin compounds in medicinal chemistry: some important examples from the last years. Current topics in medicinal chemistry. 2018 Jan 1;18(2):124-48.
44. Mukhtar A, Mansha A, Asim S, Shahzad A, Bibi S. Excited state complexes of coumarin derivatives. Journal of Fluorescence. 2022 Jan 1:1-7.
45. Patel J, Dholariya H, Patel K, Bhatt J, Patel K. Cu (II) and Ni (II) complexes of coumarin derivatives with fourth generation flouroquinolone: synthesis, characterization, microbicidal and antioxidant assay. Medicinal Chemistry Research. 2014 Aug;23:3714-24.
46. Patel J, Dholariya H, Patel K, Bhatt J, Patel K. Cu (II) and Ni (II) complexes of coumarin derivatives with fourth generation flouroquinolone: synthesis, characterization, microbicidal and antioxidant assay. Medicinal Chemistry Research. 2014 Aug;23:3714-24.
47. Ibrahim DM, Jumal J, Al-Adiwish WM. Anti-cancer Screening of Some Transition Metal Ion Complexes with Coumarin Derivatives. J. Transit. Met Complexes. 2019;2:1-5.
48. Sahoo CR, Sahoo J, Mahapatra M, Lenka D, Sahu PK, Dehury B, Padhy RN, Paidesetty SK. Coumarin derivatives as promising antibacterial agent (s). Arabian Journal of Chemistry. 2021 Feb 1;14(2):102922.
49. Karaliota, A., O. Kretsi, and C. Tzougraki. "Synthesis and characterization of a binuclear coumarin-3-carboxylate copper (II) complex." Journal of Inorganic Biochemistry 84.1-2 (2001): 33-37.
50. Koç S, Köse DA, Avcı E. Synthesis, Structural Characterization and Biological Application of Mixed Ligands Complexes of Coumaric Acid/Coumarine with Some Transition Metal Cation. European Chemical Bulletin. 2016;5(4):132-7.
51. Abdel-Kader NS, Moustafa H, El-Ansary AL, Sherif OE, Farghaly AM. A coumarin Schiff base and its Ag (i) and Cu (ii) complexes: synthesis, characterization, DFT calculations and biological applications. New Journal of Chemistry. 2021;45(17):7714-30.
52. Rastogi DK. Coumarins as ligands. Studies on metal complexes of 8-Amino-7-hydroxy-4-methylcoumarin and 7-Hydroxy4-methylcoumarin-6-carboxylic acid. Australian Journal of Chemistry. 1972;25(4):729-37..
53. Karafi, Athar, Lassaad Baklouti, and Besma Mellah. "Spectroscopic properties and stabilities of metal complexes using coumarin derivatives substituted with methyl, chloro, and nitro groups." Journal of Inclusion Phenomena and Macrocyclic Chemistry 104.5 (2024): 269-276.
54. Abou-Hussein AA, Linert W. Synthesis, spectroscopic studies and inhibitory activity against bactria and fungi of acyclic and macrocyclic transition metal complexes containing a triamine coumarine Schiff base ligand. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2015 Apr 15;141:223-32.
55. Manjunath M, Kulkarni AD, Bagihalli GB, Malladi S, Patil SA. Bio-important antipyrine derived Schiff bases and their transition metal complexes: Synthesis, spectroscopic characterization, antimicrobial, anthelmintic and DNA cleavage investigation. Journal of Molecular Structure. 2017 Jan 5;1127:314-21.