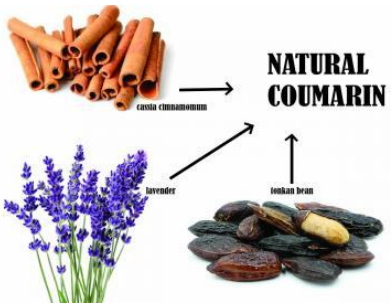

CHAPTER 09

Coumarins: Natural Anticoagulants and Anticancer Agents

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ABSTRACT: Coumarins are a class of naturally occurring phytochemicals with diverse pharmacological activities, including anticoagulant, anti-inflammatory, antioxidant, and anticancer effects. Their anticoagulant mechanism, as observed in warfarin, involves inhibition of the vitamin K epoxide reductase complex, thereby impairing the activation of key clotting factors. Anti-inflammatory effects are mediated through the downregulation of pro-inflammatory mediators such as COX-2, TNF-α, and IL-1β, and via suppression of NF-κB and MAPK signaling pathways. Coumarins also exhibit antioxidant capacity by neutralizing reactive oxygen species, thereby protecting cellular structures from oxidative injury. Moreover, compounds like esculetin, osthole, and scopoletin have demonstrated anticancer properties as they promote apoptosis, inhibit cell proliferation, and reduce the metastatic potential of tumors. Despite their broad therapeutic usages, their clinical applications are limited by poor aqueous solubility, low bioavailability, rapid metabolic clearance, and hepatotoxic risks. Recent advancements in structural modifications, hybrid compound synthesis, nanocarrier systems, and pharmacogenomics aim to enhance the efficacy and safety of coumarins. These developments present coumarins as valuable candidates in the treatment of cardiovascular, inflammatory, neurodegenerative, and oncological disorders.

Coumarins are a diverse class of naturally occurring phenolic compounds which are characterized by a benzopyrone core, specifically the 2H-1-benzopyran-2-one structure. They are widely distributed in higher plants, especially in the families Apiaceae, Rutaceae, and Fabaceae, where they function as secondary metabolites and are involved in plant defense mechanisms (Venugopala et al., 2013). The compound "coumarin" itself was first isolated in 1820 from tonka beans (*Dipteryx odorata*) by Vogel and later by Guibourt.

The biosynthesis of natural coumarins in plants generally proceeds via the phenylpropanoid pathway, beginning with phenylalanine and involving hydroxylation and lactonization steps to yield the characteristic lactone ring. Structurally, coumarins are classified into several subclasses based on their substitution patterns and ring fusions, including simple coumarins, furanocoumarins, pyranocoumarins, and bis-coumarins, among others (Venugopala et al., 2013).

Historically, coumarin-containing plants were used in folk medicine and perfumery. The sweet scent of coumarin led to its use in fragrances such as Houbigant's Fougère Royale (1882), and it was once added to foods and tobacco, although its direct use as a food additive is now restricted due to hepatotoxicity concerns in high doses (Kumar & Nayyar, 2021). Coumarin's pharmacological relevance became particularly prominent in the 20th century when the anticoagulant dicoumarol, a natural derivative formed by fungal metabolism of coumarin in spoiled sweet clover, was discovered. This led to the development of synthetic 4-hydroxycoumarin derivatives like warfarin, which are widely used as oral anticoagulants (Mazimba, 2017). Beyond anticoagulation, various coumarin derivatives have demonstrated anti-inflammatory, antimicrobial, antiviral, antioxidant, antitumor, and

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enzyme-inhibitory activities, making them promising leads in medicinal chemistry.

Coumarins are widely distributed in nature and occur in significant concentrations across various plant species. One of the most concentrated natural sources is the tonka bean (*Dipteryx odorata*), which contains high levels of coumarin, sometimes up to 10% of the dry weight, and was the first botanical source from which coumarin was isolated (Ford et al., 2021). Another notable source is sweet clover (*Melilotus officinalis*), where coumarins exist as glycosides. During microbial fermentation or spoilage, these precursors convert into dicoumarol, a natural anticoagulant that led to the development of synthetic derivatives like warfarin (Wang et al., 2021).

Citrus fruits, particularly the peels of species like *Citrus bergamia* and *Citrus aurantium*, are rich in furanocoumarins such as psoralen, bergapten, and xanthotoxin, which contribute to their phototoxic and therapeutic activities. In addition, many medicinal plants synthesize hydroxycoumarins like scopoletin, which is widely distributed in plants such as *Artemisia annua*, *Scopolia japonica*, *Morinda citrifolia*, and *Aegle marmelos*. Scopoletin and related coumarins have been reported to exert multiple pharmacological effects including anti-inflammatory, antioxidant, and neuroprotective activities (Huang et al., 2024). This chapter discusses the importance of coumarins as naturally occurring anticoagulants and anticancer agents.

ANTICOAGULANT AND CARDIOVASCULAR ACTIVITIES

The anticoagulant activity of coumarins is fundamentally linked to their interference with the vitamin K cycle, a critical biochemical process that enables the activation of coagulation proteins. Vitamin K is required for the post-translational γ-carboxylation of glutamate residues on clotting factors II (prothrombin), VII, IX, and X, as well as proteins C and S, which are essential for blood coagulation (Wang et al., 2025). It is this gamma carboxylation that allows these proteins to bind calcium ions, which is a precondition to their appropriate usage in the coagulation process.

Coumarin directly blocks the enzyme vitamin K epoxide reductase complex 1 (VKORC1), which under normal circumstances recycles vitamin K 2-epoxide back to the reduction state, active form, hydroquinone. Coumarins inhibit VKORC1, thereby depleting active vitamin K, and leads to the synthesis of inactive blood clotting factors (the undercarboxylated form), which increases the amount of time required to clot the blood and reduces the risk of developing thrombosis (Wang et al., 2025).

Following the discovery in the 1940s that a naturally occurring anticoagulant, dicoumarol could be derived from spoiled sweet clover, many attempts have been made to synthesize analogs with better pharmacokinetic and pharmacodynamic properties. Warfarin is an anticoagulant and synthetic derivative of 4-hydroxycoumarin and gives prototypical synthetic interactions with CO (Gupta et al., 2024). The structure activity relationship (SAR) of drug warfarin and it analogs focus on alteration of the 4-hydroxycoumarin scaffold. Two of the areas are critical to the potency and metabolism: the phenyl substituent at the C-3 position and alkyl or halogen substitutions at the other aromatic positions (Cuevas et al., 2020).

Warfarin and similar coumarin derivatives have been the foundation for the prevention and treatment of thromboembolic disorders for more than 60 years. They are clinically indicated in terms of the prevention of venous thromboembolism (VTE), pulmonary embolism (PE) and thrombosis of arteries, in patients with atrial fibrillation (AF), who are at risk of ischemic stroke, or with mechanical valves of the heart or some forms of individual hypercoagulability (Pitaro et al., 2022).

While dicoumarol, a naturally occurring anticoagulant, paved the way for synthetic coumarins, natural coumarins themselves generally lack the potency and pharmacokinetic predictability of synthetic drugs. Natural coumarins are widely distributed in plants such as Ferula, Angelica, and Melilotus species, and some exhibit mild antithrombotic and vasodilatory activities in experimental models (Zhang et al., 2021).

The major limitation of coumarin anticoagulants such as warfarin is their narrow therapeutic window.

The risk of bleeding, ranging from minor bruising to life-threatening hemorrhage, is a constant clinical challenge. Epidemiological data indicate major bleeding rates of approximately 1-3% per year in patients on warfarin, with minor bleeding events occurring much more frequently. Warfarin therapy requires frequent monitoring of coagulation status using the International Normalized Ratio (INR) to maintain blood clotting within a target range (usually 2.0 to 3.0). Deviations from this range significantly increase risks: an INR above 4.5 is strongly associated with hemorrhagic complications, while values below 2 may fail to prevent thrombosis (Khalid et al., 2023).

Drug-drug interactions are another major concern. Many prescribed medications, including antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), and amiodarone, can potentiate or inhibit warfarin metabolism, altering its anticoagulant effect (Lee et al., 2020). On top of that, diet adherence to such foodstuffs as leafy vegetables that are rich in vitamin K can antagonize the effect of warfarin even making the management harder.

ANTI-INFLAMMATORY AND ANTIOXIDANT PROPERTIES

Anti-inflammatory action of coumarin mainly entails inhibition of major pro-inflammatory cytokines as well as enzymes that include tumor necrosis factor-alpha (TNF-α) interleukin-1 beta (IL-1β), and cyclooxygenase-2 (COX-2). The main cytokines that coordinate inflammatory reactions are TNF-α and IL-1β that stimulate the activation of immune cells and enhance cytokine cascades. *In vitro* and *in vivo* experiments in the past few years have shown that coumarins such as esculetin and daphnetin are strong inhibitors of TNF-α and IL-1β expressions in LPS-induced macrophages. Moreover, they are found in inflammation models in animals and show a decrease in leukocyte infiltration and tissue swelling (Cheke et al., 2022).

Moreover, the expression of COX-2 and the production of pro-inflammatory prostaglandins and COX-2 stimulants like PGE2, which mediate pain and vascular permeability, are effectively inhibited by coumarins (Jung et al., 2024). This suppresses the production of prostaglandins and is one of the reasons that coumarins have anti-inflammatory and pain killing effects. Down regulation of these mediators leads to the weakening of the inflammation process on several levels both in the initiation and maintenance of the inflammation process.

On a molecular scale, the anti-inflammatory activity of coumarins has been attributed to their inhibitory activity on two signaling pathways, namely the nuclear factor kappa B (NF-κB) and mitogen- activated protein kinase (MAPK). NF-κB is a transcription regulator that plays a significant role in controlling the expression of various inflammatory genes, which include cytokines, chemokines, and the enzyme COX-2 inducible nitric oxide synthase (iNOS). Inflammatory stimulation can lead to the activation, through phosphorylation and subsequent degradation, of NF-κB inhibitor (IκB), thus unlocking and allowing NF-κB to translocate into the nucleus where it can increase the transcription of pro-inflammatory genes (Şeker Karatoprak et al., 2024).

Recent research clearly shows that fraxetin, osthole, and other coumarins suppress the activation of the NF-κB pathway, thereby inhibiting nuclear transport and transcription of the NF-κB factors in immune cells, by stabilizing IκB, additional components of the NF-κB pathway. At the same time, coumarins regulate MAPK track which includes ERK, JNK and p38, thereby influencing inflammation. Coumarins curb the downstream signaling of these kinases and transcription factors like AP-1 and prevent the increased production of inflammatory mediators, which can be achieved by inhibiting the phosphorylation of these kinases (Hu et al., 2025).

Coumarins have an attractive prospect as anti-inflammatory and antioxidant agents in long-term inflammatory situations like rheumatoid arthritis (RA), inflammatory bowel disease (IBD), neuroinflammatory illnesses and cardiovascular inflammation. In preclinical settings, coumarins have an anti-inflammatory effect on the joint, cartilage loss, and hyperplasia in RA models by inhibiting the cytokine and oxidative markers.

In IBD models, colonic inflammation and damage of the mucosa are diminished by coumarin treatment through its modulation of NF-κB and MAPK pathways together with the reintegration of the antioxidant defenses. In addition to it, neuroprotective properties of coumarins are acknowledged to a greater extent, as researchers proved their ability to attenuate the microglial activation, decrease neuroinflammation, and oxidative neuronal damage in Alzheimer's and Parkinson's disease models (Hu et al., 2025; Şeker Karatoprak et al., 2024).

ANTICANCER AND CHEMOPREVENTIVE EFFECTS

Induction of apoptosis is one of the main ways that coumarins have via which they exert their anticancer effects. As an example, esculetin was found to possess the ability to induce apoptosis in colon cancer HT-29 cells using the reactive oxygen species (ROS)-mediated mitochondrial pathway via depolarizing the mitochondrial membranes. It increases ratio of Bax/Bcl-2, and caspase-9, as well as caspase-3. Esculetin also mediates the activation of MAPK pathway and apoptosis and reduces antioxidants which confirms that its action is ROS-dependent (Sarker & Nahar, 2017).

In another case, esculetin inhibited the proliferation and anchorage-independent growth of HCT116, HCT15, and DLD1 colon cancer cell in a dose-dependent manner. It also reduced the growth of a xenograft mouse model. This was explained by downregulation of wound/beta-catenin signaling, especially, via the inhibition of downstream effectors such as cyclin D1 and c-Myc that are essential for cancer cell proliferation (Bai et al., 2016).

Osthole is a naturally occurring coumarin derived from *Cnidium monnieri*, that exhibits anticancer effects in various tumor types. Osthole caused a considerable level of apoptosis and cell cycle arrest in triple-negative breast cancer (TNBC) cells (MDA-MB-231) and were also found to be inhibitory to the STAT3 signaling pathway. This could be seen in the decreased phosphorylation and nuclear translocation of STAT3. *In vivo* studies showed that osthole decreased the volume of tumor and target gene expression of STAT3 in xenograft models, and it may likely become a chemotherapeutic agent (Wang et al., 2021).

Osthole's effects on lung cancer cells (A549) further underscores its broad-spectrum activity. In this model, osthole induced G2/M cell-cycle arrest, promoted mitochondrial dysfunction, and activated endoplasmic reticulum (ER) stress pathways. This was associated with downregulation of the PI3K/Akt and MAPK signaling pathways, both critical to tumor survival and progression (Wang et al., 2021).

Osthole promoted apoptosis in colon cancer HT-29 cells through elevation of the pro-apoptotic protein levels including Bax and caspase-3, and a reduction of Bcl-2 (anti-apoptotic), that shows the activation of intrinsic apoptotic pathway via osthole. It is interesting to note that this apoptotic effect was associated with ER-induced autophagy due to the elevated gene expression of ER stress markers, Glucose-Regulated Protein 78 (GRP78), Protein kinase R-like Endoplasmic Reticulum Kinase (PERK), and C/EBP homologous protein (CHOP) (Liu et al., 2023).

Osthole has also been effective in the metastasis of cancer. It was discovered to suppress epithelial-to-mesenchymal transition (EMT), which also plays a major role in tumor invasion and metastasis, in lung cancer models. It inhibited the TGF-β1-induced EMT in A549 cells by suppressing the NF-κB/Snail signaling pathway, which increased the epithelial marker E-cadherin and decreased the mesenchymal markers vimentin and N-cadherin (Hu et al., 2025).

Scopoletin is the other compound that has exhibited anticancer activity in prostate cancer models besides esculetin and osthole. In LNCaP (human prostate cancer cell line) cells, scopoletin arrested the cells in G2/M phase and caused an increased occurrence of cells at the sub-G0/G1 phase, which resulted in apoptosis. It was coupled by reduced expression of cyclin D1, the emergence of membrane blebs, which indicated apoptosis (Fig. 1). The abovementioned effects underscore the fact

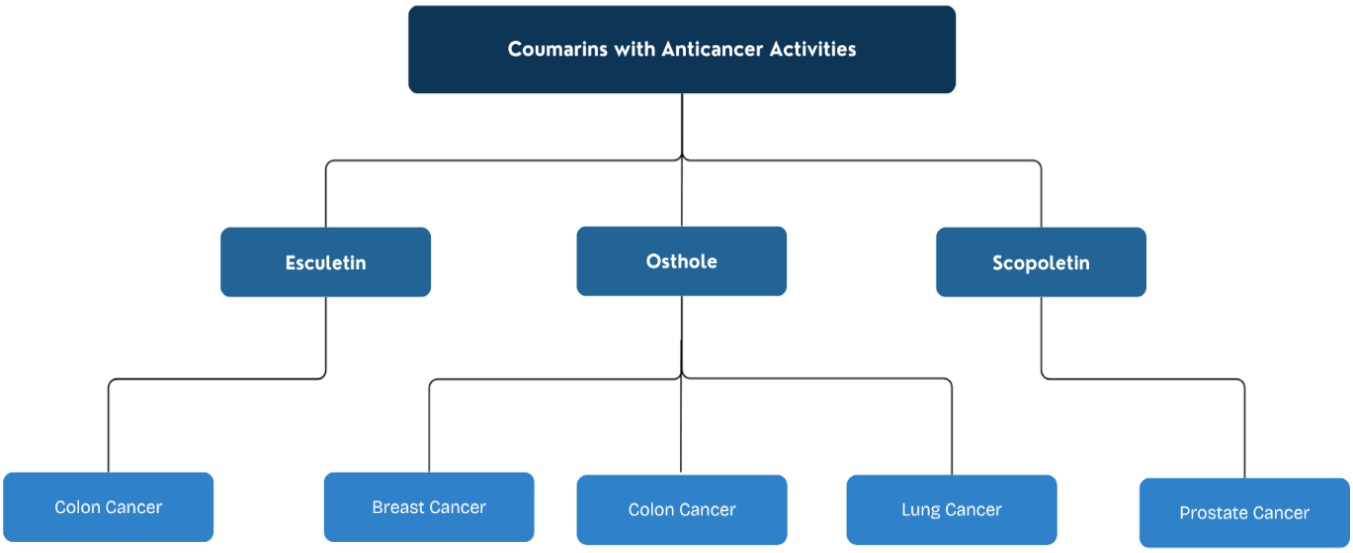

Fig 1. Anticancer activities of different coumarins

that scopoletin could interfere with the cell-cycle control pathway and stimulate programmed cell death (Ajiboye et al., 2025).

COUMARIN-BASED DRUG DEVELOPMENT

Coumarin derivatives have received popularity in the context of anticancer potential because they have the capability of interacting with a wide range of molecular targets. The latest research has been on coumarin hybrids, especially coumarin-1,2,3-triazole conjugates, which exhibit an increased rate of cytotoxicity and multi target involvement on cancerous cells. Indicatively, hybrids of coumarin with chalcone or sulfonamide moiety are found to potentially inhibit lung, breast, colon, and liver cancer through the effect of apoptosis and cell cycle arrest. The multi-pronged mechanism comprises kinase, topoisomerases, carbonic anhydrase, and topoisomerases inhibition (Chaudhary et al., 2022; Ahmed et al., 2025).

More specifically, click chemistry syntheses of coumarin artemisinin hybrids have shown to exhibit *in vitro* cytotoxicity less than 1 µM in colorectal and breast cancer cell lines, with proposed mechanism of action based on the formation of ROS and mitochondrial apoptotic pathways. Moreover, hypoxic tumor cells are selectively targeted and killed by palladium (II) complexes of coumarin derivatives because carbonic anhydrase IX is a tumor-specific enzyme expressed in hypoxic tumor cell types, which takes advantage of the tumor microenvironment (Chakraborty, 2022).

Although coumarin compounds are the most promising ones, the high-water insolubility and the fast metabolic elimination of most of them pose a challenge to its clinical application. In response, halogenation, sulfonamide substitution, and metal complexation are the methods to increase the lipophilicity of the coumarins which improves their target affinity (Verma et al., 2020). The attachment of heterocyclic moieties such as triazoles does not only enhance metabolism, but it also improves selective ligand binding to cancer related enzymes (Singh et al., 2025).

In addition, the hybridization with molecules possessing biological activity-dopamine, amino acids or peptides has been claimed to enhance the selective cytotoxicity and decrease the off-target toxicity. This is because these conjugates could take advantage of using receptor-meditated uptake or enzyme-substrate cascade and thus enhancing pharmacodynamics. To overcome bioavailability limitations, nanoformulations have been widely investigated for coumarin delivery. Liposomal encapsulation improves aqueous solubility and offers targeted delivery through enhanced permeability and retention (EPR) effects in tumors. For instance, liposomes containing coumarin and 4-

phenylbutyric acid demonstrated increased cytotoxicity against breast (MDA-MB-231) and lung (A549) cancer cells compared to free coumarin, high-lighting improved cellular uptake and controlled release (Singh et al., 2025).

Nanoparticles, including carbon nanotube and PEGylated nanographene oxide have been explored as carriers to enhance coumarin delivery by extending circulation time and enabling passive tumor targeting. Prodrug strategies, such as esterification or cleavable linker conjugates, have also been proposed to improve pharmacokinetic profiles and ensure selective activation in tumor microenvironments, though most remain at preclinical stages (Liu et al., 2023).

Clinical translation of anticancer coumarins remains limited. While warfarin and acenocoumarol are established anticoagulants, few coumarin-based anticancer agents have advanced beyond preclinical studies. One exception is Irosustat (STX64), a steroid sulfatase inhibitor containing a coumarin scaffold, which has undergone early-phase clinical trials in hormone-dependent cancers such as breast and endometrial cancer, demonstrating safety and preliminary efficacy.

The patent landscape reflects increasing innovation around coumarin hybrids, metal complexes, and delivery systems. Numerous patents have been filed covering sulfonamide coumarins, coumarin–1,2,3-triazole hybrids, and coumarin–artemisinin conjugates aimed at improved anticancer efficacy and bioavailability. However, detailed patent data are often proprietary, and few patented candidates have reached clinical evaluation, reflecting the challenges in optimizing pharmacokinetics and toxicity profiles (Venugopala et al., 2013).

SAFETY, PHARMACOKINETICS, AND THERAPEUTIC LIMITATIONS

Coumarins remain highly variable in their safety that is in strong dependence on chemical structure, dose and clinical indication. The traditional oral anticoagulants (heparins) like warfarin and acenocoumarol have a narrow therapeutic index and are related with potential bleeding such as life-threatening hemorrhage because of high probability of the incident. Their safety status requires that a close monitoring of prothrombin time [International Normalized Ratio (INR)] should be done to seek optimal therapeutic effects and to reduce adverse effects. VKORC1 and CYP2C9 are polymorphic enzymes that significantly influence warfarin metabolism and sensitivity. This complicates dose adjustment and can lead to toxicity in some populations (Şeker Karatoprak et al., 2024).

Non-anticoagulant coumarins, especially natural coumarins like coumarin itself (1,2-benzopyrone), have been reported to cause hepatotoxicity in some animal models, which has raised regulatory concerns. The European Food Safety Authority classified coumarin as potentially hepatotoxic, restricting its use in food products and cosmetics. Hepatotoxicity is believed to arise from coumarin bioactivation by cytochrome P450 enzymes, particularly CYP2A6, yielding toxic metabolites such as coumarin 3,4-epoxide. However, human hepatotoxicity cases are rare, and toxicity appears to be dose-dependent and influenced by interindividual metabolic differences (Li et al., 2021).

Coumarin pharmacokinetics display variability based on molecular structure and route of administration. Warfarin exhibits nearly complete oral absorption with peak plasma concentrations reached within 90 minutes, and a half-life ranging between 20 to 60 hours due to its enantiomeric forms being metabolized differently by CYP2C9. The S-enantiomer of warfarin is more potent and primarily metabolized by CYP2C9, whereas the R-enantiomer is metabolized by multiple CYP enzymes, contributing to interindividual variability. Most of the naturally occurring coumarins, such as simple coumarin, exhibit quick absorption but high first-pass metabolic effects in the liver, showing low bioavailability in the system. It is metabolized via hydroxylation and subsequent conjugation with glucuronic acid or sulphation, which facilitates its excretion by the kidneys (Li et al., 2021). Short half-life of most of the simple coumarins limits their systemic exposure, and thus the therapeutic functionality, unless chemically modified or formulated to allow better delivery.

There are some factors that restrain the clinical use of coumarins. To begin with, their low water

solubility hampers their bioavailability, which requires a large or frequent dose that may be more toxic. Additionally, the fast turnover of most of the coumarins limits their systemic exposure, which limits their application in systemic conditions, like cancer (Chaudhary et al., 2022).

Second, the narrow therapeutic index of anticoagulant coumarin implies that therapeutic monitoring and dose titration need to be done very frequently, which is problematic when it comes to clinical practice, particularly in resource-scarce environments. Moreover, individualized dosing is complicated due to high levels of interpatient variability based on the genetic polymorphisms of drug-metabolizing enzymes and vitamin K epoxide reductase which substantially contributes to the possibility of adverse events (Kaur & Rangra, 2024).

Third, the derivatives of coumarin have off-target effects and toxicity in the higher dosage, including hepatotoxicity, gastrointestinal disorders, and possible phototoxicity. Coumarins are not selective towards cancer cells, so they cannot be used single-handedly in oncology treatment, which constrains the choice of combination therapy or targeted delivery (Ajiboye et al., 2025).

FUTURE DIRECTIONS AND TRANSLATIONAL POTENTIAL

A paradigm shift presented by Structure-Based Drug Design (SBDD) has become an important strategy to improve coumarin derivatives. The recent advances related to high-resolution crystallography and computational model have provided the complex detail of the mode of binding of coumarin analogues with different biological targets, such as enzymes involved in cancer progression and inflammation. By integrating SBDD and high-throughput screening (HTS), a broader palette of new, more potent and selective coumarin-based molecules can be discovered in a shorter period of time. Such a combined framework shortens the schedule of developing a drug and enhances the effectiveness of molecules entering preclinical phases (Hu et al., 2025).

Coumarins and anticoagulant drugs such as warfarin in particular, are becoming more pertinent to personalized medicine models because patient variabilities influence the metabolism and the reaction to the drug (Singh et al., 2025). The development of pharmacogenomics has made it possible to perform genotype-optimized dosing to enhance the outcomes and minimize adverse effects. Furthermore, a combinatory approach of polyenic has been noted as a potential synergism of coumarins in combination drug therapy, especially in cancer, where derivatives of coumarin will have the potential to enhance and synergize commonly used chemotherapeutic agents and immune checkpoint hijackers. These combinatorial solutions have the potential of bypassing drug resistance and enhancing prognosis in the patient (Lee et al., 2020).

A positive direction in therapeutic development of coumarin is the emergence of the scope of immunomodulation and neuroprotection. Latest findings of coumarin usage *in vivo* and *in vitro* show the mediation of dominant immune mechanisms, NF-κB/MAPK signaling pathways to lessen the levels of inflammation and autoimmune disease. In neurodegenerative diseases, coumarin derivatives can be utilized due to their ability to reduce oxidative stress, prevent the formation of amyloid aggregates, and safeguard the neuronal cells against apoptosis (Zhang et al., 2021). The effects represent the main interest in the development of disease-modifying treatments in Alzheimer's and Parkinson's diseases (Gupta et al., 2024).

One of the concerns in the development of a coumarin drug is environmental sustainability. Green chemistry has made progress in the recent past where synthesis of coumarin derivatives is done by using green solvents, microwave-assisted reaction and enzyme catalyzed reactions, which result in less waste and lower energy use (Mishra et al., 2024). Moreover, the viewpoint on sustainable manufacturing of coumarins via using plant biomass and microbial fermentation states, some potentially scalable alternatives to conventional chemical synthesis in the context of international sustainability achievements.

CONCLUSION

Coumarins are naturally occurring compounds, found widely in many plant species and are recognized for their diverse therapeutic

applications. One of their primary medicinal uses is as anticoagulants, notably through the inhibition of the vitamin K cycle, which prevents proper blood clot formation. A key example is warfarin, a synthetic derivative of coumarin, commonly prescribed for conditions such as atrial fibrillation, deep vein thrombosis, and pulmonary embolism. Beyond anticoagulant activity, coumarins exhibit strong anti-inflammatory effects by suppressing pro-inflammatory cytokines and modulating signaling pathways such as NF-κB and MAPK. These mechanisms contribute to their effectiveness in treating inflammatory conditions, including arthritis, inflammatory bowel disease, and neuroinflammation. Additionally, coumarins have antioxidant properties that protect tissues from oxidative damage. Certain coumarins, such as esculetin, osthole, and scopoletin, also demonstrate anticancer potential via inducing apoptosis, inhibiting tumor cell proliferation, and blocking metastasis through multiple molecular pathways. However, their clinical applications are limited by poor water solubility, low bioavailability, rapid metabolism, and potential toxicity. Advances in structural modification, nanotechnology, and targeted drug delivery aim to overcome these challenges. Overall, coumarins represent a valuable platform for developing treatments for cardiovascular, inflammatory, neurodegenerative, and cancer-related diseases.

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