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REVIEW ARTICLE

The role of coumarin scaffold in the chemical engineering of bioactive molecules: A narrative review

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ABSTRACT

Coumarin and its derivatives are intriguing to researchers in both chemical and pharmaceutical fields because they have a unique benzopyrone scaffold and a lot of bioactive properties. This review delves into the significance of the coumarin scaffold in the design and engineering of bioactive molecules, offering insights into its chemical, biological, and pharmacological roles. Coumarins are praised for their many medical uses, such as their ability to fight cancer, reduce inflammation, kill microbes, stop blood clots, and act as an antioxidant. This is possible because they have a special chemical structure with α,β-unsaturated α-lactones and electron-rich aromatic rings. The flexibility of this scaffold is amazing; it can be changed chemically in many ways, which lets different derivatives with different biological activities be made. The historical significance of coumarins is underpinned by their natural occurrence in various plants and their pivotal role in therapeutic applications since the 19th century. Their synthetic versatility has led to advancements in drug development, particularly in creating anticoagulants, antivirals, and neuroprotective agents. In addition, coumarins have been shown to work well in cosmetic formulations, cardiovascular health, and diabetes treatments, showing that they can be used for many things. The efficient synthesis, purification, and functionalization of coumarins still face problems. This shows the need for new methods to get around problems like harsh reaction conditions and high costs. New computer techniques, such as 3D-QSAR and pharmacophore modeling, have made it easier and faster to study compounds that are built on a coumarin scaffold. These techniques have also made these compounds more therapeutically useful. This narrative review underscores the coumarin scaffold's prominence in medicinal chemistry and its future prospects as a platform for developing novel bioactive molecules. Coumarins are important for advancing science and health because they can change chemical forms easily and have a wide range of biological effects.

Keywords: coumarin scaffold; bioactive molecules; pharmacological applications; synthetic methodologies, chemical engineering

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1. Introduction

Coumarin is a natural compound and belongs to the class of benzopyrones that contains isocoumarins, furanocoumarins, pyranocoumarins, and others, as illustrated in **Figure 1**[1]. The third ones are the most important because they are found in many plants and have a lot of biological activities, biodegradability, and toxicological acceptability. The chromophore has an α,β-unsaturated α-lactone inside it that works through binding to biological targets and lactonizing[2]. The benzene ring and the C-3 and C-4 tails change how the core reacts, dissolves, and stays stable as well. Therefore, the design and optimization of new coumarin analogues have aroused the interest of pharmaceutical, agricultural, cosmetic, and stain

industries[3]. These coumarin particles consist of numerous moieties, necessitating the development of efficient synthesis methodologies. Because of these factors, it is important to look into the progress made in a quick and fresh way to make bioactive molecules that are very useful in medicinal chemistry, with a focus on the history of coumarin structure[4].

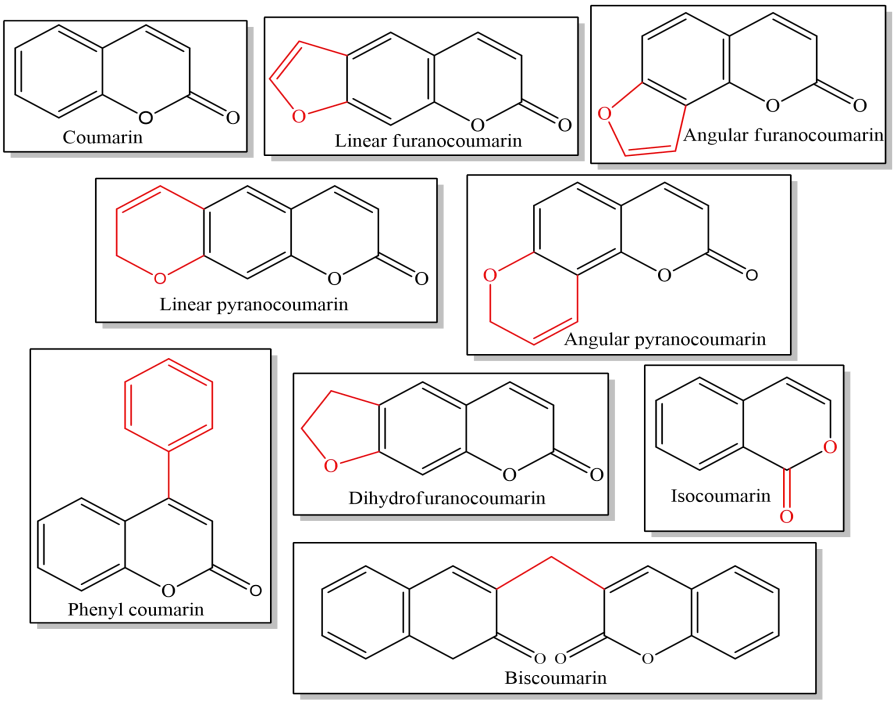

Figure 1. The chemical structures of coumarin and its related main classes.

This review covers the bioactive properties of coumarins with a historical perspective on their structures. The trends and classification of this family are analyzed, and the different methodologies for preparing these molecules are classified. Due to the large number of applications and methods, several coumarin applications and methodologies have not been mentioned. Therefore, the focus is on the most relevant and current pharmaceutical examples. We have provided summaries and conclusions on the bioactivity and chemical engineering of the coumarin framework.

2. Historical background of coumarin

Coumarins are important bioactive compounds that have attracted attention owing to their varied and diverse pharmaceutical properties. These groups of compounds, comprising both natural and synthetic forms, exhibit promising functionalities in pharmaceutical development[5]. Certain molecules that contain coumarin are bioactive because they have different functional groups that can interact with various biological molecules, like DNA, RNA, proteins, glutathione, and metals[6]. Because of this, coumarin and its derivatives can be used to take pictures of living things, kill parasites and bacteria, fight cancer and viruses, protect cells from damage, and reduce inflammation[7].

Coumarin is the prototype item of its family of chemical compounds, which is based on pyrone and chromen-2-one. The name coumarin originates from 'Coumarouna purple wood' in French. Some species of the Fabaceae family synthesize this phytoalexin in response to external stimuli[8]. The first characterization of the coumarin structure took place in 1820, followed by the first synthesis in 1868. In 1933, a group of pharmacists discovered coumarin in walnut for the first time[9]. Researchers have detected coumarin in over 50 different plant species, as well as various vegetable and dairy products. Various fruits, vegetables, and edible plants, including cinnamon, cloves, chamomiles, and Artemisia species, contain high amounts of coumarin[10]. Since the 1940s, coumarin's anticoagulant properties have led to its use in therapy. The safer

drug warfarin has replaced coumarin due to its potential to induce hepatotoxicity and allergic reactions[11]. Researchers have tried to find ways to lessen these undesirable side effects and use coumarin in drug therapy because it can stop blood clots, mostly because it reduces inflammation and protects cells from damage caused by cancer[12]. In addition to the above-mentioned properties, and perhaps more importantly, coumarin also has magnetic and photoelectric properties and can undergo metal coordination and cation transfer processes[13]. Scientists have developed coumarin-metal coordination and are now looking at lanthanide complexes that glow when mixed with coumarin scaffold derivatives. This is an important study branch because it has an effect on these luminescent probes used in biology and phototherapy[14].

3. Chemical properties of coumarin

Benzene and α-pyrone rings join to form coumarins, an important group of phenolic compounds. Scientists can use the way a two-ring substitution binds to make highly functionalized derivatives that react and behave in biology in very different ways[15]. For various decades, coumarins have been receiving scientific and practical admiration for different applications. They have several intriguing properties and a diversity of biological activities[16]. These chemicals are a "golden scaffold" for pharmacologically adjusted molecules and unique functional materials because they have so many useful effects in medicine, biology, sensors, lighting, electroluminescence, antimicrobials, and more[17]. It is easily understandable why coumarins bear the reputation of the "skeleton of pharmacologically active constituents." Being able to mix chemicals by accident is not possible because coumarins naturally react with each other in epitactic displacement and different functional group transformations[18]. Instead, we must establish rules to identify enantiomerically pure compounds in sufficient quantities. The refracted organic reactivity of coumarin derivatives comprises a diversity of reactions.

4. Biological activities of coumarin derivatives

Coumarin and its derivatives possess various intriguing biological properties, such as anti-inflammatory, anticancer, antioxidant, antimicrobial, and especially anticoagulant activity[19]. Coumarin is a key part of drug design because it has the lactone group, which is also known as the "characteristic scaffold," and electron-rich aromatic rings. Because it's not possible to make different coumarin derivatives naturally, scientists and engineers are always coming up with new ways to get it ready, such as total synthesis, extraction from natural sources, and making engineered catalysts for changing coumarin[20]. At the moment, a lot of research is being done to try making coumarin derivatives more effective against different diseases. Among important biological activities, the anticoagulant activity of these derivatives has greatly attracted the research community[21]. Numerous studies have showcased effective anticoagulant molecules, and researchers have studied and designed their scaffolds based on the coumarin skeleton. These possible blood thinner coumarin derivatives have a lot of activity and selectivity, which makes them intriguing as pharmaceutical lead compounds for future blood thinner treatments[22].

5. Synthetic strategies for coumarin derivatives

Synthetic organic chemists are interested in adding an oxygen atom to the phenyl part of the coumarin molecule because it has a lot of biological effects. For making this kind of coumarin, the easiest way is to use phenols, which are simple to get directly from the corresponding substituted hydroxylnaphthalenes[23]. Mixing flavones with cerium salts in polyphosphoric acid made it easy to obtain many 3,4-dihydrocoumarin derivatives. As long as you use ethyl glyoxylate on alumina at room temperature for an hour with NaH, you can make 3-arylcoumarins up to 86% of the time [24]. Using a Pechmann route, aromatic compounds that contain bromine can be used as building blocks to make 3-arylcoumarins. Nature typically produces pyranocoumarins chemically, using neutrophil oxidase as a catalyst. However, the high cost of using this enzyme makes the process very lengthy[25].

Oxidative cyclization easily incorporates various types of enolizable 1,3-dicarbonyl or -ketoesters into coumarin cores. The Pechmann route transforms aromatic compounds bearing an enolizable alkene moiety into 3-arylcoumarins. Three-cyclohexyl-1-crolin was mixed with the right aromatic aldehyde in diethyl ether and solid NaOH to make a lot of diryl ketones with an enolizable aldehyde[26]. Small changes in the structure of a natural compound can cause significant changes in its biological activity. 3-arylcoumarins are known to have different pharmacological effects. Adding halogen, nitro, methyl, or methoxy chains to their aromatic ring did not have a big effect on their estrogenic activity, though[27]. In **Table 1**, the main reactions used to make coumarin-based compounds are listed, along with the main pros and cons of using these reactions.

Table 1. Overview of synthetic reactions for coumarin-based derivatives; advantages and disadvantages.

Reaction name	Advantages	Disadvantages	Ref.
Pechmann Condensation	- Simple and cost-effective. - Utilizes easily available phenols and β-keto esters. - Can be catalyzed by various acids, including environmentally friendly catalysts.	- Requires acidic conditions, which may not be suitable for acid-sensitive chemicals. - May lead to side reactions with certain reactants.	[28]
Knoevenagel Condensation	- Mild reaction conditions. - Suitable for a wide range of reactants. - Produces 3-substituted coumarins efficiently.	- May require longer reaction times for less reactive reactants. - Potential formation of by-products.	[29]
Perkin Reaction	- Useful for synthesizing 3- and 4-functionalized coumarins. - Employs readily available starting ingredients.	- Requires high temperatures. - Limited to substrates that can withstand harsh conditions.	[30]
Wittig Reaction	- Allows for introducing of various substituents at the 3-position. - Provides access to a diverse range of coumarin-based derivatives.	- Requires the preparation of phosphonium salts. - May involve multiple steps, increasing complexity.	[31]
Kostanecki Reaction	- Effective for synthesizing 4-arylcoumarins. - Utilizes simple starting ingredients.	- Requires strong bases, which may not be compatible with all functional groups. - Limited substrate scope.	[20]
Baylis-Hillman Reaction	- Provides access to 3-functionalized coumarins under mild conditions. - Can be performed with various acrylate derivatives.	- Often results in low yields. - Slow reaction rates. - Limited to specific ingredients.	[32]
Michael Addition	- Useful for synthesizing 3-aroylcoumarins. - Can be performed under mild conditions.	- May require the use of strong bases. - Potential for side reactions.	[33]
Heck-Lactonization	- Allows for the synthesis of 3,4-difunctionalized coumarins. - Utilizes palladium catalysis.	- Requires expensive palladium catalysts. - Sensitive to steric hindrance around the double bond in enoates.	[34]

6. Coumarin as a pharmacophore

The point of this study was to draw attention to how important the coumarin scaffold is in molecular systems made for medical uses. So, we looked at the main bioactive molecules and molecular systems that showed the 2H-chromen-2-one scaffold and wrote a review based on chemical facts. We were able to show that the coumarin scaffold can be utilized in various ways for molecular design in order to create bioactive molecules or molecular systems that exhibit a wide range of biological activities or strengths[35]. The same activity might not be caused by the same mechanism; substituents or other scaffolds can change the properties of a molecule or molecular system; molecular systems made from this scaffold should be biosafe to avoid side effects in biomedical uses[36]. In addition to having intriguing photochemical properties that make the Fenton photoreaction work, coumarin can be used in a lot of different ways to make different structures. The considerable number of available synthetic procedures that lead to the substrate's chemical transformations evidences this versatility. Many bioactive molecules contain coumarin, making it a unique scaffold; these molecules have antibiotic, antitumor, antiviral, antioxidant, and anti-inflammatory properties,

among other things. Neurodegenerative diseases, cardiovascular diseases, and their complications can also benefit from their use[37–39].

7. Coumarin-based drug design and development

Coumarin is a benzopyrone whose name is derived from the French "couverin", a piece of cloth for covering when wet, and whose perfume is reminiscent of that of coumarin. Many plants biosynthesize this product, with its concentration varying within different organs based on genotype, developmental stage, and environment[40]. Besides being able to stabilize the membrane and work as a strong antioxidant, coumarin has many other biological effects, such as blocking a number of human enzymes and receptors[41]. However, many countries have banned its consumption due to its known nephrotoxicity. At the same time, a lot of molecules with a coumarin scaffold were made because scientists are becoming more interested in coumarin because it is safe, has strong biological activity, and is simple to make[42].

It is now known that coumarin or one of its derivatives can be used as a building block to make molecules that can interact with a wide range of known human protein receptors. A hybridization method, ligand-based design of bioactive compounds, pharmacophore modeling, or high-throughput virtual screening were used to make the design happen[43]. Major human diseases, like Alzheimer's, inflammation, AIDS, and cancer, as well as heart, parasitic, and other diseases, are affected by these molecules because they mess up important metabolic and signaling pathways[44]. About 47% of these coumarin-based agents or their analogs have reached clinical development, while 33% are already considered commercially available drugs. However, it is known that increasing the consumption of the already existing coumarin derivatives can be poisonous[45]. Also, it doesn't make sense to try to get specific biological effects from a single chemical scaffold when the pharmacodynamic spectrum is enormous and unexplored. These coumarin agents are excellent at protecting cells from damage and keeping membranes stable because they are amphoteric, the monomers are small, and the coumarin itself is structured in a certain way[46]. Therefore, from its one-dimensional use in smelling to its three-dimensional use as a drug, this journey has been made over many generations by bringing to light a wide range of coumarin derivatives.

8. Coumarins in natural sources

Natural sources of coumarins include a wide variety of plant families, such as Rutaceae, Apiaceae, Fabaceae, and Asteraceae. Various species and environmental conditions contain these compounds in varying concentrations in leaves, seeds, roots, and bark. For instance, the sweet-smelling tonka bean is rich in coumarin, giving it its characteristic aroma[47]. Other notable sources include cinnamon, sweet clover, and certain citrus fruits. These plants often use coumarins as allelopathic agents to stop competing plants from growing. This protects their ecological niche [48].

Plants use the phenylpropanoid pathway (**Figure 2**), a metabolic process that starts with phenylalanine, to make coumarins. This pathway leads to the formation of umbelliferone, a key precursor in the synthesis of various coumarin derivatives. Changes made by enzymes, like hydroxylation, methylation, and glycosylation, make the variety of coumarin compounds found in nature even wider[49]. These derivatives have many biological properties, such as the ability to stop blood clots, kill microbes, and protect cells from damage. This has made people interested in how they could be used in medicine[50].

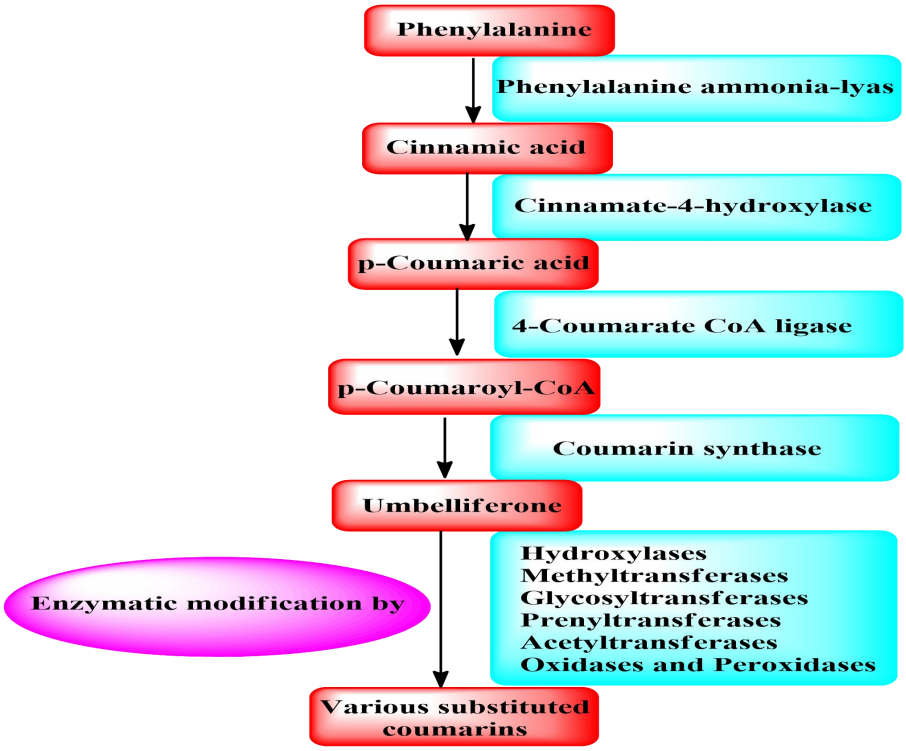

Figure 2. Schematic representation of plant-based phenylpropanoid pathway for synthesizing natural substituted coumarins.

The study of coumarins from natural sources continues to be a dynamic field, driven by their ecological significance and therapeutic potential. Improvements in analytical methods have made it possible to identify and describe new coumarin derivatives from species that had not been studied before[51]. Furthermore, these discoveries have paved the way for biotechnological approaches to enhance coumarin production in plants or microbial systems. This ongoing research shows how important coumarins are as a link between natural product chemistry and medicinal science. It also shows how important they are for both human and animal health[52].

9. Analytical methods for coumarin detection and quantification

The high frequency of pharmaceutical and commercial uses fulfills the necessity of accurate quantification methods. The development and validation of analytical methods suitable for this task is a pressing demand[53]. These examples illustrate their known applications in high-performance liquid chromatography, gas chromatography, mass spectrometry, nuclear magnetic resonance, fluorescence detection, refractive index, and electrochemical techniques[54]. Because many coumarin derivatives are stable at low temperatures, unstable at high temperatures, and sensitive to light, more effective instrumental techniques are needed[55]. These issues also need to be addressed for environmental purposes, and in this effort, solid-phase micro-extraction and high-performance liquid chromatography/mass spectrometry techniques seem to stand out[56].

The extensive research on the pharmaceutical and commercial applications of coumarins, coupled with an understanding of their chemical and biological properties, clearly underscores the necessity for the development and validation of analytical methods that can accurately determine these molecules across various matrices[57]. A number of methods have already been created, but there are still a lot of questions about their accuracy, precision, repeatability, sensitivity, and the ability to resolve and separate coumarin and its derivatives[58]. Creating these protocols is necessary not only for analyzing drugs, but also for finding coumarin and its derivatives in environmental, food, hygiene, and personal care products. These are often tested because they pose serious health risks[59]. In addition, the existence of standardized methods and the

development of new efficient instrumental techniques, which are amenable and easily available for their intended use, provide significant advantages due to the upsurge in coumarin structural types in recent years and their relatively low volatility, thermal instability, and light sensitivity[60].

For the effective detection and quantification of coumarins, one can employ quantitative analysis using spectroscopic techniques. For instance, the coumarin scaffold's excellent light absorption makes ultraviolet-visible spectroscopy a popular tool[61,62]. A simple and inexpensive way to measure amounts is with this type of spectroscopy, especially for chemicals like coumarins that have unique chromophoric properties[63]. Furthermore, one can employ high-performance liquid chromatography in conjunction with ultraviolet detection to enhance sensitivity and selectivity[64].

10. Computational approaches in coumarin research

All modern computational methods that predict chemical and biological activity use the fact that all experiments, even at their basic levels, are essentially computations. In recent years, modern methods of computational chemistry and computer-based 3D QSAR studies have played a crucial role in the outcomes of molecular modeling. The "dry lab" computers facilitate various inherent activities of the "wet" one[65]. It's easy to see in this computer view how to model ligands and proteins, small and large molecules, computer-aided drug design, 2D and 3D QSAR studies, structure-based drug design, pharmacophore modeling, and ADMET prediction work. Experts have discussed quantum mechanics, molecular mechanics, and molecular dynamics with proficiency. Modern supercomputers can effectively study withanolides, flavonoids, and calmodulin-like proteins. Experts have referred to this as a significant advancement in the field of coumarin scaffold science[66].

Examples include the study of theory, implementation, abstract computation roadmaps, successful functionalities, limitations, validations, and applications. Critical thinking philosophy helps in the selection of the most appropriate method and its best use. Scientists have also highlighted the new role of interpretable machine learning[67]. It's important to note that model selection, compared to its point in time, and decision-making based on context from dynamically constructed model libraries are all very essential. They also talked about how important it is to measure uncertainty, the range of applications, robust-tolerant QSAR models, and the difference between having many molecules and many conformations[68]. Finally, the experts have talked about how to find new drugs using computers, how proteins can act as pharmacophores, and some new publications in computational QSAR.

11. Coumarins in medicinal chemistry

Beyond their anticoagulant properties, coumarin-based derivatives exhibit promising anticancer activity. Studies have shown that they can induce apoptosis, inhibit angiogenesis, and modulate key signaling pathways involved in tumor progression. For example, some coumarins have been shown to be able to target enzymes like topoisomerases, which are needed for cancer cells to copy their DNA[69]. Also, their antioxidant properties help mitigate oxidative stress, a factor implicated in cancer and other chronic diseases like diabetes mellitus[70]. Moreover, coumarins are excellent candidates for developing anticancer drugs because they can kill cells directly and change the levels of oxidative stress[71].

Because derivatives based on coumarin can change their structure, they are also great for chemical changes that let medicinal chemists change their properties for specific medical uses[72]. Researchers can make them more effective, selective, and bioavailable by adding different functional groups or combining them with other bioactive molecules[73]. Because it is so flexible, many coumarin-based derivatives with better pharmacokinetic profiles have been made. As research progresses, coumarins continue to serve as a rich source of inspiration for novel drug development, bridging the gap between natural product chemistry and modern pharmacotherapy[74].

11.1. Coumarin in cancer research

Different heterocyclic families have recrystallized coumarin, a special heterocyclic moiety, as their basic structure. It has the power to significantly change the biological behavior of these compounds for a wider range of diseases[75]. Besides biochemical signaling and infectious agents, other areas of coumarin engineering that show a lot of promise are the extreme pharmacology of natural immune modulators, cancer theranostics, alpha-glucosidase inhibitors for diabetes, and peptidases that are involved with changes in homeostasis[76]. For example, coumarin compounds have been known for a long time to play a part in some steps of cancer cell proliferation and metastasis[77,78]. This is because they can change different signaling pathways and stop some protein enzymes from working in the nucleus of cancer cells[79]. It stands out that the search for novel and more effective anticancer compounds is of paramount importance since numerous current treatments are still very aggressive or ineffective[80]. The chemical toxicity of many classical treatments due to the non-specificity of their use is a challenge for health sciences, which can only be overcome by increasing the specificity of chemotherapy towards tumoral tissues[81,82]. In addition to the promising results obtained for some modified compounds with this important pharmacophore, the latest advances in chemical functionalization techniques favor it[83]. **Table 2** provides examples of some investigated coumarins as anticancer prospects, along with their targets of action.

Table 2. Mapping coumarin derivatives to their anticancer targets.

Coumarin derivative	Target	Ref.
7-Hydroxycoumarin	Cyclin D1 inhibition	[84]
Umbelliprenin	NF-κB and Akt signaling pathways	[85]
4-Hydroxycoumarin	Topoisomerase II inhibition	[86]
Auraptene	PI3K/Akt/mTOR signaling pathways	[87]
Scopoletin	Cell cycle arrest and apoptosis induction	[88]
Esculetin	Cell cycle arrest and apoptosis induction	[89]
Osthole	STAT3 and mTOR signaling pathways	[90]
Dicoumarol	NAD(P)H:quinone oxidoreductase (NQO1) inhibition	[91]
Psoralen	DNA intercalation	[92]
Xanthotoxin	Inhibition of the reactive oxygen species (ROS) generation	[93]
Coumarin-3-carboxylic acid	Inhibition of angiogenesis	[94]
6,7-Dimethoxycoumarin	MAPK pathway inhibition	[95]
Fraxetin	Apoptosis induction via caspase activation	[96]
Daphnetin	Inhibition of tyrosine kinases	[97]
Coumarin-3-thiosemicarbazone	DNA damage induction	[98]
Bergapten	Cell cycle arrest	[99]
Isopimpinellin	Cyclooxygenase inhibition	[100]
Imperatorin	Apoptosis via mitochondrial pathway	[101]
Pyranocoumarin	Topoisomerase I inhibition	[102]
Suberosin	Inhibition of tumor metastasis	[103]
8-Methoxypsoralen	CYP450 enzyme inhibition	[104]
Coumarin-3,6-diols	Anti-angiogenic activity	[105]
Hydroxycoumarin-aldehydes	DNA polymerase inhibition	[106]
Methoxycoumarin derivatives	Pro-apoptotic activity	[105]
Coumarin-acetate hybrids	PI3K pathway inhibition	[107]

Coumarin derivative	Target	Ref.
Coumarin-amino acid conjugates	Caspase-mediated apoptosis	[108]
Coumarin-oxime derivatives	DNA fragmentation	[109]
Coumarin-benzyl derivatives	ROS-mediated apoptosis	[110]
Nitrocoumarins	NF-κB pathway inhibition	[111]
Coumarin-imidazole hybrids	Dual kinase inhibition	[112]

Table 2. (*Continued*)

11.2. Coumarin in antimicrobial activity

There is a general idea that coumarins kill bacteria, viruses, and fungi by stopping the biosynthesis of nucleic acids and proteins. They do this by attaching covalently to DNA, nucleotides, thiols, and amino groups[113–115]. Because there are a lot of drug-resistant microorganisms and a lot of interest in antibiotics, it makes sense to look for new structures that can kill microbes and find new uses for the coumarin derivatives that are already known[116–119]. **Table 3** lists the antimicrobial effects of several coumarin derivatives, including the type of action they have and the pathogens they kill.

Table 3. Mapping coumarin derivatives to their antimicrobial targeted effects.

Coumarin derivative	Pathogen	Pathogen type	Ref.
7-Hydroxycoumarin	Escherichia coli	Bacteria	[120]
Umbelliprenin	Staphylococcus aureus	Bacteria	[121]
4-Hydroxycoumarin	Candida albicans	Fungus	[122]
Auraptene	Aspergillus niger	Fungus	[123]
Scopoletin	Pseudomonas aeruginosa	Bacteria	[124]
Esculetin	Helicobacter pylori	Bacteria	[125]
Osthole	Mycobacterium tuberculosis	Bacteria	[126]
Dicoumarol	Cryptococcus neoformans	Fungus	[127]
Psoralen	Salmonella typhimurium	Bacteria	[128]
Xanthotoxin	Trichophyton rubrum	Fungus	[129]
Fraxetin	Klebsiella pneumoniae	Bacteria	[130]
Daphnetin	Streptococcus pyogenes	Bacteria	[131]
Bergapten	Candida tropicalis	Fungus	[132]
Isopimpinellin	Aspergillus fumigatus	Fungus	[133]
Imperatorin	Vibrio cholerae	Bacteria	[134]
Suberosin	Fusarium solani	Fungus	[135]
8-Methoxypsoralen	Rhizopus oryzae	Fungus	[136]
Coumarin-3-thiosemicarbazone	Clostridium difficile	Bacteria	[137]
6,7-Dimethoxycoumarin	Plasmodium falciparum	Parasite	[138]
Coumarin-acetate hybrids	Leishmania donovani	Parasite	[139]
Coumarin-aldehyde hybrids	Trypanosoma cruzi	Parasite	[140]
Hydroxycoumarin derivatives	Schistosoma mansoni	Parasite	[141]
Coumarin-quinoline hybrids	Toxoplasma gondii	Parasite	[142]
Coumarin-chalcone conjugates	HIV-1	Virus	[143]
Coumarin-imidazole hybrids	Herpes simplex virus-1	Virus	[144]

Coumarin derivative	Pathogen	Pathogen type	Ref.
Coumarin-pyrimidine derivatives	Hepatitis C virus	Virus	[145]
Coumarin-flavonoid hybrids	Zika virus	Virus	[146]
Coumarin-salicylate hybrids	Dengue virus	Virus	[147]
Coumarin-azole derivatives	Influenza A virus	Virus	[148]

Table 3. (*Continued*)

11.3. Coumarin in antioxidant properties

Coumarins are considered among the most researched classes of molecules in terms of biological activities due to their noticeably diverse pharmacological properties[149]. Traditionally, coumarins are well-known for their extensive and wide-ranging biological activities, such as hepatoprotective, anti-inflammatory, anticoagulant, and anticancer effects[150]. Coumarins can protect the liver and regulate liver function through their antioxidant action and ROS-scavenging properties[151]. They work as antioxidants in a number of ways, such as by chelating transition metal ions, removing ROS, increasing the activity of antioxidant enzymes in cells, and stopping the activity of pro-oxidant enzymes in cells[152]. Numerous studies have clearly demonstrated their anticancer effect through antioxidant and metal ion chelation.

The main way that coumarins work as antioxidants is by neutralizing reactive oxygen or nitrogen species. However, because they are thiols or metal-chelating, they may also work in other ways[153]. The thiobarbituric acid reactive substances assay is the most common way to find out if coumarins can act as antioxidants. Some may increase the total antioxidant capacity in a cellular system, increase the expression and activity of endogenous antioxidant enzymes, or even modulate the redox status of the cell[154]. Researchers have intensively studied the relationship between new derivatives of coumarin and antioxidant properties. There is a lot of proof that natural phenolic compounds, like coumarin, can protect cells from cancer by getting rid of ROS, binding to transition metal ions, and changing the activity of antioxidant enzymes[155]. In vivo models show that a lot of coumarin-based compounds are strong antioxidants that can make more antioxidant enzymes work[156]. This means that they can change the redox status of cells in animal models. Despite several models being available to predict the antioxidant capacity of this natural compound, there is limited knowledge regarding their activity in the brain[157].

Coumarin and its derivatives belong to the group of phenolic antioxidants. The main reason these compounds are antioxidants is that they have a phenolic structure, which lets them give up hydrogen atoms or electrons to neutralize ROS and free radicals[158]. Also, coumarins are antioxidants because their aromatic rings are full of electrons. Adding substituents, such as hydroxyl or methoxy groups, to the coumarin scaffold can make it even better at getting rid of free radicals[159]. Flavonoids, stilbenes, and lignans are also with coumarins in this group, and they are all known for reducing ROS. Furthermore, coumarins help the body's antioxidant defenses by binding to transition metal ions that assist with make harmful radicals[160]. This prevents oxidative stress from damaging cells and tissues. As both free radical scavengers and metal chelators, coumarins are very useful members of the phenolic antioxidant family [161].

11.4. Coumarin in anti-inflammatory effects

The coumarin framework has sometimes been associated with anti-inflammatory effects. In studies administering the bioactive compound in various cellular or acellular assays, the coumarin moiety demonstrates positive results in inflammation models[162]. With their lipophilic character, an efficient amount of oxygen atoms in the bioactive coumarins may also be postulated in order to interact with inflammation-relevant molecular targets. This section presents the anti-inflammatory potential of structure-modified coumarins and highlights the main targets[163].

The information talks about how coumarins can help lower inflammation and how these effects can be changed by adding or removing hydrogen bond donor and acceptor pairs or by altering the way some chemicals function in the aromatic rings. The discussion also revealed intriguing results, and the compound was considered a prototype for potential anti-inflammatory coumarins[164]. All the reported examples concern oxidative stress-related inflammation in cell-based assays. We present the relationship between the coumarins's anti-inflammatory activity and their molecular targets, as listed in **Table 4**. Finally, we present a list of bioactive compounds with intriguing properties, derived either from the coumarin framework or from structural modifications[165]. There are some chemical functions and physical properties that are more important in this method because they are pharmacophoric and biologically relevant. It also helps with the design of coumarin and warfarin derivatives that might have anti-inflammatory effects[166].

Table 4. Mapping coumarin derivatives to their anti-inflammatory targets.

Coumarin derivative	Anti-inflammatory target	Ref.
7-Hydroxycoumarin	COX-2 inhibition	[167]
Esculetin	NF-κB pathway inhibition	[168]
Scopoletin	IL-6 suppression	[169]
Umbelliferone	TNF-α suppression	[170]
Osthole	iNOS downregulation	[171]
Dicoumarol	ROS scavenging	[172]
Bergapten	LOX inhibition	[173]
Imperatorin	Cytokine modulation	[174]
Auraptene	MAPK pathway inhibition	[175]
Psoralen	NF-κB pathway inhibition	[176]
Xanthotoxin	IL-1β suppression	[177]
Fraxetin	COX-1/2 dual inhibition	[178]
Daphnetin	PGE2 production inhibition	[179]
8-Methoxypsoralen	NF-κB pathway inhibition	[180]
Coumarin-3-carboxylic acid	TNF-α and IL-8 suppression	[181]
6,7-Dimethoxycoumarin	iNOS and COX-2 inhibition	[182]
Suberosin	IL-1β and TNF-α suppression	[183]
Coumarin-aldehyde hybrids	ROS scavenging	[184]
Hydroxycoumarin derivatives	COX-2 and iNOS inhibition	[185]
Coumarin-salicylate hybrids	NF-κB and IL-6 suppression	[136]

11.5. Coumarin in neuroprotective activities

Present-day research focuses on neurodegenerative-related disorders, such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, and other sporadic diseases, which undoubtedly evidence the importance of this field[186]. Neural regenerative activities refer to a great and challenging process due to the crucial associated pathways, like the ubiquitin-proteasome system, as well as the role of other signaling mechanisms, since these have a damage-repair focus[187]. Most neurological disorders have no current therapeutic solution. The development of new drugs for the treatment of the highly complex human central nervous system pathologies has proved to be a great challenge[188]. The most well-known effect of coumarins is to stop the activity of acetylcholinesterase and monoamine oxidases A and B enzymes. This shows that they protect the brain and spinal cord. Besides the repression of inflammation, such as the inhibition of nitric oxide and ROS, activation of the nuclear receptor system, or modulation of mitochondrial function,

contributes to their neuroprotective role[189]. Neuroprotection products with more than one use are important because neurodegenerative and sporadic diseases usually involve more than one system, and it is often necessary to use a pharmacological combinatorial approach to slow or stop their progression[190].

11.6. Coumarin in cardiovascular health

Cardiovascular diseases are a class of diseases that involve the heart and blood vessels. These diseases are a leading cause of human death, killing 17.9 million people every year, accounting for an estimated 31% of all deaths worldwide. In recent decades, the use of natural compounds has gained interest due to their generally reduced toxicity and low cost[191]. Over the years, many coumarin derivatives have been shown to have a number of positive effects. These effects are directly linked to protecting the heart and blood vessels, which lowers the risk of cardiovascular diseases[192]. The cell-protective and antioxidant effect of coumarin derivatives often mediates this activity, preventing damage from various pathological conditions in cardiovascular diseases[193]. Consequently, the development of novel therapeutic agents against cardiovascular diseases often proposes coumarin-based derivatives as a template[194].

11.7. Coumarin in antidiabetic potential

Diabetes has emerged as a major health threat worldwide that affects approximately 285 million people, whereas this number is assumed to be 438 million within two to three decades[195]. The large increase in children with diabetes and the problems linked to antidiabetic drugs, such as problems with the adrenal glands, pancreas, and heart, led to the creation of antidiabetic drugs[196]. Insulin accelerates glucose uptake, and peroxisome proliferator-activated receptor agonists upregulate this process. PPARγ and α work by making insulin more effective and lowering the flow of free fatty acids, respectively[197]. Coumarin has the potential to treat type 2 diabetes mellitus because it activates both PPARγ and PPARα and lowers blood sugar levels[198]. Researchers have synthesized numerous derivatives using Pechmann synthetic reaction, following general principles to exhibit maximum biological activity [199]. The related studies show that it is possible to create multidimensional scaffolds for type 2 diabetes mellitus from both a chemical and a pharmacological point of view[200].

12. Coumarin in cosmeceutical formulations

More and more people are interested in the pharmacological activity of natural and synthetic coumarin derivatives these days, especially how they can be used in different bioactive formulations. Sunlight is known to damage living skin by causing redness, hyperpigmentation, edema, skin aging, and skin cancers in humans[201]. To protect skin from these harmful effects, UV radiation protection formulas are a beneficial bioactive idea, as shown by the growing interest in researching and developing cosmetics and skin care products that contain photoactive compounds[202]. Currently, the type of hazardous radiation to human skin is categorized into UVA (320–400 nm) and UVB (280–320 nm), in a ratio of almost 10:1. However, the influence of the latter is equally more harmful, as UVB is biologically 100 times more active than UVA[203]. For that reason, the longer wavelengths of UVA radiation reach deeper into the skin because the skin tissue absorbs these two types of harmful solar radiation differently[204].

The ability of coumarins to absorb ultraviolet radiation, especially UVA and UVB radiation, makes them useful for increasing the Sun Protection Factor (SPF) in cosmetics[205]. Studies have shown that some coumarins, like 7-hydroxycoumarin and esculetin, can increase SPF values by 2 to 5 units per percentage concentration[206]. This depends on the base ingredient and other active ingredients. They protect skin cells from photodamage by absorbing the harmful light and sending it away as harmless energy[207]. Additionally, their antioxidant properties help get rid of ROS, which is another way they work[208]. Often, skincare products combine coumarins with other ultraviolet filters to broaden protection and improve formulation stability, making them valuable photoprotective agents[209].

13. Challenges and future perspectives in coumarin research

The bioactivities and potentials of coumarin and its derivatives received significant attention in the previous sections. Along with the benefits, there are a lot of problems with synthesizing, purifying, and adding functions to the coumarin scaffold. These problems make it harder for their therapeutic uses to grow and develop[210]. One of the major challenges is the efficient synthesis of structurally diverse and complex modified coumarins[211]. Classical coumarin chemical synthesis is mostly based on condensation methods, among others. These include several inherent limitations, such as harsh reaction conditions, high-cost operation, and the unwanted generation of by-products[212]. Aromatic hydrocarbons and carbonyl compounds are complex and wasteful due to their low nucleophilicity and electrophilicity rates[213]. Researchers have proposed a novel set of synthetic methods for designing a range of coumarin derivatives[214]. These showed different kinds of substituted coumarins, and the experimental part of the text gives detailed information on how to make them along with short descriptions of common reactions and compounds[215].

14. Conclusion and summary

Because of their impressive pharmacological properties, coumarin-based chemical entities constitute hot topics in the domain. We think that our most recent critical and in-depth study of the hidden contributions and illustrative examples is a good summary of the possibilities and promises that bioactive molecules designed using the coumarin scaffold can bring. On the other hand, it shows how important bioactive substances with coumarin scaffolds are and what their main target classes are in the research field. To be more specific, each group of molecules was treated and shown not as a detailed description of how they work, but as an engineering necessity for a strong and effective structure that aims for the desired activity profile. This newly acquired structural information is important for future drug-enzyme or drug-receptor interaction studies. Finally, we emphasize the advances, considering that the accelerated progress made in the field of coumarin scaffold-containing bioactive molecules reflects a significant contribution to the correlation between biological activity and chemical structure. Therefore, this enrichment of knowledge generates original insights further aimed at deeper and more profound developments for science and wellness.

Conflict of interest

The authors declare no conflict of interest.

References

1. Sharifi-Rad J, Cruz-Martins N, López-Jornet P, Lopez EPF, Harun N, Yeskaliyeva B, Beyatli A, Sytar O, Shaheen S, Sharopov F, Taheri Y, Docea AO, Calina D, Cho WC. Natural Coumarins: Exploring the Pharmacological Complexity and Underlying Molecular Mechanisms. Gil G, editor. Oxidative Medicine and Cellular Longevity. 2021;2021:6492346.
2. Bashir MK, Mustafa YF, Oglah MK. Synthesis and antitumor activity of new multifunctional coumarins. Periodico Tche Quimica. 2020;17(36):871–83.
3. Mustafa YF. Chemotherapeutic applications of folate prodrugs: A review. NeuroQuantology. 2021;19(8):99–112.
4. Mustafa YF, Mohammed ET, Khalil RR. Antioxidant and antitumor activities of methanolic extracts obtained from Red Delicious and Granny Smith apples' seeds. Systematic Reviews in Pharmacy. 2020;11(4):570–6.
5. Mustafa YF, Oglah MK, Bashir MK. Conjugation of sinapic acid analogues with 5- Fluorouracil: Synthesis, preliminary cytotoxicity, and release study. Systematic Reviews in Pharmacy. 2020;11(3):482–9.
6. Aldewachi H, Mustafa YF, Najm R, Ammar F. Adulteration of Slimming Products and its Detection Methods. Systematic Reviews in Pharmacy. 2020;11(3):289–96.
7. Hachem K, Jasim SA, Al-Gazally ME, Riadi Y, Yasin G, Turki Jalil A, Abdulkadhm MM, Saleh MM, Fenjan MN, Mustafa YF, Dehno Khalaji A. Adsorption of Pb(II) and Cd(II) by magnetic chitosan-salicylaldehyde Schiff base: Synthesis, characterization, thermal study and antibacterial activity. Journal of the Chinese Chemical Society. 2022;69(3):512–21.

8. Mustafa YF, Abdulaziza NT, Jasima MH. 4-Methylumbelliferone and its derived compounds: A brief review of their cytotoxicity. Egyptian Journal of Chemistry. 2021;64(4):1807–16.
9. Bashir MK, Mustafa YF, Oglah MK. Antitumor, antioxidant, and antibacterial activities of glycosyl-conjugated compounds: A review. Systematic Reviews in Pharmacy. 2020;11(4):175–87.
10. Mustafa YF, Mohammed NA alwahab. A promising oral 5-fluorouracil prodrug for lung tumor: Synthesis, characterization and release. Biochemical and Cellular Archives. 2021;21(Supp 1):1991–9.
11. Nejres AM, Ali HK, Behnam SP, Mustafa YF. Potential effect of ammonium chloride on the optical physical properties of polyvinyl alcohol. Systematic Reviews in Pharmacy. 2020;11(6):726–32.
12. Firoozeh AZ, Bokov DO, Salahdin OD, Abdelbasset WK, Jawad MA, Kadhi MM, Qasim MT, Kzar HH, Al-Gazally ME, Mustafa YF, Khatami M. Cytotoxicity evaluation of environmentally friendly synthesis Copper/Zinc bimetallic nanoparticles on MCF-7 cancer cells. Rendiconti Lincei Scienze Fisiche e Naturali. 2022;33:441–7.
13. Roomi AB, Widjaja G, Savitri D, Jalil AT, Mustafa YF, Thangavelu L, Kazhibayeva G, Suksatan W, Chupradit S, Aravindhan S. SnO2:Au/Carbon Quantum Dots Nanocomposites: Synthesis, Characterization, and Antibacterial Activity. Journal of Nanostructures. 2021;11(3):514–23.
14. Mustafa YF. Modern Developments in the Application and Function of Metal/Metal Oxide Nanocomposite–Based Antibacterial Agents. BioNanoScience. 2023;13:840–52.
15. Waheed SA, Mustafa YF. Benzocoumarin backbone is a multifunctional and affordable scaffold with a vast scope of biological activities. Journal of Medicinal and Chemical Sciences. 2022;5(5):703–21.
16. Jebir RM, Mustafa YF. Watermelon Allsweet: A promising natural source of bioactive products. Journal of Medicinal and Chemical Sciences. 2022;5(5):652–66.
17. Patra I, Ansari MJ, Saadoon N, Mashhadani ZI Al, Obaid NH, Alawsi T, Jabbar AH, Mustafa YF. Insights into the Electronic Properties of Coumarins: A Comparative Study Photocatalytic Degradation of Methylene Blue. Physical Chemistry Research. 2023;11(2):437–47.
18. Ismael RN, Mustafa YF, Al-Qazaz HK. Citrullus lanatus, a Potential Source of Medicinal Products: A Review. Journal of Medicinal and Chemical Sciences. 2022;5(4):607–18.
19. Abdulaziz NT, Mustafa YF. The Effect of Heat Variable on the Chemical Composition and Bioactivities of a Citrullus lanatus Seed Aqueous Extracts. Journal of Medicinal and Chemical Sciences. 2022;5(7):1166–76.
20. Jasim SF, Mustafa YF. A Review of Classical and Advanced Methodologies for Benzocoumarin Synthesis. Journal of Medicinal and Chemical Sciences. 2022;5(5):676–94.
21. Mustafa YF, Mohammed ET, Khalil RR. Synthesis, characterization, and anticoagulant activity of new functionalized biscoumarins. Egyptian Journal of Chemistry. 2021;64(8):4461–8.
22. Bansuri G, Limbasiya J, Nandasana M. Bioactivity of 7-Hydroxy 4-Methyl Coumarin. International Journal of Current Microbiology and Applied Sciences ISSN:. 2019;8(04):2737–41.
23. Mustafa YF. Classical approaches and their creative advances in the synthesis of coumarins: A brief review. Journal of Medicinal and Chemical Sciences. 2021;4(6):612–25.
24. Yang Y, Bustani GS, Alawsi T, Altalbawy FMA, Kareem AK, Gupta J, Zhu P, Hjazi A, Alawadi AH, Mustafa YF. The cardioprotective effects of cerium oxide nanoparticles against the poisoning generated by aluminum phosphide pesticide: Controlling oxidative stress and mitochondrial damage. Pesticide Biochemistry and Physiology. 2023;197:105701.
25. Abdulaziz NT, Mustafa YF. Anticancer properties of hymecromone-derived compounds: A review. International Journal of Pharmaceutical Research. 2021;13(1):2163–74.
26. Jasim SF, Mustafa YF. Synthesis, ADME Study, and antimicrobial evaluation of novel naphthalene-based derivatives. Journal of Medicinal and Chemical Sciences. 2022;5(5):793–807.
27. Mustafa YF, Zain Al-Abdeen SH, Khalil RR, Mohammed ET. Novel functionalized phenyl acetate derivatives of benzo [e]-bispyrone fused hybrids: Synthesis and biological activities. Results in Chemistry. 2023;5:100942.
28. Gupta D, Guliani E, Bajaj K. Coumarin—Synthetic Methodologies, Pharmacology, and Application as Natural Fluorophore. Topics in Current Chemistry. 2024;382(2):16.
29. Adimule VM, Nandi SS, Kerur SS, Khadapure SA, Chinnam S. Recent Advances in the One-Pot Synthesis of Coumarin Derivatives from Different Starting Materials Using Nanoparticles: A Review. Topics in Catalysis. 2022;
30. Samanth M, Bhat M. Synthesis and Importance of Coumarin Derivatives in Medicinal Chemistry: A Comprehensive Review. Russian Journal of Bioorganic Chemistry. 2024;50(5):1672–91.
31. Citarella A, Vittorio S, Dank C, Ielo L. Syntheses, reactivity, and biological applications of coumarins. Frontiers in Chemistry. 2024;12:1362992.
32. Rohman N, Ardiansah B, Wukirsari T, Judeh Z. Recent Trends in the Synthesis and Bioactivity of Coumarin, Coumarin–Chalcone, and Coumarin–Triazole Molecular Hybrids. Molecules. 2024;29(5):1026.

33. Bergagnini-Kolev M, Howe M, Burgess E, Wright P, Hamburger S, Zhong Z, Ellis SB, Ellis TK. Synthesis of trifluoromethyl substituted nucleophilic glycine equivalents and the investigation of their potential for the preparation of α-amino acids. Tetrahedron. 2021;77:131741.
34. Lončarić M, Sokač DG, Jokić S, Molnar M. Recent advances in the synthesis of coumarin derivatives from different starting materials. Biomolecules. 2020;10(1):151.
35. Kasim SM, Al-Dabbagh BM, Mustafa YF. A review on the biological potentials of carbazole and its derived products. Eurasian Chemical Communications. 2022;4(6):495–512.
36. Mustafa YF. Triple coumarin-based 5-fluorouracil prodrugs, their synthesis, characterization, and release kinetics. Journal of Molecular Structure. 2024;1301:137415.
37. Zeki NM, Mustafa YF. 6,7-Coumarin-heterocyclic hybrids: A comprehensive review of their natural sources, synthetic approaches, and bioactivity. Journal of Molecular Structure. 2024;1303:137601.
38. Younes AH, Mustafa YF. Plant-Derived Coumarins: A Narrative Review Of Their Structural And Biomedical Diversity. Chemistry & Biodiversity. 2024;21(6):e202400344.
39. Jibroo RN, Mustafa YF, Al-Shakarchi W. Heterocycles fused on a 6,7-coumarin framework: an in-depth review of their structural and pharmacological diversity. Chemical Papers. 2024;78:7239–7311.
40. Zeki NM, Mustafa YF. Digital alchemy: Exploring the pharmacokinetic and toxicity profiles of selected coumarin-heterocycle hybrids. Results in Chemistry. 2024;10:101754.
41. Mustafa YF. Synthesis of 7,8-dihydroxy-4-phenylbenzo[g]coumarins as potential multitarget anti-skin-aging candidates. Journal of Molecular Structure. 2025;1321:139806.
42. Mustafa YF. Coumarins from toxic phenol: An algorithm of their synthesis and assessment as biosafe, wide-spectrum, potent antimicrobial prospects. Applied Chemical Engineering. 2024;7(3):ACE-5527.
43. Zeki NM, Mustafa YF. Synthesis of Novel Dioxathiole-6,7-coumarin Hybrids As Cytosafe-Multifunctional Applicants: An In Vitro—In Silico Study. Russian Journal of Bioorganic Chemistry. 2024;50(5):2076–91.
44. Abdulaziz NT, Al-bazzaz FY, Mustafa YF. Natural products for attenuating Alzheimer's disease: A narrative review. Eurasian Chemical Communications. 2023;5(4):358–70.
45. Mustafa YF. Biocompatible chlorocoumarins from harmful chlorophenols, their synthesis and biomedicinal evaluation. Journal of Molecular Structure. 2024;1309:138193.
46. Mustafa YF. Harmful Free Radicals in Aging: A Narrative Review of Their Detrimental Effects on Health. Indian Journal of Clinical Biochemistry. 2024;39(2):154–67.
47. Mohammed ET, Khalil RR, Mustafa YF. Phytochemical Analysis and Antimicrobial Evaluation of Quince Seeds' Extracts. Journal of Medicinal and Chemical Sciences. 2022;5(6):968–79.
48. Jebir RM, Mustafa YF. Novel coumarins isolated from the seeds of Citrullus lanatus as potential antimicrobial agents. Eurasian Chemical Communications. 2022;4(8):692–708.
49. Mustafa YF, Bashir MK, Oglah MK, Khalil RR, Mohammed ET. Bioactivity of some natural and semisynthetic coumarin derived compounds. NeuroQuantology. 2021;19(6):129–38.
50. Kasim SM, Abdulaziz NT, Jasim MH, Mustafa YF. Resveratrol in cancer chemotherapy: Is it a preventer, protector, or fighter? Eurasian Chemical Communications. 2023;5(7):576–87.
51. Ahmed BA, Mustafa YF, Ibrahim BY. Isolation and characterization of furanocoumarins from Golden Delicious apple seeds. Journal of Medicinal and Chemical Sciences. 2022;5(4):537–45.
52. Abdelbasset WK, Elkholi SM, Ismail KA, AL-Ghamdi HS, Mironov S, Ridha HSH, Maashi MS, Thangavelu L, Mahmudiono T, Mustafa YF. Mequinol-loaded carboxymethyl cellulose/chitosan electrospun wound dressing as a potential candidate to treat diabetic wounds. Cellulose. 2022;29(14):7863–81.
53. Huldani H, Rashid AI, Turaev KN, Opulencia MJC, Abdelbasset WK, Bokov DO, Mustafa YF, Al-Gazally ME, Hammid AT, Kadhim MM, Ahmadi SH. Concanavalin A as a promising lectin-based anti-cancer agent: the molecular mechanisms and therapeutic potential. Cell Communication and Signaling. 2022;20(1):1–14.
54. Zamanian MY, Parra RMR, Soltani A, Kujawska M, Mustafa YF, Raheem G, Al-Awsi L, Lafta HA, Taheri N, Heidari M, Golmohammadi M, Bazmandegan G. Targeting Nrf2 signaling pathway and oxidative stress by resveratrol for Parkinson's disease: an overview and update on new developments. Molecular Biology Reports. 2023;50:5455–5464.
55. Abdelbasset WK, Savina SV, Mavaluru D, Shichiyakh RA, Bokov DO, Mustafa YF. Smartphone based aptasensors as intelligent biodevice for food contamination detection in food and soil samples: Recent advances. Talanta. 2023;252:123769.
56. Jiang M, Althomali RH, Ansari SA, Saleh EAM, Gupta J, Kambarov KD, Alsaab HO, Alwaily ER, Hussien BM, Mustafa YF, Narmani A, Farhood B. Advances in preparation, biomedical, and pharmaceutical applications of chitosan-based gold, silver, and magnetic nanoparticles: A review. International Journal of Biological Macromolecules. 2023;251:126390.

57. Maashi MS, Al-Mualm M, Al-Awsi GRL, Opulencia MJC, Al-Gazally ME, Abdullaev B, Abdelbasset WK, Ansari MJ, Jalil AT, Alsaikhan F, Shalaby MN, Mustafa YF. Apigenin alleviates resistance to doxorubicin in breast cancer cells by acting on the JAK/STAT signaling pathway. Molecular Biology Reports. 2022;49:8777–84.
58. Ibraheem Shelash Al-Hawary S, Omar Bali A, Askar S, Lafta HA, Jawad Kadhim Z, Kholdorov B, Riadi Y, Solanki R, ismaeel kadhem Q, Fakri Mustafa Y. Recent advances in nanomaterials-based electrochemical and optical sensing approaches for detection of food dyes in food samples: A comprehensive overview. Microchemical Journal. 2023;189:108540.
59. Javed Ansari M, Olegovich Bokov D, Abdalkareem Jasim S, Rudiansyah M, Suksatan W, Yasin G, Chupradit S, Alkaim AF, Fakri Mustafa Y, Imad Tarek D. Emerging optical and electrochemical biosensing approaches for detection of ciprofloxacin residues in food and environment samples: A comprehensive overview. Journal of Molecular Liquids. 2022;354:118895.
60. Ramírez-Coronel AA, Alameri AA, Altalbawy F, Sanaan Jabbar H, Lateef Al-Awsi GR, Iswanto AH, Altamimi AS, Shareef Mohsen K, Almulla AF, Mustafa YF. Smartphone-Facilitated Mobile Colorimetric Probes for Rapid Monitoring of Chemical Contaminations in Food: Advances and Outlook. Critical Reviews in Analytical Chemistry. 2024;54(7):2290–308.
61. Raya I, Chupradit S, Kadhim MM, Mahmoud MZ, Jalil AT, Surendar A, Ghafel ST, Mustafa YF, Bochvar AN. Role of Compositional Changes on Thermal, Magnetic and Mechanical Properties of Fe-P-C-Based Amorphous Alloys. Chinese Physics B. 2022;31(1):016401.
62. Ismael SS, Waheed NAM, Kasim SM, Mustafa YF. Novel Coumarin-Indole Hybrids as Cytotoxic Candidates: Synthesis and Antiproliferative Activity. Pharmacognosy Journal. 2023;15(6):1105–11.
63. Setia Budi H, Javed Ansari M, Abdalkareem Jasim S, Abdelbasset WK, Bokov D, Fakri Mustafa Y, Najm MAA, Kazemnejadi M. Preparation of antibacterial Gel/PCL nanofibers reinforced by dicalcium phosphate-modified graphene oxide with control release of clindamycin for possible application in bone tissue engineering. Inorganic Chemistry Communications. 2022;139:109336.
64. Mustafa YF, Faisal AF, Alshaher MM, Hassan DA. Food-Derived Micronutrients as Alleviators of Age-Related Dysfunction: A Dive into Their Effects and Cellular Mechanisms. Indian Journal of Clinical Biochemistry. 2025; https://doi.org/10.1007/s12291-024-01297-7
65. Younes HA, Mustafa YF. Sweet Bell Pepper: A Focus on Its Nutritional Qualities and Illness-Alleviated Properties. Indian Journal of Clinical Biochemistry. 2024;39:459–69.
66. Mustafa YF. Effects of heat variables on the starch content of cooked white rice: Searching for diabetes-friendly food. Bioactive Carbohydrates and Dietary Fibre. 2024;31:100395.
67. Mustafa YF. 4-Chloroskimmetine-based derivatives as potential anticancer and antibacterial prospects: Their synthesis and in vitro inspections. Results in Chemistry. 2024;7:101511.
68. Zeki NM, Mustafa YF. Novel heterocyclic coumarin annulates: synthesis and figuring their roles in biomedicine, bench-to-bedside investigation. Chemical Papers. 2024;78:4935–51.
69. Barus M, Rotar D, Bratenko M, Panasenko N, Zvarych V, Stasevych M, Vovk M. Synthesis and evaluation of antimicrobial activities of new functional derivatives of 3-[5-(4-nitrophenyl)-2-furyl]-4-pyrazole-carbaldehydes. Biointerface Research in Applied Chemistry. 2021;11(4):12159–69.
70. Mustafa YF. Nutraceutical-based telomerase inhibitors: Renewed hope for cancer therapy. Phytomedicine Plus. 2024;4(2):100537.
71. Jibroo RN, Mustafa YF, Al-Shakarchi W. Synthesis and evaluation of linearly fused thiadiazolocoumarins as prospects with broad-spectrum bioactivity. Results in Chemistry. 2024;7:101494.
72. Younes AH, Mustafa YF. Novel coumarins from green sweet bell pepper seeds: Their isolation, characterization, oxidative stress-mitigating, anticancer, anti-inflammatory, and antidiabetic properties. Journal of Molecular Structure. 2024;1312:138629.
73. Younes AH, Mustafa YF. Unveiling the Biomedical Applications of Novel Coumarins Isolated From Capsicum Annuum L. Seeds by a Multivariate Extraction Technique. Chemistry and Biodiversity. 2024;21(6):e202400581.
74. Zeki NM, Mustafa YF. Coumarin hybrids: a sighting of their roles in drug targeting. Chemical Papers. 2024;78:5753–5772.
75. Mustafa YF, Ismael RN, Jebir RM. Natural coumarins from two cultivars of watermelon seeds as biosafe anticancer agents, an algorithm for their isolation and evaluation. Journal of Molecular Structure. 2024;1295(P1):136644.
76. Mustafa YF. Coumarins from carcinogenic phenol: synthesis, characterization, in silico, biosafety, anticancer, antioxidant, and anti-inflammatory assessments. Chemical Papers. 2024;78:493–504.
77. Jibroo RN, Mustafa YF. Linearly ring-fused coumarins: A review of their cancer-fighting attributes. Results in Chemistry. 2024;8:101611.

78. Mustafa YF. Synthesis of novel 6-aminocoumarin derivatives as potential –biocompatible antimicrobial and anticancer agents. Journal of Molecular Structure. 2025;1320:139658.
79. Mustafa YF. Synthesis, in silico analysis, and biomedical effects of coumarins derived from resveratrol. Phytomedicine Plus. 2024;3(4):100501.
80. Budi HS, Younus LA, Lafta MH, Parveen S, Mohammad HJ, Al-qaim ZH, Jawad MA, Parra RMR, Mustafa YF, Alhachami FR, Karampoor S, Mirzaei R. The role of miR-128 in cancer development, prevention, drug resistance, and immunotherapy. Frontiers in Oncology. 2023;12:1067974.
81. Abdulaziz NT, Mustafa YF. Antibacterial and Antitumor Potentials of Some Novel Coumarins. International Journal of Drug Delivery Technology. 2022;12(1):239–47.
82. Mustafa YF, Hassan DA, Faisal AF, Alshaher MM. Synthesis of novel skipped diene-3-halocoumarin conjugates as potent anticancer and antibacterial biocompatible agents. Results in Chemistry. 2024;11:101846.
83. Waheed SA, Mustafa YF. Synthesis and evaluation of new coumarins as antitumor and antioxidant applicants. Journal of Medicinal and Chemical Sciences. 2022;5(5):808–19.
84. El-Etrawy AAS, Ramadan A, Sherbiny FF, Zeid IF, Abdel-Rahman AAH, Hawata MA. Coumarin–amino acid hybrids as promising anticancer agents: design, synthesis, docking studies and CK2 inhibition. RSC Advances. 2024;14(34):24671–86.
85. Shahzadi I, Ali Z, Baek SH, Mirza B, Seok A. Assessment of the antitumor potential of umbelliprenin , a naturally occurring sesquiterpene coumarin. Biomedicines. 2020;8(5):126.
86. Zaki I, El-Sayed ESH, Radwan EM. Synthesis and Antiproliferative Activity of Some New Coumarin Derivatives Derived from 8-Hydroxycoumarin. Russian Journal of Bioorganic Chemistry. 2021;47(2):514–23.
87. Kamran S, Sinniah A, Abdulghani MAM, Alshawsh MA. Therapeutic potential of certain terpenoids as anticancer agents : A scoping review. Cancers. 2022;14(5):1100.
88. Li C long, Han X cheng, Zhang H, Wu J sheng, Li B. Effect of scopoletin on apoptosis and cell cycle arrest in human prostate cancer cells in vitro. Tropical Journal of Pharmaceutical Research April. 2015;14(4):611–7.
89. Hossain R, Tuj F, Shova Z, Akter M, Mogal R, Saha HR, Sarkar BC. Esculetin unveiled : Decoding its anti-tumor potential through molecular mechanisms — A comprehensive review. Cancer Reports. 2023;7(1):e1948.
90. Lv X, Yang H, Zhong H, He L, Wang L. Osthole exhibits an antitumor effect in retinoblastoma through inhibiting the PI3K / AKT / mTOR pathway via regulating the hsa _ circ _ 0007534 / miR-214-3p axis. Pharmaceutical Biology. 2022;60(1):417–26.
91. Matias-Barrios VM, Radaeva M, Song Y, Alperstein Z, Lee AR, Schmitt V, Lee J, Ban F, Xie N, Qi J, Lallous N, Gleave ME, Cherkasov A, Dong X. Discovery of New Catalytic Topoisomerase II Inhibitors for Anticancer Therapeutics. Frontiers in Oncology. 2021;10:633142.
92. Visser BJ, Sharma S, Chen PJ, Mcmullin AB, Bates ML, Bates D. Psoralen mapping reveals a bacterial genome supercoiling landscape dominated by transcription. Nucleic Acids Research. 2022;50(8):4436–49.
93. Agarwal U, Pannu A, Tonk RK, Jaiswal P, Jain K. The potential of xanthotoxin in the treatment of cognitive disorders: current insights and future perspectives. Future Journal of Pharmaceutical Sciences. 2024;10(1):147.
94. Gaber A, Alsanie WF, Alhomrani M, Alamri AS, El-deen IM, Refat MS. Synthesis and characterization of some new coumarin derivatives as probable breast anticancer MCF-7 drugs. Crystals. 2021;11(5):565.
95. Zeki NM, Mustafa YF. Synthesis and Pharmacological Profiles of 6,7-Dihydroxycoumarin and Its Derivatives: A Concise Review. Iraqi Journal of Pharmacy. 2023;20(Supplementary Issue 1):174–88.
96. de Oliveira AA, Mendoza VO, Priviero F, Webb RC, Nunes KP. Age-Related Decline in Vascular Responses to Phenylephrine Is Associated with Reduced Levels of HSP70. Biomolecules. 2022;12(8):1125.
97. Wei Z, Wei N, Su L, Gao S. The molecular effects underlying the pharmacological activities of daphnetin. Frontiers in Pharmacology. 2024;15:1407010.
98. Mosa AI, Ibrahim MM, Aldhlmani SA. Spectroscopic and solution studies of some transition metal complexes of new 4-hydroxy coumarin. Journal of Solution Chemistry. 2013;42:2364–83.
99. Liang Y, Xie L, Liu K, Dai X, Wang X, Li X. Bergapten : A review of its pharmacology , pharmacokinetics , and toxicity. Phytotherapy Research. 2021;35(11):6131–47.
100. Revankar HM, Bukhari SN, Kumar GB, Qin H li. Coumarins scaffolds as COX inhibitors. Bioorganic Chemistry. 2017;71:146–59.
101. Deng M, Xie L, Zhong L, Liao Y, Liu L, Li X. Imperatorin: A review of its pharmacology, toxicity and pharmacokinetics. European Journal of Pharmacology. 2020;879(April).
102. Bhattarai N, Kumbhar AA, Pokharel YR, Yadav PN. Anticancer Potential of Coumarin and its Derivatives. Mini-Reviews in Medicinal Chemistry. 2021;21(19):2996–3029.

103. Nodooshan SJ, Amini P, Ashrafizadeh M, Tavakoli S, Farhood B. Suberosin attenuates the proliferation of MCF-7 breast cancer cells in combination with radiotherapy or hyperthermia. Current Drug Research Reviews Formerly: Current Drug Abuse Reviews. 2021;13(12):148–53.
104. Wu A, Lu J, Zhong G, Lu L, Qu Y, Chen Z. Xanthotoxin (8-methoxypsoralen): A review of its chemistry, pharmacology, pharmacokinetics, and toxicity. Phytotherapy Research. 2022;36(10):3805–32.
105. Şeker Karatoprak G, Dumlupınar B, Celep E, Kurt Celep I, Küpeli Akkol E, Sobarzo-Sánchez E. A comprehensive review on the potential of coumarin and related derivatives as multi-target therapeutic agents in the management of gynecological cancers. Frontiers in Pharmacology. 2024;15:1423480.
106. Saleem A, Bukhari SM, Zaidi A, Farooq U, Ali M, Khan A, Khan S, Shah KH, D AM, Khan FA. Enzyme inhibition and antibacterial potential of 4-Hydroxycoumarin derivatives. Brazilian Journal of Pharmaceutical Sciences. 2020;56:e18654.
107. Avdović EH, Milanović Ž, Simijonović D, Antonijević M, Milutinović M, Vojinović R. An effective, green synthesis procedure for obtaining coumarin– hydroxybenzohydrazide derivatives and assessment of their antioxidant activity and redox status. Antioxidants. 2023;12(12):2070.
108. Al-Harbi LM, Nassar HS, Moustfa A, Alosaimi AM, Mohamed HM, Khowdiary MM, Elhenawy AA. Novel coumarin amino acid derivatives: Design, synthesis, docking, absorption, distribution, metabolism, elimination, toxicity (ADMET), quantitative structure–activity relationship (QSAR) and anticancer studies. Materials Express. 2020;10(9):1375–94.
109. Chandran N, Bose K, Thekkantavida AC, Thomas RR, Anirudhan K, Bindra S, Mathew B. Oxime derivatives: A valid pharmacophore in medicinal chemistry. ChemistrySelect Review. 2024;9(27):e202401726.
110. Yadav AK, Shrestha RM, Yadav PN. Anticancer mechanism of coumarin-based derivatives. European Journal of Medicinal Chemistry. 2024;267:116179.
111. Kumar M, Singla R, Dandriyal J, Jaitak V. Coumarin derivatives as anticancer agents for lung cancer therapy: A review. Anti-Cancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry - Anti-Cancer Agents. 2018;18(7):964–84.
112. Irfan A, Rubab L, Rehman MU, Anjum R, Ullah S, Marjana M, Qadeer S, Sana S. Coumarin sulfonamide derivatives: An emerging class of therapeutic agents. Heterocyclic Communications. 2020;26(1):46–59.
113. Mustafa YF. Emerging trends and future opportunities for coumarin-heterocycle conjugates as antibacterial agents. Results in Chemistry. 2023;6:101151.
114. Rudiansyah M, Jasim SA, Mohammad pour ZG, Athar SS, Jeda AS, Doewes RI, Jalil AT, Bokov DO, Mustafa YF, Noroozbeygi M, Karampoor S, Mirzaei R. Coronavirus disease 2019 (COVID-19) update: From metabolic reprogramming to immunometabolism. Journal of Medical Virology. 2022;94(10):4611–27.
115. Jebir RM, Mustafa YF. Natural products catalog of allsweet watermelon seeds and evaluation of their novel coumarins as antimicrobial candidates. Journal of Medicinal and Chemical Sciences. 2022;5(5):831–47.
116. Mustafa YF. New Coumarin-Metronidazole Composites: Synthesis, Biocompatibility, and Anti-anaerobic Bacterial Activity. Russian Journal of Bioorganic Chemistry. 2024;50(1):201–10.
117. Zeki MN, Mustafa YF. Synthesis and evaluation of novel ring-conjugated coumarins as biosafe broad-spectrum antimicrobial candidates. Journal of Molecular Structure. 2024;1309:138192.
118. Kamal IK, Mahmood AT, Mustafa YF. Synthesis of Eugenol-Derived Coumarins as Broad-Spectrum Biosafe Antimicrobial Agents. Russian Journal of Bioorganic Chemistry. 2024;50(6):2240–51.
119. Mahmood AT, Kamal IK, Mustafa YF. Coumarin Backbone as a Door-Opening Key for Investigating Chloroxylenol as Oral Antimicrobial Agents: an In Vitro–In Silico Study. Russian Journal of Bioorganic Chemistry. 2024;50(6):2252–68.
120. Farshori NN, Banday MR, Ahmad A, Khan AU, Rauf A. 7-Hydroxy-coumarin derivatives: Synthesis, characterization and preliminary antimicrobial activities. Medicinal chemistry research. 2011;20:535–41.
121. Safdari H, Neshani A, Sadeghian A, Ebrahimi M, Iranshahi M, Sadeghian H. Potent and selective inhibitors of class A β-lactamase: 7-prenyloxy coumarins. The Journal of antibiotics. 2014;67(5):373–7.
122. Jia C, Zhang J, Yu L, Wang C, Yang Y, Rong X, Xu K, Chu M. Antifungal Activity of Coumarin Against Candida albicans Is Related to Apoptosis. Frontiers in Cellular and Infection Microbiology. 2019;8:00445.
123. Ali EM, Alkuwayti MA, Aldayel MF, Abdallah BM. Coumarin derivative, 5′-hydroxy-auraptene, extracted from Lotus lalambensis, displays antifungal and anti-aflatoxigenic activities against Aspergillus flavus. Journal of King Saud University - Science. 2021;33(1):101216.
124. Antika LD, Tasfiyat AN, Hikmat H, Septama AW. Scopoletin: A review of its source, biosynthesis, methods of extraction, and pharmacological activities. Zeitschrift für Naturforschung C. 2022;77(7–8):303–16.
125. Ju S, Tan Y, Wang Q, Zhou L, Wang KUN, Wen C, Wang M. Antioxidant and anti- inflammatory effects of esculin and esculetin. Experimental and Therapeutic Medicine. 2024;27(6):1–14.

126. Zhang X, Liu Y, Shen Z, Wang S, Wu C, Liu D. Osthole ameliorates myonecrosis caused by Clostridium perfringens type A infection in mice. One Health Advances. 2023;1(1):27.
127. Luo L, Yang J, Wang C, Wu J, Li Y, Zhang X, Li H, Zhang H, Zhou Y, Lu A, Chen S. Natural products for infectious microbes and diseases: An overview of sources, compounds, and chemical diversities. Science China Life Sciences. 2022;65(6):1123–45.
128. Swer H, Rathi B, Wanjari A, Raut P, Shinde A, Chunchuwar M, Katore A. Antibacterial activity of Psoralea cordifolia Linn .: A systematic review. International Journal of Pharmaceutical Investigation. 2024;14(4):1061–8.
129. Hasanuddin S, Meilanda E, Ramadhan DSF, Gozali D. Inhibitory activity, metabolite contents determination, and in silico prediction of parsley leaves fraction (Petrocelinum crispum MILL) as antifungal agent of Malassezia furfur. Chem. 2022;15(2):1539–46.
130. Sarfraz I, Rasul A, Jabeen F, Younis T, Zahoor MK, Arshad M, Ali M. Fraxinus: A plant with versatile pharmacological and biological activities. Evidence-Based Complementary and Alternative Medicine. 2017;2017:4269868.
131. Javed M, Saleem A, Xaveria A, Akhtar MF. Daphnetin: A bioactive natural coumarin with diverse therapeutic potentials. Frontiers in Pharmacology. 2022;13:993562.
132. Safar AA, Ghafoor AO, Dastan D. Screening of chemical characterization, antifungal and cytotoxic activities of essential oil constituents of Tagetes erecta L. from Erbil, Kurdistan Region-Iraq. Polish Journal of Environmental Studies. 2020;29(3):2317–26.
133. Almalki MA. In-vitro antibacterial, antifungal, antibiofilm, and antioxidant potentials of isopimpinellin recovered from Citrullus colocynthis. International Journal of Pharmacy and Pharmaceutical Sciences. 2016;8(4):117–22.
134. Kozioł E, Skalicka-Woźniak K. Imperatorin–pharmacological meaning and analytical clues: profound investigation. Phytochemistry Reviews. 2016;15(4):627–49.
135. Mahdi SA, Ahmed AA, Yousid E, Zainulabdeen K, Ahmed D, Alsayed R, Bufaroosha M. A research study in the synthesis and the applications of coumarin derivatives. Journal of Sustainable Materials Processing and Management. 2022;2(2):69–77.
136. Emam SH, Sonousi A, Osman EO, Hwang D, Kim GD, Hassan RA. Design and synthesis of methoxyphenyl-and coumarin-based chalcone derivatives as anti-inflammatory agents by inhibition of NO production and down-regulation of NF-κB in LPS-induced RAW264. 7 macrophage cells. Bioorganic Chemistry. 2021;107:104630.
137. Zhu F di, Fu X, Ye H chun, Ding H xin, Feng G. Antibacterial activities of coumarin-3-carboxylic acid against Acidovorax citrulli. Frontiers in Microbiology. 2023;14:1207125.
138. Häußler D, Gütschow M. Synthesis of a Fluorescent-Labeled Bisbenzamidine Containing the Central (6, 7-Dimethoxy-4-coumaryl) Alanine Building Block. Heteroatom Chemistry. 2015;26(5):367–73.
139. Mandlik V, Patil S, Bopanna R, Basu S, Singh S. Biological activity of coumarin derivatives as anti-leishmanial agents. PLoS One. 2016;11(10):e016458.
140. Pasricha S, Gahlot P. Synthetic strategies and biological potential of coumarin-chalcone hybrids: A new dimension to drug design. Current Organic Chemistry. 2020;24(4):402–38.
141. Tsivileva OM, Koftin O V, Evseeva N V. Coumarins as fungal metabolites with potential medicinal properties. Antibiotics. 2022;11(9):1156.
142. Zhao YQ, Li X, Guo HY, Shen QK, Quan ZS, Luan T. Application of quinoline ring in structural modification of natural products. Molecules. 2023;28(18):6478.
143. Xu Z, Chen Q, Zhang Y, Liang C. Coumarin-based derivatives with potential anti-HIV activity. Fitoterapia. 2021;150:104863.
144. Li Z, Kong D, Liu Y, Li M. Pharmacological perspectives and molecular mechanisms of coumarin derivatives against virus disease. Genes & diseases. 2022;9(1):80–94.
145. Alwan ES, Mohareb RM. Synthesis of biologically active chromene, coumarin, azole, azine and thiophene derivatives from 1, 3-diketone. Organic Communications. 2021;14(3):163–227.
146. Fotopoulos I, Hadjipavlou-Litina D. Hybrids of coumarin derivatives as potent and multifunctional bioactive agents: A review. Medicinal Chemistry. 2020;16(3):272–306.
147. De S, Aamna B, Sahu R, Parida S, Behera SK, Dan AK. Seeking heterocyclic scaffolds as antivirals against dengue virus. European Journal of Medicinal Chemistry. 2022;240:114576.
148. Al-Elweet D, El-Sayed W, Alminderej FM, Albadri AE. 1, 2, 4-Triazole as promising scaffold: Synthetic and ciological aspects. Journal of Qassim University for Science,. 2023;2(2):61–94.
149. Jasim SF, Mustafa YF. New fused-coumarin composites: Synthesis, anticancer and antioxidant potentials evaluation. Eurasian Chemical Communications. 2022;4(7):607–19.
150. Mustafa YF. Coumarins derived from natural methoxystilbene as oxidative stress-related disease alleviators: Synthesis and in vitro-in silico study. Journal of Molecular Structure. 2024;1302:137471.

151. Ismael RN, Mustafa YF, Al-Qazaz HK. Cancer-curative potential of novel coumarins from watermelon princess: A scenario of their isolation and activity. Eurasian Chemical Communications. 2022;4(7):657–72.
152. Mustafa YF. Combretastatin A4-based coumarins: synthesis, anticancer, oxidative stress-relieving, anti-inflammatory, biosafety, and in silico analysis. Chemical Papers. 2024;78:3705–3720.
153. Bloh A hameed, Khamis MF, Altekrety AAA, Mustafa YF, Almashhadani HA, Kadhim MM. Total Oxidants, Lipid Peroxidation and Antioxidant Capacity in the Serum of Rheumatoid Arthritis Patients. Journal of Pharmaceutical Negative Results. 2022;13(3):231–5.
154. Mustafa YF. 3-mercaptocoumarins as potential bioactive candidates: From novel synthesis to comparative analysis. Journal of Molecular Structure. 2025;1320:139657.
155. Mustafa YF, Abdulaziz NT. Biological potentials of hymecromone-based derivatives: A systematic review. Systematic Reviews in Pharmacy. 2020;11(11):438–52.
156. Khalil RR, Mohammed ET, Mustafa YF. Evaluation of in vitro antioxidant and antidiabetic properties of Cydonia Oblonga seeds' extracts. Journal of Medicinal and Chemical Sciences. 2022;5(6):1048–58.
157. Oglah MK, Mustafa YF. Synthesis, antioxidant, and preliminary antitumor activities of new curcumin analogues. Journal of Global Pharma Technology. 2020;12(2):854–62.
158. Yahya MQ, Mustafa YF. Transforming Poisonous Phenol into Biosafe Antimicrobial Coumarins: Synthesis and Evaluation. Russian Journal of Bioorganic Chemistry. 2024;50(4):1595–608.
159. Ban AA, Ibrahim BY, Mustafa YF. The Protective Role of Natural Coumarins Derivatives and Anpro Supplement Against Aflatoxin B1 Pollution in the Quails Coturnix Japonica Diet. Mesopotamia Journal of Agriculture. 2023;51(1):1–13.
160. Jasim MHM, Mustafa YF. Synthesis of Acetaminophen-Based Coumarins as Selective COX-2 Inhibitors: An in vitro-in silico Study. Chemistry & Biodiversity. 2024;21(10):e202401309.
161. Abdulaziz NT, Mohammed ET, Khalil RR, Mustafa YF. Unrevealing the total phenols, total flavonoids, antioxidant, anti-inflammatory, and cytotoxic effects of Garden Cress seed ethanolic extracts. Review of Clinical Pharmacology and Pharmacokinetics - International Edition. 2024;38(2):187–96.
162. Rohmah MK, Salahdin OD, Gupta R, Muzammil K, Qasim MT, Al-qaim ZH, Abbas NF, Jawad MA, Yasin G, Mustafa YF, Heidary A, Abarghouei S. Modulatory role of dietary curcumin and resveratrol on growth performance, serum immunity responses, mucus enzymes activity, antioxidant capacity and serum and mucus biochemicals in the common carp, Cyprinus carpio exposed to abamectin. Fish and Shellfish Immunology. 2022;129:221–30.
163. Khalil RR, Mohammed ET, Mustafa YF. Various promising biological effects of Cranberry extract: A review. Clinical Schizophrenia and Related Psychoses. 2021;15(S6):1–9.
164. Al-Shakarchi W, Abdulaziz NT, Mustafa YF. A review of the chemical, pharmacokinetic, and pharmacological aspects of quercetin. Eurasian Chemical Communications. 2022;4(7):645–56.
165. Mustafa YF, Bashir MK, Oglah MK. Influence of albocarbon-cyclic hybridization on biomedical activities: A review. Journal of Medicinal and Chemical Sciences. 2022;5(4):518–35.
166. Zeki NM, Mustafa YF. Annulated Heterocyclic[g]Coumarin Composites: Synthetic Approaches and Bioactive Profiling. Chemistry and Biodiversity. 2024;21(3):e202301855.
167. El-Haggar R, Al-Wabli RI. Anti-inflammatory screening and molecular modeling of some novel coumarin derivatives. Molecules. 2015;20(4):5374–91.
168. Jayakumar T, CJ H, Yen TL, CW H, Sheu JR, PS B, Huang WC, Hsieh CH, Hsia CH. Activation of Nrf2 by Esculetin mitigates inflammatory responses through suppression of NF-κB signaling Cascade in RAW 264.7 cells. Molecules. 2022;27(16):5143.
169. Dou Y, Tong B, Wei Z, Li Y, Xia Y, Dai Y. Scopoletin suppresses IL-6 production from fibroblast-like synoviocytes of adjuvant arthritis rats induced by IL-1β stimulation. International Immunopharmacology. 2013;17(4):1037–43.
170. Avendaño-Ortiz J, Redondo-Calvo FJ, Lozano-Rodríguez R, Terrón-Arcos V, Bergón-Gutiérrez M, Rodríguez-Jiménez C, Rodríguez JF, del Campo R, Gómez LA, Bejarano-Ramírez N, Pérez-Ortiz JM, López-Collazo E. Thiosulfinate-Enriched Allium sativum Extract Exhibits Differential Effects between Healthy and Sepsis Patients: The Implication of HIF-1α. International Journal of Molecular Sciences. 2023;24(7):6234.
171. Zafar S, Sarfraz I, Rasul A, Shah MA, Sarker SD. Osthole: A multifunctional natural compound with potential anticancer, antioxidant and anti-inflammatory activities. Mini Reviews in Medicinal Chemistry. 2021;21(18):2747–63.
172. Silva VLM, Reis RS, Pais AM, Ferreira T, Oliveira PA, Ferreira R, Cardoso SM, Rad JS, Butnariu M, Costea MA, Grozea I. Dicoumarol : From chemistry to antitumor benefits. Chinese Medicine. 2022;17(1):145.

173. Medicine O, Longevity C. Retracted: Pharmacological properties of bergapten: Mechanistic and therapeutic aspects. Oxidative medicine and cellular longevity. 2022;2022(1):8615242.
174. Ge JW, Deng SJ, Xue ZW, Liu P, Xu Y. Imperatorin inhibits mitogen-activated protein kinase and nuclear factor kappa-B signaling pathways and alleviates neuroinflammation in ischemic stroke. CNS Neuroscience & Therapeutics. 2022;28(1):116–25.
175. Abd-Elhalem SS, Al-Doori MH, Hassen MT. Macrophage Polarization Towards M2 Phenotype by Curcuminoids Through NF-κB Pathway Inhibition in Adjuvant-Induced Arthritis. International Immunopharmacology. 2023;119(2):110231.
176. Lee Y, Hyun CG. Anti-inflammatory effects of psoralen derivatives on RAW264. 7 cells via regulation of the NF-κB and MAPK signaling pathways. International Journal of Molecular Sciences. 2022;23(10):5813.
177. Kurach Ł, Kulczycka-mamona S, Kowalczyk J, Skalicka-wo K, Boguszewska-czubara A, El Sayed N, Osmani M, Iwaniak K, Budzyńska B. Mechanisms of the procognitive effects of xanthotoxin and umbelliferone on LPS-induced amnesia in mice. International Journal of Molecular Sciences. 2021;22(4):1779.
178. Gagliotti Vigil de Mello S V, Frode TS. In vitro and in vivo experimental model-based approaches for investigating anti-inflammatory properties of coumarins. Current Medicinal Chemistry. 2018;25(12):1446–76.
179. Li T, Yang G, Hao Q, Zhang X, Zhang X. Daphnetin ameliorates the expansion of chemically induced hepatocellular carcinoma via reduction of inflammation and oxidative stress. Journal of Oleo Science. 2022;71(4):575–85.
180. Li J, Zhang Z, Qiu J, Huang X. 8-Methoxypsoralen has Anti-inflammatory and Antioxidant Roles in Osteoarthritis Through SIRT1/NF-κB Pathway. Frontiers in Pharmacology. 2021;12(September):1–15.
181. Skalicka-Woźniak K, Orhan IE, Cordell GA, Nabavi SM, Budzyńska B. Implication of coumarins towards central nervous system disorders. Pharmacological Research. 2016;103:188–203.
182. Zhu JJ, Jiang JG. Pharmacological and nutritional effects of natural coumarins and their structure–activity relationships. Molecular nutrition & food research. 2018;62(14):1701073.
183. Karabulut Uzunçakmak S, Halıcı Z, Karakaya S, Kutlu Z, Sağlam YS, Bolat İ, Aydın P, Kılıç CS. Suberosin alleviates sepsis-induced lung injury in A rat model of cecal ligation and puncture. Journal of InvestIgatIve surgery. 2023;36(1):2136802.
184. Thakur A, Singla R, Jaitak V. Coumarins as anticancer agents: A review on synthetic strategies, mechanism of action and SAR studies. Vol. 101, European Journal of Medicinal Chemistry. 2015.
185. Rostom B, Karaky R, Kassab I, Veit\'\ia MSI. Coumarins derivatives and inflammation: Review of their effects on the inflammatory signaling pathways. European Journal of Pharmacology. 2022;922:174867.
186. Zeki NM, Mustafa YF. Coumarin hybrids for targeted therapies: A promising approach for potential drug candidates. Phytochemistry Letters. 2024;60:117–33.
187. Jebir MR, Mustafa YF. Kidney stones: natural remedies and lifestyle modifications to alleviate their burden. International Urology and Nephrology. 2024;56(3):1025–33.
188. Zeki NM, Mustafa YF. Natural linear coumarin-heterocyclic conjugates: A review of their roles in phytotherapy. Fitoterapia. 2024;175:105929.
189. Mahmood AAJ, Mustafa YF, Abdulstaar M. New coumarinic azo-derivatives of metoclopramide and diphenhydramine: Synthesis and in vitro testing for cholinesterase inhibitory effect and protection ability against chlorpyrifos. International Medical Journal Malaysia. 2014;13(1):3–12.
190. Widjaja G, Doewes R iqbal, Rudiansyah M, Sultan MQ, Ansari MJ, Izzat SE, Al Jaber MS, Kzar HH, Mustafa YF, Hammid AT, Turki Jalil A, Aravindhan S. Effect of tomato consumption on inflammatory markers in health and disease status: A systematic review and meta-analysis of clinical trials. Clinical Nutrition ESPEN. 2022;50:93–100.
191. Hussein HK, Aubead NM, Kzar HH, Karim YS, Amin AH, Al-Gazally ME, Ahmed TI, Jawad MA, Hammid AT, Jalil AT, Mustafa YF, Saleh MM, Heydari H. Association of cord blood asprosin concentration with atherogenic lipid profile and anthropometric indices. Diabetology & Metabolic Syndrome. 2022;14(1):74.
192. Mahmudiono T, Jasim SA, Karim YS, Bokov DO, Abdelbasset WK, Akhmedov KS, Yasin G, Thangavelu L, Mustafa YF, Shoukat S, Najm MAA, Amraei M. The effect of flaxseed oil consumtion on blood pressure among patients with metabolic syndrome and related disorders: A systematic review and meta-analysis of randomized clinical trials. Phytotherapy Research. 2022;36(10):3766–73.
193. Al-Shakarchi W, Saber Y, Merkhan M, Mustafa Y. Acute toxicity of coumacines: An in vivo study. Georgian medical news. 2023;(338):126–31.
194. Hjazi A, Sukmana BI, Ali SS, Alsaab HO, Gupta J, Ullah MI, Romero-Parra RM, Alawadi AHR, Alazbjee AAA, Mustafa YF. Functional role of circRNAs in osteogenesis: A review. International Immunopharmacology. 2023;121:110455.

195. Huldani H, Kozlitina IA, Alshahrani M, Daabo HMA, Almalki SG, Oudaha KH, Alawadi AH, Alsalamy A, Joshi SK, Mustafa YF. Exosomes derived from adipose stem cells in combination with hyaluronic acid promote diabetic wound healing. Tissue and Cell. 2023;85:102252.
196. Jasim SF, Mustafa YF. Synthesis and Antidiabetic Assessment of New Coumarin-Disubstituted Benzene Conjugates: An In Silico-In Virto Study. Journal of Medicinal and Chemical Sciences. 2022;5(6):887–99.
197. Tayyib NA, Ramaiah P, Alshahrani SH, Margiana R, Almalki SG, Kareem AK, Zabibah RS, Shbeer AM, Ali SHJ, Mustafa YF. Soluble receptor for advanced glycation end products (sRAGE) is associated with obesity rates: a systematic review and meta-analysis of cross-sectional study. BMC Endocrine Disorders. 2023;23(1):275.
198. Shelash Al-Hawary SI, Abdalkareem Jasim S, M. Kadhim M, Jaafar Saadoon S, Ahmad I, Romero Parra RM, Hasan Hammoodi S, Abulkassim R, M. Hameed N, K. Alkhafaje W, Mustafa YF, Javed Ansari M. Curcumin in the treatment of liver cancer: From mechanisms of action to nanoformulations. Phytotherapy Research. 2023;37(4):1624–39.
199. Waheed SA, Mustafa YF. The in vitro effects of new albocarbon-based coumarins on blood glucose-controlling enzymes. Journal of Medicinal and Chemical Sciences. 2022;5(6):954–67.
200. Turki Jalil A, Alameri AA, Iqbal Doewes R, El-Sehrawy AA, Ahmad I, Ramaiah P, Kadhim MM, Kzar HH, Sivaraman R, Romero-Parra RM, Ansari MJ, Fakri Mustafa Y. Circulating and dietary advanced glycation end products and obesity in an adult population: A paradox of their detrimental effects in obesity. Frontiers in Endocrinology. 2022;13:966590.
201. Mirmazloum I, Slavov AK, Marchev AS. The Untapped Potential of Hairy Root Cultures and Their Multiple Applications. International Journal of Molecular Sciences. 2024;25(23):12682.
202. Kim DJ, Jung MS, Jin HU, Kim MS, An CE. Anti-Melanogenic Effects of Umbelliferone: In Vitro and Clinical Studies. Molecules. 2024;29(23):5571.
203. Mallick SR, Hassan J, Hoque MA, Sultana H, Kayesh E, Ahmed M, Ozaki Y, Al-Hashimi A, Siddiqui MH. Color, proximate composition, bioactive compounds and antinutrient profiling of rose. Scientific Reports. 2024;14(1):21690.
204. Lee YJ, Hyun CG. Mechanistic Insights into the Stimulatory Effect of Melanogenesis of 4-Methylcoumarin Derivatives in B16F10 Melanoma Cells. International Journal of Molecular Sciences. 2024;25(22):12421.
205. Jasim SA, Al-Mosawi RH, Khalikov K, Abdelbasset WK, Ahmad I, Shoukat S, Jawad MA, Hafsan H, Mustafa YF, Norbakhsh M. Dietary quercetin improved growth, body composition, haematology, immunity and resistance to Aeromonas hydrophila infection in common carp (Cyprinus carpio). Aquaculture Research. 2022;53(18):6910–20.
206. Al-Shakarchi W, Saber Y, Merkhan MM, Mustafa YF. Sub Chronic Toxicity Study of Coumacines. Pharmacognosy Journal. 2023;15(1):160–4.
207. Mustafa YF. Synthesis, characterization and preliminary cytotoxic study of sinapic acid and its analogues. Journal of Global Pharma Technology. 2019;11(9):1–10.
208. Mustafa YF, Abdulaziz NT. Hymecromone and its products as cytotoxic candidates for brain cancer : A brief review. NeuroQuantology. 2021;19(7):175–86.
209. Younis MA, Hamid OA, Dhaher R, Saber Y, Al-shakarchi W, Merkhan MM, Mustafa YF. Characterization of the renal safety profiles of coumacines. Pharmakeftiki. 2023;35(4):57–63.
210. Mustafa YF, Khalil RR, Mohammed ET. Antimicrobial activity of aqueous extracts acquired from the seeds of two apples' cultivars. Systematic Reviews in Pharmacy. 2020;11(2):382–7.
211. Mustafa YF, Khalil RR, Mohammed ET. Synthesis and antitumor potential of new 7-halocoumarin-4-acetic acid derivatives. Egyptian Journal of Chemistry. 2021;64(7):3711–6.
212. Mustafa YF, Bashir MK, Oglah MK. Original and innovative advances in the synthetic schemes of coumarin-based derivatives: A review. Systematic Reviews in Pharmacy. 2020;11(6):598–612.
213. Mustafa YF. Synthesis, characterization, and biomedical assessment of novel bisimidazole–coumarin conjugates. Applied Nanoscience (Switzerland). 2023;13(3):1907–18.
214. Mustafa YF, Kasim SM, Al-Dabbagh BM, Al-Shakarchi W. Synthesis, characterization and biological evaluation of new azo-coumarinic derivatives. Applied Nanoscience (Switzerland). 2023;13:1095–1102.
215. Mustafa YF, Najem MA, Tawffiq ZS. Coumarins from Creston apple seeds: Isolation, chemical modification, and cytotoxicity study. Journal of Applied Pharmaceutical Science. 2018;8(8):49–56.