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The therapeutic, physicochemical, and pharmaceutical properties of the active compounds in *Ammi visnaga*: an in silico study

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ABSTRACT

The flowering plant *Ammi visnaga* from the Apiaceae family is rich in secondary metabolites with established traditional benefits and promising therapeutic applications. Notable compounds include γ-pyrones (e.g., khellin and visnagin), coumarins, flavonols, isoflavones, and essential oils. These metabolites exhibit diverse pharmacological effects such as anti-inflammatory, antitumor, antimicrobial, antiviral, anti-diabetic, anticoagulant, antioxidant, and neuroprotective activities. γ-Pyrones are particularly prominent in *A. visnaga* and have been linked to treatments for respiratory and cardiovascular conditions. Flavonols like quercetin, kaempferol, and rhamnetin contribute to its antioxidant and anti-inflammatory profile, while isoflavones like genistein and daidzein possess phytoestrogenic properties, potentially reducing cancer risk and alleviating menopausal symptoms. The essential oils of *A. visnaga* are enriched with bioactive components like linalool and thymol, which provide aromatherapeutic benefits and antimicrobial properties. The study's comprehensive analysis of the physicochemical properties, pharmacokinetics, and pharmacological effects of these metabolites using databases like PubChem and SwissADME highlights their potential for pharmaceutical and cosmeceutical applications. It is an in silico study. The high bioavailability of certain compounds suggests their suitability for oral formulations, and their potential to cross the blood-brain barrier may offer neuropharmacological opportunities. However, the presence of Pgp substrates and CYP inhibitors requires careful consideration to avoid drug interactions. The essential oils' antifungal and antibacterial properties indicate natural alternatives to synthetic treatments. The findings emphasize the importance of further research into the formulation of *A. visnaga*-derived natural medicines and the development of sustainable, economically viable synthesis methods.

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Introduction

Chronic inflammatory diseases are a significant global health issue, encompassing conditions such as arthritis, asthma, inflammatory bowel disease, cardiovascular disease, and cancer. These diseases not only pose substantial health challenges but also place strain on healthcare systems. The development of these diseases is a result of intricate interactions among the immune system, environmental factors, and genetics, leading to persistent inflammation (1). Certain compounds, including visnagolide, khellin, and visnaginol, have been found to have anti-inflammatory and antitumor properties. Aromatic compounds like scopoletin and umbelliferone, as well as polyphenolic compounds such as quercetin, rutin, and apigenin, provide antioxidant and antimicrobial benefits. The quantity and quality of these compounds can vary depending on various factors. Ammi visnaga, a plant containing these beneficial compounds, has been utilized in traditional medicine practices, with modern

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research supporting its effectiveness in treating various ailments (2, 3).

γ-Pyrones and Coumarins

γ-Pyrones are a class of furanochromones prominent in *A. visnaga*. The major γ-pyrone compounds found in this species are khellin and visnagin, known for their pharmacological properties, particularly in treating respiratory and cardiovascular conditions (4). Other notable γ-pyrones include 4-norvisnagin, khellinol, visamminol, ammiol, and khellol, which have also been isolated from the plant's fruits. The presence of these γ-pyrones suggests significant therapeutic potential in these areas (2, 4).

Coumarins

Coumarins, another group of secondary metabolites prevalent in *A. visnaga*, can be further subdivided into pyranocoumarins and furanocoumarins (2). Coumarins show potential in various therapeutic areas such as antimicrobial, antiviral, anti-diabetic, anticoagulant, anti-cancer, antioxidant, and anti-inflammatory activities. They occur naturally in plant tissues, indicating a role in plant defense. Studies have shown that coumarins have anti-cancer properties, inhibit tumor growth, induce cell death, and have antioxidant effects, protecting cells from damage. Coumarins also show promise in diabetes treatment by enhancing insulin secretion and improving glucose metabolism. They exhibit antiviral properties, particularly against HIV, and may help treat neurodegenerative diseases like Alzheimer's and Parkinson's. Coumarins also offer cardiovascular benefits through their antihypertensive and vasodilatory effects. However, their safety profile is complex, with concerns about toxicity and drug interactions (5).

Pyranocoumarins such as visnadin and cis-khellactone-3'-β-d-glucopyranoside have been isolated from the fruits, while furanocoumarins like xanthotoxin, ammoidin, and psoralen are found in smaller quantities. These compounds exhibit various biological activities, including anti-inflammatory, anticoagulant, and phototoxic properties (6).

Flavonols

Flavonols, a subgroup of flavonoids characterized by a 3-hydroxyflavone structure, are found in *A. visnaga*. The major aglycones identified are quercetin, kaempferol, rhamnocitrin, and rhamnetin. Aglycones are the non-sugar parts of glycosides, compounds where a sugar is bound to a non-carbohydrate molecule. The conjugation of these flavonols with glucose or rutinose moieties enhances their bioavailability and stability. Identified flavonol glycosides include quercetin-3-glucoside, kaempferol-3-glucoside, isorhamnetin 3-β-d-glucoside, rhamnetin-3-O-glucoside, isorhamnetin-3-O-glucoside, and quercetin-7,3,3'-O-triglucoside. The presence of these compounds suggests potential health benefits due to the antioxidant and anti-inflammatory properties associated with flavonols (7).

Isoflavonoids

Isoflavonoids are intriguing phytochemicals that resemble estradiol and affect the body in various ways. Their complex metabolism varies across species and individuals, reflecting intricate interactions between nutrients, receptors, and diet's impact on health. Isoflavones like genistein and daidzein have been studied for their potential health benefits, especially concerning hormone-related diseases, due to their interaction with estrogen receptors. Their bioactivity is complicated by different glycoside forms and metabolism by gut microflora (8).

Flavones

Neuroinflammation plays a crucial role in diseases like Alzheimer's, Parkinson's, and multiple sclerosis. Flavones, characterized by a 2-phenylchromen-4-one structure, are found in *A. visnaga*. Identified flavones include apigenin, luteolin, and chrysoeriol, contributing to the plant's pharmacological profile due to various biological activities like antioxidant, anti-inflammatory, and neuroprotective effects (9).

Isoflavones

Isoflavones, another subgroup of flavonoids characterized by a 3-phenylchromen-4-one structure, are rich in *A. visnaga*. Isoflavones like daidzin, genistin, sissotrin, isoformononetin, formononetin, prunetin, biochaninA, coumestrol, daidzein, and 6,7,4'-trihydroxyisoflavone are known for their phytoestrogenic properties, which can mimic estrogen's effects in the body and are linked to preventing menopausal symptoms and reducing cancer risk, especially breast cancer (10). Flavonoids, present in many fruits and vegetables, may help reduce neuroinflammation due to their antioxidant and anti-inflammatory effects. Their unique structure allows them to affect different cellular targets and important signaling pathways. Flavonoids offer neuroprotective benefits by neutralizing free radicals, inhibiting microglial activation, regulating inflammatory genes, and reducing inflammation through various mechanisms. Some can cross the blood-brain barrier, indicating potential for treating neurodegenerative diseases (11).

The essential oils from Ammi visnaga

The essential oils of *Ammi visnaga L*. contain a

variety of bioactive compounds that are useful in industries such as pharmaceuticals, cosmetics, and aromatherapy. The nonterpenoid and monoterpenoid compounds found in the plant's fruits and umbels are particularly important due to their biological activities and therapeutic properties. Key components of these essential oils include isoamyl 2-methylbutyrate, isoamyl isobutyrate, isobutyl-2-methylbutyrate, 2-methylbutyl 2-methylbutyrate, and isoamyl isovalerate, which contribute to the plant's unique aroma (2).

Monoterpenes such as linalool and thymol are also significant in *A. visnaga* oils. Linalool, with its floral scent, is known for its calming effects, making it useful in aromatherapy for influencing mood and emotional health. It is also widely used in perfumes and fragrant products. Thymol, known for its antiseptic and antimicrobial properties, is found in plants like thyme and oregano. Its presence in *A. visnaga* essential oils suggests similar benefits, potentially fighting microbial infections and acting as an antifungal agent (12).

These antifungal properties could provide natural alternatives to synthetic antifungal treatments. The essential oils may also target bacterial strains, enhancing their therapeutic use. In cosmetics, *A. visnaga* essential oils can serve as natural preservatives and effective components in skincare due to their antimicrobial and anti-inflammatory properties. The esters and linalool can offer moisturizing and soothing benefits, which are desirable in skincare. Their antioxidant capabilities can protect the skin from environmental damage. The anti-inflammatory properties of these oils may help in creating natural treatments for skin issues and inflammation-related disorders. Research suggests that the high level of monoterpenes in *A. visnaga* may reduce inflammation by modulating immune responses (13-16).

Sterols and Fatty Acids

β-Sitosterol is a plant-based sterol similar to cholesterol and is mainly found in fruits, vegetables, nuts, and seeds. It is known for lowering cholesterol levels by competing with cholesterol for absorption in the gut. Additionally, it has possible anti-inflammatory, anticancer, and antidiabetic properties. β-Sitosterol-glucoside has a sugar molecule attached to β-sitosterol, which may affect how it is absorbed and used in the body (17).

Fatty acids are key parts of fats and oils and are important for many body functions. Palmitic acid has 16 carbons and is saturated, while palmitoleic acid has one double bond and is monounsaturated. Stearic acid is saturated with 18 carbons. These acids form cell membranes and supply energy (2).

Petroselinic acid, a rare monounsaturated fatty acid, has anti-inflammatory effects and may aid cholesterol management. Linoleic acid, an essential polyunsaturated fatty acid, supports immune function and cell membrane fluidity, while linolenic acid, an omega-3 fatty acid, is crucial for heart and brain health. Arachidic acid, a saturated fatty acid, plays a role in inflammation and cardiovascular signaling. Tetracosanoic acid, a longer-chain saturated fatty acid, is studied for its impact on skin barrier function (Figure 1, 2)(After References) (2).

Methodology for extracting bioactive compounds from Ammi visnaga (L.)

The study by Zineb El Jabboury et al. in 2024 examines how to improve the extraction of phenolic compounds from Ammi visnaga (L.) using a combination of water, methanol, and ethanol. It focuses on the plant's aerial parts, including flowers, leaves, and stems, which are known for their beneficial bioactive compounds. The researchers found that a mixture of 50% ethanol and 50% methanol, with varying amounts of water, was effective for extraction. This combination was successful because the additional water helped dissolve polar phenolic compounds, ultimately enhancing the total phenolic content (TPC) and antioxidant activity. The quaternary mixture yielded positive results, revealing the presence of various bioactive substances such as chlorogenic acid and rutin, thus highlighting the plant's health benefits (18).

In another study conducted by Zineb El Jabboury et al. in 2024, the researchers sought to determine the best solvent for extracting total phenolic content (TPC) from roots. The selected solvents - methanol, water, and ethanol - vary in polarities, which can impact the extraction results. By utilizing a response surface methodology (RSM), they systematically adjusted the solvent proportions to identify the optimal blend for maximizing TPC. The ideal mixture was determined to be 10% methanol, 50% water, and 40% ethanol, striking a balance in polarity necessary to dissolve phenolic compounds and effectively interact with the plant matrix. A. visnaga roots' rich phenolic profile, suggesting their potential in pharmacological applications and as natural antioxidants (19).

Martials and Methods

This is an in silico study. A thorough literature review was conducted to evaluate the medicinal usage of A. visnaga in traditional medicine management. A comprehensive search of databases, including PubMed, ScienceDirect, and Scopus, was performed using relevant keywords related to herbal and traditional medicine. The molecular models of the studied compounds of the A. visnaga plant were obtained from the PubChem database (20). The primary outcomes of these

studies were analyzed, and the physicochemical properties and pharmacokinetics of compounds found in A. visnaga were calculated using the SwissADME online software (21-23). This investigation aimed to clarify the potential of A. visnaga as a therapeutic agent in herbal medicine. Leveraging the database's reliable predictive models and user-friendly interface provided valuable insights into the compound's bioavailability, absorption, distribution, metabolism, and excretion (21-27).

Predicting Physicochemical Properties and Pharmacokinetics

The SwissADME web tool has become a valuable resource for drug development researchers, offering a comprehensive platform for predicting key physicochemical properties and pharmacokinetic parameters. By utilizing user-friendly interfaces and reliable predictive models such as BOILED-Egg and iLOGP, researchers can quickly and accurately forecast critical parameters without the need for extensive computational expertise or specialized software. Our research team has extensively used SwissADME's online software, proving it to be an indispensable asset in the discovery and development of novel therapeutic agents (21-23).

Results

Physicochemical properties of studied compounds

The Fraction Csp3 index value for the compounds Arachidic Acid, Stearic Acid, Beta-Sitosterol, Isoamyl 2-methylbutyrate, Isobutyl isovalerate, Petroselinic acid, Bicyclo[3.1.0]hex-2-ene, 2-methyl-5-(1-methylethyl)-, and α-Pinène is greater than or equal to 0.8.

The compounds with the highest number of hydrogen bond acceptors have between 10-16 hydrogen bond acceptors and include Quercetin-3-O-rutinoside, Kaempferol-3-rutinoside, Isorhamnetin 3-O-β-D-glucoside, Prim-O-glucosylcimifugin, Kaempferol-3-glucoside, Khellinin, Sissotrin, Genistin, and Quercetin 3-sulfate.

The compounds Bicyclo[3.1.0]hex-2-ene, 2-methyl-5-(1-methylethyl)-, α-Pinène, 2-Nonyne, alpha-Terpinene, Limonene, are neither hydrogen bond acceptors nor hydrogen bond donors.

The compounds Quercetin-3-O-rutinoside, Kaempferol-3-rutinoside, Isorhamnetin 3-O-β-D-glucoside, Kaempferol-3-glucoside, and Genistin have the highest number of hydrogen bond donors with 6-10 hydrogen bonds.

The compounds including Quercetin-3-O-rutinoside, Kaempferol-3-rutinoside, Beta-Sitosterol, Pimolin, Isorhamnetin 3-O-β-D-glucoside, Prim-O-glucosylcimifugin, and Sissotrin have the highest molar refractivity values, ranging from 110 to 141.

The compounds Quercetin-3-O-rutinoside, Kaempferol-3-rutinoside, Isorhamnetin 3-O-β-D-glucoside, Kaempferol-3-glucoside, Quercetin 3-sulfate, and Genistin have the highest polar surfaces, ranging from 170 to 269.43 Å2.

The compounds Beta-Sitosterol, Arachidic Acid, Stearic Acid, Petroselinic acid, Citronellyl propionate, Samidin, Dihydrosamidin, Pimolin, and Geranyl acetate have the highest iLOGP values, ranging from 3 to 5.

The compounds Quercetin-3-O-rutinoside, Kaempferol-3-rutinoside, Quercetin 3-sulfate, Kaempferol-3-glucoside, Rhamnocitrin 3-O-sulfate, Quercetin, Kaempferol, 6,7,4'-Trihydroxyisoflavone, Daidzein, Coumestrol, Luteolin, Apigenin, and Khellinin have lower iLOGP values to a lesser extent. Most of the compounds have good solubility in aqueous liquids. The compounds Isophorone and Prim-O-glucosylcimifugin have the highest solubility (Table 1, Figure 3)(After References).

Pharmaceutical Properties of Studied Compounds

Most of the studied compounds have good gastrointestinal absorption, but the glycosylated and sulfated compounds studied have low gastrointestinal drug absorption. The compounds Daidzin, Genistin, Sissotrin, Bicyclo[3.1.0]hex-2-ene, 2-methyl-5-(1-methylethyl)-, α-Pinène, alpha-Terpinene, Limonenecid, and Beta-Sitosterol also have low gastrointestinal absorption.

The dominant compounds in the studied plant are permeable to the blood-brain barrier and can enter the central nervous system. These include Khellin, Visnagin, Khellinol, Khellol, Khellinone, Xanthotoxin, Bergapten, Psoralen, Isoformononetin, Formononetin, Daidzein, Linalool, Isoamyl 2-methylbutyrate, 3-methylbutyrate, Thymol, Citronellol Propionate, Croacine, Geranyl Acetate, Isobutyl Isovalerate, Nerol, Bicyclo[3.1.0]Hex-2-ene, α-Pine, Alpha-Terpinene, Limonene, Pimolin, Cimifugin, Kaempferol-3-rutinoside, Quercetin-3-O-rutinoside, Isorhamnetin 3-O-β-D-glucoside, Genistin, Sissotrin, and Pgp substrate. Compounds like Cimifugin, Khellin, Visnagin, Khellinol, Khellol, Khellinone, Xanthotoxin, Bergapten, Psoralen, Isoformononetin, Formononetin, Daidzein, Thymol, Croacine, Ammiol, Visammiol, Rhamnazin, Quercetin, Lutein, Kategorin, Prunetin, Biochanin A, Coumestrol, 6,7,4'-Trihydroxyisoflavone, Stearic Acid, Petroselinic acid, Quercetin 3-sulfate, and Arachidic Acid can enable the cytochrome enzyme CYP1A2. Compounds like Samidin, Dihydrosamidin, and Khellin inhibit the enzyme CYP2C19. Compounds

like Samidin, Dihydrosamidin, Khellin, Rhamnazin, Chryseriol, Petroselinic acid, Pimolin, α-Pinène, Limonene inhibit the enzyme CYP2C9. Compounds like Rhamnazin, Chryseriol, Khellinol, Isoformononetin, Formononetin, Daidzein, Quercetin, Kaempferol, Apigenin, Luteolin, Prunetin, Biochanin A, Coumestrol, and 6,7,4'-Trihydroxyisoflavone have the ability to inhibit the enzyme CYP2C6. Compounds like Rhamnazin, Chryseriol, Khellinol, Isoformononetin, Formononetin, Daidzein, Quercetin, Kaempferol, Apigenin, Luteolin, Prunetin, Biochanin A, 6,7,4'-Trihydroxyisoflavone, Samidin, Dihydrosamidin, Vihydrosamidinol, Kl, and Sissotrin are CYP3A4 enzyme inhibitors. Compounds like Petroselinic acid, Beta-Sitosterol, Stearic Acid, and Arachidic Acid have the highest skin absorption with a log Kp (cm/s) greater than -2.60. Compounds like Thymol, Nerol, Geranyl acetate, Citronellyl propionate, 2-Nonyne, alpha-Terpinene, α-Pinène, Limonene, and others have a log Kp (cm/s) greater than -5.0. The three compounds Petroselinic acid, Stearic Acid, and Arachidic Acid have the highest bioavailability score with a value of 0.85. For the rest of the compounds, this rate was less than or equal to 0.55 (Table 2, Figure 4)(After References).

Discussions

The study of the physicochemical properties of various compounds from *Ammi visnaga* provides a comprehensive understanding of their potential pharmaceutical applications and formulation considerations. The phytochemical diversity of the plant includes γ-pyrones, coumarins, and flavonols, each with distinct therapeutic properties. The presence of these compounds suggests that the plant may be a valuable source of natural agents for treating respiratory and cardiovascular conditions, as well as possessing antimicrobial, antiviral, anti-cancer, antioxidant, and anti-inflammatory properties (2-17).

The high bioavailability scores of compounds like petroselinic acid, stearic acid, and arachidic acid indicate good oral absorption, which is essential for the development of effective drugs. These compounds can be administered in oral formulations with high likelihood of systemic absorption. Conversely, compounds with lower bioavailability scores, such as khellinol and samidin, may require alternative strategies such as drug delivery systems or chemical modifications to enhance their oral bioavailability (21).

The prediction of the compounds' ability to cross the blood-brain barrier (BBB) is crucial for understanding their neuropharmacological potential. Compounds like khellin, visnagin, and khellinol, which are identified as BBB permeants, may have therapeutic applications in treating central nervous system disorders, provided they are not substrates of P-glycoprotein (Pgp) and do not exhibit significant CYP inhibition. The potential Pgp substrate nature of these compounds could affect their distribution in the brain and interactions with other medications (23).

The inhibitory effects on CYP enzymes by some compounds, such as khellin, visnagin, khellinol, ammiol, and others, are noteworthy. CYP inhibition can lead to changes in drug metabolism and increased susceptibility to drug-drug interactions, which must be carefully evaluated during the development of pharmacological agents. These interactions can either amplify the therapeutic effects or result in adverse outcomes, necessitating careful monitoring and dosage adjustments when these compounds are administered with other medications (18, 20).

Log Kp values, which reflect skin permeability, are particularly relevant for the development of topical preparations. High log Kp values in compounds like petroselinic acid, stearic acid, and arachidic acid indicate their suitability for transdermal drug delivery. This property can be exploited in the formulation of cosmeceuticals and pharmaceuticals requiring localized action, such as anti-inflammatory and antioxidant agents for skin health (21, 23).

Synthetic accessibility scores provide an assessment of the ease with which these compounds can be produced synthetically. Lower scores suggest that these compounds are more readily obtainable from natural sources, which is advantageous for sustainable and economically viable production. This is especially important for compounds that are structurally complex or occur in low concentrations in the plant material (21).

The molecular properties of these compounds, such as the number of hydrogen bond acceptors and donors, fraction Csp3, molar refractivity, topological polar surface area (TPSA), and octanol-water partition coefficient (iLOGP), contribute to their solubility and pharmacokinetic behavior. For

instance, the compounds Quercetin-3-O-rutinoside, Kaempferol-3-rutinoside, Isorhamnetin 3-O-β-D-glucoside, and Kaempferol-3-glucoside have the highest number of hydrogen bond donors, which might influence their solubility and bioavailability. Those with higher TPSA values, such as Quercetin-3-O-rutinoside, Kaempferol-3-rutinoside, Isorhamnetin 3-O-β-D-glucoside, and Kaempferol-3-glucoside, may have higher polarity, affecting their absorption and distribution (21, 22).

The analysis of these physicochemical properties and pharmacokinetic parameters can guide the selection of compounds for specific therapeutic targets and inform the design of suitable drug delivery systems. For instance, compounds with high polarity and hydrogen bond donor/acceptor counts may require formulation strategies that enhance their solubility in non-aqueous vehicles for better absorption, such as the use of cyclodextrins or liposomes (21, 22).

Conclusion

The bioavailability scores indicate that compounds such as stearic acid, petroselinic acid, and arachidic acid have high oral bioavailability, making them valuable for drug development. The high scores of stearic acid and arachidic acid suggest that they are well-suited for oral administration. The presence of γ-pyrones and flavonols suggests potential effectiveness in treating respiratory and cardiovascular issues. Monoterpene constituents found in essential oils, such as linalool and thymol, possess antimicrobial and antifungal properties beneficial for skincare. However, the presence of Pgp substrates and CYP inhibitors necessitates careful consideration in drug development to prevent interactions and enhance outcomes. Data presented in Tables 1 and 2 support further research for drug formulation and natural medicines. Compounds with lower bioavailability scores, like khellinol, may require novel approaches to enhance their bioavailability, while log Kp values indicate potential for skin delivery. Synthetic accessibility scores underscore the importance of sustainable, cost-effective methods for obtaining these bioactive compounds.

Conflict of Interest

The author has no conflicts of interest in this study.

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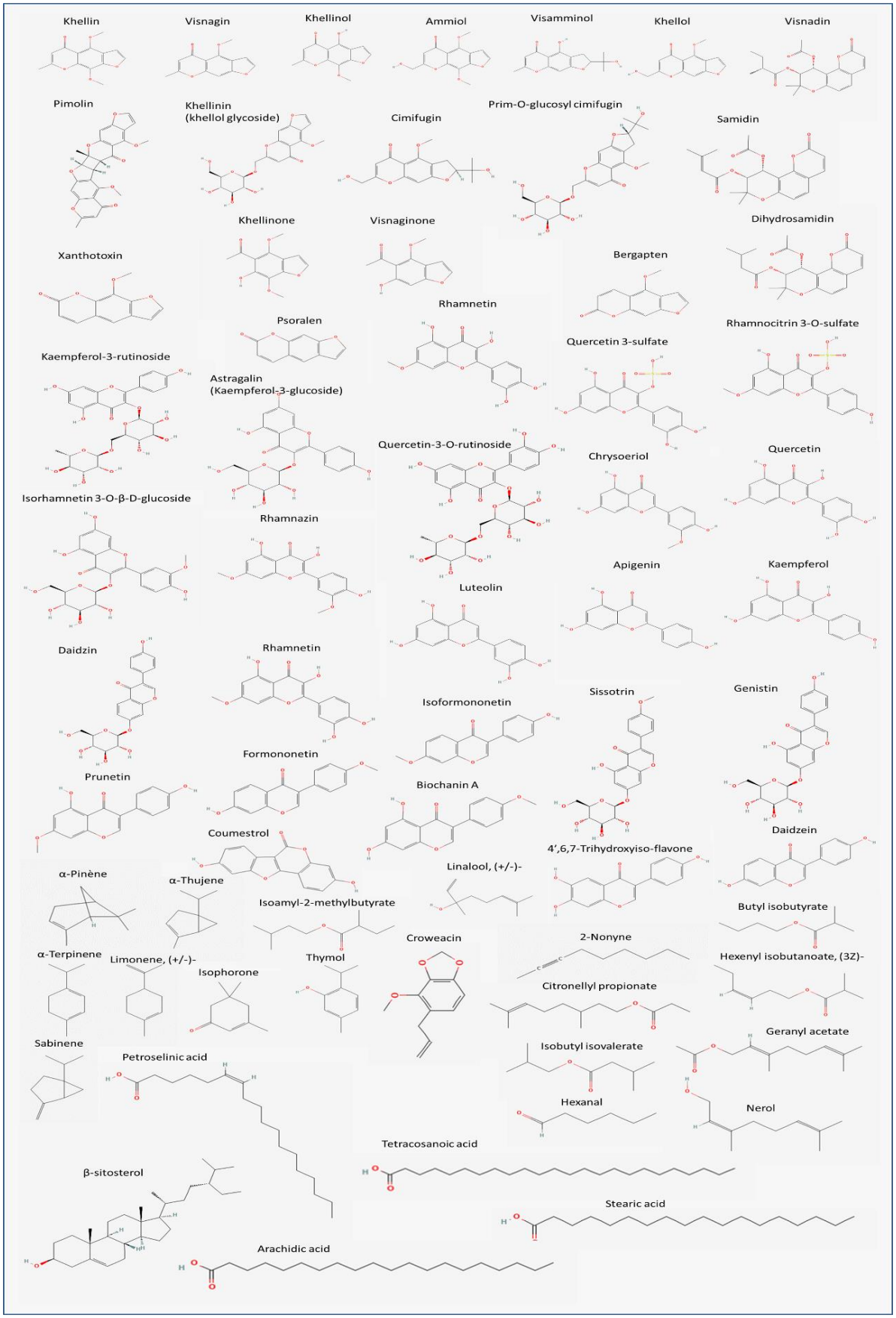

Figure 1. 2-*D structure of bioactive compounds in A. visnaga*

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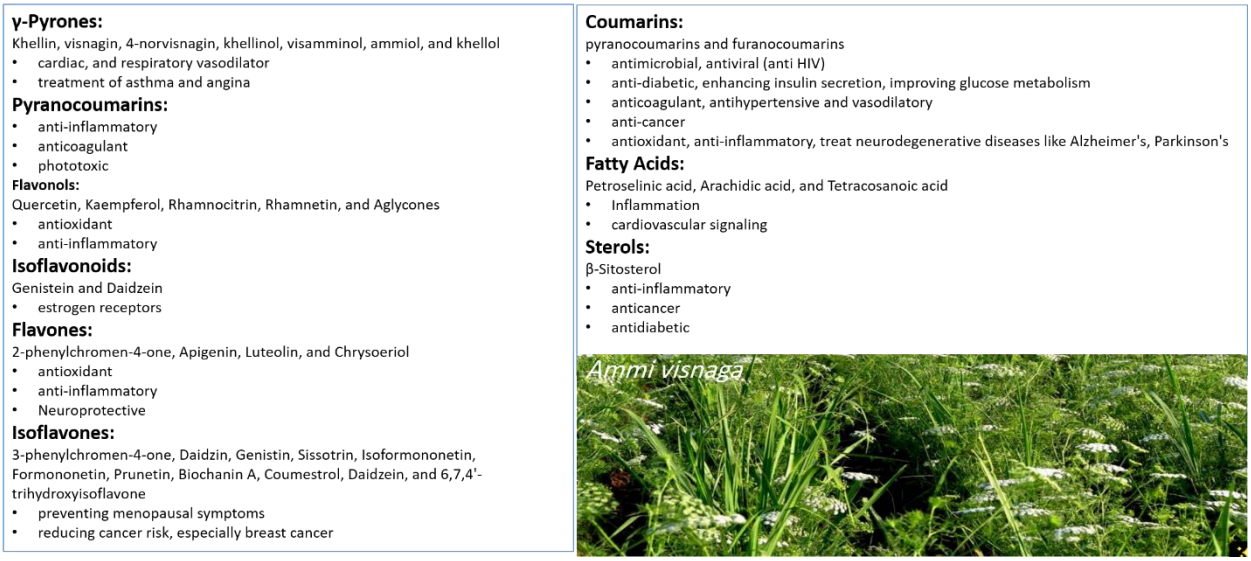

Figure 2. *Therapeutic properties of bioactive compounds found in the plant Ammi visnaga (1).*

Table 1. Pharmaceutical Properties of Studied Compounds.

Molecule	GI absorption	BBB permeant	Pgp substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	log Kp (cm/s)	Bioavailability Score	Synthetic Accessibility
Khellin	High	Yes	No	Yes	No	Yes	No	Yes	-6.28	0.55	3.16
Visnagin	High	Yes	No	Yes	No	No	No	Yes	-6.08	0.55	2.89
Khellinol	High	Yes	No	Yes	No	No	Yes	Yes	-6.03	0.55	2.97
Ammiol	High	No	No	Yes	No	No	No	Yes	-7.27	0.55	3.22
Visammiol	High	No	No	Yes	No	No	No	No	-6.48	0.55	3.63
Khellol	High	Yes	No	Yes	No	No	No	Yes	-7.06	0.55	2.96
Pimolin	High	No	Yes	No	No	Yes	No	Yes	-6.74	0.55	5.16
Khellinin	Low	No	No	No	No	No	No	No	-9.18	0.55	5.13
Cimifugin	High	No	Yes	Yes	No	No	No	No	-7.71	0.55	3.85
Prim-O-glucosylcimifugin	Low	No	No	No	No	No	No	No	-9.83	0.55	5.70
Khellinone	High	Yes	No	Yes	No	No	No	No	-6.21	0.55	2.67
Samidin	High	No	No	No	Yes	Yes	No	Yes	-6.24	0.55	4.56
Dihydrosamidin	High	No	No	No	Yes	Yes	No	Yes	-6.38	0.55	4.58
Xanthotoxin	High	Yes	No	Yes	No	No	No	No	-6.20	0.55	2.97
Bergapten	High	Yes	No	Yes	No	No	No	No	-6.25	0.55	2.90
Psoralen	High	Yes	No	Yes	No	No	No	No	-6.25	0.55	3.06
Kaempferol-3-rutinoside	Low	No	Yes	No	No	No	No	No	-9.91	0.17	6.48
Kaempferol-3-glucoside	Low	No	No	No	No	No	No	No	-8.52	0.17	5.29
Quercetin 3-sulfate	Low	No	No	Yes	No	No	No	No	-7.36	0.11	3.54
Rhamnocitrin 3-O-sulfate	Low	No	No	No	No	No	No	No	-7.02	0.11	3.54
Quercetin-3-O-rutinoside	Low	No	Yes	No	No	No	No	No	-10.26	0.17	6.52
Isorhamnetin 3-O-β-D-glucoside	Low	No	Yes	No	No	No	No	No	-8.73	0.17	5.44
Rhamnazin	High	No	No	Yes	No	Yes	Yes	Yes	-6.76	0.55	3.41
Quercetin	High	No	No	Yes	No	No	Yes	Yes	-7.05	0.55	3.23
Kaempferol	High	No	No	Yes	No	No	Yes	Yes	-6.70	0.55	3.14
Apigenin	High	No	No	Yes	No	No	Yes	Yes	-5.80	0.55	2.96
Luteolin	High	No	No	Yes	No	No	Yes	Yes	-6.25	0.55	3.02
Chryseriol	High	No	No	Yes	No	Yes	Yes	Yes	-5.93	0.55	3.06
Daidzin	Low	No	No	No	No	No	No	No	-8.36	0.55	5.01
Genistin	Low	No	Yes	No	No	No	No	No	-8.33	0.55	5.12

Sissotrin	Low	No	Yes	No	No	No	No	Yes	-8.18	0.55	5.23
Isoformononetin	High	Yes	No	Yes	No	No	Yes	Yes	-5.95	0.55	2.86
Formononetin	High	Yes	No	Yes	No	No	Yes	Yes	-5.95	0.55	2.81
Prunetin	High	No	No	Yes	No	No	Yes	Yes	-5.91	0.55	2.96
Biochanin A	High	No	No	Yes	No	No	Yes	Yes	-5.91	0.55	2.89
Coumestrol	High	No	No	Yes	No	No	Yes	No	-5.98	0.55	3.16
Daidzein	High	Yes	No	Yes	No	No	Yes	Yes	-6.10	0.55	2.79
6,7,4'-Trihydroxyisoflavone	High	No	No	Yes	No	No	Yes	Yes	-6.45	0.55	2.86
Linalool, (+_-)-	High	Yes	No	No	No	No	No	No	-5.13	0.55	2.74
Isoamyl 2-methylbutyrate	High	Yes	No	No	No	No	No	No	-5.08	0.55	2.08
ALPHA-THUJENE	Low	Yes	No	No	No	No	No	No	-5.11	0.55	3.99
(Bicyclo[3.1.0]hex-2-ene)											
α-Pinène	Low	Yes	No	No	No	Yes	No	No	-3.95	0.55	4.44
alpha-Terpinene	Low	Yes	No	No	No	No	No	No	-4.11	0.55	3.63
Limonene, (+_-)-	Low	Yes	No	No	No	Yes	No	No	-3.89	0.55	3.46
Isophorone	High	Yes	No	No	No	No	No	No	-5.94	0.55	2.67
2-Nonyne	Low	Yes	No	No	No	No	No	No	-4.20	0.55	3.80
Hexenyl isobutanoate, (3Z)-	High	Yes	No	No	No	No	No	No	-5.26	0.55	2.39
Thymol	High	Yes	No	Yes	No	No	No	No	-4.87	0.55	1.00
Citronellyl propionate	High	Yes	No	No	No	No	No	No	-4.58	0.55	2.84
Croweacin	High	Yes	No	Yes	No	No	No	No	-5.50	0.55	2.42
Geranyl acetate	High	Yes	No	No	No	No	No	No	-4.63	0.55	2.72
Isobutyl isovalerate	High	Yes	No	No	No	No	No	No	-5.34	0.55	1.53
Nerol	High	Yes	No	No	No	No	No	No	-4.71	0.55	2.58
Stearic Acid	High	No	No	Yes	No	No	No	No	-2.19	0.85	2.54
Petroselinic acid	High	No	No	Yes	No	Yes	No	No	-2.60	0.85	3.07
Arachidic Acid	Low	No	No	Yes	No	No	No	No	-1.61	0.85	2.77
Beta-Sitosterol	Low	No	No	No	No	No	No	No	-2.20	0.55	6.30

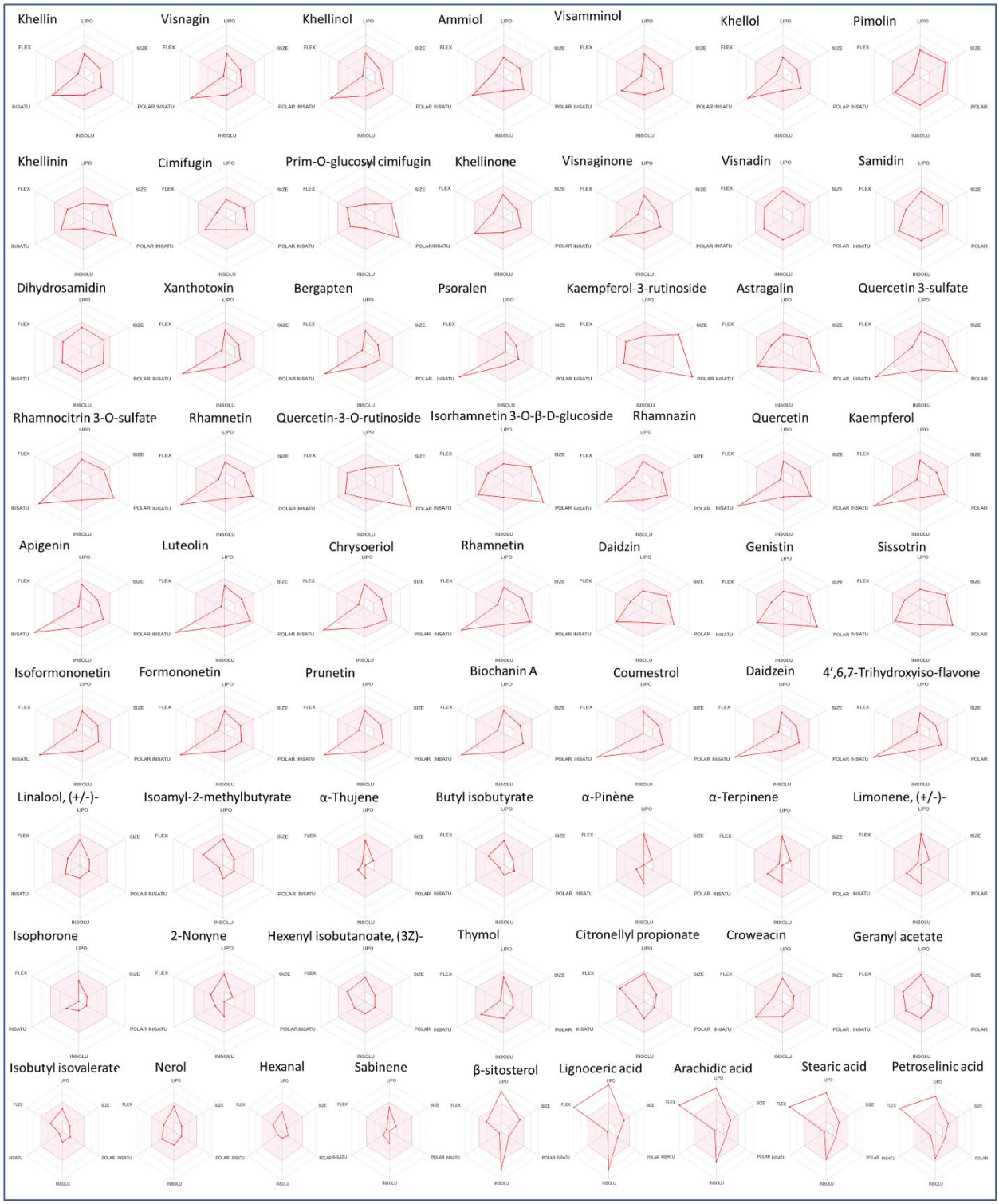

Figure 3. *Radar scale of physicochemical and bioavailability of bioactive compounds in A. visnaga*

Table 2. Pharmaceutical Properties of Studied Compounds.

Pimolin	Khellol	Visammiol	Ammiol	Khellinol	Visnagin	Khellin	Molecule
C26H20O8	C13H10O5	C15H16O5	C14H12O6	C13H10O5	C13H10O4	C14H12O5	**Formula**
460.43	246.22	276.28	276.24	246.22	230.22	260.24	**MW**
34	18	20	20	18	17	19	**Heavy atoms**
19	13	10	13	13	13	13	**Aromatic heavy atoms**
0.31	0.15	0.40	0.21	0.15	0.15	0.21	**Fraction Csp3**
2	2	1	3	1	1	2	**Rotatable bonds**
8	5	5	6	5	4	5	**H-bond acceptors**
0	1	2	1	1	0	0	**H-bond donors**
121.18	64.88	74.44	71.37	65.74	63.71	70.21	**Molar Refractivity (MR)**
97.34	72.81	79.90	82.04	72.81	52.58	61.81	**Topological Polar Surface Area (TPSA)**
3.29	2.18	2.73	2.47	2.59	2.44	2.63	**iLOGP**
3.36	1.53	2.00	1.53	2.11	2.32	2.29	**Consensus Log P**
-5.08	-2.42	-3.19	-2.47	-3.40	-3.21	-3.25	**ESOL Log S**
3.83e-03	9.27e-01	1.77e-01	9.32e-01	9.72e-02	1.42e-01	1.46e-01	**ESOL Solubility (mg/ml)**
Moderately soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	**ESOL Class**

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Kaempferol-3-glucoside	Kaempferol-3-rutinoside	Psoralen	Bergapten	Xanthotoxin	Dihydrosamidin	Samidin	Khellinone	Prim-O-glucosylcimifugin	Cimifugin	Khellinin
C21H20O11	C27H30O15	C11H6O3	C12H8O4	C12H8O4	C21H24O7	C21H22O7	C12H12O5	C22H28O11	C16H18O6	C19H20O10
448.38	594.52	186.16	216.19	216.19	388.41	386.40	236.22	468.45	306.31	408.36
32	42	14	16	16	28	28	17	33	22	29
16	16	13	13	13	10	10	9	10	10	13
0.29	0.44	0.00	0.08	0.08	0.48	0.38	0.25	0.59	0.44	0.42
4	6	0	1	1	6	5	3	6	3	5
11	15	3	4	4	7	7	5	11	6	10
7	9	0	0	0	0	0	1	5	2	4
108.13	139.36	52.26	58.75	58.75	102.51	102.03	61.42	112.45	80.07	97.26
190.28	249.20	43.35	52.58	52.58	92.04	92.04	68.90	168.28	89.13	151.96
1.29	0.79	2.01	2.29	2.22	3.42	3.49	2.22	2.32	2.59	1.96
-0.09	-1.13	2.12	2.16	2.16	3.19	3.18	1.80	-0.22	1.42	-0.11
-3.18	-3.42	-2.73	-2.93	-2.98	-4.15	-4.31	-2.85	-1.97	-2.28	-2.03
2.97e-01	2.24e-01	3.44e-01	2.53e-01	2.29e-01	2.78e-02	1.88e-02	3.32e-01	4.97e+00	1.60e+00	3.84e+00
Soluble	Soluble	Soluble	Soluble	Soluble	Moderately soluble	Moderately soluble	Soluble	Very soluble	Soluble	Soluble

Daidzin	Chryseriol	Luteolin	Apigenin	Kaempferol	Quercetin	Rhamnazin	Isorhamnetin 3-O-β-D-glucoside	Quercetin-3-O-rutinoside	Rhamnocitrin 3-O-sulfate	Quercetin 3-sulfate
C21H20O9	C16H12O6	C15H10O6	C15H10O5	C15H10O6	C15H10O7	C17H14O7	C22H22O12	C27H30O16	C16H12O9S	C15H10O10S
416.38	300.26	286.24	270.24	286.24	302.24	330.29	478.40	610.52	380.33	382.30
30	22	21	20	21	22	24	34	43	26	26
16	16	16	16	16	16	16	16	16	16	16
0.29	0.06	0.00	0.00	0.00	0.00	0.12	0.32	0.44	0.06	0.00
4	2	1	1	1	1	3	5	6	4	3
9	6	6	5	6	7	7	12	16	9	10
5	3	4	3	4	5	3	7	10	3	5
104.09	80.48	76.01	73.99	76.01	78.03	86.97	114.63	141.38	90.68	88.23
149.82	100.13	111.13	90.90	111.13	131.36	109.36	199.51	269.43	151.88	183.11
2.42	2.44	1.86	1.89	1.70	1.63	2.81	2.58	0.46	1.40	0.87
0.63	2.18	1.73	2.11	1.58	1.23	2.02	0.12	-1.51	1.49	0.83
-2.97	-4.06	-3.71	-3.94	-3.31	-3.16	-3.56	-3.26	-3.30	-3.81	-3.60
4.42e-01	2.61e-02	5.63e-02	3.07e-02	1.40e-01	2.11e-01	9.04e-02	2.63e-01	3.08e-01	5.93e-02	9.71e-02
Soluble	Moderately soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble

Isoamyl 2-methylbutyrate	Linalool, (+_-)-(1)	6,7,4'-Trihydroxyisoflavone	Daidzein	Coumestrol	Biochanin A	Prunetin	Formononetin	Isoformononetin	Sissotrin	Genistin
C10H20O2	C10H18O	C15H10O5	C15H10O4	C15H8O5	C16H12O5	C16H12O5	C16H12O4	C16H12O4	C22H22O10	C21H20O10
172.26	154.25	270.24	254.24	268.22	284.26	284.26	268.26	268.26	446.40	432.38
12	11	20	19	20	21	21	20	20	32	31
0	0	16	16	17	16	16	16	16	16	16
0.90	0.60	0.00	0.00	0.00	0.06	0.06	0.06	0.06	0.32	0.29
6	4	1	1	0	2	2	2	2	5	4
2	1	5	4	5	5	5	4	4	10	10
0	1	3	2	2	2	2	1	1	5	6
51.47	50.44	73.99	71.97	73.81	78.46	78.46	76.44	76.44	110.58	106.11
26.30	20.23	90.90	70.67	83.81	79.90	79.90	59.67	59.67	159.05	170.05
3.02	2.70	1.71	1.77	1.80	2.55	2.50	2.49	2.42	3.02	2.44
2.77	2.66	1.89	2.24	2.46	2.44	2.43	2.66	2.65	0.81	0.42
-2.53	-2.40	-3.37	-3.53	-3.87	-3.92	-3.92	-3.73	-3.73	-3.40	-3.18
5.11e-01	6.09e-01	1.15e-01	7.51e-02	3.61e-02	3.43e-02	3.43e-02	5.03e-02	5.03e-02	1.79e-01	2.85e-01
Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Soluble

Geranyl acetate	Croweacin	Citronellyl propionate	Thymol	Hexenyl isobutanoate, (3Z)-	2-Nonyne	Isophorone	Limonene, (+_-)-	alpha-Terpinene	α-Pinène	Bicyclo[3.1.0]hex-2-ene, 2-methyl-5-(1-methylethyl)-
C12H20O2	C11H12O3	C13H24O2	C10H14O	C10H18O2	C9H16	C9H14O	C10H16	C10H16	C10H16	C10H16
196.29	192.21	212.33	150.22	170.25	124.22	138.21	136.23	136.23	136.23	136.23
14	14	15	11	12	9	10	10	10	10	10
0	6	0	6	0	0	0	0	0	0	0
0.58	0.27	0.77	0.40	0.70	0.78	0.67	0.60	0.60	0.80	0.80
6	3	8	1	6	4	0	1	1	0	1
2	3	2	1	2	0	1	0	0	0	0
0	0	0	1	0	0	0	0	0	0	0
60.13	53.10	65.42	48.01	50.99	43.54	42.73	47.12	47.12	45.22	45.22
26.30	27.69	26.30	20.23	26.30	0.00	17.07	0.00	0.00	0.00	0.00
3.27	2.63	3.57	2.32	2.84	2.96	2.09	2.72	2.70	2.63	2.67
3.30	2.45	3.68	2.80	2.64	3.44	2.11	3.37	3.30	3.44	3.15
-3.21	-2.90	-3.30	-3.19	-2.35	-2.88	-1.77	-3.50	-3.30	-3.51	-2.41
1.22e-01	2.41e-01	1.07e-01	9.74e-02	7.68e-01	1.64e-01	2.36e+00	4.33e-02	6.89e-02	4.24e-02	5.25e-01
Soluble	Soluble	Soluble	Soluble	Soluble	Soluble	Very soluble	Soluble	Soluble	Soluble	Soluble

Beta-Sitosterol	Arachidic Acid (1)	Petroselinic acid	Stearic Acid	Nerol	Isobutyl isovalerate
C29H50O	C20H40O2	C18H34O2	C18H36O2	C10H18O	C9H18O2
414.71	312.53	282.46	284.48	154.25	158.24
30	22	20	20	11	11
0	0	0	0	0	0
0.93	0.95	0.83	0.94	0.60	0.89
6	18	15	16	4	5
1	2	2	2	1	2
1	1	1	1	1	0
133.23	100.03	89.94	90.41	50.40	46.66
20.23	37.30	37.30	37.30	20.23	26.30
5.05	4.56	4.16	4.30	2.75	2.83
7.24	6.62	5.68	5.93	2.78	2.41
-7.90	-6.44	-5.41	-5.73	-2.78	-2.20
5.23e-06	1.13e-04	1.09e-03	5.26e-04	2.59e-01	1.00e+00
Poorly soluble	Poorly soluble	Moderately soluble	Moderately soluble	Soluble	Soluble

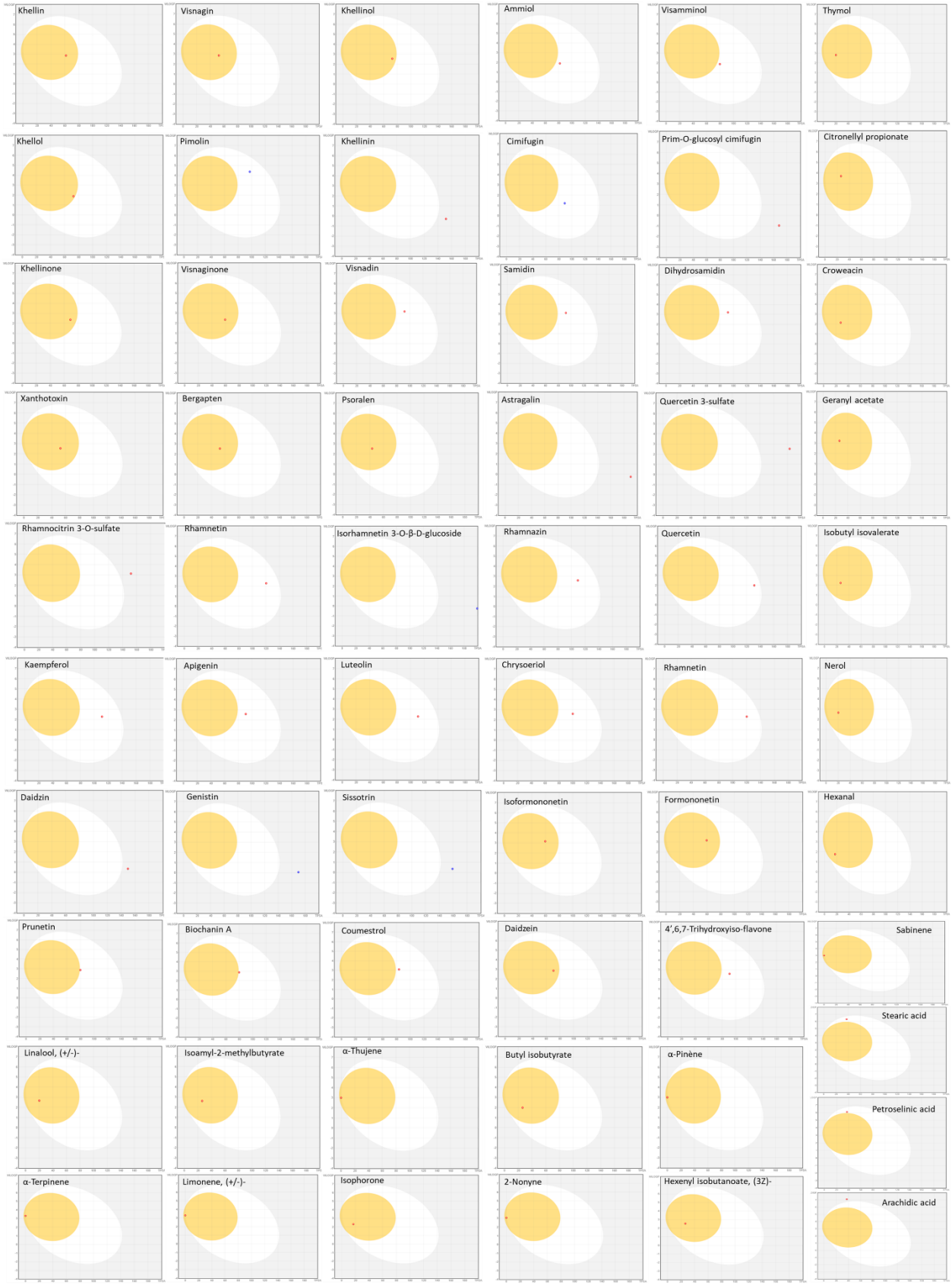

Figure 4. *The egg plot is a visual tool that illustrates how a compound interacts with biological barriers such as the blood-brain barrier (BBB) and the digestive system. The yellow area indicates the compound's capability to cross the BBB, while the white area represents its potential for absorption in the digestive system. Blue dots on the plot signify the compound entering the central nervous system (CNS) through P-glycoproteins, whereas red dots indicate its exit from the CNS, impacting its effectiveness and duration.*