

## Ethnomedicinal, ecological, phytochemical, nutritional and pharmacological aspects of *Sanguisorba officinalis* L. (Rosaceae): A comprehensive review

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### Abstract

The medicinal properties of *Sanguisorba* species have been known since the 16<sup>th</sup> century and have been used in traditional folk medicine ever since. The genus *Sanguisorba* includes approximately 148 species and subspecies and belonging to Rosaceae family distributed mainly in East Asia and southern Europe. The most widespread species in the genus *Sanguisorba* is *Sanguisorba officinalis* L. Currently available *S. officinalis* L. reports in the literature were mostly found on Google Scholar, Pubmed, Web of Science, Lens.org and Scopus. This review provides a detailed and focused analysis of *S. officinalis* L., deliberately centering on its unique properties and existing literature, without drawing comparative analysis with other species within the *Sanguisorba* genus. This article focuses on the taxonomy, habitat, distribution, ethno-medicinal uses, botanical characterization, nutritional composition, chemical composition, pharmacological effects, insect interactions, and conservation status of *S. officinalis*. Moreover, the present work attempts to compile various phytochemical and bioactivity investigations conducted on *S. officinalis*; the resulting data consistently highlight its therapeutic prospects, as evidenced by the wide range of secondary metabolites and biological activities reported. Despite its promising potential, limited clinical data and standardization issues present challenges for its integration into modern medicine. The mechanisms of action, safety profile, and therapeutic efficacy of *S. officinalis* warrant further investigation.

**Keywords:** antioxidant capacity; ethnobotany; flavonoids; interspecific relationships; phytochemistry; *Sanguisorba officinalis* L.; tannins

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## Introduction

The rose family (Rosaceae) comprises 85 genera and over 2000 species (Traian, 1956; Latif, 2004; DeVore and Pigg, 2007; Bunse *et al.*, 2020). The genus *Sanguisorba* belongs to the family Rosaceae, subfamily Rosideae, tribe Sanguisorbae and includes approximately 148 species and subspecies distributed mainly in East Asia and southern Europe (Traian, 1956; Nordborg, 1966; Latif, 2004; Park *et al.*, 2021). *Sanguisorba officinalis* L., is a perennial herbaceous plant which is native to Europe, North Africa, North America and parts of Asia, and it's often found in meadows, pastures and damp grasslands (Bączek, 2014; Liu *et al.*, 2020).

*Sanguisorba* derives its name from the Latin sanguis (blood) and sorbere (absorb), alluring to the syptic properties of some species (Pawlaczyk-Graja *et al.*, 2016). The letter “L” in the name of the plant *S. officinalis* L., comes from Carl Linnaeus, who discovered this plant (Linnaeus, 1753). When analyzing *S. officinalis* L., the name “*officinalis*” is derived from the Latin word “*officina*”, which represents a storage room, a name given to plants with specific medicinal effects (Jang *et al.*, 2018). Dioscorides and Pliny assigned the name *Poterium Sanguisorba*, which comes from the Greek word “*poterion*”, which means cup, referring to the shape of the *Sanguisorba* flowers (Nordborg, 1966; Latif, 2004; Li *et al.*, 2020).

The names given *S. officinalis* varies depending on the language spoken, so it is called “Great burnet” in English, “*Salvastrella maggiore*” in Italian, “*Grosser Wiesenknopf*” in German, “*Krovochlebka*” in Russian, “*Sorbestrea*” in Romanian and “*Pimprenelle officinale*” in French (Shikov *et al.*, 2021; Tocai (Moțoc) 2024).

*S. officinalis* is a plant known for its medicinal properties, exhibits a wide range of pharmacological activities such as anti-inflammatory, astringent, hemostatic, and antimicrobial qualities, in a variety of healing traditions, most notably in Chinese and European herbal medicine (Gan *et al.*, 2010b; Council of Europe, 2010). *Sanguisorba officinalis* has long played a significant role in conventional medicine (Zhang *et al.*, 2012b; Sun *et al.*, 2013; Yasueda *et al.*, 2020). In Traditional Chinese Medicine (TCM), it is referred to as Di Yu and is used to treat gastrointestinal disorders, stop bleeding, and reduce inflammation (Gan *et al.*, 2010a). In European herbalism, it was used for its astringent and wound-healing effects (Council of Europe European Pharmacopoeia 7th). Many of these traditional uses have started to be validated by modern scientific studies, which have shown the plant's potential in pharmacology because of its tannins, flavonoids, and triterpenes content (Nonaka *et al.*, 1982; Sun *et al.*, 2012; Zhu *et al.*, 2019).

The young leaves of *S. officinalis* have a cucumber-like flavor and can be used in salads, soups, and sauces (Tocai *et al.*, 2021; Tocai (Moțoc) *et al.*, 2022). The integration of ecological and conservation perspectives with traditional pharmacological analysis represents a key methodological advancement, thus establishing the novelty and increased scientific scope of this review. This strategic coupling significantly broadens the impact of the analysis by promoting a holistic understanding of the medicinal potential of *S. officinalis* in the essential context of sustainability, biodiversity conservation and resource management, thus transcending purely biomedical or phytochemical considerations.

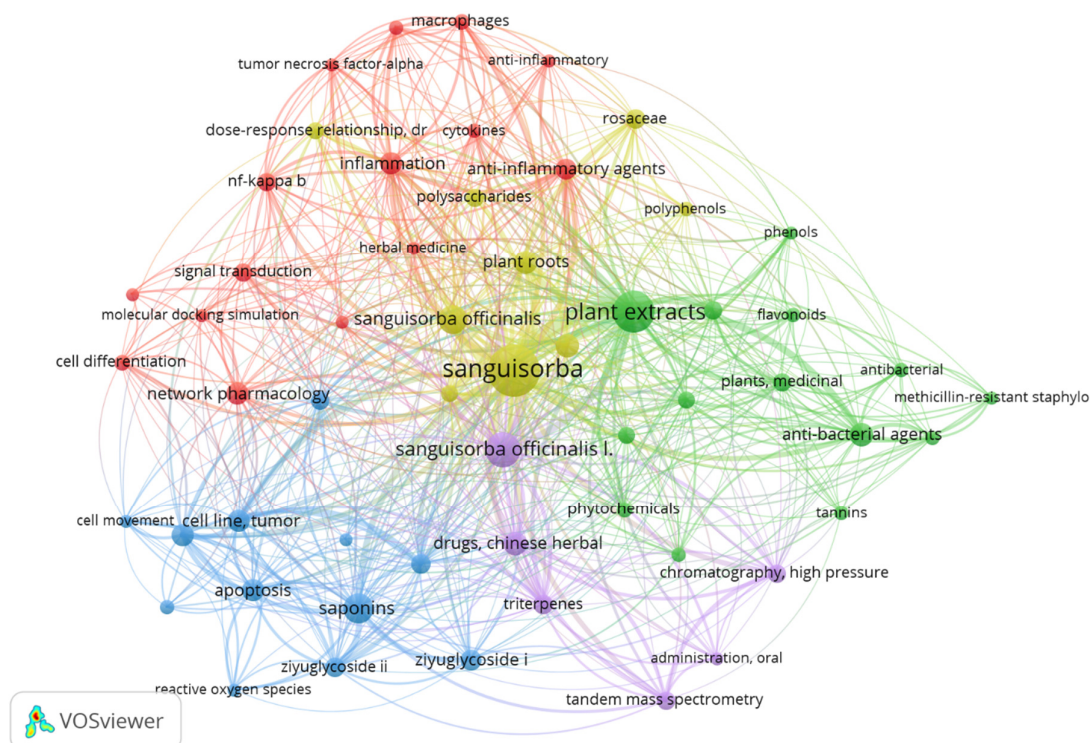
## Research Methodology

### *Bibliometric analysis of the topic in the literature*

Bibliometric data analyses were implemented with the intent to reveal the research environment and thematic movement related to *S. officinalis* and its documented medicinal properties. To create a strong and confirmed foundation for further quantitative evaluation, an extensive amount of scientific literature was gathered from the most reputable, peer-reviewed databases, which are, Scopus, PubMed, and Web of Science. The resulting map (Figure 1), was merged from each of the three sources where the selection criterion was set at five minimum occurrences of a keyword out of 1379 words using the VOSviewer software version 1.6.20.

This requirement was only met by 86 words. From the 638 articles gathered from databases used between 2015-2025 (Pubmed with 156 articles, Scopus with 238 and Web of Science with 244), the greatest attention paid to *S. officinalis* was registered in 2023, with 25.87% of the total results.

Each label is represented by a colored node in the network visualization map (Figure 1).



**Figure 1.** Keyword map of the most common terms

The size of the node depends on how frequently the item is used. The more often an item is used, the larger its label becomes. Beyond this, the thickness of the connecting line and the internode show how frequently the labels occur together. There is a stronger connection between nodes that share the same color. There are 5 clusters created from the keywords on the list. Notably, the map illustrates the links between the 86 keywords that were chosen because they appeared at least five times in the corpus of the literature.

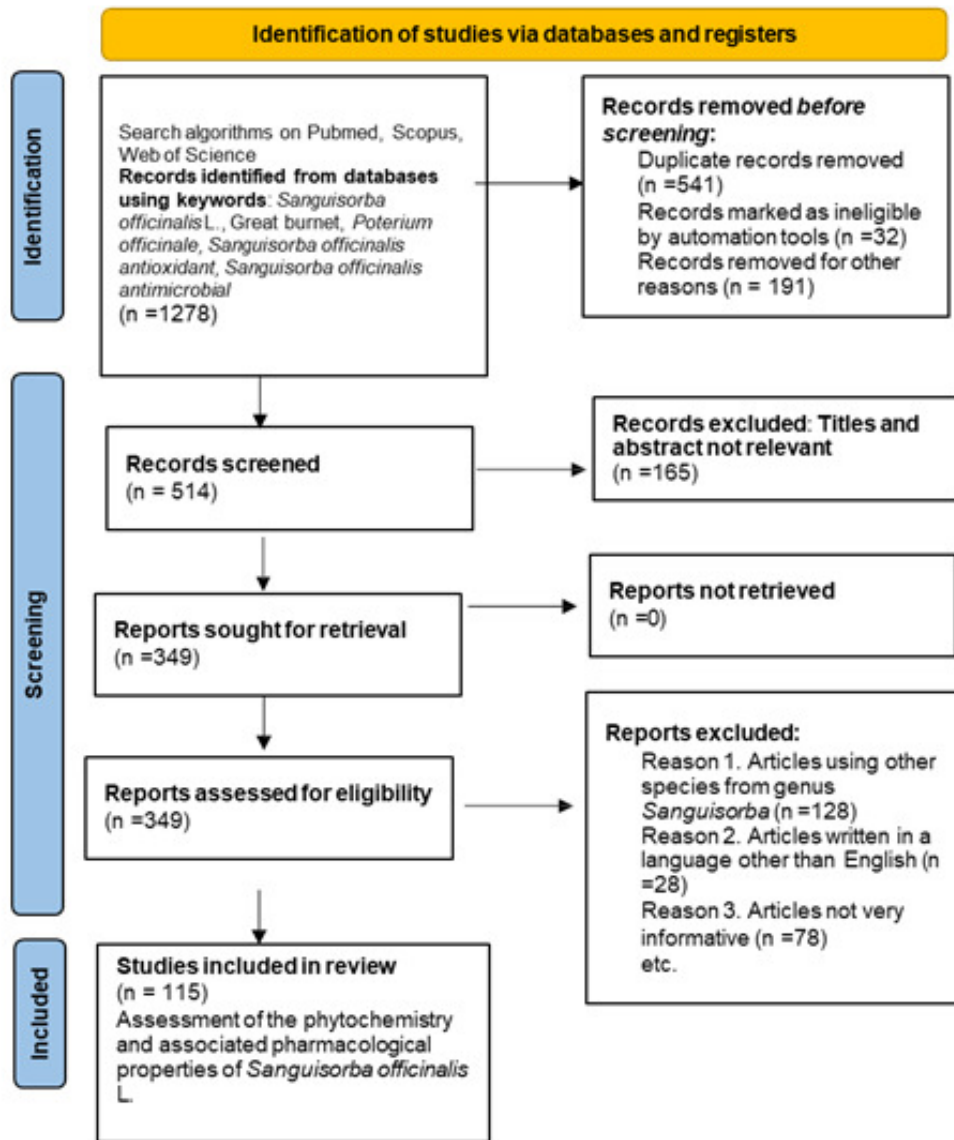
The red one of the clusters identified as a major point of a very densely concentrated scientific investigation. The scientific literature on the anti-inflammatory and immunomodulatory aspects of *S. officinalis* is predominant. From the co-occurrence of the words: inflammation, macrophages, and cytokines that the relief of chronic and acute inflammations has been the most extensively studied issues. A large number of studies elucidating mechanisms is typical, and the special emphasis seems to be on the NF- $\kappa$ B signaling pathway and different signal transduction networks. The second cluster, the green one is focused on plant extracts, antibacterial drugs, and specific chemical classes (flavonoids, phenols), which point to the deep investigation of the antimicrobial activities of *S. officinalis*. Their research is vital for the resolution of the antimicrobial resistance issue, which was a worldwide health crisis, as evidenced by the pinpointing of methicillin-resistant *Staphylococcus* (MRSA). The announcement of tannins and phenolic acids as the foremost bioactive compounds demonstrates that secondary metabolites are decisive for the organisms to have made their therapeutic properties. The blue cluster is focused on the *S. officinalis*'s antineoplastic activity, which is noted using such words as apoptosis, cell line models, tumor activity, and reactive oxygen species (ROS). Studies within this category focus on the pro-apoptotic and anti-tumorigenic activities of *S. officinalis* compounds. The

shared usage to investigate compounds such as Ziyuglycoside I and II suggests focus on a single triterpenoid saponin. The mechanistic focus encompasses the induction of oxidative stress pathways and the modulation of cell signaling to suppress proliferation and inhibit cell movement, positioning *S. officinalis* research at the forefront of natural product oncology. The yellow cluster concentrated not only on the chemical classes like triterpenes, phytochemicals, but the advanced analytical techniques such as chromatography (HPLC), tandem mass spectrometry which indicates that analytical chemistry is of paramount importance in the research lifecycle. The point is very necessary as it is the foundation for standardization of herbal formulations, enabling quality control, and supplying the chemical information that is required to figure out the pharmacokinetics and the mechanism of the *S. officinalis*'s active components. The last cluster, is mainly characterized by the centrality of its vertices, inter-cluster connectivity, and the terms *Sanguisorba*, plant extracts, herbal medicine, and *S. officinalis* in specific. The frequent co-occurrence of these words in numerous thematic clusters such as ethnopharmacology, phytochemistry, and various biomedical applications, reflects the interdisciplinary nature of the research domain of this medicinal plant.

The frequency analysis of keywords provides a clear demarcation between established foundational concepts and emergent methodological trends. As a result, most of the current research are pinpointing the exact molecular targets and complicated biological pathways that originate the therapeutic effects of *S. officinalis* constituents. The bibliometric field discloses a solid and long-standing interest in the inflammatory, antibacterial, and anticancer properties of *S. officinalis*.

The literature search strategy and selection process are summarized in a PRISMA flowchart (Figure 2), which complements the bibliometric analysis (Page *et al.*, 2021). The systematic review embraced 115 research works concerning the phytochemistry and pharmacology of *S. officinalis* and rejected 236 papers mostly because they focused on other species of *Sanguisorba*, or were non-English articles, or did not have enough information (Figure 2).

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only



**Figure 2.** PRISMA flowchart illustrating the identification, screening, eligibility, and inclusion of studies on *S. officinalis*

### Taxonomy, Habitat, and Distribution

The genera *Sanguisorba* L. and *Poterium* L. were first described as separate genera by Linnaeus (1753), but later these two genera were grouped into a single genus under the names *Sanguisorba* (Bertoloni, 1833; Nordborg, 1966) or *Poterium* (Bentham and Hooker, 1865). Since then, the genus has undergone many other taxonomic changes (Eriksson *et al.*, 2015).

Botanists such as Nordborg (1966), Traian (1956) and Ciocârlan (2009) have distinguished the genus *Sanguisorba* including the name *Poterium* (Traian, 1956; Nordborg, 1966; Ciocârlan, 2009).

Nordborg presented a thorough description of *S. officinalis*'s habitat, which includes meadows and shrubby formations, open grassy slopes, woodland borders, bog edges, and stream banks. *S. officinalis* grows on limestone and damp clayey soil, which is frequently combined with gravel (Nordborg, 1966). Nowadays, *S. officinalis* is primarily distributed across temperate regions of the Northern Hemisphere, including parts of Europe, Asia, and North America and thrives in moist, nutrient-rich environments, often found in wetlands, meadows, and along riverbanks (Liu *et al.*, 2020; Park *et al.*, 2021; Tocai (Moşoc) *et al.*, 2022; Tocai (Moşoc), 2024).

*S. officinalis* prefers a moist but well-drained soil, in areas exposed to the sun or partial shade. *S. officinalis* is resistant to both low temperatures in winter and to extreme heat (Karkanis *et al.*, 2014; Zhao *et al.*, 2017; Tocai *et al.*, 2021). The flowering stage ranges from July to September (Nordborg, 1966; Bunse *et al.*, 2021; Park *et al.*, 2021).

WFO (World Flora Online) mentions fourteen subspecies of *S. officinalis*, which are shown in Table 1 (World Flora Online Consortium, <http://www.worldfloraonline.org/organisation/WFO>) (accessed on 13 June 2025) (World Flora Online consortium, 2024).

**Table 1.** The subspecies of *S. officinalis*

| No. | Taxonomic Variations of <i>S. officinalis</i>                                           | References                |
|-----|-----------------------------------------------------------------------------------------|---------------------------|
| 1.  | <i>Sanguisorba officinalis</i> var. <i>altissima</i> Moench ex Steud.                   | WFO Taxon Details (2024a) |
| 2.  | <i>Sanguisorba officinalis</i> var. <i>auriculata</i> (Scop.) Steud.                    | WFO Taxon Details (2024b) |
| 3.  | <i>Sanguisorba officinalis</i> var. <i>carnea</i> (Fisch. ex Link) Regel ex Maxim       | WFO Taxon Details (2024c) |
| 4.  | <i>Sanguisorba officinalis</i> var. <i>glandulosa</i> (Kom.) Vorosch.                   | WFO Taxon Details (2024d) |
| 5.  | <i>Sanguisorba officinalis</i> var. <i>hispanica</i> (Mill.) Willd.                     | WFO Taxon Details (2024e) |
| 6.  | <i>Sanguisorba officinalis</i> var. <i>longa</i> Kitag                                  | WFO Taxon Details (2024f) |
| 7.  | <i>Sanguisorba officinalis</i> var. <i>longifila</i> Bertol.                            | WFO Taxon Details (2024g) |
| 8.  | <i>Sanguisorba officinalis</i> subsp. <i>microcephala</i> (C.Presl) Calder & R.L.Taylor | WFO Taxon Details (2024h) |
| 9.  | <i>Sanguisorba officinalis</i> subsp. <i>montana</i> (Jord. ex Boreau) Grelli           | WFO Taxon Details (2024i) |
| 10. | <i>Sanguisorba officinalis</i> subsp. <i>officinalis</i>                                | WFO Taxon Details (2024j) |
| 11. | <i>Sanguisorba officinalis</i> f. <i>pilosella</i> (Ohwi) H.Hara                        | WFO Taxon Details (2024k) |
| 12. | <i>Sanguisorba officinalis</i> var. <i>polygama</i> (F.Nyl.) Mela & Cajander            | WFO Taxon Details (2024l) |
| 13. | <i>Sanguisorba officinalis</i> var. <i>sabauda</i> (Mill.) Steud.                       | WFO Taxon Details (2024m) |

Nordborg expanded the range of distribution of *S. officinalis* from Europe to Southeast and South Asia, treating it as a species group with up to 24 taxonomic entities that were officially published or named taxa (Nordborg, 1966; Chase *et al.*, 2016).

**Ethno-Medicinal Uses of *S. officinalis***

Historically, *S. officinalis* was widely used in European folk medicine for its astringent and cooling qualities even the name “*Sanguisorba*” literally means “blood absorber” reflecting its use in stopping bleeding (Svitlana *et al.*, 2018; Yasueda *et al.*, 2020; Council of Europe (2010). In Table 2., the uses of the *S. officinalis* in traditional medicine are presented according to geographical area.

**Table 2.** Ethnomedicinal uses of *S. officinalis*

| Species                  | Geographical area                    | Used part         | Application                                                                       | References                                    |
|--------------------------|--------------------------------------|-------------------|-----------------------------------------------------------------------------------|-----------------------------------------------|
| <i>S. officinalis</i> L. | Korea                                | Root              | Regenerate the skin and alleviate inflammation                                    | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
|                          | Korea                                | Whole plant       | Treat hemorrhoids and female diseases                                             | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
|                          | Korea                                | Root              | Treat urticaria, eczema, allergic dermatitis                                      | (Shin <i>et al.</i> , 2002)                   |
|                          | Korea and Japan                      | Leaves            | Used to manage diarrhea. Dysentery, and ulcerative colitis                        | (Jang <i>et al.</i> , 2018)                   |
|                          | China                                | Whole plant       | Hemorrhaging and burns                                                            | (Zhang <i>et al.</i> , 2012b)                 |
|                          | China                                | Root              | Treatment of dermatitis, eczema, incised wounds                                   | (Yokozawa <i>et al.</i> , 2002)               |
|                          | China                                | Root              | Reducing blood toxicity and enhancing immunity of cancer patients                 | (Wang <i>et al.</i> , 2012)                   |
|                          | Germany and other European Countries | Whole plant       | Wound healing and immune modulation                                               | (Melzig 2024; Council of Europe (2010))       |
|                          | Romania                              | Root              | For treating enterocolitis and hemorrhoids                                        | (Tocai (Moțoc) <i>et al.</i> , 2022)          |
|                          | Romania                              | Whole plant       | Sit baths for women with vaginal inflammation. Infections, or postpartum recovery | (Tocai (Moțoc) <i>et al.</i> , 2022)          |
|                          | Poland                               | Roots and rhizome | Treating hemorrhoids and colon cancer                                             | (Mirgos <i>et al.</i> , 2012)                 |
|                          | Russia                               | Root              | Treat stomatitis and gingivitis                                                   | (Egorova <i>et al.</i> , 2018)                |
|                          | Siberia                              | Root              | Used for treating fever. Wounds. And stomach pain                                 | (Shikov <i>et al.</i> , 2021)                 |
| Turkey                   | Whole plant                          | Treat goiter      | (Tuzlacı and Erol, 1999)                                                          |                                               |

In 2024, a book was launched in Romanian entitled "Aspects related to ecology, phytochemical profile, pharmacological actions, culinary applications of the species *Sanguisorba officinalis* L. and *Sanguisorba minor* Scop.", which describes the two species of the genus *Sanguisorba*, including culinary aspects, especially recipes with *S. officinalis* leaves such as: pesto, Caesar salad, tabouleh salad with quinoa or cream cheese with herbs for meat (Tocai (Moțoc), 2024).

These traditional uses highlight the diverse applications of *Sanguisorba officinalis* in herbal medicine.

### Botanical Characterization

A distinguishing feature of the genus *Sanguisorba* is its elongated, imparipinnate leaves and the small, tetrameric or trimerous flowers, which lack petals (Figure 3) (Simpson, 2010; Wang *et al.*, 2020). According to Nordborg's categorization, *S. officinalis* has chromosome number of  $2n = 28,56$  (Nordborg, 1966; Mishima *et al.*, 2002; Park *et al.*, 2021; Tocai (Moşoc) *et al.*, 2022).



**Figure 3.** Macroscopic visualization of *S. officinalis* L. whole plant (A), leaf (B), root (C), and flower with visible nectarines (D) (original images)

*S. officinalis* grows to a height of anything between 20-100 cm and has a basal rosette, which is approximately one foot in diameter (Figure 3A) (Traian, 1956; Im *et al.*, 2017).

*S. officinalis* has compound, pinnate leaves with growth rates up to 10 inches to 15 inches long, with seven to fifteen oval-shaped, jagged leaflets, each up to one to two inches long and a whitish hue underneath (Figure 3B) (Nordborg, 1966; Tocai (Moşoc) *et al.*, 2022; Tocai (Moşoc), 2024). A number of erect stems grow from the middle of the rosette and they produce thick, long-stalked, round to club-shaped tiny red flowers in clusters (Traian, 1956; Tocai (Moşoc) *et al.*, 2022; Tocai (Moşoc), 2024). The root of *Sanguisorba officinalis* is irregularly shaped and slightly curved. Furthermore, it has a thick, brown rhizome that is branched and has grayish-brown or dark brown roots with longitudinal wrinkles (Figure 3C) (Zhang *et al.*, 2005; Sun *et al.*, 2012; Zhang *et al.*, 2012b; Svitlana *et al.*, 2018).

Throughout the Rosaceae family, the floral formula is  $K_{(3-5(-10))}$ ,  $C_{(0-3-5(-10))}$ ,  $A_{(1-10\text{-many})}$ ,  $\hat{G}_{1\text{-many}}$  (Simpson, 2010), but the *Sanguisorba* species has  $K_4C_0A_{2\text{-many}}\hat{G}_{1\text{-many}}$  (Byng 2014), where K means a calyx of 4 petals, in these species the corolla does not exist, and A indicates the number of stamens may be two or more, and  $\hat{G}$  indicates the number of carpels, which can be more than 1 (Tocai (Mořoc) *et al.*, 2023a). Flowers have oval or short-cylindrical heads, about 15-30 mm long, on long erect peduncles, dark brown-red or nearly black-purple, bisexual (Figure 3D)(Kim *et al.*, 2008; Lee *et al.*, 2011; Wang *et al.*, 2020). *S. officinalis* usually has 6-colporate pollen, a feature unique within the Rosaceae family. *S. officinalis* it can be propagated by seeds. The seeds need to be sown in a cold frame either in spring or autumn (Holloway and Matheke, 2003; Lee *et al.*, 2011; Li *et al.*, 2020).

*S. officinalis* blooms in the period July-September, more precisely the flowers bloom from the second half of July to August, and the formation of the fruit begins from September to November (Kim *et al.*, 2008; Yang *et al.*, 2015; Pawlaczyk-Graja *et al.*, 2016; Bunse *et al.*, 2020; Tocai *et al.*, 2021). *S. officinalis* has a scent of cucumber (Im *et al.*, 2017). *S. officinalis* may release allelochemicals that inhibit the germination and growth of competing plant species, thereby shaping community composition (El Amrani, 2023). While *S. officinalis* plays a significant role in its ecosystem, it is essential to consider that invasive species can disrupt these interactions, potentially leading to declines in native biodiversity and altering ecosystem functions (El Amrani, 2023).

*S. officinalis* can be confused with some species, first of all, it can be confused with *S. minor*, but this one only grows up to 15-40 cm tall, has more rounded leaflets and a more rounded flower head (Tocai *et al.*, 2021; Tocai (Mořoc) *et al.*, 2022, 2023a). Another species with which it can be confused is *Pimpinella saxifraga* but is a smaller plant, has very similar lower leaves but very different white flowers (Zhang *et al.*, 2012b; Tocai (Mořoc) *et al.*, 2023a).

### The Nutritional Composition of *S. officinalis*

Beyond their essential function as sources of nutritional intake and caloric energy for human populations, plants furnish a diverse spectrum of extractive resources vital to various industrial, medicinal, and structural applications (Liu *et al.*, 2020). A scheme to classify *S. officinalis* nutrients according to their biochemical properties and physiological function is presented in Table 3.

**Table 3.** Nutritional composition of *S. officinalis*

| Class                  | Compound                         | Roots            | Aerial parts<br>(stems and<br>leaves) | Flower | Seeds | References                                    |
|------------------------|----------------------------------|------------------|---------------------------------------|--------|-------|-----------------------------------------------|
| Organic acid           | Ascorbic acid                    | (0.12 ± 0.005) % | (0.32 ± 0.0001) %                     | n.d.   | n.d.  | (Svitlana <i>et al.</i> , 2018)               |
| Organic acid           | Malic acid                       | n.d.             | n.d.                                  | 18.8   | n.d.  | (Bunse <i>et al.</i> , 2020)                  |
| Organic acid           | Salicylic acid                   | n.d.             | n.d.                                  | 19.6   | n.d.  | (Bunse <i>et al.</i> , 2020)                  |
| Organic acid           | Threonic acid                    | n.d.             | n.d.                                  | 20.8   | n.d.  | (Bunse <i>et al.</i> , 2020)                  |
| Organic acid           | Pelargonic acid                  | n.d.             | n.d.                                  | 15.1   | n.d.  | (Bunse <i>et al.</i> , 2020)                  |
| Unsaturated fatty acid | Dihomo- $\gamma$ -linolenic acid | 18.573           | n.d.                                  | n.d.   | n.d.  | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
| Unsaturated fatty acid | Linolenic acid                   | n.d.             | n.d.                                  | n.d.   | 39%   | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
| Unsaturated fatty acid | Linoleic acid                    | n.d.             | n.d.                                  | n.d.   | 36%   | (Bunse <i>et al.</i> , 2021)                  |
| Unsaturated fatty acid | Oleic acid                       | n.d.             | n.d.                                  | n.d.   | 17%   | (Bunse <i>et al.</i> , 2021)                  |

|                        |                          |                              |                               |      |      |                               |
|------------------------|--------------------------|------------------------------|-------------------------------|------|------|-------------------------------|
| Unsaturated fatty acid | Eicosenoic acid          | n.d.                         | n.d.                          | n.d. | 0.5% | (Bunse <i>et al.</i> , 2021)  |
| Saturated fatty acids  | Palmitic acid            | n.d.                         | n.d.                          | n.d. | 4%   | (Bunse <i>et al.</i> , 2021)  |
| Saturated fatty acids  | Stearic acid             | n.d.                         | n.d.                          | n.d. | 2%   | (Bunse <i>et al.</i> , 2021)  |
| Saturated fatty acids  | Arachidic acid           | n.d.                         | n.d.                          | n.d. | 2%   | (Bunse <i>et al.</i> , 2021)  |
| Sterols                | B-sitosterol             | 30.64 mg·100 g <sup>-1</sup> | 100.40 mg·100 g <sup>-1</sup> | n.d. | n.d. | (Mirgos <i>et al.</i> , 2012) |
| Sterols                | B-sitosterol D-glucoside | 83.54 mg·100 g <sup>-1</sup> | 209.66 mg·100 g <sup>-1</sup> | n.d. | n.d. | (Mirgos <i>et al.</i> , 2012) |
| Sterols                | Campesterol              | 63.38 mg·100 g <sup>-1</sup> | 282.54 mg·100 g <sup>-1</sup> | n.d. | n.d. | (Mirgos <i>et al.</i> , 2012) |
| Sterols                | Brassicasterol           | 0.46 mg·100 g <sup>-1</sup>  | 11.10 mg·100 g <sup>-1</sup>  | n.d. | n.d. | (Mirgos <i>et al.</i> , 2012) |
| Sterols                | Stigmasterol             | 2.34 mg·100 g <sup>-1</sup>  | 8.70 mg·100 g <sup>-1</sup>   | n.d. | n.d. | (Mirgos <i>et al.</i> , 2012) |
| Monosaccharide         | Fructose                 | 17.64%                       | n.d.                          | n.d. | n.d. | (Zhang <i>et al.</i> , 2012a) |
| Monosaccharide         | Glucose                  | 20.16%                       | n.d.                          | n.d. | n.d. | (Zhang <i>et al.</i> , 2012a) |
| Monosaccharide         | Xylose                   | 11.54%                       | n.d.                          | n.d. | n.d. | (Zhang <i>et al.</i> , 2012a) |

n.d.-not detected

*S. officinalis* contains a variety of organic acids, sterols, lipids, sugars and fatty acids, where linolenic acid, linoleic acid and oleic acid were the predominant unsaturated fatty acids.

### Phytochemical Composition of *S. officinalis*

Plants of the genus *Sanguisorba* have a rich phytochemical composition (Zhang *et al.*, 2012a; Szejka *et al.*, 2017; Tocai (Mořoc) *et al.*, 2022). In *S. officinalis* are found a wide range of secondary metabolites belonging to classes such as triterpenoids, flavonoids, tannins and phenolic acids, which are presented in Table 4.

**Table 4.** Content of terpenoids and polyphenolic compounds (mg/g d.w. (dry weight) identified in different organs of *S. officinalis* using data from current literature (2018–2022)

| Compounds                       | Roots         | Leaves        | Flowers       | Aerial parts (leaves and stems) | References                           |
|---------------------------------|---------------|---------------|---------------|---------------------------------|--------------------------------------|
| <b>Triterpenes</b>              |               |               |               |                                 |                                      |
| Sanguisorbin B                  | n.d.          | 300.60 ± 6.01 | 262.53 ± 5.25 | 253.28 ± 5.07                   | (Lachowicz <i>et al.</i> , 2020)     |
| Ziyuglycoside I                 | 47.96 ± 13.39 | n.d.          | n.d.          | n.d.                            | (Shen <i>et al.</i> , 2019)          |
|                                 | 10.99 ± 1.83  | n.d.          | n.d.          | n.d.                            | (Li <i>et al.</i> , 2018)            |
|                                 | 19 ± 1.2      | n.d.          | n.d.          | n.d.                            | (Wu <i>et al.</i> , 2018)            |
|                                 | 9.09 ± 0.58   | n.d.          | n.d.          | n.d.                            | (Fan <i>et al.</i> , 2020)           |
| Ziyuglycoside II                | 10.99 ± 0.99  | n.d.          | n.d.          | n.d.                            | (Li <i>et al.</i> , 2018)            |
| <b>Tannins</b>                  |               |               |               |                                 |                                      |
| 2,3-Hexahydroxydiphenyl-glucose | 15.3 ± 1.27   | 6.95 ± 0.13   | 12.64 ± 0.37  | n.d.                            | (Tocai (Mořoc) <i>et al.</i> , 2022) |
|                                 | 12.33 ± 0.25  | n.d.          | n.d.          | n.d.                            | (Lachowicz <i>et al.</i> , 2020)     |
| Sanguiin H-10                   | 9.01 ± 0.58   | 1.95 ± 0.025  | 8.29 ± 0.045  | n.d.                            | (Tocai (Mořoc) <i>et al.</i> , 2022) |
|                                 | n.d.          | 5.33 ± 0.11   | 130.92 ± 2.62 | 4.14 ± 0.08                     | (Lachowicz <i>et al.</i> , 2020)     |
| Punicalagin gallate             | 3.76 ± 0.025  | 9.23 ± 0.161  | 11.13 ± 0.087 | n.d.                            | (Tocai (Mořoc) <i>et al.</i> , 2022) |
| Sanguiin H-1                    | 7.69 ± 0.043  | 8.27 ± 0.015  | 19.67 ± 0.035 | n.d.                            | (Tocai (Mořoc) <i>et al.</i> , 2022) |
|                                 | 2.95 ± 0.06   | 1.01 ± 0.02   | n.d.          | 0.15 ± 0.01                     | (Lachowicz <i>et al.</i> , 2020)     |
| Sanguiin H-4                    | 352.14 ± 7.04 | n.d.          | n.d.          | n.d.                            | (Lachowicz <i>et al.</i> , 2020)     |
| Sanguiin H-6                    | n.d.          | 10.13 ± 0.20  | 2.57 ± 0.05   | 1.22 ± 0.02                     | (Lachowicz <i>et al.</i> , 2020)     |

|                                                    |                |                 |                 |               |                                      |
|----------------------------------------------------|----------------|-----------------|-----------------|---------------|--------------------------------------|
| Sanguiin H-7                                       | 4.42 ± 0.09    | n.d.            | n.d.            | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| Galoyl-bis-hexahydroxydiphenyl-glucoside, isomer 1 | 2.73 ± 0.032   | n.d.            | n.d.            | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | 145.15 ± 2.90  | 8.65 ± 0.17     | 165.31 ± 3.31   | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| Galoyl-bis-hexahydroxydiphenyl-glucoside, isomer 2 | 2.83 ± 0.02    | n.d.            | n.d.            | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
| Ellagic acid hexoside                              | n.d.           | 2.28 ± 0.036    | 3.37 ± 0.02     | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | n.d.           | 7.16 ± 0.14     | 5.76 ± 0.12     | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| Ellagic acid pentoside                             | 0.29 ± 0.041   | n.d.            | 2.60 ± 0.264    | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | 18.07 ± 0.36   | 15.22 ± 0.3     | 14.50 ± 0.29    | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| Pedunculagin                                       | n.d.           | n.d.            | 2.55 ± 0.05     | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| Lambertianin C                                     | 898.98 ± 17.98 | 2232.84 ± 44.66 | 3029.28 ± 60.59 | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| Sanguisorbic acid dilactone                        | n.d.           | 6.61 ± 0.13     | n.d.            | 10.95 ± 0.22  | (Lachowicz <i>et al.</i> , 2020)     |
| Sanguisorbic acid glucoside                        | n.d.           | 109.18 ± 2.18   | n.d.            | 13.43 ± 0.27  | (Lachowicz <i>et al.</i> , 2020)     |
| <b>Flavonoids</b>                                  |                |                 |                 |               |                                      |
| C-type (epi)catechin trimer                        | 10.48 ± 0.045  | n.d.            | n.d.            | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
| Cyanidin-glucoside                                 | n.d.           | n.d.            | 0.49 ± 0.04     | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | n.d.           | n.d.            | 19.56 ± 0.39    | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| B-type (epi)catechin dimer, isomer 1               | 17.23 ± 0.01   | 6.08 ± 0.04     | 5.06 ± 0.037    | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | n.d.           | 33.03 ± 0.66    | 111.05 ± 2.22   | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| Catechin                                           | 20.40 ± 0.045  | 7.43 ± 0.01     | 2.90 ± 0.035    | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | 38.2 ± 0.5     | n.d.            | n.d.            | n.d.          | (Zhang <i>et al.</i> , 2012b)        |
|                                                    | 374.41 ± 7.49  | 160.08 ± 3.20   | 46.77 ± 0.9     | 133.37 ± 2.67 | (Lachowicz <i>et al.</i> , 2020)     |
| Fisetinidol-(4 $\alpha$ -8)-catechin               | 12.3 ± 0.2     | n.d.            | n.d.            | n.d.          | (Zhang <i>et al.</i> , 2012b)        |
| Corilagin                                          | 7.42 ± 0.01    | n.d.            | n.d.            | n.d.          | (Tu <i>et al.</i> , 2021)            |
|                                                    | 29.73 ± 0.59   | n.d.            | n.d.            | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| Cyanidin-malonylglucoside                          | n.d.           | n.d.            | 0.25 ± 0.037    | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | n.d.           | n.d.            | 14.40 ± 0.29    | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| B-type (epi)catechin dimer, isomer 2               | 11.19 ± 0.041  | 2.04 ± 0.035    | 5.76 ± 0.026    | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | n.d.           | 15.04 ± 0.30    | 136.33 ± 2.73   | n.d.          | (Lachowicz <i>et al.</i> , 2020)     |
| Quercetin- galloy-glucoside                        | n.d.           | 2.89 ± 0.03     | 6.21 ± 0.135    | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
| Quercetin-glucoside                                | n.d.           | 18.62 ± 0.051   | 9.26 ± 0.032    | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | n.d.           | 15.00 ± 0.30    | n.d.            | 4.15 ± 0.08   | (Lachowicz <i>et al.</i> , 2020)     |
| Kaempferol-glucuronide                             | n.d.           | 7.62 ± 0.015    | 1.88 ± 0.035    | n.d.          | (Tocai (Moşoc) <i>et al.</i> , 2022) |
|                                                    | n.d.           | 163.18 ± 3.26   | 137.89 ± 2.76   | 65.65 ± 1.31  | (Lachowicz <i>et al.</i> , 2020)     |
| Kaempferol-di-O-rhamnoside                         | n.d.           | 0.59 ± 0.01     | 5.23 ± 0.10     | 0.31 ± 0.01   | (Lachowicz <i>et al.</i> , 2020)     |

|                                             |                  |                   |                    |                   |                                      |
|---------------------------------------------|------------------|-------------------|--------------------|-------------------|--------------------------------------|
| Taxifolin 7-O- $\beta$ -D-glucopyranoside   | 43.41 $\pm$ 0.87 | n.d.              | n.d.               | n.d.              | (Lachowicz <i>et al.</i> , 2020)     |
| Quercetin rhamnosyl-rutinoside              | n.d.             | 3.11 $\pm$ 0.06   | 5.93 $\pm$ 0.12    | 2.54 $\pm$ 0.05   | (Lachowicz <i>et al.</i> , 2020)     |
| Quercetin 3-O-acetylglucoside               | n.d.             | 54.56 $\pm$ 1.09  | 47.89 $\pm$ 0.96   | 26.73 $\pm$ 0.53  | (Lachowicz <i>et al.</i> , 2020)     |
| <b>Phenolic acids</b>                       |                  |                   |                    |                   |                                      |
| 3-Caffeoylquinic acid (Neochlorogenic acid) | 3.06 $\pm$ 0.08  | 1.00 $\pm$ 0.105  | 2.08 $\pm$ 0.068   | n.d.              | (Tocai (Mořoc) <i>et al.</i> , 2022) |
| Caffeic acid-glucoside                      | 8.68 $\pm$ 0.04  | 2.35 $\pm$ 0.04   | 5.36 $\pm$ 0.228   | n.d.              | (Tocai (Mořoc) <i>et al.</i> , 2022) |
| 5-Caffeoylquinic acid (Chlorogenic acid)    | 4.64 $\pm$ 0.025 | 1.57 $\pm$ 0.03   | 2.24 $\pm$ 0.045   | n.d.              | (Tocai (Mořoc) <i>et al.</i> , 2022) |
|                                             | n.d.             | 436.44 $\pm$ 8.73 | 673.42 $\pm$ 13.47 | 129.09 $\pm$ 2.58 | (Lachowicz <i>et al.</i> , 2020)     |
| Caffeoylquinic acid                         | n.d.             | 47.52 $\pm$ 0.95  | 23.07 $\pm$ 0.46   | n.d.              | (Lachowicz <i>et al.</i> , 2020)     |
| p-Coumaroylquinic acid                      | 7.34 $\pm$ 0.025 | 2.75 $\pm$ 0.03   | 3.07 $\pm$ 0.043   | n.d.              | (Tocai (Mořoc) <i>et al.</i> , 2022) |
|                                             | n.d.             | 42.55 $\pm$ 0.85  | 87.17 $\pm$ 1.74   | n.d.              | (Lachowicz <i>et al.</i> , 2020)     |
| Ellagic acid                                | 2.30 $\pm$ 0.026 | n.d.              | n.d.               | n.d.              | (Tocai (Mořoc) <i>et al.</i> , 2022) |
|                                             | 13.49 $\pm$ 0.27 | 26.90 $\pm$ 0.54  | 17.69 $\pm$ 0.35   | n.d.              | (Lachowicz <i>et al.</i> , 2020)     |
| Rosmarinic acid                             | n.d.             | 8.39 $\pm$ 0.17   | n.d.               | 2.98 $\pm$ 0.06   | (Lachowicz <i>et al.</i> , 2020)     |
| 3-Feruloylquinic acid                       | n.d.             | 4.95 $\pm$ 0.10   | 11.46 $\pm$ 0.23   | 3.17 $\pm$ 0.06   | (Lachowicz <i>et al.</i> , 2020)     |
| Disuccinoyl-caffeoylquinic acid             | n.d.             | 89.00 $\pm$ 1.78  | 69.02 $\pm$ 1.38   | 31.51 $\pm$ 0.63  | (Lachowicz <i>et al.</i> , 2020)     |

n.d.-not detected. Data are expressed as mean value  $\pm$  SD (n = 3).

The total phenol content of *S. officinalis* aerial parts, roots, and leaves or flowers is shown in Table 5.

**Table 5.** The content of phytochemicals (polyphenols, flavonoids) in roots, leaves, aerial parts and flowers of *S. officinalis* from recent data in the specialized literature (2013–2024)

| Species                  | Botanical part used          | Type of extract    | Total polyphenols           | Total flavonoids          | References                           |
|--------------------------|------------------------------|--------------------|-----------------------------|---------------------------|--------------------------------------|
| <i>S. officinalis</i> L. | Whole plant                  | Ethanollic Extract | 9.37 $\pm$ 0.22 mg GAE/g    | n.d.                      | (Li <i>et al.</i> , 2013)            |
|                          | Aerial parts (stems+ leaves) | Aqueous Extract    | 0.726 $\pm$ 0.007 mg GAE/mg | 0.143 $\pm$ 0.004 QE/mL   | (Gawron-Gzella <i>et al.</i> , 2016) |
|                          | Roots                        | Extract ethanollic | 76.56 $\pm$ 0.48 mg GAE/mg  | 63.20 $\pm$ 0.66 mg CE/ml | (Byun <i>et al.</i> , 2021)          |

|                              |                     |                                      |                                       |                                               |
|------------------------------|---------------------|--------------------------------------|---------------------------------------|-----------------------------------------------|
| Whole plant                  | Ethanollic Extract  | 75.71 ± 5.64 mg GAE/g                | n.d.                                  | (Gan <i>et al.</i> , 2010a)                   |
| Whole plant                  | Methanol extract    | 92.6 ± 0.4 mg GAE g <sup>-1</sup> DW | 34.73 ± 0.93 mg CE g <sup>-1</sup> DW | (Ginovyian <i>et al.</i> , 2020)              |
| Aerial parts (stems+ leaves) | Aqueous Extract     | 0.35 ± 0.003 mg/mL                   | n.d.                                  | (Byun <i>et al.</i> , 2021)                   |
| Roots                        | Aqueous Extract     | 87.01 ± 2.21 mg GAE/g                | n.d.                                  | (Shen <i>et al.</i> , 2021)                   |
| Roots                        | Ethanollic Extract  | 8.56 mg GAE/mL                       | n.d.                                  | (Tocai <i>et al.</i> , 2021)                  |
| Stems                        | Ethanollic Extract  | 0.59 mg GAE/mL                       | n.d.                                  | (Tocai <i>et al.</i> , 2021)                  |
| Leaves                       | Ethanollic Extract  | 2.79 mg GAE/mL                       | n.d.                                  | (Tocai <i>et al.</i> , 2021)                  |
| Aerial parts (stems+ leaves) | Ethanollic Extract  | 2.1 g GA/L                           | n.d.                                  | (Muzykiewicz-Szymańska <i>et al.</i> , 2024a) |
| Aerial parts (stems+ leaves) | Ethanollic Extract  | 196 ± 3 mg GA/L                      | n.d.                                  | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
| Flowers                      | Ethanollic Extract  | 0.41 mg GAE/mL                       | n.d.                                  | (Tocai <i>et al.</i> , 2021)                  |
| Aerial parts (stems+ leaves) | Methanollic extract | 92.6 ± 0.4 mg GAE/mL                 | 34.73 ± 0.93 mg QE/mL                 | (Ginovyian <i>et al.</i> , 2020)              |

n.d.- not detected; GAE/ gallic acid equivalents; QE- quercetin equivalents; RE- rutin equivalents; CE- catechin equivalents; g GA/L- gallic acid equivalents; DW- dry weight.

## Pharmacology Studies

Research studies have shown that *S. officinalis* has anti-infectious, anti-inflammatory, antitumor, anti-allergic, anti-wrinkle, neurodegenerative, anxiolytic effects (Ban *et al.*, 2008; Musche *et al.*, 2008; Kim *et al.*, 2008; Liu *et al.*, 2016; Wu *et al.*, 2018; Fan *et al.*, 2020).

### Antioxidant capacity

In order to prevent the damaging effects of free radicals on our body cells, antioxidants provide our cells with protection. As a result, studying antioxidant activity is considered important as it can lead to the discovery of therapeutically effective bioactive molecules (Kasote *et al.*, 2015). Therefore, Table 6 presents the latest results regarding the antioxidant effect of *S. officinalis* extracts as evaluated by different methods.

Data from Table 6 indicate that the antioxidant capacity of *S. officinalis* strongly depends on the nature of extraction solvent and the plant part used.

**Table 6.** *In vitro* antioxidant activity of *S. officinalis* from literature searching

| Sample                                                 | Method | Result                         | References                                    |
|--------------------------------------------------------|--------|--------------------------------|-----------------------------------------------|
| Ethanollic extract of <i>S. officinalis</i> L. 47% v/v | DPPH   | 12.9 mmol Trolox/L             | (Muzykiewicz-Szymańska <i>et al.</i> , 2024a) |
|                                                        | FRAP   | 19.4 mmol FeSO <sub>4</sub> /L | (Muzykiewicz-Szymańska <i>et al.</i> , 2024a) |
| Ethanollic extract of <i>S. officinalis</i> L. 96% v/v | DPPH   | 127 ± 2 mg Trolox/L            | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
|                                                        | ABTS   | 128 ± 10                       | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
|                                                        | DPPH   | 186 ± 0 mg Trolox/L            | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |

|                                                           |      |                              |                                               |
|-----------------------------------------------------------|------|------------------------------|-----------------------------------------------|
| Ethanollic extract of <i>S. officinalis</i> L. 70% v/v    | ABTS | 854 ± 1 mg Trolox/L          | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
| Ethanollic extract of <i>S. officinalis</i> L. 40% v/v    | DPPH | 183 ± 0 mg Trolox/L          | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
|                                                           | ABTS | 854 ± 2 mg Trolox/L          | (Muzykiewicz-Szymańska <i>et al.</i> , 2024b) |
| Methanollic extract of <i>S. officinalis</i> leaves       | ABTS | 6.63 ± 0.1 mmol/g            | (Lachowicz <i>et al.</i> , 2020)              |
|                                                           | FRAP | 0.30 ± 0.01 mmol/g           | (Lachowicz <i>et al.</i> , 2020)              |
| Ethanollic extract of <i>S. officinalis</i>               | DPPH | 94.61%                       | (Tocai <i>et al.</i> , 2021)                  |
|                                                           | FRAP | 23.32 µmol TE/g              | (Tocai <i>et al.</i> , 2021)                  |
| Methanollic extract of <i>S. officinalis</i> aerial parts | DPPH | IC <sub>50</sub> =2.95 mg/mL | (Gawron-Gzella <i>et al.</i> , 2016)          |

Substantial differences were observed among ethanollic extracts of varying concentrations. Using the DPPH assay, extracts obtained with 40-70% ethanol showed the highest antioxidant activity, suggesting that solvents of intermediate polarity favor the recovery of active compounds. However, most available studies suggest that the ideal polarity for extracting the maximum amount of antioxidant compounds is in the middle range of ethanol percentages 40% to 70%, because the highest potencies in DPPH were found within this range (Muzykiewicz-Szymańska *et al.*, 2024b). The ABTS assay for methanollic extract of *S. officinalis* leaves was 6.63 ± 0.1 mmol/g while for an ethanollic extract are given in different units (Lachowicz *et al.*, 2020).

The identified studies do not provide the critical step in identifying and quantifying those responsible compounds for antioxidant activity, such as phenolics and flavonoids. This prevents standardization of the extract on a chemical fingerprint, which is necessary for quality control in a therapeutic agent. The efficacy that can be predicted from the *in vitro* assay might not accurately reflect the efficacy *in vivo* due to the fact that parameters such as bioavailability, metabolism, and concentration in the target organ are not observed. Future research must be designed with animal models that demonstrate such antioxidant properties translate into physiologically relevant effects-for example, reduction in markers of oxidative stress or protection against diseases mediated by free radicals.

#### *Antimicrobial effects*

The accumulation of data from several studies has identified *S. officinalis* as a promising plant source of natural antimicrobial agents (Chen *et al.*, 2015; Gawron-Gzella *et al.*, 2016; Su *et al.*, 2019; Shen *et al.*, 2021; Tocai (Mořoc) *et al.*, 2022; Muzykiewicz-Szymańska *et al.*, 2024b). Antimicrobial activity is of wide spectrum, concerns MDR strains, and the investigation of the mechanism of action was documented. The literature is out for the excellent activity of this extract against both Gram-positive and Gram-negative bacteria. Excellent bacteriostatic activity was recorded against key pathogens like *Staphylococcus aureus* (including MRSA), *S. epidermidis*, *Micrococcus luteus*, and *Bacillus subtilis* (Chen *et al.*, 2015; Gawron-Gzella *et al.*, 2016). One particular note is its inhibition of MRSA resistance, positioning *S. officinalis* as a potential adjunct or alternative therapy in the face of escalating *Staphylococcal* antibiotic resistance (Chen *et al.*, 2015). Activity extends to Gram-negative species, including *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa* (Gawron-Gzella *et al.*, 2016; Tocai (Mořoc) *et al.*, 2022; Muzykiewicz-Szymańska *et al.*, 2024b), and *Vibrio vulnificus* (Su *et al.*, 2019). The low MIC values 160 to 320 µg/ml. against *Helicobacter pylori*, including MDR strains (Shen *et al.*, 2021), further indicate the opportunities for this agent in tackling difficult gastrointestinal infections. Such consistency in the results from various extract types (ethanollic, methanollic, water) and plant parts used root, leaves, flowers present evidence of the presence of multiple, potent, and stable bioactive compounds. *S. officinalis* is one of the most sought-after plants in the global search for novel antimicrobials. The existing literature is great testimony to its therapeutic potential. The academic approach now needs to change from documenting *in vitro* activity through more demanded translational research on compound

identification, mechanisms of action, standardization, and preclinical *in vivo* validation to realize its role in combating antibiotic-resistant infections.

#### *Antifungal activity*

Gawron-Gzella *et al.* (2016), studied antifungal activity, which the analyzed extracts (methanol and aqueous) showed moderate activity against *C. albicans* (0.60 mg ml<sup>-1</sup> for both extract). For comparison, nystatin, a positive control antifungal agent, had MIC values ranging from 16 to 32 µg/mL against *C. albicans* (Gawron-Gzella *et al.*, 2016).

#### *Antiviral activity*

Liang *et al.* (2013), demonstrated that the extract of *S. officinalis* (SOE) effectively blocks the entry of both CCR5-tropic and CXCR4-tropic strains of HIV-1 (ADA and HXB2), showing specific antiviral activity against HIV-1 without affecting other viruses such as VSV, SARS-CoV, and influenza. It reported an IC<sub>50</sub> of 1.91 ± 0.16 mg/mL for HIV-1ADA and 3.70 ± 0.53 mg ml<sup>-1</sup> for HIV-1HXB2, meaning how much concentration is needed to stop viral replication by 50% (Liang *et al.*, 2013).

#### *Anti-inflammatory effect*

The cumulative evidence strongly places *S. officinalis* as a polyvalent therapeutic candidate, not only with broad antimicrobial activity but with significant anti-inflammatory and immunomodulatory properties. A key strength of the recent literature has been a shift toward investigating the molecular mechanisms of its bioactivity, in particular about inflammatory pathways. The established antimicrobial activity against critical pathogens, including MRSA and *H. pylori*, is complemented by evidence of potent anti-inflammatory effects. This dual activity is highly desirable, as many serious bacterial infections are exacerbated by an uncontrolled host inflammatory response. Demonstrating that the hot water extract of *S. officinalis* (HSO) potently inhibits ATP-induced NLRP3 inflammasome activation in macrophages (Seo *et al.*, 2018) is truly groundbreaking. The NLRP3 inflammasome is the major part of the innate immune response that has been linked to a nebulous of inflammatory maladies, and, in a thrillingly pivotal way, to the mechanisms of septic shock. Seo *et al.* (2018) report that the suppression by HSO of IL-1β secretion (one of the most important downstream products of NLRP3 activation) along with the beneficial effect in a murine model of septic shock, serve as the strongest evidence that *S. officinalis* can be the source of less cytokine storm in sepsis-induced organ failure. The large P < 0.001 results for IL-1β reduction in the septic model give a robust statistical confidence for this immunomodulatory action. Isolation and study of specific compounds provide important underpinning for the activity seen in the bulk extract, taking the research beyond crude extracts to pharmacological validation (Seo *et al.*, 2018).

The anti-inflammatory efficacy of polyphenols isolated from *Sanguisorbae Radix* namely Quercetin (QC), (+)-Catechin (CC), and Gallic Acid (GA) through the modulation of core cellular signaling pathways was clearly demonstrated by Jang *et al.* (2019). QC, CC, and GA were found to have reduced in a concentration-dependent manner the phosphorylation of NF-κB and IKK which resulted in the blockage of NF-κB pathway activation. NF-κB is a master regulator of proinflammatory genes, including iNOS and COX-2. These compounds similarly to NF-κB inhibition, suppressed iNOS and COX-2 expression that resulted in reduced levels of the inflammatory mediators such as PGE2 (e.g., 38.8% reduction by QC at 50 µg mL<sup>-1</sup>) and TNF-α (21.9%). The simultaneous suppression of the MAPK signaling pathway comprising ERK, p38, and JNK phosphorylation thus providing further evidence for a broad-spectrum regulatory action of the cellular stress and inflammatory response mechanisms. While it is crucial to the recognition of active substances, e.g., QC, CC, and GA, and the ingredients in the HSO ethyl acetate fraction, these works have only partly connected a bridge of a pivotal gap, among which is the connection of the isolated compounds with *in vivo* or

inflammasome-specific effects. An especially rigorous approach to translation, particularly for formulation and safety, is needed. In this connection, the zebra fish embryo toxicity assessment of Quercetin represents a positive step in determining safety margin requirements-the compound was considered safe below 25  $\mu\text{g mL}^{-1}$ . The higher tested concentrations, 50  $\mu\text{g mL}^{-1}$ , induce yolk swelling and melanin loss among the embryos, and at this point it is difficult to determine whether this could translate to *in vivo* mammalian toxicity or teratogenicity (Jang *et al.*, 2019).

The difference in the results obtained with various extracts, including hot water versus ethanolic, and plant parts necessitates the chemical standardization of the final therapeutic product based on the identified active components Quercetin Content (QC), Catechin Content (CC), Gallic Acid (GA), and so on-for further studies. Since systemic infections/inflammation, such as sepsis, demand treatment with the oral route of administration, the oral bioavailability of the active principles needs to be calculated. Quercetin, for example, has very poor oral bioavailability, which may limit the therapeutic efficacy recorded in the septic shock model. This aspect of formulation should be addressed in future studies concerning strategies like liposome/nanoparticle formulations to increase the absorption and targeting of tissues.

#### *Cytotoxic activity on cancer cells*

The basic studies revealed that the cytotoxic effect of *S. officinalis* is mostly through programmed cell death or apoptosis; however, different groups of studies have different mechanistic pathways and components. Wang *et al.* (2012) provided *in vitro* and *in vivo* critical evidence that *S. officinalis* causes apoptosis in a dose-dependent manner. Their research referred to the apoptosis as mitochondrial-dependent, which was supported by the increase of cleaved caspase-9 and BAX, and the release of cytochrome c. Moreover, this team linked the cytotoxicity to the inhibition of angiogenesis as a result of the downregulation of VEGF mRNA levels in breast cancer xenografts (Wang *et al.*, 2012).

Choi *et al.* (2012) focused more narrowly by demonstrating that the methanol extract of *S. officinalis* drastically impedes cell proliferation because of the diminished production of Mcl-1, anti-apoptotic protein-myeloid cell leukemia-1. It is very significant because Mcl-1 is a protein that is often overexpressed in some types of human cancer, thus providing a key molecular target (Choi *et al.*, 2012).

Zhu *et al.* (2016) recognized one active component, Ziyuglycoside I, that through the activation of the extrinsic apoptotic pathway performs its action. Their elaborate work indicated a dose-dependent increase of Fas/APO1 and FasL leading to caspase-8 activation and the following connection of the Fas associated death domain (FADD) protein. This study provided an important link to p53-mediated G2/M arrest, showing a role at multiple points of cytotoxic intervention. Thus, these authors collectively established a multi-pathway model for *S. officinalis* cytotoxicity, showing that the effectiveness of the crude extract derives from its ability to activate both the intrinsic and extrinsic apoptotic cascades concurrently, coupled with targeting anti-apoptotic mechanisms of defense (Zhu *et al.*, 2016).

One highly translational relevant application was done by Liu *et al.* (2016), who showed that a combination of *S. officinalis* root with the conventional chemotherapy agent 5-fluorouracil significantly enhanced cytotoxic effects on colorectal cancer cells lines (Liu *et al.*, 2016). This suggests its possible use as an adjuvant therapy, considering statistical significance exists with respect to reduced cell viability and enhanced apoptosis ( $P < 0.05$ ). Their subsequent study in Liu *et al.* (2018) recommended that the extract, tannins, and saponins suppress the Wnt signaling pathway, one of the most important pathways driving colorectal cancer cells, through a solid mechanistic explanation for such synergy observed with 5-fluorouracil (Liu *et al.*, 2018).

Most importantly, Wang *et al.* (2019) investigated the critical clinical challenge of metastasis. In this article, the Ziyuglycoside II (Ziyu II) mediated inhibitions focused on the metastatic cascade in human triple-negative breast carcinoma MDA-MB-231 cells. They used detailed assays (Western blot, Transwell) to prove that Ziyu II reverses epithelial-mesenchymal transition (EMT), by decreasing the mesenchymal marker

Vimentin and increasing the epithelial marker E-cadherin. These findings are critical for preventing the spread of highly aggressive cancers (Wang *et al.*, 2019).

Chen *et al.* (2017) demonstrated that total saponins from *S. officinalis* enhance hematopoietic recovery in a myelosuppression mouse model. This is a critical counter-effect to the cytotoxic activity, showing that the extract can selectively protect healthy progenitor cells while promoting the death of cancer cells (Chen *et al.*, 2017). This line of research is clinically validated by Xu *et al.* (2022), who refer to the approved use of the Chinese patent medicine “Diyu Shengbai Tablet” (containing *S. officinalis*) to treat leukopenia caused by anti-cancer therapies (Xu *et al.*, 2022). The authors showed that *S. officinalis* is comprised of compounds that are cytotoxic to cancer cells (Ziyuglycosides, tannins) and other compounds (saponins) that are protective to healthy immune/hematopoietic cells. This indicates a surprising and useful therapeutic selectivity, which certainly requires more clinical trials.

#### *Neuroprotective effects*

Nguyen *et al.* (2008), used treatment with *S. officinalis* root (at doses of 10, 30, and 50 mg/ml) significantly reduced H<sub>2</sub>O<sub>2</sub>-induced neuronal death, with MTT absorbance values of 74.9%, 80.3%, and 83.1%, respectively. In a rat model of middle cerebral artery occlusion (MCAO), *S. officinalis* root treatment significantly reduced infarct volume and edema, as well as improved neurological scores compared to the vehicle-treated control group (Nguyen *et al.*, 2008).

#### *Anti-wrinkle*

Tsukahara *et al.* (2001) described that using *S. officinalis* extract inhibits two important molecular promoters of skin aging in human keratinocytes: Inhibition of the production of endothelin-1, a peptide involved in UV-B-induced pigmentation; this places the extract as an active principle with possible use in the management of hyperpigmentation disorders; and inhibition of fibroblast-derived elastase production, which is directly related to wrinkle formation. The early study served to bifurcate the potential of *S. officinalis* into the two most important cosmetic areas—illumination and wrinkle reduction—through the identification of specific enzymes and peptides as targets, thus setting the stage for later focused studies (Tsukahara *et al.*, 2001).

Kim *et al.* (2008) provided the crucial step of translating *in vitro* activity to *in vivo* clinical validation. The authors screened various extracts, finding that *S. officinalis* root extract showed the highest free radical scavenging capacity (IC<sub>50</sub> = 7.4 mg ml<sup>-1</sup>) among the tested plants. They subsequently focused on a specific compound, Ziyuglycoside I. In a clinical trial setting, their test formulation containing Ziyuglycoside I demonstrated a statistically significant improvement in skin roughness ( $\Delta R3 = 0.03 \pm 0.02$ ) compared to the placebo group after 12 weeks ( $p < 0.05$ ). Furthermore, dermatologists’ visual evaluations confirmed a significant anti-wrinkling effect. The authors moved beyond crude extract observation to validate the efficacy of a single, standardized component (Ziyuglycoside I) in a placebo-controlled, statistically robust clinical setting, providing the strongest evidence yet for its use in cosmetic formulations (Kim *et al.*, 2008).

Byun *et al.* (2021) addressed the practical challenge of extract standardization and maximization of activity of *S. officinalis* for commercial production. They methodically investigated different ethanol concentrations, concluding that the 80% ethanol extract of *S. officinalis* yielded the highest content of total polyphenols and flavonoids, and, consequently, the best total antioxidant activity. This study solidified the link between the chemical content and biological effect, showing significant correlation coefficients (0.830 and 0.872) between polyphenol/flavonoid content and antioxidant activity. Critically, all extracts showed better inhibitory activity against both collagenase and elastase than the positive control, with the 80% ethanol extract being the most potent. By defining 80% ethanol as the optimal extraction concentration, the authors offer a

practical method for maximizing the yield of the bioactive compounds responsible for the anti-wrinkle (collagenase/elastase inhibition) and skin-protective (antioxidant) properties (Byun *et al.*, 2021).

All the authors, have provided compelling evidence for the dermatological utility of *S. officinalis*. The progress from the identification of the *in vitro* mechanism by Tsukahara *et al.* (2001), to the successful clinical trial by Kim *et al.* (2008) and finally to the optimization of the extraction by Byun *et al.* (2021) demonstrates a mature and practical research group. The extract from *S. officinalis* functions as a multimodal agent: reducing oxidative stress, inhibiting matrix-degrading enzymes (elastase and collagenase), and suppressing pigmentation signaling (endothelin-1).

#### *Cardiovascular effects*

*Sanguisorbae Radix* extract (SRE) exhibits a vasorelaxant and hypotensive effect through dual mechanisms. SRE relaxed the phenylephrine (PE)-constricted thoracic aortic rings in a concentration-dependent manner. At the lower concentration, the effect was dependent on the endothelium and was predominantly dependent on the NO/cGMP pathway and was not associated with prostaglandins as indomethacin had no effect on the response. In contrast to higher concentrations, 300 and 1000  $\mu\text{g mL}^{-1}$ , SRE showed an endothelium-independent effect by blocking the influx of extra cellular  $\text{Ca}^{2+}$  and inhibited Angiotensin II-induced contraction. Treatment with SRE at 1000  $\text{mg kg}^{-1}$  results in a significant reduction of both systolic and diastolic blood pressure in spontaneously hypertensive rats after 4 and 8 h. Briefly, SRE lowers blood pressure by making the vessels to be dilated which is caused by the increase of NO signaling and then the blockade of calcium channels in the vascular smooth muscle cells. As with all other studies on *S. officinalis*, the active compound(s) responsible for the concentration-dependent effects remain unknown. Isolation and standardization are the next necessary steps to translate these highly promising *in vivo* results into a consistent, clinically viable drug (Jung *et al.*, 2023).

Jin *et al.* (2025) offers robust, multifaceted evidence regarding the vasodilatory mechanism of the n-butanol extract of *S. officinalis* root, which should be critically discussed in the completeness and novelty of the mechanistic pathway identified, the translational potential, and critical gaps remaining between the *in vitro/ex vivo* findings and clinical use. This is highly valued because the study does not only confirm vasodilation but elucidates a complex, multi-targeted molecular pathway; this level of mechanistic detail strengthens the therapeutic relevance of *S. officinalis* for cardiovascular applications. The authors meticulously confirmed the involvement of the canonical endothelium-dependent vasodilation cascade and introduced a novel regulatory component. The abolition of vasorelaxation upon endothelium removal and inhibition by L-NAME (NOS inhibitor) and ODQ (sGC inhibitor) provides conclusive proof of the Nitric Oxide (NO), cyclic GMP (cGMP) pathway being the primary mediator. This confirms the biological relevance of the observed Akt/eNOS phosphorylation and NO production increase in HUVECs. The inhibitory effect of wortmannin (Akt inhibitor) directly places the PI3K-Akt signaling pathway upstream of eNOS activation, confirming the central regulatory mechanism for NO synthesis. The most critical and novel finding is the reliance on Store-Operated  $\text{Ca}^{2+}$  Entry (SOCE) pathways. The study successfully bridges *in vitro* and *ex vivo* findings with preliminary *in vivo* data. The demonstrated reduction in rat systolic blood pressure is a direct indication of antihypertensive potential, translating the vasorelaxation seen in isolated aortas to a systemic effect. While this goes hand in hand—the reduction of heart rate and blood pressure—the same precautions, such as avoiding excessive bradycardia, which could limit its therapeutic window, are necessary. The absence of action on L-type  $\text{Ca}^{2+}$  channels insinuates that BSO possibly offers a safer profile or a different mechanism of action compared to the established  $\text{Ca}^{2+}$  channel blockers and hence may bypass some of the associated side effects. While the study is mechanistically strong, a few gaps have to be filled in for clinical translation. The mechanism is attributed to the crude n-butanol extract (BSO) (Jin *et al.*, 2025). An important next step includes performing bioactivity-guided fractionation to isolate and identify which compounds are responsible for the Akt/eNOS

phosphorylation and modulation of SOCE-saponins, tannins, or flavonoids. Only with a standardized, purified compound can clinical trials proceed. The *in vivo* data are limited to acute effects: reduction in blood pressure and heart rate. Future studies must be directed at investigating long-term efficacy in chronic hypertension models, and critically, assessing toxicity and pharmacokinetics of BSO or its active component.

#### *Other biological activities*

Shin (2010) provided evidence of the utility of *S. officinalis* in an OVA-induced asthma-induced respiratory disease model. *S. officinalis* ethanolic extract was effective at suppressing eosinophilia and total cell counts in the bronchoalveolar lavage fluid (BALF) of asthmatic mice. This directly impacts inflammatory cell recruitment associated with asthma. Importantly, the OVA challenge-generated levels of reactive oxygen species (ROS) were attenuated by the extract of *S. officinalis*. While this was a foundational study in the context of respiratory applications, this is the most preliminary of the three studies, based mainly on cell counts and ROS levels. Lack of detailed molecular signaling analysis was evident in the later studies, that is, induction of specific enzymes or their pathways. The implication of anti-inflammatory impact driven by antioxidant action was strong; the targets at the cellular level remain broad (Shin, 2010).

Zheng *et al.* (2023) gave an in-depth analysis of *S. officinalis* extract in metabolic syndrome using both *in vitro* (3T3-L1 adipocytes) and *in vivo* (high-fat diet (HFD)-obese mice) models. The extract suppressed the HFD-driven body weight gain and white adipose tissue (WAT) weight without food intake suppression. It reduced fat hypertrophy and hepatic steatosis by reducing glucose, lipids, and leptin within the serum. The authors gave deep mechanistic insight into the action via AMPK pathway and thermogenic factors. Increased levels of Adiponectin, AMPK phosphorylation, PPAR $\alpha$ , and UCP-1 expression point toward enhanced energy expenditure and fat oxidation. They have explicitly linked the effect with antioxidant enzymes showing *S. officinalis* increasing SOD1 and SOD2 expression in WAT, which in turn reduced ROS and lipid peroxides and quantified the Quercitrin content of  $10.31 \pm 0.31 \text{ mg g}^{-1}$ , which is one step toward standardization required for clinical application (Zheng *et al.*, 2023).

Nam *et al.* (2023) focused their efforts on one of the most specific and severe complications of metabolic dysfunction: Non-Alcoholic Fatty Liver Disease (NAFLD) and subsequent fibrosis, using the challenging model known as L-amino-acid-defined, high-fat diet (CDAHFD). The *S. officinalis* extract (SOEE) markedly reduced hepatic lipid accumulation and NAFLD activity score (NAS). However, most importantly, they were able to document liver fibrosis inhibition after receiving SOEE, by greatly decreasing Sirius-Red-stained areas and lowering hydroxyproline levels. The authors showed the decrease of hepatic MDA, which is a lipid peroxidation marker, along with an increase in the mRNA expression of anti-oxidative enzymes (catalase (Cat), superoxide dismutase 1 (Sod1), and glutathione peroxidase I (Gpx1)) and represented the upregulation of Cpt1a, relating to an increase in fat oxidation. More precisely, they declared that SOEE significantly lowered mRNA levels of the liver-fibrosis-related genes (collagen type I alpha 1 (Col1a1), collagen type III alpha 1 (Col3a1), and transforming growth factor beta 1 (Tgfb1)). (Nam *et al.*, 2023).

Where both Zheng *et al.* (2023) and Nam *et al.* (2023) link *S. officinalis* to antioxidant protection and metabolic improvement (fat oxidation), the contribution of Nam *et al.* (2023) is the fact that their focus is on fibrosis as an endpoint—a most clinically relevant outcome for long-term NAFLD prognosis. Conversely, Zheng *et al.* (2023) provide superior data on the systemic anti-obesity mechanism (thermogenesis and leptin reduction). The finding by Nam *et al.* (2023) that SOEE did not significantly reduce ALT/AST (liver injury markers) is a critical limitation when compared to the reference drug obeticholic acid (OCA), suggesting that while SOEE successfully prevents steatosis and fibrosis, it may be less effective at reversing acute liver injury. These authors have collectively established that *S. officinalis* is a potent redox regulator whose efficacy extends from the systemic disorder of obesity to organ-specific pathologies like asthma and liver fibrosis. Future research must now connect the specific bioactive components like Quercitrin, quantified by Zheng *et al.* (2023) to the

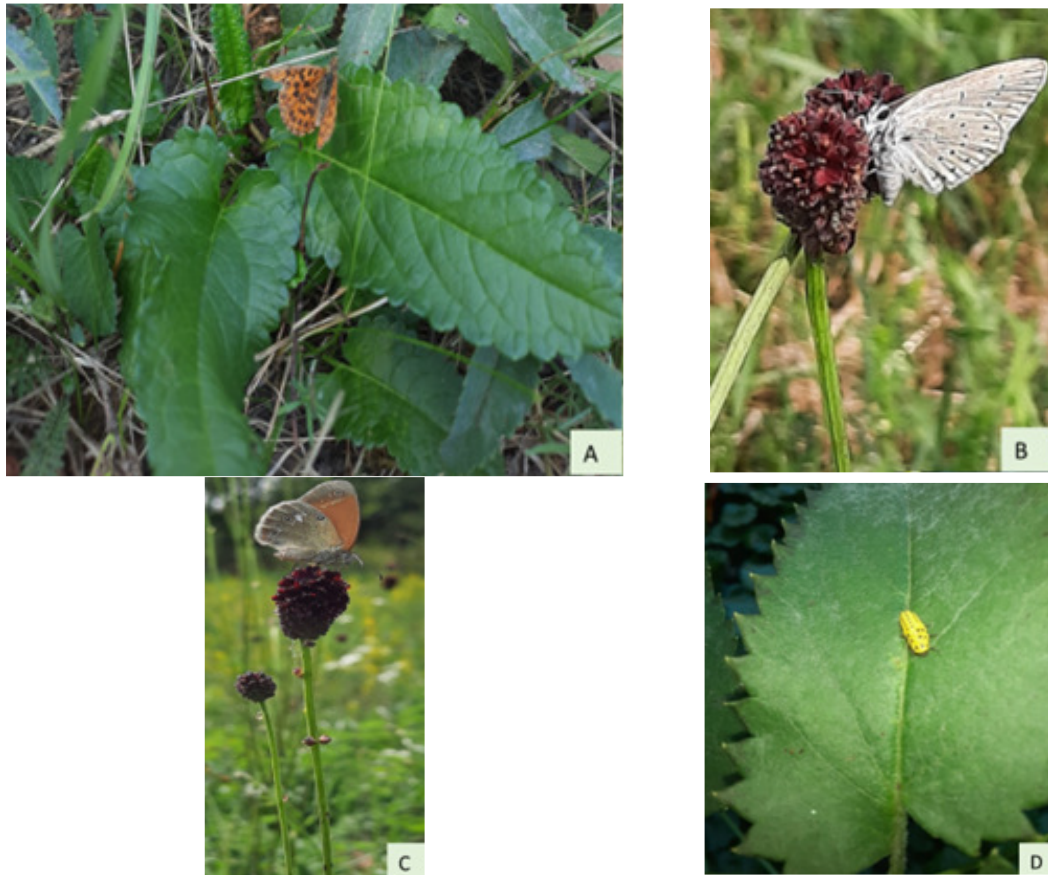
different molecular outcomes (AMPK/UCP-1 activation vs. fibrosis gene suppression) demonstrated by these distinct studies.

### Plant-Insect Relationships

*S. officinalis* is a pollinator because using its flowers, bees, butterflies, and moths transfer pollen from one flower to another, making pollination easier (Tolman and Lewington, 2009; Decourtye *et al.*, 2011; Rákosy and Goia, 2021). It is a host plant for various insects, providing them with nectar and pollen (Tolman and Lewington, 2009; Rákosy and Goia, 2021; Tocai (Mořoc), 2024).

Insects which are attracted to the colourful flowers of *Sanguisorba officinalis* L. that are easily seen from a distance because they are taller than most of the other wildflowers around them (Tolman and Lewington, 2009; Tocai (Mořoc) *et al.*, 2023b; Tocai (Mořoc), 2024).

*Sanguisorba officinalis* is a valuable plant for pollinators, attracting bees and other beneficial insects to gardens and meadows (Figure 4) (Abrahamczyk *et al.*, 2023; Tocai (Mořoc), 2024). *S. officinalis* may benefit from mutualistic relationships with pollinators and seed dispersers, which are crucial for its reproduction and the maintenance of plant diversity in the ecosystem (Abrahamczyk *et al.*, 2023).





**Figure 4.** Insects observed on *S. officinalis*: *Boloria dia* on leaf (A), *Phengaris (Maculinea) teleius* on flower (B), *Coenonympha glycerion* on flower (C), Larva of *Psyllobora vigintiduopunctata* on leaf (D), *Andrena wilkella* on flower (E), and *Phimenes flavopictus* on flower (F) (original images)

*Andrena wilkella* (Figure 4E) and *Phimenes flavopictus* (Figure 4F) belong to the same order *Hymenoptera*, while *Phengaris (Maculinea) teleius* (Figure 4B), *Coenonympha glycerion* (Figure 4C) and *Boloria dia* (Figure 4A) belong to the order *Lepidoptera*, *Psyllobora vigintiduopunctata* (Figure 4D) belongs to the order *Coleoptera* (Tolman and Lewington, 2009; Walters, 2010; Everson, 2014).

Mining bees (*Andrena* spp.) (Figure 4E) are solitary bees that nest in underground tunnels and can be found in the spring. There is great diversity among bee species in their foraging behaviour and flower preferences. For example, male bees and parasitic bees do not collect pollen, but they still visit flowers to collect nectar (Kline *et al.*, 2022).

*Phimenes flavopictus* (Figure 4F) is a solitary insect which lays one to several eggs in a nest. It then provides its young with insects, including caterpillars and beetle larvae (Nguyen *et al.*, 2016).

*Coenonympha glycerion* (Figure 4C) is a widespread species, and is found in sheltered grassy habitats, including subalpine meadows, forest glades and pastures. This butterfly is not included in the Global and National Red Lists, but is listed in the European Red List as Least Concern, as it is not currently a vulnerable or endangered species (Rákósy and Goia, 2021).

*Boloria dia* (Figure 4A) is most often found in shrub-rich meadow habitats or forest glades. This species lays numerous larvae from March to May on *Viola hirta*, feeding during the day or resting hidden in the moss around the plants (Radchuk *et al.*, 2013; Rákósy and Goia, 2021). It was found for the first time in the field resting on *S. officinalis*.

*Psyllobora vigintiduopunctata* (Figure 4D) is an insect that could reduce the impact of powdery mildew, playing an important ecological role (Dillen *et al.*, 2017).

*Phengaris (Maculinea) teleius* (Figure 4B), belongs to the family *Lycaenidae*. It is a diurnal butterfly and can only survive in places where both ants and the host plant *S. officinalis* are present (Musche *et al.*, 2008; van Swaay *et al.*, 2012; Popović *et al.*, 2022). The species of the genus *Maculinea* belongs to one of the most studied groups of butterflies in Europe and Asia (Pech *et al.*, 2004). *S. officinalis* is the major food source of the European large blue butterflies *Phengaris (Maculinea) nausithous* and *Phengaris (Maculinea) teleius* (Batáry *et al.*, 2007; Rákósy *et al.*, 2010; Rákósy and Goia, 2021). These butterflies lay their eggs in the flower heads of *S. officinalis*, where the larvae can feed on the seeds of this plant before they fall to the ground (Musche *et al.*, 2008; Rákósy *et al.*, 2010). The caterpillars that fall to the ground are carried by ants to their nests, where they can feed on ant larvae (Pech *et al.*, 2004). Tocai (Moțoc) *et al.* (2023), conducted field studies on the species *S. officinalis* in the Săcădat region between 2020-2022 (Tocai (Moțoc) *et al.*, 2023b), when they accidentally identified *P. teleius* butterflies in the Săcădat area. The observations were made in the Săcădat locality, in

northwestern Romania, an area located on the border between plains and hills. The flora of the Săcădat commune is characteristic of a steppe area with a moderate plain climate. *Podosphaera ferruginea* is a powdery mildew which can attack *S. officinalis* affects caterpillar performance of the endangered *Phengaris teleius* (Śliwińska *et al.*, 2019). The association of the beetle *Psyllobora vigintiduopunctata* with *S. officinalis* is at the core of the ecosystem where the infection of the fungal pathogen *Podosphaera ferruginea* is effectively impeded. The instrument of this regulation notably elevates *S. officinalis*'s physical health and its architectural stability thus, producing an advantageous microhabitat that is absolutely necessary for the insect's further growth and survival.

All of these insects rediscovering and finding out their role each, support seed set and genetic diversity through cross-pollination and contribute to the overall health of meadow ecosystems.

### Conservation Status

*S. officinalis*, plays a pivotal role in the lifecycle and habitat of *Maculinea teleius* that is why it is necessary for as many populations of *S. officinalis* as possible. A major influence on the wild populations of *S. officinalis* is the loss of habitat from farming growth and city building (Hazrati *et al.*, 2023). Changed climate can influence the development and spread of this plant, adding more difficulty to saving it (Muzykiewicz-Szymańska *et al.*, 2024a). In spite of these problems, there is growing awareness of the importance of healthy ways and plans to keep *S. officinalis* safe, but the conflict between old ways and current needs still presents a big problem for growing it and keeping it secure (Bunse *et al.*, 2020; Tocai (Moțoc) *et al.*, 2023b; Muzykiewicz-Szymańska *et al.*, 2024a).

### Conclusion

This review aligns with and broadens the current knowledge base in ethnopharmacology and phytochemistry by illustrating biochemically clear correlations between the traditional use of *S. officinalis* and the plant metabolites identified. The isolation of tannins, flavonoids, triterpenoids, and phenolic acids is in agreement with Traditional Chinese Medicine and European herbalism, which have been utilizing the species for the purposes of keeping healthy blood circulation, providing anti-inflammatory effects, and aiding in the healing of the skin for a very long time. This review, by gathering and presenting phytochemical data for different parts of *S. officinalis* and methods of the extract, draws attention to the differences in the content of chemical compounds and the problem of the possible standardization of the plant material, which issues have not been acknowledged in previous studies. Hence, our integration not only confirms the long-standing ethnopharmacological uses of *S. officinalis* but points out the crucial research gaps that would facilitate the effective incorporation of this species into evidence-based pharmacotherapy. The triterpenoid saponins and polyphenolic compounds are the most promising chemical constituents in the synthesis of current data, which underlines the observed therapeutic efficacy of *S. officinalis*. Among those, the triterpenoid saponins Ziyuglycoside I and II represent a prime candidate for further antineoplastic drug development, documenting an induction of pro-apoptotic effects due to modulation of cellular signaling and oxidative stress pathways. On the other hand, such highly concentrated polyphenolic components as the key tannin Lambertianin C are directly associated with the robust and frequently validated anti-inflammatory, hemostatic, and antimicrobial activities of *S. officinalis*. An understanding of *S. officinalis*' biological effects requires in-depth biochemical and clinical studies. To establish the plant's efficacy, further studies must be conducted on its pharmacodynamic activities. It is imperative to study the pharmacokinetics of the major bioactive constituents of *S. officinalis* so

as to validate their safeties. Polyphenolic components present in this plant (roots, stems, leaves and flowers) have been thoroughly reviewed in connection with the nutritional and phytochemical profile for an assessment of a possible link between the biological activities of *S. officinalis* and its main bioactive compounds.

### Authors' Contributions

Conceptualization and Writing-Original draft: ACT, AGT; Data curation: RAC, DU; Software analysis and Visualization: AML, AB; Writing-Review and Editing: ACT, SIV.

All authors read and approved the final manuscript.

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### Conflict of Interests

The authors declare that there are no conflicts of interest related to this article.

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