Review

SOLIDAGO VIRGAUREA L.: A REVIEW OF ITS ETHNOMEDICINAL USES, PHYTOCHEMISTRY, AND PHARMACOLOGICAL ACTIVITIES

Cornelia Fursenco¹†, Tatiana Calalb¹†, Livia Uncu¹, Mihaela Dinu*², Robert Ancuceanu²

¹ Faculty of Pharmacy, Nicolae Testemitanu SUMPh, 66 Mălina Mică Street, MD-2025, Chisinau, Republic of Moldova; cornelia.fursenco@usmf.md

² Faculty of Pharmacy, Carol Davila University of Medicine and Pharmacy, 6 Traian Vuia Street, Sector 2, 020956, Bucharest, Romania; robert.ancuceanu@umfcd.ro

* Correspondence: mihaela.dinu@umfcd.ro

† Denotes equal contribution

Abstract: *Solidago virgaurea* L. (European goldenrod, Woundwort), Asteraceae, is a familiar medicinal plant in Europe and other parts of the world, widely used and among the most researched species from its genus. The aerial parts of European goldenrod have long been used for urinary tract conditions and as an anti-inflammatory agent in the traditional medicine of different peoples. Its main chemical constituents are flavonoids (mainly derived from quercetin and kaempferol), C6-C1 and C6-C3 compounds, terpenes (mostly from the essential oil), and a large number of saponin molecules (mainly virgaureasaponins and solidagosaponins). Published research on its potential activities is critically reviewed here: antioxidant, antiinflammatory, analgesic, spasmolitic, antihypertensive, diuretic, antibacterial, antifungal, antiparasite, cytotoxic and antitumor, antimutagenic, antiadipogenic, antidiabetic, cardioprotective, and antisenescence. The evidence concerning its potential benefits is mainly derived from non-clinical studies, some effects are rather modest, whereas others are more promising, but need more confirmation in both non-clinical models and clinical trials.

Keywords: Solidago vigaurea L.; European goldenrod; Asteraceae; ethnomedicinal; phytochemistry; distribution; pharmacological activity

---

1. Introduction

The genus *Solidago* comprises about 190 species and infraspecific taxons (subspecies and varieties) with an accepted status and about 330 species and intraspecific taxons with an ambiguous status [1]. They are widespread throughout the world, most of them originating from North America or confined to this part of the world [2]. Most of *Solidago* species are herbaceous flowering plants, which occur in the spontaneous flora or are cultivated as decorative plants [3]. Raw materials of goldenrods have a long and wide use history in the traditional medicine of different parts of the world: *S. virgaurea* L. (European goldenrod) is the most used in Europe and Asia; *S. canadensis* L. (Canadian goldenrod), *S. gigantea* Aiton (Giant goldenrod) and *S. odora* Aiton − in North America; *S. chilensis* Meyen − in South America [4,5]. According to the Flora Europaea, on the continent there are 5 representatives of the genus *Solidago*: *S. virgaurea* L., *S. canadensis* L., *S. gigantea* Aiton., *S. altissima* L. and *S. graminifolia* L. Salisb.) [6]. Today, *S. graminifolia* is considered a synonym for *Euthamia graminifolia* (L.) Nutt. [7]. *S. canadensis* and *S. gigantea*, although of North American origin, have become widespread across Europe and are considered "serious invaders", whereas *S. rugosa*, of the same origins, has been reported in a few Western European countries [8].

The aerial parts of European goldenrod have been known and used for centuries as anti-inflammatory, spasmolytic, and diuretic remedies in the traditional medicine for the treatment

of numerous diseases, especially as a urological agent in kidney and bladder inflammation, urolithiasis, and cystitis [3,4,8–12]. According to the European Medicines Agency, *S. virgaurea* is one of the most used and studied species of the *Solidago* genus in Europe [9].

The growing interest for the species *S. virgaurea* as a medicinal plant led us to carry out this review using the most relevant and recent international research studies. The scientific community interest in *S. virgaurea* is booming. Figure 1 depicts the cumulative number of articles (total of 580) published on *S. virgaurea* in the period 1944-2020. For this purpose, two well-known and worldwide applied scientific databases (MEDLINE (PubMed) and HINARI), as well as Google Scholar, were used. The number of published paper on this species has escalated in the last two decades (2000-2020).
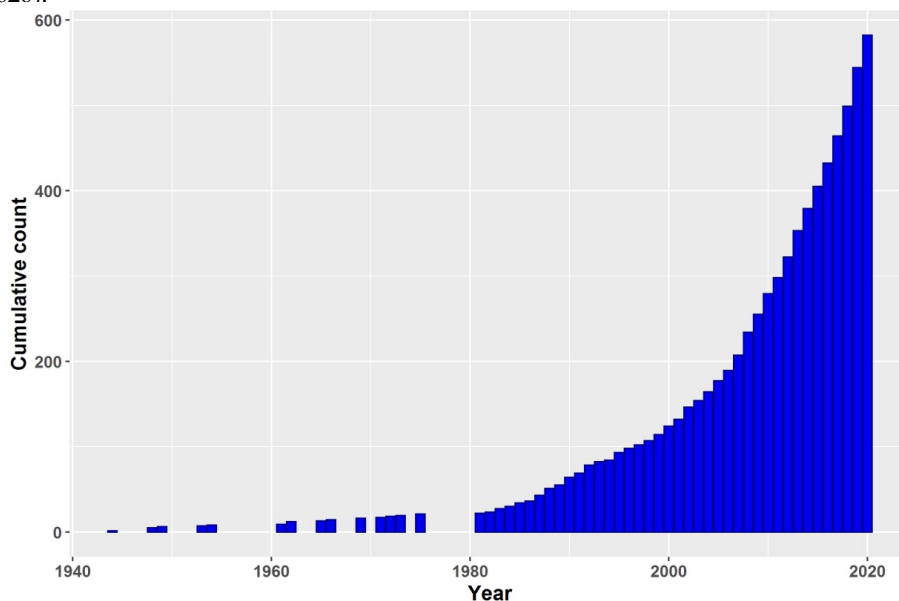

Figure 1. Cumulative number of citations on S. virgaurea. Source: PubMed

2. General description, taxonomy, and distribution

S. virgaurea is a perennial herb provided with an oblique, woody rhizome, of a cylindrical shape and devoid of knots, on which stem scars are visible (fig. 2A). The round, erect stem may achieve a height of up to 1m, and is ramified and pubescent at the topside. The leaves, with an alternate arrangement are simple, slightly pubescent on the adaxial face and pubescent on the abaxial one. Basal leaves have ovate or ovate-elliptic blades with an acute tip and a winged petiole, whereas upper leaves have short stalks and linear-lanceolate or elliptic blades, with margins either serrated or entire (fig. 2B,C). The radiate flower heads have morphologically distinguished ray (female, tongue-like) and disc yellow florets (hermaphrodite, tubular). The flowers capitula are grouped in a simple raceme or in panicles (fig. 2D). The receptacle is glossy and flat. The fruit is a cylindrically-shaped achene, with 8-10 ribs and a pappus derived from the modified calyx [13].

A recent morpho-anatomical local study focused on the morphological and anatomical investigation of *S. virgaurea* from flora of the Republic of Moldova, and its herbal product *Solidaginis virgaureae herba,* was done by Calalb T. et al. [13]. The anatomical features of the highest interest for the exact identification of *S. virgaurea,* established in this study, include: repartition of stomata on both sides of the leaf, anomocytic arrangement of stomata, cone-shaped or fan-shaped multicellular trichomes on both epidermises, as well as glandular trichomes, dorsiventral structure of the leaf with vascular bundles collateral and open, and secretory ducts in the stem. The anomocytic stomata reported for the leaf is consistent with the findings of Szymura M. and Wolsky K. [14], who also established that anomotetracytic stomata were the most widespread type in other *Solidago* taxa collected from Poland. The presence of two categories of multicellular trichomes (cone-shaped and fan-shaped) on the goldenrod leaf was also reported by other sources [14,15]:   by Buynov MV. on *S. dahurica* leaf [16], by Douglas M. et al. on *S. chilensis* leaf [17], and by Fedotova VV. on *S. caucasica* leaf

[18]. Care is needed for a correct identification, because in the 19th Century, a scientific paper written by a medical doctor (based on his personal experience repeated several times) drew the attention to the risks of confusing this medicinal plant with a non-effective (and likely dangerous for the health) *Senecio nemorensis* L. [19]
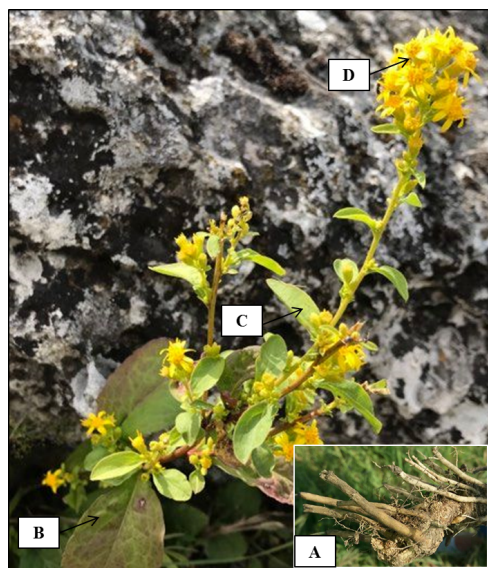

Figure 2. S. virgaurea (original photo): A – oblique rhizome, B – basal leaves, C – cauline leaves, D – radiate flower heads

According to a number of sources [20,21] *S. virgaurea* is regarded as a taxonomic group or complex, and it consists of perennial herbaceous species extensively distributed from Europe to East Asia. As a group, it is generally divided longitudinally: in Europe the genus is represented by *S. virgaurea* L., in Siberia and most of the Far East by *S. dahurica* (Kitag.) Kitag. ex Juz. Together with *S. spiraeifolia* Fisch. ex Herder, whereas in the Far East region of Russia known as Chukotka and in North America the genus is represented by *S. multiradiata* Ait. [22].

The European *S. virgaurea* L. has been described as "an exceedingly polymorphic taxon", and a multitude of narrowly related taxa have been included within it at different levels (varieties, subspecies, and even species) [22,23]. In a European country (Czech Republic) flora, discussing the variability S. Slavik (2004) has identified 17 taxa as belonging to *S. virgaurea* L. group (leaving aside taxa from Japan), of which a number of six are qualified as subspecies, whereas a number of eleven as "microspecies" [22,24]). The Atlas of the British and Irish flora [25] describes *S. virgaurea* as highly variable, with many distinct forms for distinct habitats (ecotypes). Strong correlations have been claimed between *S. virgaurea* genotypes and their geography, and a strong ability to rapidly evolve and ecologically diversify has been recognized for the species [26].

3. Synonyms and common names

According to the Assessment Report on *Solidago virgaurea*, realized by the European Medicines Agency [9] and the World Flora Online [1], the main synonyms in use are: *Amphiraphis leiocarpa* Benth., *Amphiraphis pubescens* DC., *Aster virgaurea* (L.) Kuntze, *Dectis decurrens* Rafin. (Lour.), and *Doria virgaurea* Scop. *S. patagonica* Phil. is currently an accepted name [1], although it was reported that one Argentine specimen identified as *S. patagonica* was in fact an escaped cultivar of S. virgaurea [27].

The most often used common name for *S. virgaurea*, as well as for other *Solidago* species is goldenrod. Sometimes the "European" qualifier is added to this vernacular name and in this paper, in order to avoid confusion with other species of the genus, we will hereafter use this name

(European goldenrod). According to the American Botanical Council other common names in use are: Solidago, Virgaurea, Woundwort, Aaron's rod, and Yellowweed [28]. The dried flowering aboveground parts are the subject of a European herbal monograph [29].

4. Ethnomedicinal uses

S. virgaurea has a diversity of medicinal uses in the territories where it is spread. Probably its most widely known ethnopharmacological uses are related to kidney disorders (being often found in teas intended to help passing kidney calculi), urinary tract infections, the overactive bladder syndrome, and prostatic diseases [30–32], the urologic uses of the plant going back at least to the writings of   Arnold von Villanova (1240-1311) [33]. Traditionally, the aerial parts of the plant have been used for healing and antiseptic properties [9], as well as for the treatment of diabetes, allergies, and gastro-intestinal disorders [8,32]. Likewise, infusions or decoctions prepared from European goldenrod is used in the traditional medicine in many parts of the world for its antibacterial and anti-inflammatory effects [34], including inflammation of the oral cavity and throat, when used as a mouth rinse [32]. Further scientific studies have shown the growing importance of European goldenrod as a source for herbal drugs [35]. In many European countries, the herbal product derived from the species has often been in combination products [9].

Germany

Hieronymus Bock (1498-1554), one of the first modern botanists in Germany, conjectured that Germanic tribes had been using the plant for medicinal purposes, mentioning that they regarded it as a "miracle herb" (*Wunderkraut*) [36]. It is believed that the German father of Reformation, Martin Luther (1438-1546), had a good opinion on goldenrod and used it often to care for his physical infirmities with its help [33]. One of the first reports on its diuretic and anti-inflammatory effects are ascribed to the „father of German botany" (1525-1590), Jacobus Theodorus Tabernaemontanus [37], who stated that it "also cleanses the kidneys and urinary tract of all coarse mucus"[36]. The name *Heydnisch Wundkraut* (heathen woundwort) attributed in the German territories to the plant in the Middle Ages alludes to the same healing properties of the plant. Another vernacular name, *Unsegenkraut* (*curse herb)*, alludes to less medicinal properties, although in an era where disease was often attributed to witchcraft and metaphysical causes, it may still reflect medicinal properties of the plant [38]. In German folk medicine, goldenrod was used for the treatment of urinary retention, kidney stones, and hemorrhoids [36]. Since the middle 19th Century, its use was slowly forgotten in Germany, to be revived only relatively recently, with the renewed interest for the herbal therapy [36].

Currently, a well-established use is accepted in Germany for inflammatory diseases of the urinary tract collection system, urolithiasis and renal gravel. A variety of extracts are used, particularly dried extracts obtained from the aerial parts (*Solidaginis virgaureae herba*) using 30-60% ethanol as an extraction solvent [9]. A monograph of the species was introduced in DAB in 2002, which also acknowledged *S. canadensis* and *S. gigantea* as valid species, despite certain differences in the spectrum of their phytochemicals [33].

Czech Republic

The herbal drug obtained from *S. virgaurea* is included in the Czech Pharmacopoeia 2009 [39]. A drink obtained from the aerial parts of the plant is used as an adjuvant treatment in inflammatory conditions of the urinary system, as well as for the prevention of kidney and bladder calculi [9]. It is not clear, though, whether such uses represent an old Czech tradition, as a Czech paper on the species only cited foreign sources when referring to the traditional medicinal use of the species [39].

Poland

Traditionally, the infusion prepared of dried aerial parts of S. virgaurea has been used as a diuretic and as an adjuvant in treatment of minor complaints of the urinary tract [9]. In a Polish source, it is stated that raw material of this herb is characterized by diuretic, detoxifying, anti-inflammatory, and bile secretion enhancing properties [35]. A Polish source mentions its disinfectant properties as the most important among the traditional uses, but also its useful effects in accelerating wound healing and in skin care [40].

Russian Federation

In Russian folk medicine, European goldenrod is used for a variety of conditions, from gallstone disease to indigestion, and from rheumatism to gout. For external use, fresh leaves are recommended in abscesses and boils   [41]. Other Russian sources [35,42] state that most common uses of this species include prevention and treatment of various diseases of the kidneys, bladder, and prostate gland (i.e., the traditional use most widely acknowledged in Europe). In the Russian folk tradition the European goldenrod is also known as a hemostatic and astringent agent, as well as a good remedy for respiratory diseases (tonsillitis, laryngitis, acute respiratory diseases), gallstone diseases, and pulmonary tuberculosis [41].

Ukraine

The use in tuberculosis is also well established in the Ukraine folk medicine, where the name of the plant, *zolotushnik*, alludes to its use in decoctions as "a good remedy against scrofula (*zolotukha*)", but the plant was also believed to have diuretic effects [43].

Bulgaria

According to a Bulgarian source, the aerial parts of *S. vigaurea* L. are used as a diuretic, antihypertensive, and expectorant, as well as in the therapy of renal deficiency and gout [44].

Romania and the Republic of Moldova

S. virgaurea has a long history of use in the Romanian traditional phytotherapy. The herbal product *Solidaginis virgaureae herba* has been in used in herbal therapy and marketed by specialized outlets since 1990 [45]. Ethnopharmacological uses of this plant are mostly related to maintaining the health of the urinary tract and the normal functioning of the digestive system. Traditionally, it is recommended as a diuretic, saluretic, anti-inflammatory, antiseptic, healing or a sedative agent. For external use, the most common application consists in administering an infusion or decoction of the aerial parts or blooming tops in the treatment of wounds or ulcers of the oral cavity [46,47]. The external use in rickets, also acknowledged by Romanian traditional sources [48], does not seem to have great benefit, considering the current knowledge of this disease and its causes.

Korea

The root and aerial parts of *S. virgaurea* subsp. *gigantea* (Nakai) Kitam have been used as an appetite stimulant and diuretic in Korean folk medicine, whereas the immature aerial parts are used in the same area as food [49,50].

China

Decoctions obtained from the whole plant were used for their antibacterial activity, and in respiratory tract infections for its expectorant and anti-inflammatory properties [51].

Other uses

Besides its medicinal uses, *S. virgaurea* has been recognized as a first-class alternative source for the floriculture business, both on the old continent and in the new world [32]. It has also been proposed to be used as a rotation crop as a means of containing noxious weeds in an organic agriculture context [35]. *Solidago* spp., including *S. virgaurea*, have been claimed to have potential utility for phytoremediation purposes, based on their ability to transfer iron from soil to plants near iron processing industrial sites [35];   however, studies on other oligo-elements (such as zinc) have not identified particular hyperaccumulator properties for the plant [52], and whereas a number of papers have been published on the phytoremediation potential of *S. canadensis* [53,54], we could find none on *S. virgaurea*. The pollen of the latter is of good quality, and its availability may contribute to long-lived bees, able to survive a hard winter [55].

5. Phytochemistry

Extracts of *S. virgaurea* contain C6-C1 glycosides (virgaureoside, leiocarposide) and aglycones (vanillic acid, gallic acid) [4,9,56–58], C6-C3 polyphenolic acids (caffeic, chlorogenic, ferulic, synapic, 3-hydroxyphenylacetic acid, 3,4-dihydroxyphenylacetic, homovanilic, acids) [3,9,10,45,53–57], a number of flavonoid molecules (mostly quercetin and kaempferol glycosides, as well as the free aglycons and small amounts of cyanidin derivatives) [3,4,9,45,49,59,60,63–67], oleanane-type triterpene saponins [9,68–75], essential oils containing and monoterpenes (alpha- and beta-pinene, myrcene, limonene, sabinene) [35,76–79] and sesquiterpenes (germacrene D β-caryophyllene, *α*-humulene,), clerodane-type diterpenes [80], polysaccharides [81], and polyacetylenes [82]   (tab. 1). The European Pharmacopoeia monograph for *Solidaginis virgaureae herba* regards flavonoids as quality markers and for the product requires a content of at least 0.5% and maximum 1.5%, expressed as hyperoside [83].

It has been speculated [3] that a number of the active compounds of *S. virgaurea* extracts (leiocarposide, polyphenolic acids, flavonoids, saponins) exert a synergistic activity in displaying the reported anti-inflammatory effects of the product [56,84]. The antioxidant activity has been attributed to the polyphenolic compounds [3,85–87], while flavonoids are thought to be responsible for the spasmolytic effects [3,31,88].

Flavonoids

Among the flavonoids, rutin, quercetrin, astragalin, nicotiflorin, biorobin, and narcissin have been considered "the most representative" [64], and they are accompanied by their aglycons [49,95]. More recently, flavanones aglycones and glycosides have also been detected and quantified in the different parts of the plant: eriodictyol (the largest amount in the flowers, followed by leaves and then stems, mostly as glycosides), naringenin (similar quantitative distribution in flowers, leaves, and stems, mostly as glycosides), and very small amounts of hesperitin (not assessed separately in each aerial parts) [102]. Eriodictyol and naringenin are present in the form of both R and S enantiomers, whereas hesperitin was detected only as the S enantiomer [102]. All flavonoid heterosides seem to be 3-O-glycosides, as for the majority of *Solidago* species (the notable exception being *S. graminifolia* (L.) Salisb, in which mono- and di-C-glycosylflavonoids have also been reported [58], but which now is considered a synonym for the *Euthamia graminifolia* (L.) Nutt [1]). The presence of flavonoid-C-heterosides in *S. virgaurea* has also been occasionally claimed in secondary sources [59], but we could not locate a primary reference reporting them. Cyanidin-3-gentiobioside is the main anthocyanin present in the leaves, but at least one other cyaniding-glycosyde was reported in very small amounts [103]. Flavonoid glycosides tend to be better extracted in ethanol of

70% or higher concentrations [94]. As mentioned above, hyperoside is considered the key flavonoid by the European Pharmacopoeia [83]. However, in one paper quercitrin was the major phytochemical from a quantitative standpoint [95], whereas other sources reported rutin as the dominant flavonoid [59,60] (a mean content 196.42 mg100 g-1 reported by [59]). A qualitative and quantitative comparative study of flavonoids from extracts of four *Solidago* spp. reported in Romanian flora was carried out by Dobjanschi L. et al. [38,49], who found a total flavonoid content for *S. virgaurea* of 4.06%., expressed as rutin. They also found that for *S. virgaurea* specific was the presence of rutin and hyperoside, whereas quercitrin (unlike the findings of V. Kraujalienė et al.) was absent [45,66]. Spasmolytic effects (as discussed below) [31,88], diuretic activity [10], have been attributed to the flavonoids, and other effects have also been specifically ascribed (at least partially) to some flavonoids, e.g. antiadipogenic effects to kaempferol-3-O-rutinoside [104].

Table 1. Chemical compounds identified in *S. virgaurea*

Chemical compounds	Place/Country of collection	References
Flavonoids (Fig. 3)		
Quercetin,	Poland, Italy,	Fuchs L. [93]
Quercetin-3-O-glucoside (isoquercitrin)	Hungary, Korea,	Budzianowski J. *et al.* [63],
Quercetin-3-O-galactoside (hyperoside)	Romania, Lithuania	Borkowski B. and Skrzypczakowa L.
Quercetin-3-O-rhamnoside (quercitrin)		[60],
Quercetin-3-O-rutinoside (rutin)		Chodera A. *et al.* [67],
Quercetin-3-O-arabinopyranoside		Roslon W. *et al.* [59],
(avicularin)		Pietta P. *et al.* [64],
Kaempferol-3-O-glucoside (astragalin)		Apáti P. *et al.* [94],
Kaempferol-3-O-rhamnoside (afzelin)		Choi SZ. *et al.* [49],
Kaempferol-3-O-rutinoside (nicotiflorin)		Tamas M. [65],
Kaempferol-3-O-robinobioside		Dobjanschi L. *et al.* [45,66]
(biorobin)		Kraujaliene V. et al. [95]
Myricetin 3-rhamnoside (myricitrin)		
Isorhamnetin-3-O-rutinoside (narcissin)		
Cyanidin-3-gentiobioside		
mono-C-glycosylflavones (?)		
di-C-glycosylflavones (?)		
C6-C1 compounds (Fig. 4)		
Benzoic acid	Poland	Kalemba D. [61]
3-Hydroxybenzoic acid	Egypt	Abdel Motaal A. *et al.* [10]
4-Hydroxybenzoic acid	Korea	Choi SZ. *et al.* [49],
3,4-Dihydroxybenzoic (protocatechuic) acid		Thiem, B. *et al.* [58]
Salicylic acid		Bajkacz S. et al. [62]
Gentisic acid		Sung JH et al. [50]
Vanillic acid		
Gallic acid		
Leiocarposide		

2-methoxybenzyl-2,6-dimethoxybenzoate		
C6-C2 and C6-C3 compounds (Fig. 5)		
Caffeic acid,	Poland	Kalemba D. [61]
Chlorogenic acid	Egypt	Abdel Motaal A. *et al.* [10]
5-O-caffeoylquinic (neochlorogenic) acid	Korea	Choi SZ. *et al.* [49],
3,5-di-O-caffeoylquinic acid	Iran	Thiem B. *et al.* [58]
3,4-di-O-caffeoylquinic acid		Bajkacz S. et al. [62]
4,5-di-O-caffeoylquinic acid		Haghi G., Hatami A. [96]
3,4,5-tri-O-caffeoylquinic acid		Roslon W. et al. [59]
Methyl 3,5-di-O-caffeoylquinate		Kraujalienė V et al. [95]
3-hydroxyphenylacetic acid		M. Marksa et al. [97]
3,4-dihydroxyphenylacetic acid		D. Fraisse et al. [98]
5-p-Coumaroylquinic acid		Borkowski B. and Skrzypczakowa L.
Homovanilic acid		[60]
p-Coumaric acid		Jaiswal R. et al. [99]
Ferulic acid		
Sinapic acid		
Rosmarinic acid		
Coumarins		
7-hydroxy-coumarin (umbelliferone)	Czech Republic	Dobias P. et al. [100]
Terpene derivatives (Fig. 6)		
α-Pinene,	Poland, Japan,	Kalemba D. [76]
β-Pinene,	Italy,	Kalemba D. and Thiem B. [77],
Sabinene	Russian Federation ,	Fujita S. [78],
Myrcene	USA	Bertoli A. *et al.* [79]
Limonene	Denmark	Tkachev AV. *et al.* [35]
β-Ocimene	Korea	Goswami A et al. [101]
Germacrene-D,		Starks CM. *et al.* [80]
β-Caryophyllene,		Lam J. [82]
α-Humulene,		Choi S. [49]
Clerodane diterpenes		
2,8-(cis)-(cis)-Matricaria ester		
Matricaria γ-lactones		
Lachnophyllum lactone		
ent-germacra-4(15),5,10(14)-trien-1β-ol		
β-dictyopterol		
Saponins (Fig. 7)		
Virgaureasaponins 1-6	Germany,	Bader G. *et al.* [34,56-59],
Solidagosaponins X-XXIX	France, Romania	Chevalier M. *et al.* [62],
Bellisaponin BA2	Japan	Laurençon L. *et al.* [63],

Erythrodiol-3-acetate	Dobjanschi L. *et al.* [61]
	Inose Y. *et al.* [60]
	Sung JH et al. [50]
	Carbohydrates and other compounds
Polysaccharides	Russian Federation Pychenkova PA. [68]
α-tocopherol quinone	Korea Sung JH et al. [50]
2-phyten-1-ol	

Kaempferol-3-O-glucoside (astragalin))

Kaempferol-3-O-rhamnoside (afzelin)

Kaempferol-3-O-robinobioside (biorobin)

Myricetin 3-rhamnoside (myricitrin)

Isorhamnetin-3-O-rutinoside (narcissin)

Cyanidin-3-gentiobioside

Quercetin

Quercetin-3-O-glucoside (isoquercitrin)

Quercetin-3-O-galactoside (hyperoside)

Quercetin-3-O-rhamnoside (quercitrin)

Quercetin-3-O-rutinoside (rutin)
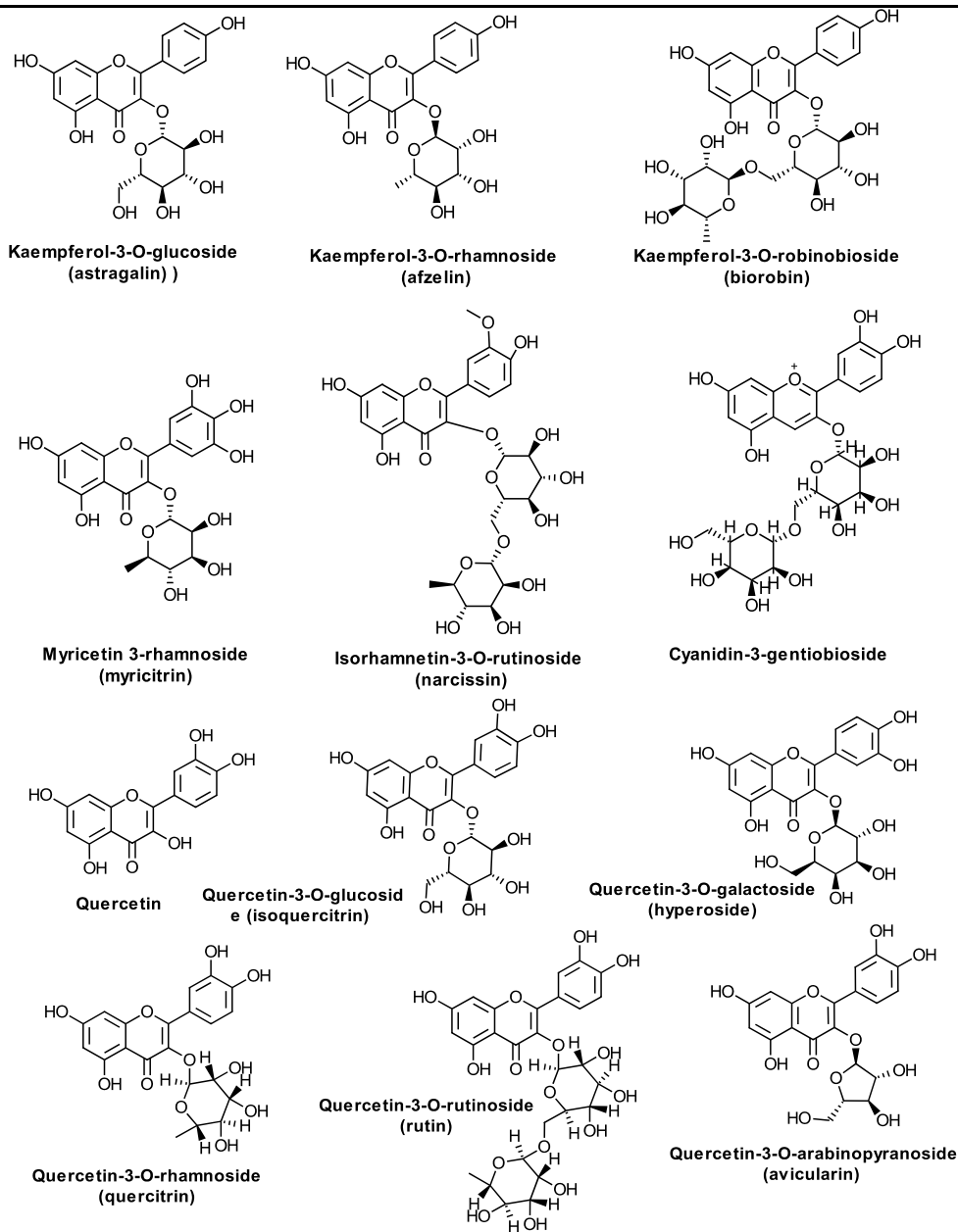
Quercetin-3-O-arabinopyranoside (avicularin)

Figure 3. Representative flavonoids from *S. virgaurea* L.

C6-C1 compounds

Several main compounds with a C6-C1 have apparently been reported up to date in *S. virgaurea*, two glycosides and two aglycones: virgaureoside A, a bis-desmosidic glycoside derived from benzoic acid (2-beta-D-glucopyranosyloxybenzoic acid-2'-beta-D-glucopyranosyloxybenzyl ester) [89], leiocarposide (2'-hydroxybenzyl-3-methoxybenzoate 2',4-diglucoside)[56], vanillic acid, gallic acid [9,90], benzoic acid, 3-hydroxybenzoic acid, 4-hydroxybenzoic acid, 3,4-dihydroxybenzoic (protocatechuic) acid, and 2,5-dihydroxibenzoic (gentisic) acid [61,62]. Such derivatives of the benzoic acid are often occurring in the family Asteraceae [91].

A somewhat detailed history of the discovery of the two phenolic glycosides was provided by L. Skrzypczak et al. [91]. Leiocarposide is currently considered the most important and was found to be maximally biosynthesized in the flower buds (1.60%) and in the two-year leaves, post-blooming (1.05%) [92]. Similar contents (0.4-1.6%) were reported by other researchers, depending on a number of variables such as plant height at harvest, collection time, or the natural state of the herbal samples [58]. Leiocarposide has attracted interest for its pharmacological potential, being explored for its hypothesized anti-inflammatory, analgesic, antilithiatic, and diuretic effects, as discussed below. For plants cultivated *in vitro*, the content of leiocarposide is lower than that of naturally growing plants (0.18% vs. 0.2-1.0%) [58].
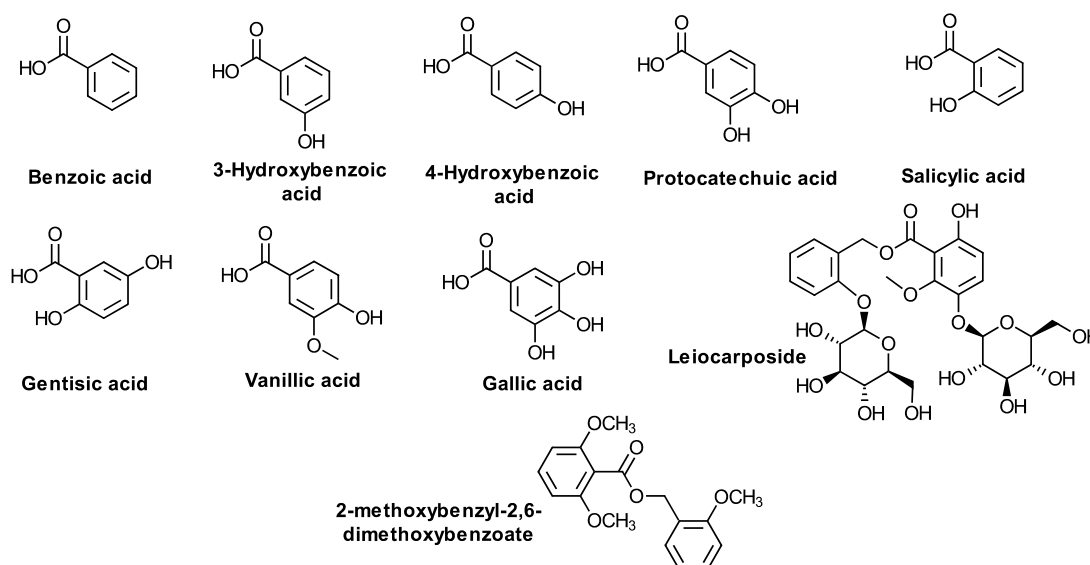

Figure 4. C6-C1 compounds from *S. virgaurea* L.

C6-C2 and C6-C3 compounds

A variety of C6-C3 phenolic acids have been identified in different studies. Among the most important are the caffeoylquinic derivatives (chlorogenic acid, but also 5-O-caffeoylquinic (neochlorogenic) acid, 5-p-coumaroylquinic acid, 3,5-di-O-caffeoylquinic, 3,4-di-O-caffeoylquinic, 4,5-di-O-caffeoylquinic acids, methyl 3,5-di-O-caffeoylquinate, and 3,4,5-tri-O-caffeoylquinic acid, the latter showing superior anti-inflammatory effects over the di-caffeoylquinic derivatives.) [10,49,58,59,62,99]. Caffeic, p-coumaric, ferulic, sinapic, 3-hydroxyphenylacetic, 3,4-dihydroxyphenylacetic (DOPAC), and homovanilic acids were also reported in phytochemical studies of *S. virgaurea* L [62]. In one study, whereas chlorogenic acid was detected and measured (by HPLC), ellagic and rosmarinic acids could not be detected [96]. Chlorogenic acid content may vary considerably, as shown in one study that measured it in samples collected from 20 sites, which found concentrations as low as 158.99 mg/100g and as high as 441.50 mg/kg [59]. Similarly, rosmarinic acid varied in the same study between 256.38 mg/100 g and 898.70 mg/100 g [59], whereas (as mentioned), in a different study, it could not be detected at all [96]. As already discussed in the literature [97], a number of variables, such as the herbal part, ontogenetic development stage,

and ambient conditions have a considerable influence on the qualitative and quantitative content in phenolic compounds of the species.
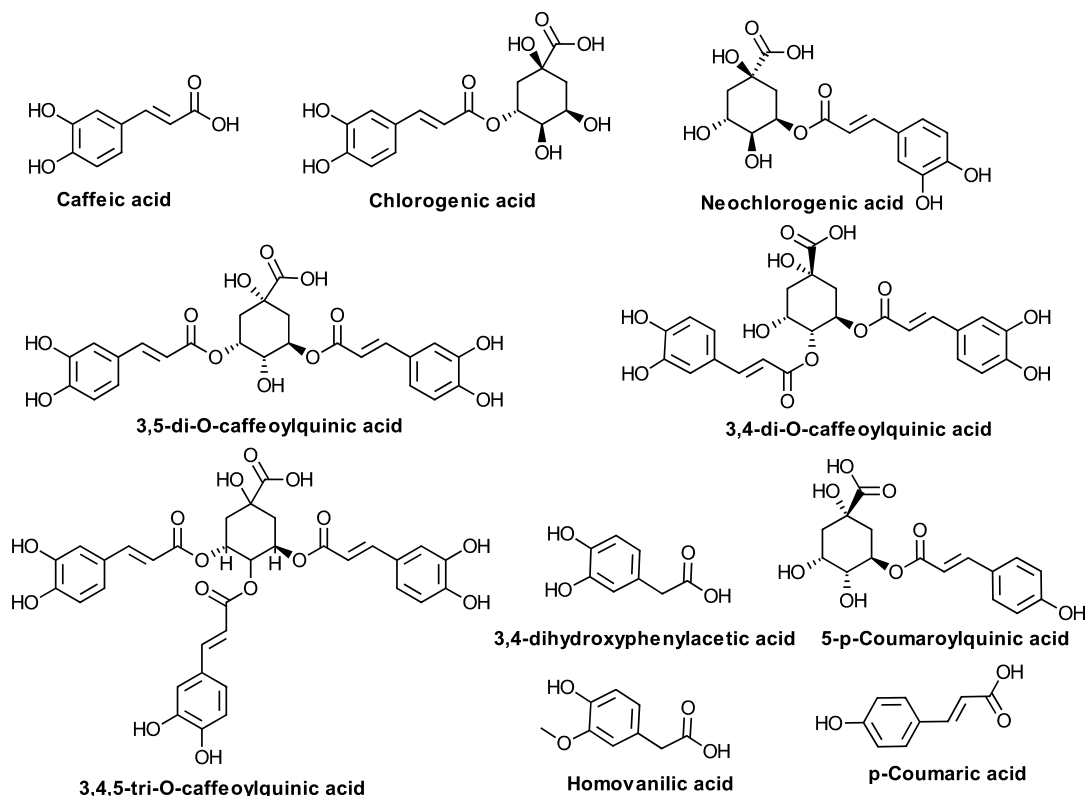

Figure 5. C6-C2 and C6-C3 compounds from *S. virgaurea* L.

Coumarins

Up to date, a single paper *[100]* reported the presence of a coumarine compound in *Solidago virgaurea*: umbeliferone (7-hydroxy-coumarin). Esculetin and scopoletin were not detected in the species *[100]*.

Terpene derivatives

A number of over 60 compounds have been described in the essential oil obtained from the flowering tops of *S. virgaurea* L collected in Poland [76], whereas in specimens from Lithuania, 106 compounds were identified in flowers and 95 in leaves [105]. The key compounds (as found in three samples from three different sites of Poland) were the monoterpenes α-pinene (27.4-34.1%), myrcene (7.8-17.9%), β-pinene (5.4-7.5%), limonene (3.0-14.1%), and sabinene (0.4-11.8%), as well as the sesquiterpenes germacrene D (8.2-17.0%), and in smaller amounts α–humulene, β-caryophyllene, and α–muurolene [76]. In Lithuanin specimens, the composition reported recently was rather different: in the leaves the most important compounds detected were caryophyllene oxide, trans-verbenol, spathulenol, humulene epoxide II, α –pinene (only 5.21%), and germacrene D; in flowers of the same origin, the most important compounds were caryophyllene oxide, humulene epoxide II, germacrene D, trans-verbenol, spathulenol, and bornyl acetate [105].

Looking at all compounds grouped by chemical structure, the largest proportion in the Polish samples consisted of monoterpene hydrocarbons (58-73%) and sesquiterpene hydrocarbons (17-31%); oxygenated monoterpenes and sesquiterpenes (about 3% each), benzoic acid and salicilyc acids (about 1%) represent less than 10% of the total oil [76]. The essential oil of specimens cultivated

in vitro by micropropagation was similar in its monoterpene contents, but the sesquiterpenes were apparently less represented for *S. virgaurea* L. in this case [77]. A.V. Tkachev et al. (2006) compared the composition of the essential oil from the aerial parts harvested from two different heights in the Russian Altai and found that the product harvested at a lower height (290 m) are richer in essential oil (0.22%), which contains higher amounts of *α*-pinene and myrcene as compared to the oil (0.07 %) obtained from plants harvested at a more elevated height (650 m) [35]. The key compounds in this study were almost the same as in the specimens from Poland, the only notable exception being a higher content in β-caryophyllene for both specimens (maximum content in the Polish specimens was 3.3%, whereas in the Russian specimens the minimum content was 6.3%) [35,76].

Besides the essential oil terpenes, from the aerial parts of *S. virgaurea* L. a number of at least 12 *cis*-clerodane lactones were reported in the 1980s, eight of which were new at the time of reporting [101]. In 2010 an additional set of nine new clerodanes were isolated from the species (most likely the aerial part, although up to date many clerodanes have been isolated from roots of different *Solidago* species), seven of which have the relatively atypical feature of a carboxylic acid at C-19 (solidagoic acids C-I) [80].

A number of polyacetylene compounds have been reported in the roots of the species (matricaria ester, two matricaria-*γ*-lactones, one lachnophyllum lactone), that show considerable seasonal variation [82]. Only the matricaria ester could be detected in the aboveground shoots, whereas the other compounds are absent from the aerial parts [82].
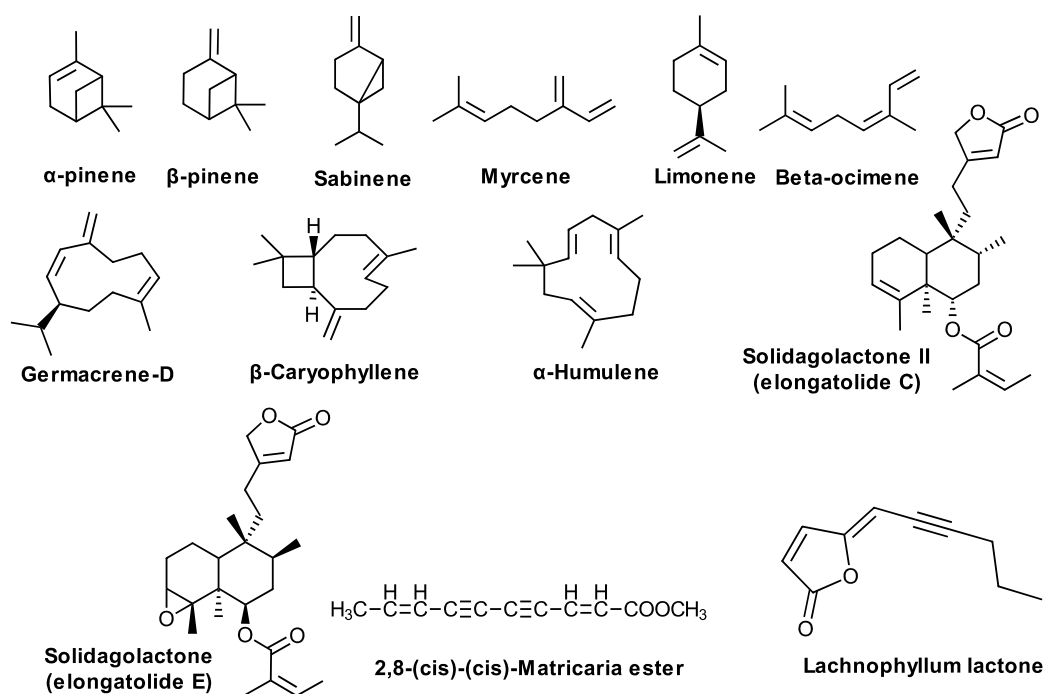

Figure 6. Terpenes from *S. virgaurea* L.

Saponins

The saponins of *S. virgaurea* L. have been an object of study as early as the 1930s, but the first data on their structure were provided by K. Hiller et al. in 1975 [106].   In the 1980s, G. Bader et al. were among the first to isolate and establish the chemical structures of deacylated saponins found in the aerial parts, named by the authors virgaureasponins 1-3 [37,68,70,107]. Around the same time, in Japan Y. Inose et al. isolated and elucidated, from samples of Japanese origin, the structures of oleanane-type solidagosaponins I-XX, many of them glycosylated in position 16 of the aglycone alone or besides position 3 [51,72], and later the same group further identified solidagosaponins XXI-XXIX [108]. The same Japanese researchers reported the presence of bellisaponin BA2 [108],

which had been isolated previously from *Bellis perennis* L. [109]. Later another European group isolated virgaureasaponins 4-6 from *S. virgaurea* ssp. *alpestris* [75]. Quantitatively, the saponin content is similar between *S. virgaurea*, *S. gigantean,* and *S. canadensis* [73]. Unlike *S. canadensis* and *S. gigantea*, which are derived from byogenin and have more complex sugar chains, the saponins isolated from *S. virgaurea* are derived from polygalacic acid and are acylated by carboxylic acids [37]. As for many phytochemicals, some of the saponins have multiple synonyms, sometimes confusing; for instance, solidagosaponin XVIII is also known as virgaureasaponin C [75].
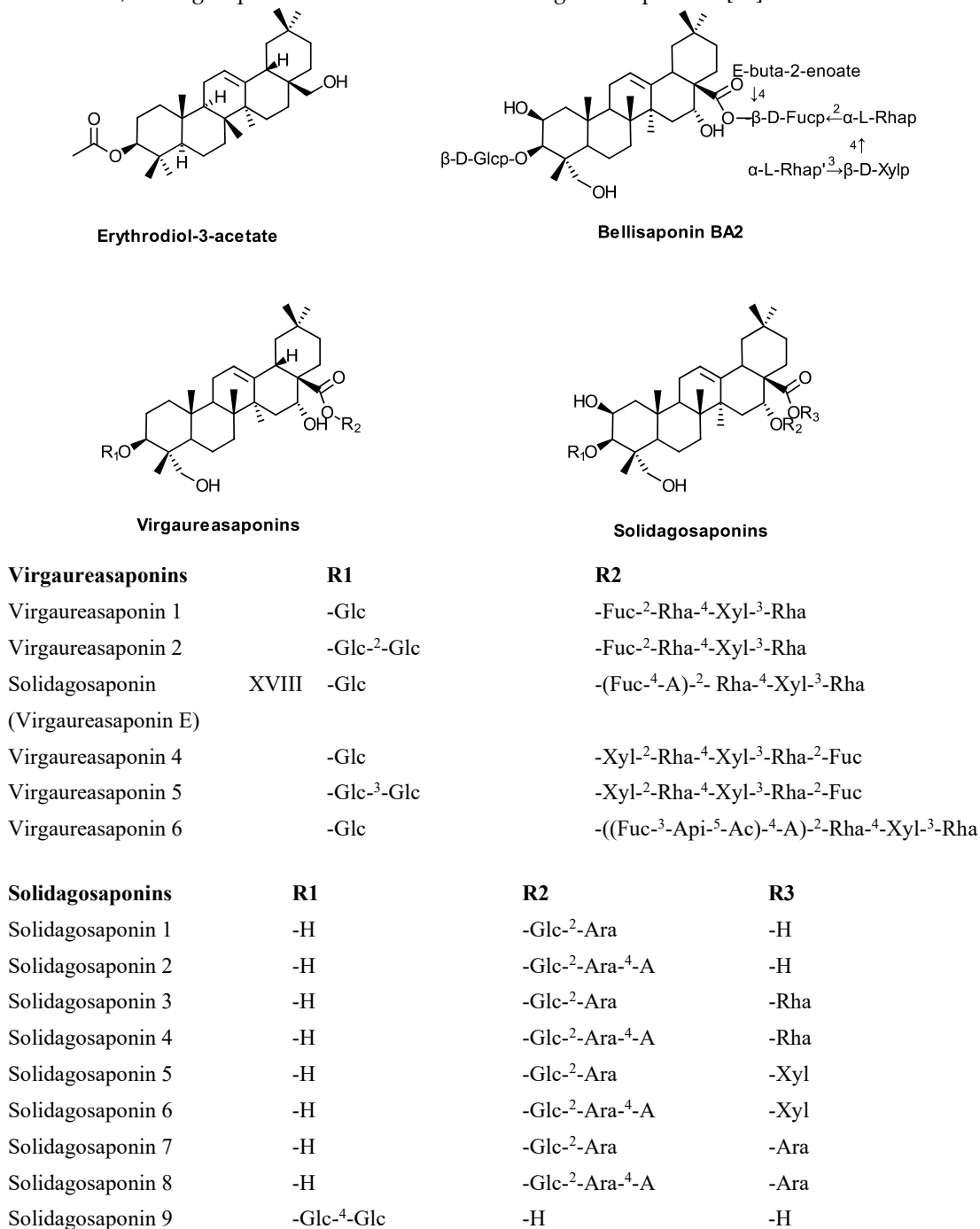
Erythrodiol-3-acetate

Bellisaponin BA2

Virgaureasaponins

Solidagosaponins

Virgaureasaponins		R1	R2
Virgaureasaponin 1		-Glc	-Fuc-^{2}-Rha-^{4}-Xyl-^{3}-Rha
Virgaureasaponin 2		-Glc-^{2}-Glc	-Fuc-^{2}-Rha-^{4}-Xyl-^{3}-Rha
Solidagosaponin (Virgaureasaponin E)	XVIII	-Glc	-(Fuc-^{4}-A)-^{2}- Rha-^{4}-Xyl-^{3}-Rha
Virgaureasaponin 4		-Glc	-Xyl-^{2}-Rha-^{4}-Xyl-^{3}-Rha-^{2}-Fuc
Virgaureasaponin 5		-Glc-^{3}-Glc	-Xyl-^{2}-Rha-^{4}-Xyl-^{3}-Rha-^{2}-Fuc
Virgaureasaponin 6		-Glc	-((Fuc-^{3}-Api-^{5}-Ac)-^{4}-A)-^{2}-Rha-^{4}-Xyl-^{3}-Rha

Solidagosaponins	R1	R2	R3
Solidagosaponin 1	-H	-Glc-^{2}-Ara	-H
Solidagosaponin 2	-H	-Glc-^{2}-Ara-^{4}-A	-H
Solidagosaponin 3	-H	-Glc-^{2}-Ara	-Rha
Solidagosaponin 4	-H	-Glc-^{2}-Ara-^{4}-A	-Rha
Solidagosaponin 5	-H	-Glc-^{2}-Ara	-Xyl
Solidagosaponin 6	-H	-Glc-^{2}-Ara-^{4}-A	-Xyl
Solidagosaponin 7	-H	-Glc-^{2}-Ara	-Ara
Solidagosaponin 8	-H	-Glc-^{2}-Ara-^{4}-A	-Ara
Solidagosaponin 9	-Glc-^{4}-Glc	-H	-H

Figure 7. Saponins from *S. virgaurea* L.

Polysaccharides

Both inflorescences and leaves of *S. virgaurea* L. contain polysaccharides. Those isolated from inflorescences contain uronic acids (over 40%, mostly galacturonic acid), galactose (13-18%), glucose (7-12.5%), rhamnose (4-7.5%), arabinose (2-8%), and xylose (1-2%) residues [81]. The amount and the proportion among the components vary along the growing stages of the plant [81]. J. Saluk-Juszczak (2010) reported quite different proportions of sugars for the polyphenolic-polysaccharide conjugates isolated from the flower heads (rhamnose 22.4%, fucose 5.0%, arabinose 19.2%, xylose 2.6%, mannose 1.3%, glucose 13.0%, galactose 14.0%) [110].

6. Pharmacology

6.1. Antioxidant Properties

Joining the nutritional vocabulary of the masses at least three decades ago, the concept of "antioxidants" remains one poorly understood in the field of life sciences, and the clinical relevance of antioxidants is still rather fuzzy, with many knowledge gaps [111]. However, partly because the assessment of antioxidant potential is easily accessible and relatively cheap, for many herbal products the antioxidant properties are evaluated repeatedly, and *S. virgaurea* makes no exception, the first study on this topic dating from 1995 [87]. In this study, ethanolic extracts of the plant were shown *in vitro* to inhibit lipoxygenase and xanthine oxidase pathways [87]. A methanol extract obtained from the young shoots and leaves had stronger antioxidant effects (measured in vitro with a DPPH-based assay) than an extract prepared with hot water [86]. Autoclaving of an 80% ethanol extract resulted in decreased scavenging effects on DPPH and ABTS (associated with a decline in polyphenol and flavonoid contents), but it increased the chelating effects on ferrous ions [112]. Although a slightly higher antioxidant effect was observed when using pressurized fluid extraction over the ultrasonic extraction method on *S. virgaurea* L. leaves (94.0% vs. 89.% inhibition), the difference was not statistically significant [100]. Both leaf and stem powders, as well as extracts obtained from those parts, prevented lipid oxidation when applied on ground pork samples [113,114]. Among 23 herbal species examined for their antioxidant effect in one study, *S. vigaurea* L. had an average antioxidant activity (in decreasing order, it occupied the 11th position out of 23) [44].

The key component and marker of the antioxidant properties of *S. virgaurea* was found by M. Marksa et al. (2020) to be 3,5-dicaffeoylquinic acid (about half of the whole scavenging activity, as for *S. canadensis* and *S. ×niederederi*, but unlike *S. gigantea*, for which the main component responsible is chlorogenic acid) [97]. For several *Solidago* species tested, the scavenging activities were stronger for the leaf products than for the inflorescences [97]. The radical neutralizing properties of quercetin derivatives from *Solidago* species was shown to be considerably lower to that of the cafeoylquinic derivatives, but it is higher than that of kaempferol derivatives, whose antioxidant potential is insignificant [97]. Di-caffeoylquinic acids have a stronger radical scavenging effect than mono-caffeoylquinic acids [97].

6.2. Antiinflammatory effects

The antiinflammatory activity of *S. virgaurea* extracts or components isolated from the species has been repeatedly evaluated, confirmed and ascribed to different phytochemicals from its composition. In a rat model, H. J. Jacker et al. (1981) showed that a triterpene saponin fraction administered i.v. at a low dose (1.25-2.5 mg/kg) caused a significant decrease of edema, as measured by pletysmograph [9,115]. Although J. Metzner et al. (1984) reported some anti-inflammatory effect for leiocarposide (200 mg/kg) in a carrageenan-induced edema model in rats, the effect was obviously inferior to that of phenylbutazone (e.g. 3% vs. 53% two hours post-administration and 27% vs. 54% reduction five hours post-administration) [9,56]. Rutin and quercetin, as well as 3,5-dicaffeoylquinic acid were shown by M. Melzig et al. (2000) to inhibit leukocyte elastase, an effect considered synergistic with the radical scavenging of the same molecules in exerting their anti-inflammatory activity [33,84]. Instead, saponins and leiocarposide did not demonstrate any such elastase inhibition; the same authors claimed that ester saponins stimulate the release of ACTH by their interaction with cell membranes of the pituitary cells, and thus, consecutively,

glucocorticoids with anti-inflammatory effects [33,84]. 3,4,5-O-tricaffeoylquinic acid was identified among phenolic compounds from *S. virgaurea* as having the highest anti-inflammatory effect (88% of that of indomethacin) in rats (carrageenan-based rat paw edema)   and to inhibit TNF-α and IL-1β [10]. On the other hand, other studies reported stimulation of TNF-α secretion by macrophages, an effect induced by different phytochemicals of the species (2-methoxybenzyl-2-hydroxybenzoate, benzyl-2-hydroxy-6-methoxybenzoate) [116], and it remains to be investigated in what contexts and under the influence of what variables one or the other effect will predominate.

Aqueous and ethanolic extracts of *S. virguarea* have demonstrated an ability to reduce paw edema and arthritic paw volume in rat models of inflammation [117]. Some inhibition of dihydrofolate reductase has been described for a hydroalcoholic extract of the species, and this has been suggested as contributing to the anti-inflammatory effects of the *S. virgaurea* extracts, being known that inhibitors of the enzyme, such as methotrexate, do have anti-inflammatory activity [118–120].

A standardized combination of alcoholic extracts of *S. vigaurea*, *Populus tremula* L., and *Fraxinus excelsior* L. has been developed as an anti-rheumatic drug and has been relatively extensively investigated [117,121,122].

6.3. Analgesic activity

An *in vitro* study evaluated the analgesic potential of a methanol seed extract by assessing its affinity for three receptors involved in acute pain signaling (bradykinin, neurokinin 1, and calcitonin gene related peptide). The extract exhibited substantial binding to the bradykinin receptor, but this effect was canceled by PVP treatment, allowing the authors to speculate that it should probably be ascribed to non-specific binding of tannins or other polyphenols [123]. In the hot plate test on mice, leiocarposide demonstrated very similar analgesic effects to aminophenazone for the first hour, but those effects almost disappeared post-administration after the second hour [56].

6.4. Spasmolytic and antihypertensive activity

Ex vivo data obtained on isolated smooth muscles from guinea pig gut showed a modest spasmolytic effect for a *S. virgaurea* ethanol extract (less than 15% of the papaverine effect) [9,124]. As mentioned below, extracts of *S. virgaurea* have demonstrated anti-muscarinic effects on isolated bladder, inhibiting the M2 and M3 receptors [31]. It has been stated that all species of the genus have "hypotensive activity", including *S. virgaurea*, which demonstrated such an effect in dogs, for a leaf extract, at a dose of 150/kg [119,125,126]. Aqueous extract from flowers and from leaves, administered by i.v. route in rats, at doses of 180 and 360 mg/kg found no reduction of blood pressure after the first 2-5 minutes, for both organs [127], despite isolated interpretations to the contrary [119]. This has been speculatively related to a potential contribution of flavonoids, based on the reported vasodilatory effects mediated by the inhibition of protein kinase C resulting in the relaxation of the arterial smooth muscle [88]. In that study, flavonols had a stronger effect than flavones, which in their turn had a more potent effect than flavanols [88], and as shown above, *S. virgaurea* key flavonoids are derivatives of flavonols (quercetin and kaempferol).

6.5. Diuretic effects and benefits in other urinary tract conditions

As shown above, many folk traditions attribute a diuretic activity to extracts prepared from *S. virgaurea* L. In academic sources, it is mentioned at least starting with the 17th Century, when Shcroeder's "Thesaurus pharmacologicus" points out to it; throughout the 20th Century different sources also cite this pharmacological effect in relationship to *S. virgaurea* products [9].

The diuretic effects have been attributed to the flavonoid fraction (particularly quercetin and its derivatives), which was shown to inhibit the neutral endopeptidase resulting in an enhanced urinary flow [84,97]. The inhibition of neutral endopeptidase leads to an increase in the plasma concentration of natriuretic peptides, which have strong natriuretic properties [128]. A. Chodera et al. (1991) found that this flavonoid fraction (25 mg/kg b.w.) increase the urine output in rats by about 88%, and causes a decrease in the excretion of sodium and potassium, accompanied by an increase in

calcium excretion [9,67]. These results are in contradiction with those reported later by U. Kaspers et al. (1998), who found no increase in urine volume or electrolytes for the flavonoid fraction [9,129]. Instead, they reported that the hydroxycinnamic acid fraction (100 mg/kg) and the saponin fraction (25-100 mg/kg) had an effect comparable with those of furosemide [9,129], including an increase in sodium and potassium excretion, unlike the data reported by A. Chodera et al. (1991), which claimed a decrease in the excretion of these ions [9,67].

Besides the flavonoidic fraction, leiocarposide (25 mg/kg, i.p.) was also shown by A. Chodera et al. (1985) to have diuretic activity, equivalent to about 75% of the furosemide effect [9,130]. The same authors have demonstrated that the i.p. route results in higher efficacy (about 30%) than the oral route, that it has a slow onset (around 5 hours), and it lasts for up to 24 hours [9,119,131]. The aglycone part of the glycoside (leiocarpic acid) is devoid of diuretic activity (at the same dose, 25 mg/kg i.p.) [9,132].

Besides the assumed diuretic effects, S. virgaurea has been declared "the plant that is most frequently extracted to yield preparations for the treatment of bladder dysfunction including the overactive bladder syndrome" [31]. In this sense, clinical data in patients with dysuria have claimed that *S. virgaurea* reduces the frequency of urination (as well as the pain associated with it). In a relatively large (n=512 patients), but open-label and uncontrolled study of patients with chronic recurrent overactive bladder, 96% of the subjects receiving 424.8 mg of *S. vigraurea* extract, t.i.d., reported an improvement in the clinical global impression and a significant drop in painful micturition and in the need to urinate [133]. In a smaller study (n=74), also open-label, carried out on female patients with dysuria, a reduction of the same symptoms was observed in 69% of the patients [133]. These results are somewhat puzzling because diuretics tend to rather increase the frequency of urination, but the diuretic data come from non-clinical studies with an isolated compound (leiocarposide) or the flavonoid fraction, and not with an extract as such. On the other hand, the open-label character and the lack of a control group indicate a low quality of these data and stronger evidence is needed to conclude on the effect *S. virgaurea* have on the urinary tract. *In vitro* data have demonstrated that extracts of the plant have anti-muscarinic effects on the M2 and M3 receptors, which results in the inhibition of the bladder contraction [31].

Leiocarposide (25 mg/kg p.o.) administered for six weeks significantly inhibited the growth of human-derived urinary calculi transferred into the rat bladder. [57]

6.6. Antibacterial activity

An investigation of the antibacterial potential of two extracts, one alcoholic and one lipophilic (with hexane), found that the alcoholic had the lowest MIC for *Staphyllococcus aureus*, whereas the lipophilic one for *S. aureus* and *P. aeruginosa* [134]. The MIC values varied between 2.95 and 11.8 mg/ml for the ethanolic; for the hexane extract MIC was 3.5 mg/ml for *Staphyllococcus aureus*, *Staphyllococcus faecalis*, and *Pseudomonas aeruginosa*, and higher than 3.5 mg/ml for the other microorganisms tested [134]. Although values lower than 16 mg/ml have been considered sometimes as showing a strong antibacterial effect [135], other authors have used more stringent criteria: MIC values <100 μg/mL have been proposed to be highly active, those between 100 and 500 μg/mL active, those between 500 and 1000 μg/mL moderately active, those between 1000 and 200 μg/mL of low activity, and those with MIC > 2000 μg/mL inactive [136,137]. It has also been suggested that in order to "be considered a promising activity, a crude extract must demonstrate a MIC under 100 μg/ml" (and a pure compound less than 16 μg/ml) [138]. Other studies have also assessed various extracts for their antimicrobial effects, but MIC or MBC (minimal bactericidal concentration) was also for most species higher than 2000 μg/mL [139–141]. In the light of these criteria from the literature, the activities observed in this study are not "promising" and because they are higher than 2000 μg/mL should rather be considered inactive.

In a study comparing (among others) the ethanol and aqueous extracts obtained from leaves and stems of *S. virgaurea* (agar disc diffusion method), inhibition zones were detected only for the ethanol extract and only on *Bacillus subtilis*, *Micrococcus flavus* (Gram-positive), and the Gram-negative *Morganella morganii* [142]. Another study also reported no inhibitory effect on

several microbial species of an aqueous extract [74]. It has been suggested that inhibition zones smaller than 9 mm should be considered inactive, those ranging between 9 and 12 mm, moderately active, those ranging between 13 and 18 mm, active, and those larger than 18 mm should be classified as very active [136,143]. Since in this study all inhibition zones were less than 9 mm in size [142], the ethanol extract should also be regarded as virtually inactive. A. Brantner and J. Grein (1994), though, reported inhibition zones of around 11 mm on *Staphylococcus aureus* and *Escherichia coli* for an aqueous extract prepared from the aerial parts of the plant [140]. A methanol extract produced inhibition zones of 15 mm for *Staphylococcus aureus* and *Bacillus cereus*, and of 20 mm for *Enterobacter fecalis* [86] (i.e., the extract could be considered active and very active, respectively, on these microbial species).

A root extract was fractioned in a bioassay-guided manner and the active compounds responsible for the antibacterial effects (on *Bacillus subtilis* and *Xanthomonas euvesicatoria*, a plant pathogen) were identified as two isomers of the matricaria ester. For the extract, the MIC determined was 172 µg/mL for *B. subtilis*, and 86 µg/mL for *X. euvesicatoria* [32]. Nine clerodante-type diterpenes have been evaluated for their activity on *S. aureus*, and all had a modest activity, considerably inferior to that of vancomycin (the lowest MIC, observed for the second clerodane compound, was 30 µg/mL, 15 times higher than that of vancomycin and over the 16 µg/mL for a pure compound to be considered "active") [80]. A. V. Tkachev et al. (2006) claimed complete inhibition of *S. aureus* for the essential oil [35], but these positive results were observed only with the undiluted essential oil and the ½ dilution, which is of very little clinical significance for systemic use.

Inhibition of bacterial cell division, impairment of plasmalema or cell membranes inside the cell resulting in cell lysis [134,144], and inhibition of dihydrofolate reductase [9,118] have been suggested as potential mechanisms for the supposed antibacterial effects of *S. virgaurea* extracts. The effect has been attributed to several phytochemical groups: phenolic acids and flavonoids [134], terpenes and essential oils [35,134], matricaria ester isomers [32], and clerodante-type diterpenes [80]. Considering the modest antibacterial activity reported by most studies, the discussion of these mechanisms (which are supported in a general way by the general literature on these phytochemicals [145–148]) is, in our view, rather moot.

6.7. Antifungal activity

G. Bader et al. investigated the antifungal potential of *S. virgaurea* extracts and reported that deacylated saponins tend to have a stronger effect on different *Candida* species and *Cryptococcus neoformans* than the corresponding mixture of ester saponins, and among the deacylated saponins, the bidesmosides had stronger activity than monodesmosides [9,68,69,119,149]. S. Pepeljnjak et al. (1998) claimed antimycotic activity on several dermatophyte species (*Trichophyton mentagrophytes*, *Microsporum gypseum* and *Microsporum canis*) for a hydroalcoholic extract (75%) [150], but the MIC values (between 9.7% and 50%) seem too high to support the claim for clinical purposes, the effect being modest at best. M. Chevalier et al. (2012), reported no inhibitory effect of an aqueous extract from *S. virgaurea* on four strains of *Candida albicans* on agar mediums or in liquid medium, but they found that it was able to inhibit the transition between yeast and hyphal growth, a significant inhibition of biofilm formation, as well as a decrease of pre-formed biofilms of *C. albicans*, an effect speculatively attributed to the saponin fraction of the extract [74]. This attribution seems reasonable considering the inherent surfactant properties of saponins, as well as their haemolytic and iron chelator qualities, iron being necessary for the growth and development of *Candida* [74,151]. To confirm this, the same research group carried out a bioassay-guided fractionation that led to the isolation of six triterpene saponins (oleanane-type), of which four caused significant inhibition of *C. albicans* yeast-hyphal switch [75]. What is the clinical relevance of this effect only time will tell.

6.8. Antiparasite activity

In a murine experiment, at a dose of 500 mg/kg bw, an extract of the aboveground parts of S. virgaurea showed the largest effect on *Acanthamoeba*, prolonging the survival of the animals to an average time of 12 days, whereas the controls had a mean survival time of only 4 days. Other three

species tested in the same experiment were associated with shorter survival times [152]. An extract obtained from the stems did not have any remarkable activity on the parasitic nematode *Haemonchus contortus* [153].

6.9. Cytotoxic and antitumor activity

In murine models of sarcoma (allogenic sarcoma-180 and syngenic DBA/2-MC.SC-1 fibrosarcoma), significant antitumor activity was claimed for virgaureasaponin E administered in low doses (1 mg/kg/day) [9,70,71,154]. This effect of viragurea saponin E may at least partly be related to its ability to induce TNFα release from macrophages, as well as to an induction of cytotoxic macrophages [154]. Data for saponins from several species, including *S. virgaurea* L., evaluated on YAC-1 (T cell lymphoma) and P-815 cells (mouse mastocytoma), indicated that the glycosylation pattern (at 3 or 28 carbon atom position) has an influence on the cytotoxicity and that similarly to the antifungal effect, bisdesmosides derived from the polygalacic acid tend to be more active than their related prosapogenins [155]. Not only virgaureasaponin E is able to activate macrophages and TNF-α secretion, but also two C6-C1 compounds of the herbal product (2-methoxybenzyl-2-hydroxybenzoate, benzyl-2-hydroxy-6-methoxybenzoate) [116].

A methanol extract of *S. virgaurea* ssp. gigantean was reported to be active against the melanoma cell line SK-MEL-2 [50]. Fractionation guided by cytotoxicity led to the isolation of three active compounds from the hexane-soluble fraction, evaluated on five human tumor cell lines: erythrodiol-3-acetate, α-tocopherol quinone, and 2-phyten-l-ol [50]. However, the ED_{50} varied between 5.9 and 54.8 μM, which qualified the activity as rather modest (the most active one, with ED_{50} less than 10 μM on four out of the five cancer cell lines was the α-tocopherol quinone) [50]. It should also be considered, though, that if one important mechanism of antitumor activity is the stimulation of cytotoxic macrophages and TNFα release, as discussed above [154], a mere cytotoxicity test may not be appropriate to assess the antitumor potential of these extracts.

Experiments on PC3 cells have shown that whereas aqueous and ethanol extracts had strong cytotoxic activity, chloroform extracts were devoid of such activity [34]. Extracts prepared from stems were markedly less active than those prepared from leaves or flowers [34]. The same authors also found that pre-treatment with protease leads to an almost complete loss of effect, which indicates that a protein is responsible for this activity [34]. A rodent model of prostate cancer (AT6.1) showed that i.p. administration in SCID mice of an active fraction corresponding to a molecular weight of about 40,000 Da (at a low dose of 5 mg/kg, once every three days) resulted in a significant reduction in tumor volume as compared with the non-treated animals [34]. Since SCID mice have immune deficiencies consisting of the lack of B and T lymphocytes, the authors speculated that the effect of this fraction is due to a direct cytotoxic effect rather than being mediated by the immune system [34]. This was also supported by the caspase-3 increase in cells treated with the fraction and the flow cytometric analysis, which suggested that the fraction causes cell cycle arrest (in the G0/G1 phase), triggering then apoptosis [34]. Since SCID mice, though, have macrophages, an immune contribution should not be necessarily excluded, in the absence of direct evidence to the contrary.

Ent-germacra-4(15),5,10(14)-trien-1β-ol, β–dictyopterol, and 3,5-di-O-caffeoyl quinic acid exhibited "moderate cytotoxicity" against five cancer cell lines, with ED_{50} values varying between 1.52-18.57 μM (the most active – ED_{50} between 1.52 and 18.57 μM – being β–dictyopterol) [49]. Methyl 3,5-dicaffeoyl quinate (MDQ) has demonstrated antioxidant activities, as well as antiproliferative effects in vitro, in HT-29 cell, by inducing cell cycle arrest and apoptosis through inhibition of the PI3K/Akt and ERK signaling pathways [156].

6.10. Antimutagenic activity

Hexane extracts of three *Solidago* species demonstrated antimutagenic activity in a *S. typhimurium* test, the most active apparently being *S. virgaurea* L; instead, the ethanolic extracts were devoid of any such antimutagenic effects [134].

6.11. Antiadipogenic and antidiabetic activities

Following an impressive screening of about 300 plant extracts, kaempferol-3-O-rutinoside was isolated from a butanol fraction of a water extract of *S. virgaurea*, showing strong anti-adipogenic effects in vitro and supressing PPAR-γ and C/EBPα expression [104]. Of a number of several phenolic derivatives of the species, evaluated in vitro for their anti-adipogenic potential, 5-di-O-caffeoylquinic acid was found to have the most potent inhibitory effect [157]. A 10% ethanolic extract of *S. virgaurea* also showed good anti-adipogenic effects *in vitro* and *in vivo* in a murine model, causing a decrease in body weight, liver weight, and the magnitude of the adipose tissues [158]. Such experimental data are worth further investigation of the species for its potential use for weight loss purposes.

In an alloxan-induced diabetic rat model, a hydroalcoholic extract of *S. virgaurea* caused a decline in glycemia, TNF-α, serum amylase activity, and pancreatic malondialdehyde, as well as a rise in serum insulin, hepatic glycogen, pancreatic SOD, and catalase activities[159] .

6.12. Cardioprotective effects

In a rat model, a protective effect against cardiotoxicity (induced with isoproterenol) was claimed for a methanolic extract of *S. virgaurea* L. [160].

6.13. Antisenescence effects

An alcoholic extract of *Solidago virgaurea* subsp. *alpestris* was claimed to exert anti-senescence effects in vitro on fibroblasts [161], opening a door towards the possibility to use it as for anti-aging purposes in topical or systemic preparations.

7. Conclusions

S. virgaurea L. is a native species in Europe, with a long tradition of medicinal use for a variety of therapeutic purposes in different geographical reasons: urinary tract conditions, gastro-intestinal conditions, diabetes, allergies, as well as for healing and antiseptic purposes. The largest body of research has been limited to non-clinical experiments up to date, having a wide variability with respect to design, methodological quality, and evidence strength. Many of the relevant studies have been performed before 2000, published in other languages than English, and are not easily accessible today. Clinical investigation has been very limited in scope and volume, and the little clinical data available are not of the highest quality (no clinical randomized, controlled, double-blind study has been published thus far). Whereas some of the pharmacological activities have not been promising (e.g. the antibacterial, antifungal, or cytotoxic effects seem rather modest), others seem more interesting and invite to further research (e.g. antiadipogenic, antisenescence, or the beneficial effects in dysuria and overactive/irritable bladder).

References

1.   World Flora Online Consortium WFO (2020): World Flora Online. Available online: http://www.worldfloraonline.org (accessed on 03 August 2020).

2.   Beck, J.B.; Semple, J.C.; Brull, J.M.; Lance, S.L.; Phillips, M.M.; Hoot, S.B.; Meyer, G.A. Genus-Wide Microsatellite Primers for the Goldenrods (*Solidago* ; Asteraceae). *Applications in Plant Sciences* **2014**, *2*, 1300093, doi:10.3732/apps.1300093.

3.   Toiu, A.; Vlase, L.; Vodnar, D.C.; Gheldiu, A.-M.; Oniga, I. Solidago graminifolia L. Salisb. (Asteraceae) as a Valuable Source of Bioactive Polyphenols: HPLC Profile, In Vitro Antioxidant and Antimicrobial Potential. *Molecules* **2019**, *24*, 2666, doi:10.3390/molecules24142666.

4.   Woźniak, D.; Ślusarczyk, S.; Domaradzki, K.; Dryś, A.; Matkowski, A. Comparison of Polyphenol Profile and Antimutagenic and Antioxidant Activities in Two Species Used as Source of *Solidaginis herba* - Goldenrod. *Chemistry & Biodiversity* **2018**, *15*, e1800023, doi:10.1002/cbdv.201800023.

5.   Goulart, S.; Moritz, M.I.G.; Lang, K.L.; Liz, R.; Schenkel, E.P.; Fröde, T.S. Anti-inflammatory evaluation of Solidago chilensis Meyen in a murine model of pleurisy. *Journal of Ethnopharmacology* **2007**, *113*, 346–353, doi:10.1016/j.jep.2007.07.003.

6.   Tutin, T.G.; Heywood, V.H.; Burges, N.A.; Moore, D.M.; Valentine, D.H.; Walters, S.M.; Webb, D.A. *Flora Europaea. Volume 4. Plantaginaceae To Compositae (And Rubiaceae)*; Zenodo, 1976;

7.   Native Plant Trust. Go Botany.

8.   Móricz, Á.M.; Jamshidi-Aidji, M.; Krüzselyi, D.; Darcsi, A.; Böszörményi, A.; Csontos, P.; Béni, S.; Ott, P.G.; Morlock, G.E. Distinction and valorization of 30 root extracts of five goldenrod (Solidago) species. *Journal of Chromatography A* **2020**, *1611*, 460602, doi:10.1016/j.chroma.2019.460602.

9.   European Medicines Agency Assessment Report on Solidago virgaurea L., Herba 2008.

10.   Abdel Motaal, A.; Ezzat, S.M.; Tadros, M.G.; El-Askary, H.I. *In vivo* anti-inflammatory activity of caffeoylquinic acid derivatives from *Solidago virgaurea* in rats. *Pharmaceutical Biology* **2016**, *54*, 2864–2870, doi:10.1080/13880209.2016.1190381.

11.   Yarnell, E. Botanical medicines for the urinary tract. *World Journal of Urology* **2002**, *20*, 285–293, doi:10.1007/s00345-002-0293-0.

12.   Cai, T.; Caola, I.; Tessarolo, F.; Piccoli, F.; D'Elia, C.; Caciagli, P.; Nollo, G.; Malossini, G.; Nesi, G.; Mazzoli, S.; et al. Solidago, orthosiphon, birch and cranberry extracts can decrease microbial colonization and biofilm development in indwelling urinary catheter: a microbiologic and ultrastructural pilot study. *World J Urol* **2014**, *32*, 1007–1014, doi:10.1007/s00345-013-1173-5.

13.   Calalb, T.; Fursenco, C.; Ionita, O.; Ghendov, V. The morpho-anatomical study of Solidago virgaurea L. species from the flora of Republic of Moldova. *East European Science Journal 2–1*, 4–13.

14.   Szymura, M.; Wolski, K. Leaf Epidermis Traits as Tools to Identify Solidago L. Taxa in Poland. *Acta Biologica Cracoviensia Series Botanica* **2011**, *53*, doi:10.2478/v10182-011-0006-3.

15.   Dobjanschi, L.; Vostinaru, O.; Tamas, M. Criteria for Solidago Species Differentiation. *Acta Univ. Cibiniensis, Seria F Chemia* **2005**, *8*, 41–44.

16.   Buynov, M.; Goryachkina, Y.; Fedoseyeva, G. *Otlichitel'nyye morfologicheskiye i anatomo-diagnosticheskiye priznaki vidov zolotarnikov – kanadskogo, obyknovennogo, daurskogo: uchebnoye posobiye*; IGMU: Irkutsk, 2013;

17.   Souza, D.M.F.D.; Sá, R.D.; Araújo, E.L.; Randau, K.P. Anatomical, phytochemical and histochemical study of Solidago chilensis Meyen. *Anais da Academia Brasileira de Ciências* **2018**, *90*, 2107–2120, doi:10.1590/0001-3765201720160280.

18.   Fedotova, V.; Chelombit'sh, V. Anatomo-diagnosticheskoye izucheniye zolotarnika kavkazskogo (Solidago caucasica Kem.-Nath.) flory Severnogo Kavkaza. In *Razrabotka, issledovaniye i marketing novoy farmatsevticheskoy produktsii: sb. nauch. tr.*; Vyp. 67: Pyatigorsk, 2012.

19.   Bley, L.F. Ueber Verwechselung der herba Solidaginis virgaureae mit herba Senecion. nemorensis. *Archiv der Pharmazie* **1850**, *113*, 34–37, doi:10.1002/ardp.18501130112.

20.   Semple, J. An intuitive phylogeny and summary of chromosome number variation in the goldenrod genus Solidago (Asteraceae: Astereae). *Phytoneuron* **2016**, *2016–32*, 1–9.

21.   Sakaguchi, S.; Kimura, T.; Kyan, R.; Maki, M.; Nishino, T.; Ishikawa, N.; Nagano, A.J.; Honjo, M.N.; Yasugi, M.; Kudoh, H.; et al. Phylogeographic analysis of the East Asian goldenrod (Solidago virgaurea complex, Asteraceae) reveals hidden ecological diversification with recurrent formation of ecotypes. *Ann. Bot.* **2018**, *121*, 489–500, doi:10.1093/aob/mcx182.

22.   Kiełtyk, P.; Mirek, Z. Taxonomy of the Solidago virgaurea Group (Asteraceae) in Poland, with Special Reference to Variability along an Altitudinal Gradient. *Folia Geobotanica* **2014**, *49*, 259–282, doi:10.1007/s12224-013-9180-2.

23.   Yuzepchuk, S. Zolotarnik –Solidago L. In *Flora SSSR 25*; Shishkin, B., Ed.; Izdatel'stvo Akademii Nauk SSSR: Moskva, Leningrad, 1959; pp. 31–50.

24.   Slavík, B. Solidago L. – zlatobýl. In *Květena České Republiky 7 (Flora of the Czech Republic 7)*; Slavík, B., Štěpánková, J., Eds.; Academia: Prague, 2004; pp. 114–123.

25.   Botanical Society of Britain and Ireland; Biological Records Center; UK Center for Ecology and Hydrology; Joint Nature Conservation Committee Online Atlas of the British and Irish flora - Solidago virgaurea. Available online: https://www.brc.ac.uk/plantatlas/plant/solidago-virgaurea (accessed on 28 August 2020).

26.   Sakaguchi, S.; Horie, K.; Ishikawa, N.; Nagano, A.J.; Yasugi, M.; Kudoh, H.; Ito, M. Simultaneous evaluation of the effects of geographic, environmental and temporal isolation in ecotypic populations of *Solidago virgaurea*. *New Phytologist* **2017**, *216*, 1268–1280, doi:10.1111/nph.14744.

27.   Laphitz, R.M.L.; Semple, J.C. A Multivariate Morphometric Analysis of the *Solidago chilensis* Group in South America and Related Taxa in North America (Asteraceae, Astereae) [1]. *Annals of the Missouri Botanical Garden* **2015**, *100*, 423–441, doi:10.3417/2014023.

28.   American Botanical Council Solidago virgaurea L. Available online: http://cms.herbalgram.org/MedPlantID/BotanicalEntries/Solidago_virgaurea.html (accessed on 28 August 2020).

29.   European Medicines Agency Community Herbal Monograph on Solidago Virgaurea L., Herba, EMEA/HMPC/285758/2007 2008. Available online: https://www.ema.europa.eu/en/documents/herbal-monograph/final-community-herbal-monograph-solidago-virgaurea-l-herba_en.pdf (accessed on 28 August 2020).

30.   Blum, H. Goldenrod has increasing importance as a herbal drug. *Gemuse* **1999**, 431–432.

31.   Borchert, V.E.; Czyborra, P.; Fetscher, C.; Goepel, M.; Michel, M.C. Extracts from Rhois aromatica and Solidaginis virgaurea inhibit rat and human bladder contraction. *Naunyn-Schmiedeberg's Archives of Pharmacology* **2004**, *369*, 281–286, doi:10.1007/s00210-004-0869-x.

32.   Móricz, Á.M.; Ott, P.G.; Häbe, T.T.; Darcsi, A.; Böszörményi, A.; Alberti, Á.; Krüzselyi, D.; Csontos, P.; Béni, S.; Morlock, G.E. Effect-Directed Discovery of Bioactive Compounds Followed by Highly Targeted Characterization, Isolation and Identification, Exemplarily Shown for *Solidago virgaurea*. *Analytical Chemistry* **2016**, *88*, 8202–8209, doi:10.1021/acs.analchem.6b02007.

33.   Melzig, M.F. Goldenrod – a classical exponent in the urological phytotherapy. *Wiener Medizinische Wochenschrift* **2004**, *154*, 523–527, doi:10.1007/s10354-004-0118-4.

34.   Gross, S.C.; Goodarzi, G.; Watabe, M.; Bandyopadhyay, S.; Pai, S.K.; Watabe, K. Antineoplastic activity of Solidago virgaurea on prostatic tumor cells in an SCID mouse model. *Nutrition and cancer* **2002**, *43*, 76–81.

35.   Tkachev, A.V.; Korolyuk, E.A.; Letchamo, W. Volatile Oil-Bearing Flora of Siberia VIII: Essential Oil Composition and Antimicrobial Activity of Wild *Solidago virgaurea* L. from the Russian Altai. *Journal of Essential Oil Research* **2006**, *18*, 46–50, doi:10.1080/10412905.2006.9699382.

36.   Heger, M. Entzündliche Erkrankungen der Urogenitalorgane. In *Naturheilverfahren in der Urologie*; Springer Berlin Heidelberg: Berlin, Heidelberg, 2003; pp. 55–102 ISBN 978-3-662-08920-0.

37.   Bader, G.; Wray, V.; Hiller, K. The Main Saponins from the Aerial Parts and the Roots of *Solidago virgaurea* subsp. *virgaurea* *. *Planta Medica* **1995**, *61*, 158–161, doi:10.1055/s-2006-958038.

38.   A. Vogel Plant Encylopedia Solidago virgaurea L. Available online: https://www.avogel.com/plant-encyclopaedia/solidago_virgaurea.php (accessed on 28 August 2020).

39.   Tománková, V.; Vlčková, A.; Anzenbacher, P.; Bachleda, P.; Anzenbacherová, E. Užívání přípravků ze zlatobýlu obecného (Solidago virgaurea) neovlivňuje metabolizmus současně podávaných léčiv. *Klin Farmakol Farm* **2016**, *30*, 11–15.

40.   Nawłoć pospolita (Solidago virgaurea). Available online: https://www.plantago-sklep.pl/blog/nawloc-pospolita/ (accessed on 28 August 2020).

41.   Malankina, Y. Zolotarnik: lekarstvennyye svoystva i primeneniye. Available online: https://www.greeninfo.ru/grassy/solidago_canadensis.html/Article/_/aID/5959 (accessed on 28 August 2020).

42.   Suleymanova, F.S.; Nesterova, O.V.; First Moscow State Medical University named after I.M.Sechenov, Moscow, Russian Federation; Matyushin, A.A.; First Moscow State Medical University named after I.M.Sechenov, Moscow, Russian Federation The historical background and prospects of Canadian goldenrod

(Solidago canadensis L.) herb medicinal use. *The Journal of scientific articles "Health and Education millennium"* **2017**, *19*, 142–149, doi:10.26787/nydha-2226-7425-2017-19-4-142-149.

43.   Kolosova, V. Name – Text – Ritual: The Role of Plant Characteristics in Slavic Folk Medicine. *Folklorika* **2005**, *X*, 44–61.

44.   Kiselova, Y.; Ivanova, D.; Chervenkov, T.; Gerova, D.; Galunska, B.; Yankova, T. Correlation between theIn Vitro antioxidant activity and polyphenol content of aqueous extracts from bulgarian herbs. *Phytotherapy Research* **2006**, *20*, 961–965, doi:10.1002/ptr.1985.

45.   Dobjanschi, L.; Paltinean, R.; Vlase, L.; Babota, M.; Fritea, L.; Tamas, M. Comparative phytochemical research of Solidago genus: S. graminifolia. Note I. Flavonoids. *Acta Biologica Marisiensis* **2018**, *1*, 18–26.

46.   Calalb, T.; Bodrug, M. *Botanica faramaceutică*; CEP Medicina: Chisinau, 2009;

47.   Tamas, M.; Toader, S. Acțiunea diuretică a unor specii de Solidago. *Clujul Medical* **1989**, *62*, 75–79.

48.   Petran, M.; Dragos, D.; Gilca, M. Historical ethnobotanical review of medicinal plants used to treat children diseases in Romania (1860s-1970s). *J Ethnobiol Ethnomed* **2020**, *16*, 15, doi:10.1186/s13002-020-00364-6.

49.   Choi, S.Z.; Choi, S.U.; Lee, K.R. Pytochemical constituents of the aerial parts fromsolidago virga-aurea var. gigantea. *Archives of Pharmacal Research* **2004**, *27*, 164–168, doi:10.1007/BF02980100.

50.   Sung, J.H.; Lee, J.O.; Son, J.K.; Park, N.S.; Kim, M.R.; Kim, J.G.; Moon, D.C. Cytotoxic constituents fromSolidago virga-aurea var.gigantea MIQ. *Archives of Pharmacal Research* **1999**, *22*, 633–637, doi:10.1007/BF02975338.

51.   Inose, Y.; Miyase, T.; Ueno, A. Studies on the Constituents of Solidago virga-aurea L.I. Structural Elucidation of Saponins in the Herb. *CHEMICAL & PHARMACEUTICAL BULLETIN* **1991**, *39*, 2037–2042, doi:10.1248/cpb.39.2037.

52.   Dmuchowski, W.; Gozdowski, D.; Brągoszewska, P.; Baczewska, A.H.; Suwara, I. Phytoremediation of zinc contaminated soils using silver birch (Betula pendula Roth). *Ecological Engineering* **2014**, *71*, 32–35, doi:10.1016/j.ecoleng.2014.07.053.

53.   Bielecka, A.; Królak, E. The accumulation of Mn and Cu in the morphological parts of Solidago canadensis under different soil conditions. *PeerJ* **2019**, *7*, e8175, doi:10.7717/peerj.8175.

54.   Bielecka, A.; Królak, E. Solidago canadensis as a bioaccumulator and phytoremediator of Pb and Zn. *Environ Sci Pollut Res Int* **2019**, *26*, 36942–36951, doi:10.1007/s11356-019-06690-x.

55.   Oldroyd, B.P. What's Killing American Honey Bees? *PLoS Biology* **2007**, *5*, e168, doi:10.1371/journal.pbio.0050168.

56.   Metzner, J.; Hirschelmann, R.; Hiller, K. [Antiphlogistic and analgesic effects of leiocarposide, a phenolic bisglucoside of Solidago virgaurea L]. *Pharmazie* **1984**, *39*, 869–870.

57.   Chodera, A.; Dabrowska, K.; Bobkiewicz-Kozłowska, T.; Tkaczyk, J.; Skrzypczak, L.; Budzianowski, J. [Effect of leiocarposide on experimental urinary calculi in rats]. *Acta Pol Pharm* **1988**, *45*, 181–186.

58.   Thiem, B.; Wesołowska, M.; Skrzypczak, L.; Budzianowski, J. Phenolic compounds in two Solidago L. species from in vitro culture. *Acta Pol Pharm* **2001**, *58*, 277–281.

59.   Roslon, W.; Osinska, E.; Mazur, K.; Geszprych, A. Chemical characteristics of European goldenrod (Solidago virgaurea L. subsp. virgaurea) from natural sites in central and Eastern Poland. *Acta Scientiarum Polonorum, Hortorum Cultus* **2014**, *13*, 55–65.

60.   Borkowski, B.; Skrzypczakowa, L. Polyphenolic Compounds in Herbs of the Species Solidago L. *Acta Pol Pharm.* **1962**, 491–495.

61.   Kalemba, D. Phenolic acids in four Solidago species. *Pharmazie* **1992**, *47*, 471–472.

62.   Bajkacz, S.; Baranowska, I.; Buszewski, B.; Kowalski, B.; Ligor, M. Determination of Flavonoids and Phenolic Acids in Plant Materials Using SLE-SPE-UHPLC-MS/MS Method. *Food Analytical Methods* **2018**, *11*, 3563–3575, doi:10.1007/s12161-018-1332-9.

63.   Budzianowski, J.; Skrzypczak, L.; Wesolowska, M. Flavonoid patterns in the genus Solidago. *Pharm. Weekblad.* **1987**, *Sci Ed 9*, 230.

64.   Pietta, P.; Gardana, C.; Mauri, P.; Zecca, L. High-performance liquid chromatographic analysis of flavonol glycosides of Solidago virgaurea. *Journal of Chromatography A* **1991**, *558*, 296–301.

65.   Tamas, M. Cercetări chemotaxonomice la genul Solidago. *Contrib Bot (Cluj-Napoca)* **1986**, 110–113.

66.   Dobjanschi, L.; Fritea, L.; Patay, E.B.; Tamas, M. Comparative study of the morphological and phytochemical characterization of Romanian Solidago species. *Pak J Pharm Sci* **2019**, *32*, 1571–1579.

67.   Chodera, A.; Dabrowska, K.; Sloderbach, A.; Skrzypczak, L.; Budzianowski, J. [Effect of flavonoid fractions of Solidago virgaurea L on diuresis and levels of electrolytes]. *Acta Pol Pharm* **1991**, *48*, 35–37.

68.   Bader, G.; Binder, K.; Hiller, K.; Ziegler-Böhme, H. The antifungal action of triterpene saponins of Solidago virgaurea L. *Die Pharmazie* **1987**, *42*, 140.

69.   Bader, G.; Kulhanek, Y.; Ziegler-Böhme, H. Zur antimyzetischen Wirksamkeit von polygalasäureglycosiden. *Pharmazie* **1990**, *45*, 618–620.

70.   Bader, G.; Plohmann, B.; Franz, G. Saponin from Solidago virgaurea L. Possible Agents for Therapy of Cancer? In. 44th Annual Congress of the Society for Medicinal Plant Research and a Joint Meeting with the Czech Biotechnology Society. Abstracts of Lectures and Poster Presentations, Prague, September, 1996, pp. 3-7

71.   Bader, G.; Wray, V.; Just, U.; Hiller, K. Enzymatic hydrolysis of the cytotoxic triterpenoid glycoside virgaureasaponin 1. *Phytochemistry* **1998**, *49*, 153–156.

72.   Inose, Y.; Miyase, T.; Ueno, A. Studies on the Constituents of Solidago virga-aurea L. II. Structures of Solidagosaponins X-XX. *CHEMICAL & PHARMACEUTICAL BULLETIN* **1992**, *40*, 946–953, doi:10.1248/cpb.40.946.

73.   Dobjanschi, L.; Zdrinca, M.; Muresan, M.; Vicas, S.; Antonescu, A. The thin layer chromatography analysis of saponins belonging to Solidago species. *Fascicula Protectia Mediului* **2013**, *21*, 56–60.

74.   Chevalier, M.; Medioni, E.; Prêcheur, I. Inhibition of Candida albicans yeast–hyphal transition and biofilm formation by Solidago virgaurea water extracts. *Journal of Medical Microbiology* **2012**, *61*, 1016–1022, doi:10.1099/jmm.0.041699-0.

75.   Laurençon, L.; Sarrazin, E.; Chevalier, M.; Prêcheur, I.; Herbette, G.; Fernandez, X. Triterpenoid saponins from the aerial parts of Solidago virgaurea alpestris with inhibiting activity of Candida albicans yeast-hyphal conversion. *Phytochemistry* **2013**, *86*, 103–111, doi:10.1016/j.phytochem.2012.10.004.

76.   Kalemba, D. Constituents of the essential oil of Solidago virgaurea L. *Flavour and fragrance journal* **1998**, *13*, 373–376.

77.   Kalemba, D.; Thiem, B. Constituents of the essential oils of four micropropagated Solidago species. *Flavour and Fragrance journal* **2004**, *19*, 40–43.

78.   Fujita, Y.; Fujita, S.; Hayama, Y. Miscellaneous contributions to the essential oils of plants from various territories. Components of the essential oils of Solidago virgaurea Linn.ssp. Nippon Nogei Kagaku Kaishi. 1990, 64: 1729–1732 (Jpn). *Chemical Abstracts* **1991**, *114*, 98252d.

79.   Bertoli, A.; Cioni, P.L.; Flamini, G.; Morelli, I.; Spinelli, G.; Tomei, P.E. Constituents of the Essential Oil of *Solidago litoralis* , an Endemic Plant from Northern Tuscany (Italy). *Journal of Essential Oil Research* **1999**, *11*, 215–216, doi:10.1080/10412905.1999.9701114.

80.   Starks, C.M.; Williams, R.B.; Goering, M.G.; O'Neil-Johnson, M.; Norman, V.L.; Hu, J.-F.; Garo, E.; Hough, G.W.; Rice, S.M.; Eldridge, G.R. Antibacterial clerodane diterpenes from Goldenrod (Solidago virgaurea). *Phytochemistry* **2010**, *71*, 104–109, doi:10.1016/j.phytochem.2009.09.032.

81.   Pychenkova, P.A. Dynamics of the amount and characteristics of the polysaccharides ofSolidago virgaurea. *Chemistry of Natural Compounds* **1987**, *23*, 246–247, doi:10.1007/BF00598770.

82.   Lam, J. Polyacetylenes of Solidago virgaurea: their seasonal variation and NMR long-range spin coupling constants. *Phytochemistry* **1971**, *10*, 647–653.

83.   Council of Europe *European Pharmacopoeia (Ph. Eur.)*; 10th Edition.; Council of Europe: Strasbourg, 2019;

84.   Melzig, M.; Löser, B.; Bader, G.; Papsdorf, G.; others European goldenrod as an anti-inflammatory drug: investigations into the cyto-and molecular pharmacology for a better understanding of the anti-inflammatory activity of preparations from Solidago virgaurea. *Zeitschrift für Phytotherapie* **2000**, *21*, 67–70.

85.   Vuolo, M.M.; Lima, V.S.; Junior, M.R.M. Phenolic compounds: structure, classification, and antioxidant power. In *Bioactive compounds*; Elsevier, 2019; pp. 33–50.

86.   Demir, H.; Acik, L.; Bali, E.B.; Koç, L.Y.; Kaynak, G. Antioxidant and antimicrobial activities of Solidago virgaurea extracts. *African Journal of Biotechnology* **2009**, *8*.

87.   Meyer, B.; Schneider, W.; Elstner, E. Antioxidative properties of alcoholic extracts from Fraxinus excelsior, Populus tremula and Solidago virgaurea. *Arzneimittel-forschung* **1995**, *45*, 174.

88.   Duarte, J.; Utrilla, P.; Jimenez, J.; Tamargo, J.; Zarzuelo, A.; others Vasodilatory effects of flavonoids in rat aortic smooth muscle. Structure-activity relationships. *General pharmacology* **1993**, *24*, 857–862.

89.   Hiller, K.; Dube, G.; Zeigan, D. Virgaureoside a a new bisdesmosidic phenol glycoside from solidago virgaurea. *Die Pharmazie* **1985**, *40*, 795–796.

90.   Paun, G.; Neagu, E.; Albu, C.; Radu, G.L. Verbascum phlomoides and Solidago virgaureae herbs as natural source for preventing neurodegenerative diseases. *Journal of Herbal Medicine* **2016**, *6*, 180–186, doi:10.1016/j.hermed.2016.08.001.

91.   Skrzypczak, L.; Wesołowska, M.; Thiem, B.; Budzianowski, J. Solidago L. Species (Goldenrod): In Vitro Regeneration and Biologically Active Secondary Metabolites. In *Medicinal and Aromatic Plants XI*; Bajaj, Y.P.S., Ed.; Biotechnology in Agriculture and Forestry; Springer Berlin Heidelberg: Berlin, Heidelberg, 1999; Vol. 43, pp. 384–403 ISBN 978-3-642-08363-1.

92.   Bader, G.; Janka, M.; Hannig, H.; Hiller, K. Zur quantitativen Bestimmung von Leiocaposid in Solidago virgaurea L. *Die Pharmazie* **1990**, *45*, 380–381.

93.   Fuchs, L. Isolierung Von Quercitrin Aus Solidago Virga Aurea L., S. Serotina Ait Und S. Canadensis L. *Scientia pharmaceutica* **1949**, *17*, 128–131.

94.   Apáti, P.; Szentmihályi, K.; Kristó, Sz.T.; Papp, I.; Vinkler, P.; Szoke, É.; Kéry, Á. Herbal remedies of Solidago—correlation of phytochemical characteristics and antioxidative properties. *Journal of Pharmaceutical and Biomedical Analysis* **2003**, *32*, 1045–1053, doi:10.1016/S0731-7085(03)00207-3.

95.   Kraujalienė, V.; Pukalskas, A.; Venskutonis, P.R. Biorefining of goldenrod (Solidago virgaurea L.) leaves by supercritical fluid and pressurized liquid extraction and evaluation of antioxidant properties and main phytochemicals in the fractions and plant material. *Journal of Functional Foods* **2017**, *37*, 200–208, doi:10.1016/j.jff.2017.07.049.

96.   Haghi, G.; Hatami, A. Simultaneous Quantification of Flavonoids and Phenolic Acids in Plant Materials by a Newly Developed Isocratic High-Performance Liquid Chromatography Approach. *Journal of Agricultural and Food Chemistry* **2010**, *58*, 10812–10816, doi:10.1021/jf102175x.

97.   Marksa, M.; Zymone, K.; Ivanauskas, L.; Radušienė, J.; Pukalskas, A.; Raudone, L. Antioxidant profiles of leaves and inflorescences of native, invasive and hybrid Solidago species. *Industrial Crops and Products* **2020**, *145*, 112123, doi:10.1016/j.indcrop.2020.112123.

98.   Fraisse, D.; Felgines, C.; Texier, O.; Lamaison, J.-L. Caffeoyl Derivatives: Major Antioxidant Compounds of Some Wild Herbs of the <i>Asteraceae</i> Family. *Food and Nutrition Sciences* **2011**, *02*, 181–192, doi:10.4236/fns.2011.230025.

99.   Jaiswal, R.; Kiprotich, J.; Kuhnert, N. Determination of the hydroxycinnamate profile of 12 members of the Asteraceae family. *Phytochemistry* **2011**, *72*, 781–790, doi:10.1016/j.phytochem.2011.02.027.

100. Dobiáš, P.; Pavlíková, P.; Adam, M.; Eisner, A.; Beňová, B.; Ventura, K. Comparison of pressurised fluid and ultrasonic extraction methods for analysis of plant antioxidants and their antioxidant capacity. *Open Chemistry* **2010**, *8*, 87–95, doi:10.2478/s11532-009-0125-9.

101. Goswami, A.; Barua, R.N.; Sharma, R.P.; Baruah, J.N.; Kulanthaivel, P.; Herz, W. Clerodanes from solidago virgaurea. *Phytochemistry* **1984**, *23*, 837–841, doi:10.1016/S0031-9422(00)85038-4.

102. Kruk, J.; Baranowska, I.; Buszewski, B.; Bajkacz, S.; Kowalski, B.; Ligor, M. Flavonoids enantiomer distribution in different parts of goldenrod (*Solidago virgaurea* L.), lucerne (*Medicago sativa* L.) and phacelia (*Phacelia tanacetifolia* Benth.). *Chirality* **2019**, *31*, 138–149, doi:10.1002/chir.23041.

103. Bjorkman, O.; Holmgren, P. Preliminary Observations on Anthocyanins and Other Flavonoid Compounds and Respiration Rates in Different Ecotypes of Solidago virgaurea. *Physiologia Plantarum* **1958**, *11*, 154–157, doi:10.1111/j.1399-3054.1958.tb08433.x.

104. Jang, Y.; Wang, Z.; Lee, J.-M.; Lee, J.-Y.; Lim, S. Screening of Korean Natural Products for Anti-Adipogenesis Properties and Isolation of Kaempferol-3-O-rutinoside as a Potent Anti-Adipogenetic Compound from Solidago virgaurea. *Molecules* **2016**, *21*, 226, doi:10.3390/molecules21020226.

105. Nkuimi Wandjou, J.G.; Quassinti, L.; Gudžinskas, Z.; U. Nagy, D.; Cianfaglione, K.; Bramucci, M.; Maggi, F. Chemical composition and antiproliferative effect of essential oils of four Solidago species (S. canadensis, S. gigantea, S. virgaurea and S.× niederederi). *Chemistry & Biodiversity* **2020**, doi:10.1002/cbdv.202000685.

106. Hiller, K.; Genzel, S.; Murach, M.; Franke, P. Zur Kenntnis der Saponine der Gattung Solidago. 1 Mitteilung: Uber die Saponine von Solidago virgaurea L. *Pharmazie* **1975**, *30*, 188–190.

107. Bader, G.; Wray, V.; Hiller, K. Virgaureasaponin 3, a 3,28-bisdesmosidic triterpenoid saponin from Solidago virgaurea. *Phytochemistry* **1992**, *31*, 621–623, doi:10.1016/0031-9422(92)90047-T.

108. Miyase, T.; Inose, Y.; Ueno, A. Studies on the Constituents of Solidago virga-aurea L. III. Structures of Solidagosaponins XXI-XXIX. *CHEMICAL & PHARMACEUTICAL BULLETIN* **1994**, *42*, 617–624, doi:10.1248/cpb.42.617.

109. Schöpke, T.; Wray, V.; Rzazewska, B.; Hiller, K. Bellissaponins BA1 and BA2, acylated saponins from Bellis perennis. *Phytochemistry* **1991**, *30*, 627–631.

110. Saluk-Juszczak, J.; Pawlaczyk, I.; Olas, B.; Kołodziejczyk, J.; Ponczek, M.; Nowak, P.; Tsirigotis-Wołoszczak, M.; Wachowicz, B.; Gancarz, R. The effect of polyphenolic-polysaccharide conjugates

from selected medicinal plants of Asteraceae family on the peroxynitrite-induced changes in blood platelet proteins. *International Journal of Biological Macromolecules* **2010**, *47*, 700–705, doi:10.1016/j.ijbiomac.2010.09.007.

111. Salehi, B.; Martorell, M.; Arbiser, J.L.; Sureda, A.; Martins, N.; Maurya, P.K.; Sharifi-Rad, M.; Kumar, P.; Sharifi-Rad, J. Antioxidants: Positive or Negative Actors? *Biomolecules* **2018**, *8*, doi:10.3390/biom8040124.

112. Woo, J.H.; Shin, S.L.; Jeong, H.S.; Lee, C.H. Influence of Applied Pressure and Heat Treatment on Antioxidant Activities of Young Leaves from Achillea alpina and Solidago virgaurea subsp. gigantea. *Korean J. Plant Res.* **2010**, *23*, 123~130.

113. Kim, Y.-J.; Kim, H.-Y.; Choe, J.-H.; Park, J.-H.; Ham, Y.-K.; Yeo, E.-J.; Hwang, K.-E.; Kim, C.-J. Antioxidant activity of goldenrod (Solidago virgaurea) leaf and stem powder on raw ground pork during chilled storage. *Korean Journal for Food Science of Animal Resources* **2013**, *33*, 1–8.

114. Choe, J.; Choi, Y.; Kim, H.; Han, D.; Kim, H.; Kim, Y.; Park, J.; Chung, H.; Kim, C. Effects of goldenrod (Solidago virgaurea) leaf and stem extracts on oxidative stability in cooked ground pork during chilled storage. In Proceedings of the International Congress of Meat Science and Technology; 2011; pp. 7–12.

115. Jacker, H.; Voigt, G.; Hiller, K. Zum antiexsudativen verhalten einiger triterpensaponine. *Pharmazie* **1982**, *37*, 380–382.

116. Choi, S.Z.; Choi, S.U.; Bae, S.Y.; neung Pyo, S.; Lee, K.R. Immunobioloical activity of a new benzyl benzoate from the aerial parts ofSolidago virga-aurea var. gigantea. *Archives of pharmacal research* **2005**, *28*, 49.

117. El-Ghazaly, M.; Khayyal, M.; Okpanyi, S.; Arens-Corell, M. Study of the anti-inflammatory activity of Populus tremula, Solidago virgaurea and Fraxinus excelsior. *Arzneimittel-forschung* **1992**, *42*, 333–336.

118. Strehl, E.; Schneider, W.; Elstner, E.F. Inhibition of dihydrofolate reductase activity by alcoholic extracts from Fraxinus excelsior, Populus tremula and Solidago virgaurea. *Arzneimittelforschung* **1995**, *45*, 172–173.

119. ESCOP Solidago virgaurea. In *Monographs on the medicinal uses of plant drugs*; European Scientific Cooperative on Phytotherapy Thieme: Exeter Stuttgart New York, 2003; pp. 487–91 ISBN 1-58890-233-1.

120. Schweitzer, B.I.; Dicker, A.P.; Bertino, J.R. Dihydrofolate reductase as a therapeutic target. *The FASEB Journal* **1990**, *4*, 2441–2452, doi:10.1096/fasebj.4.8.2185970.

121. Bonaterra, G.A.; Schwarzbach, H.; Kelber, O.; Weiser, D.; Kinscherf, R. Anti-inflammatory effects of Phytodolor® (STW 1) and components (poplar, ash and goldenrod) on human monocytes/macrophages. *Phytomedicine* **2019**, *58*, 152868, doi:10.1016/j.phymed.2019.152868.

122. Von Kruedener, S.; Schneider, W.; Elstner, E. A combination of Populus tremula, Solidago virgaurea and Fraxinus excelsior as an anti-inflammatory and antirheumatic drug. A short review. *Arzneimittel-forschung* **1995**, *45*, 169–171.

123. Sampson, J.H.; Phillipson, J.D.; Bowery, N.G.; O?Neill, M.J.; Houston, J.G.; Lewis, J.A. Ethnomedicinally selected plants as sources of potential analgesic compounds: indication ofin vitro biological activity in receptor binding assays. *Phytotherapy Research* **2000**, *14*, 24–29, doi:10.1002/(SICI)1099-1573(200002)14:1<24::AID-PTR537>3.0.CO;2-9.

124. Westendorf, J.; Vahlensieck, W. Spasmolytische und kontraktile Einflüsse eines pflanzlichen Kombinations-präparates auf die glatte Muskulatur des isolierten Meerschweinchendarms. *Arzneim-Forsch/Drug Res.* **1981**, *31*, 40–3.

125. Rácz, G.; Rácz-Kotilla, E.; Józsa, J. Hypotensive Activity-A Possible Pharmacotaxonomic Character of Solidago L. In Proceedings of the II International Symposium on Spices and medicinal Plants 96; 1979; pp. 15–18.

126. Raczkotilla, E.; Racz, G. Hypotensive and sedative effect of extracts obtained from Soldidago virgaurea L.[golden rod, drug plants]. *Planta Medica* **1978**.

127. Lasserre, B.; Kaiser, R.; Chanh, P.H.; Ifansyah, N.; Gleye, J.; Moulis, C. Effects on rats of aqueous extracts of plants used in folk medicine as antihypertensive agents. *Naturwissenschaften* **1983**, *70*, 95–96.

128. Mangiafico, S.; Costello-Boerrigter, L.C.; Andersen, I.A.; Cataliotti, A.; Burnett, J.C. Neutral endopeptidase inhibition and the natriuretic peptide system: an evolving strategy in cardiovascular therapeutics. *European Heart Journal* **2013**, *34*, 886–893, doi:10.1093/eurheartj/ehs262.

129. Kaspers, U.; Poetsch, F.; Nahrstedt, A.; Chatterjee, S. Diuretic effects of extracts and fractions obtained from different Solidago species. In Proceedings of the Naunyn-Schmiedebergs Archives Of Pharmacology; Springer Verlag 175 Fifth Ave, New York, NY 10010 USA, 1998; Vol. 358, pp. R495–R495.

130. Chodera, A.; Dabrowska, K.; Seńczuk, M.; Wasik-Olejnik, A.; Skrzypczak, L.; Budzianowski, J.; Ellnain-Wojtaszek, M. [Diuretic effect of the glycoside from a plant of the Solidago L. genus]. *Acta poloniae pharmaceutica* **1985**, *42*, 199–204.

131. Chodera, A.; Dąbrowska, K.; Skrzypczak, L.; others Biological activity of Leiocarposide from Solidago L. *Acta Agron Acad Sci Hung* **1985**, *34*, 112.

132. Budzianowski, J. Die urologische Wirkung des Leiocarposids. *Drogenreport* **1999**, *12*, 20–21.

133. Edwards, S.E.; Rocha, I.; Williamson, E.M.; Heinrich, M. *Phytopharmacy: an evidence-based guide to herbal medical products*; Wiley Blackwell: Chichester, West Sussex, UK ; Hoboken, NJ, 2015; ISBN 978-1-118-54345-0.

134. Kolodziej, B.; Kowalski, R.; Kędzia, B. Antibacterial and antimutagenic activity of extracts aboveground parts of three Solidago species: Solidago virgaurea L., Solidago canadensis L. and Solidago gigantea Ait. *Journal of Medicinal Plants Research* **2011**, *5*, 6770–6779.

135. Bussmann, R.W.; Malca-García, G.; Glenn, A.; Sharon, D.; Chait, G.; Díaz, D.; Pourmand, K.; Jonat, B.; Somogy, S.; Guardado, G.; et al. Minimum inhibitory concentrations of medicinal plants used in Northern Peru as antibacterial remedies. *J Ethnopharmacol* **2010**, *132*, 101–108, doi:10.1016/j.jep.2010.07.048.

136. Silva, A.C.O.; Santana, E.F.; Saraiva, A.M.; Coutinho, F.N.; Castro, R.H.A.; Pisciottano, M.N.C.; Amorim, E.L.C.; Albuquerque, U.P. Which approach is more effective in the selection of plants with antimicrobial activity? *Evidence-Based Complementary and Alternative Medicine: eCAM* **2013**, *2013*, 308980, doi:10.1155/2013/308980.

137. Saraiva, M. In vitro evaluation of antioxidant, antimicrobial and toxicity properties of extracts of Schinopsis brasiliensis Engl. (Anacardiaceae). *African Journal of Pharmacy and Pharmacology* **2011**, *5*, 1724–1731, doi:10.5897/AJPP11.428.

138. Bueno, J. In Vitro Antimicrobial Activity of Natural Products Using Minimum Inhibitory Concentrations: Looking for New Chemical Entities or Predicting Clinical Response. *Medicinal & Aromatic Plants* **2012**, *01*, doi:10.4172/2167-0412.1000113.

139. Thiem, B.; Goślińska, O. Antimicrobial activity of Solidago virgaurea L. from in vitro cultures. *Fitoterapia* **2002**, *73*, 514–516.

140. Brantner, A.; Grein, E. Antibacterial activity of plant extracts used externally in traditional medicine. *Journal of Ethnopharmacology* **1994**, *44*, 35–40, doi:10.1016/0378-8741(94)90096-5.

141. Brantner, A. Die antimikrobielle Wirkung von Solidago- haltigen Phytourologica. *Drogen-report* **1999**, *12*, 27–28.

142. Nair, R.; Kalariya, T.; Chanda, S. Antibacterial Activity of Some Plant Extracts Used in Folk Medicine. *Journal of Herbal Pharmacotherapy* **2008**, *7*, 191–201, doi:10.1080/15228940802152836.

143. Alves, T.M. de A.; Silva, A.F.; Brandão, M.; Grandi, T.S.M.; Smânia, E. de F.A.; Smânia Júnior, A.; Zani, C.L. Biological screening of Brazilian medicinal plants. *Memórias do Instituto Oswaldo Cruz* **2000**, *95*, 367–373, doi:10.1590/S0074-02762000000300012.

144. Kalemba, D. Constituents and biological activity of the essential oils of some Solidago and Artemisia species. *Scientific Papers Technical University of Lodz* **2000**, *857*, 1–118.

145. Xie, Y.; Yang, W.; Tang, F.; Chen, X.; Ren, L. Antibacterial activities of flavonoids: structure-activity relationship and mechanism. *Curr. Med. Chem.* **2015**, *22*, 132–149, doi:10.2174/0929867321666140916113443.

146. Liu, J.; Du, C.; Beaman, H.T.; Monroe, M.B.B. Characterization of Phenolic Acid Antimicrobial and Antioxidant Structure–Property Relationships. *Pharmaceutics* **2020**, *12*, 419, doi:10.3390/pharmaceutics12050419.

147. Guimarães, A.C.; Meireles, L.M.; Lemos, M.F.; Guimarães, M.C.C.; Endringer, D.C.; Fronza, M.; Scherer, R. Antibacterial Activity of Terpenes and Terpenoids Present in Essential Oils. *Molecules* **2019**, *24*, doi:10.3390/molecules24132471.

148. Wińska, K.; Mączka, W.; Łyczko, J.; Grabarczyk, M.; Czubaszek, A.; Szumny, A. Essential Oils as Antimicrobial Agents—Myth or Real Alternative? *Molecules* **2019**, *24*, 2130, doi:10.3390/molecules24112130.

149. Bader, G.; Seibold, M.; Tintelnot, K.; Hiller, K. Cytotoxicity of triterpenoid saponins. Part 2: Relationships between the structures of glycosides of polygalacic acid and their activities against pathogenic Candida species. *Pharmazie* **2000**, *55*, 72–74.

150. Pepeljnjak, S.; Kuštrak, D.; Vukušić, I. Investigation of the Antimycotic Activities of Solidago virgaurea and Solidago gigantea Exstracts. In Proceedings of the Program and Abstracts; 1998; p. K18.

151. Matsuda, H. Studies on chemical structures and pharmacological activities of triterpene saponins. *Natural Medicines* **1999**, *53*, 223–228.

152. Derda, M.; Hadaś, E.; Thiem, B. Plant extracts as natural amoebicidal agents. *Parasitology Research* **2009**, *104*, 705–708, doi:10.1007/s00436-008-1277-9.

153. Váradyová, Z.; Pisarčíková, J.; Babják, M.; Hodges, A.; Mravčáková, D.; Kišidayová, S.; Königová, A.; Vadlejch, J.; Várady, M. Ovicidal and larvicidal activity of extracts from medicinal-plants against Haemonchus contortus. *Experimental Parasitology* **2018**, *195*, 71–77, doi:10.1016/j.exppara.2018.10.009.

154. Plohmann, B.; Bader, G.; Hiller, K.; Franz, G. Immunomodulatory and antitumoral effects of triterpenoid saponins. *Die Pharmazie* **1997**, *52*, 953–957.

155. Bader, G.; Plohmann, B.; Hiller, K.; Franz, G. Cytotoxicity of triterpenoid saponins. Part 1: Activities against tumor cells in vitro and hemolytical index. *Pharmazie* **1996**, *51*, 414–417.

156. Hu, W.; Shen, T.; Wang, M.-H. Cell cycle arrest and apoptosis induced by methyl 3,5-dicaffeoyl quinate in human colon cancer cells: Involvement of the PI3K/Akt and MAP kinase pathways. *Chemico-Biological Interactions* **2011**, *194*, 48–57, doi:10.1016/j.cbi.2011.08.006.

157. Jang, Y.S.; Kim, H.-Y.; Zuo, G.; Lee, E.H.; Kang, S.K.; Lim, S.S. Constituents from Solidago virgaurea var. gigantea and their inhibitory effect on lipid accumulation. *Fitoterapia* **2020**, *146*, 104683, doi:10.1016/j.fitote.2020.104683.

158. Wang, Z.; Kim, J.H.; Jang, Y.S.; Kim, C.H.; Lee, J.-Y.; Lim, S.S. Anti-obesity effect of *Solidago virgaurea* var. *gigantea* extract through regulation of adipogenesis and lipogenesis pathways in high-fat diet-induced obese mice (C57BL/6N). *Food & Nutrition Research* **2017**, *61*, 1273479, doi:10.1080/16546628.2016.1273479.

159. Sanad, F.A.-A.; Ahmed, S.F.; El-Tantawy, W.H. Antidiabetic and hypolipidemic potentials of *Solidago virgaurea* extract in alloxan-induced diabetes type 1. *Archives of Physiology and Biochemistry* **2020**, 1–8, doi:10.1080/13813455.2020.1722705.

160. El-Tantawy, W.H. Biochemical effects of Solidago virgaurea extract on experimental cardiotoxicity. *Journal of Physiology and Biochemistry* **2014**, *70*, 33–42, doi:10.1007/s13105-013-0277-0.

161. Lämmermann, I.; Terlecki-Zaniewicz, L.; Weinmüllner, R.; Schosserer, M.; Dellago, H.; de Matos Branco, A.D.; Autheried, D.; Sevcnikar, B.; Kleissl, L.; Berlin, I.; et al. Blocking negative effects of senescence in human skin fibroblasts with a plant extract. *npj Aging and Mechanisms of Disease* **2018**, *4*, doi:10.1038/s41514-018-0023-5.