European Goldenrod

Summary and Pharmaceutical Comment

Phytochemical details have been documented for European goldenrod but no constituents have yet been identified to support its pharmacological actions. The traditional use of European goldenrod as a diuretic has been well documented but there is a lack of sufficient clinical data to support this use, or a possible mechanism of action. There is also a lack of clinical safety and toxicity data for European goldenrod and further investigation of these aspects is required.

Species (Family)

Solidago virgaurea L. (Asteraceae)

Synonym(s)

Goldenrod

Part(s) Used

Flowering aerial parts

Pharmacopoeial and Other Monographs

In ***BHC 2006*** (Goldenrod, European); ***BHP 2006*** (Goldenrod, European); ***BP 2012*** (European Goldenrod).

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The whole or cut, dried, flowering aerial parts of *Solidago virgaurea* L.

European goldenrod is also included in the Complete German Commission E, ESCOP 2003, HMPC monographs and Martindale 37th edition.

Constituents

The following is compiled from several sources, including general references.[1,2]

Diterpenes Nine *cis*-clerodane diterpenes (cannaclerodanolide, (5α,8α)-3,13-clerodadien-16,15:18,19-diolide, and solidagoic acids C–I) have been identified from plant material harvested in southeastern Bulgaria.[3] *cis*-Clerodane lactones, including solidagolactones II, III, V, VII, VIII and seven related compounds have been isolated from plant material of Indian origin (Khasi Hills, Meghalaya).[4]

Essential oils The main components found in steam-distilled oil from fresh flowering tops collected in the Russian Altai at 290 m (0.22% pure yellow light oil) were α-pinene (36.5%), myrcene (14.8%), β-caryophyllene (10.5%), germacrene D (8.2%), β-pinene (7.1%), and limonene+β-phellandrene (6.4%). Similarly at 650 m (0.07% pure yellow light oil) the main components included benzyl benzoate (57.0%), β-caryophyllene (6.3%), germacrene D (6.0%), α-pinene (4.4%), and α-humulene (4.4%).[5] The aerial parts at flowering stage collected from three sites in Poland yielded 0.32–0.38% essential oil described as 'intense and spicy, with a wormwood note'. Among 60 constituents identified, germacrene D, limonene, myrcene, α- and β-pinene, and sabinene were major components.[6] Essential oil yield and composition of aerial parts differs slightly between micropropagated and wild harvested material.[7]

Flavonoids The following flavonol aglycones have been found: kaempferol, quercetin, and isorhamnetin; also flavonol glycosides: 3-arabinosides, 3-galactosides, 3-glucosides, 3-robinobiosides, and 3-rutinosides of kaempferol and quercetin, 3-galactoside, 3-glucoside, and 3-rutinoside of isorhamnetin, rhamnetin 3-rhamnoglucoside (glycosidic linkage unspecified).[8,9] Kaempferol 3-robinobioside, kaempferol 3-rutinoside, quercetin 3-rutinoside (rutin), isorhamnetin 3-rutinoside, and trace amounts of quercetin 3-rhamnoside (quercitrin) have been detected using HPLC.[10] Flavonoid content of the leaves is 1.44–1.98%, buds 0.67%, flowers 1.14%, and the fruits 0.36%.[11]

Other phenolics Chlorogenic acids: 5-caffeoyl-, *cis*-5-caffeoyl-, 5-*p*-coumaroyl-, *cis*-5-*p*-coumaroyl-, and 3,5-dicaffeoyl- (3 isomers) quinic acids detected in LC-MS/MS analysis of leaf extracts.[12] Phenolic and hydroxycinnamic acids: caffeic, *p*-coumaric, ferulic, gentisic, *p*-hydroxybenzoic, protocatechuic, salicylic, sinapic, and vanillic acids as minor constituents.[13] Phenolic glucosides[14,15] (content in different above-ground tissues): leiocarposide (0.07–0.52% by photometric methods; 0.13–2.07% by HPLC) and virgaureoside A (0.01–0.14% by photometric methods).[16,17] Tannins (catechin based) mentioned in early literature.[1]

Polysaccharides Preliminary data indicates polysaccharide content of 5–8% in material of Russian origin collected at different flowering stages. Monosaccharide composition: galacturonic acid (43–45%), galactose (13–17%), glucose (7–12%), arabinose (5–8%), rhamnose (4–7%), xylose (1–1.5%).[18]

Saponins Major saponins of aerial parts (material sourced from the Botanical Garden, Berlin-Blankenfelde) comprise four acylated 3,28-bisdesmosides of polygalacic acid including solidagosaponins XIV and XVIII (also referred to as virgaureasaponins B–E, although these names not widely adopted); all were also present in roots.[1,19] Note that virgaureasaponins 1–3 (3,28-bisdesmosides of polygalacic acid) reported in earlier studies are deacylated saponins isolated from alkaline hydrolysates of aerial parts. Solidagosaponins I-XXIX, virgaureasaponins 1 and 2, and belissaponin BA_2, obtained from hot water extracts of fresh whole plants (collected Shizuoka, Japan), comprise a 3-monodesmoside, 3,28-bisdesmosides, 3,16,28-tridesmosides, 16-monodesmosides, and 16,28-bisdesmosides of polygalacic acid, with many acylated examples.[20–22]

Other plant parts Polyacetylenes have been found in the roots. Fresh material collected in Norway (Trondheim) contained 8 g/kg matricaria ester (methyl ester of 2*Z*,8*Z*-decadiene-4,6-diynoic acid), however the above-ground parts lacked these compounds.[23] Levels of polyacetylenes in Danish material (collected Marselisborg and Svejbæk) showed seasonal variation with a maximum average amount of matricaria ester 0.56 g/kg fresh roots in December. Four other polyacetylenes were also identified.[24]

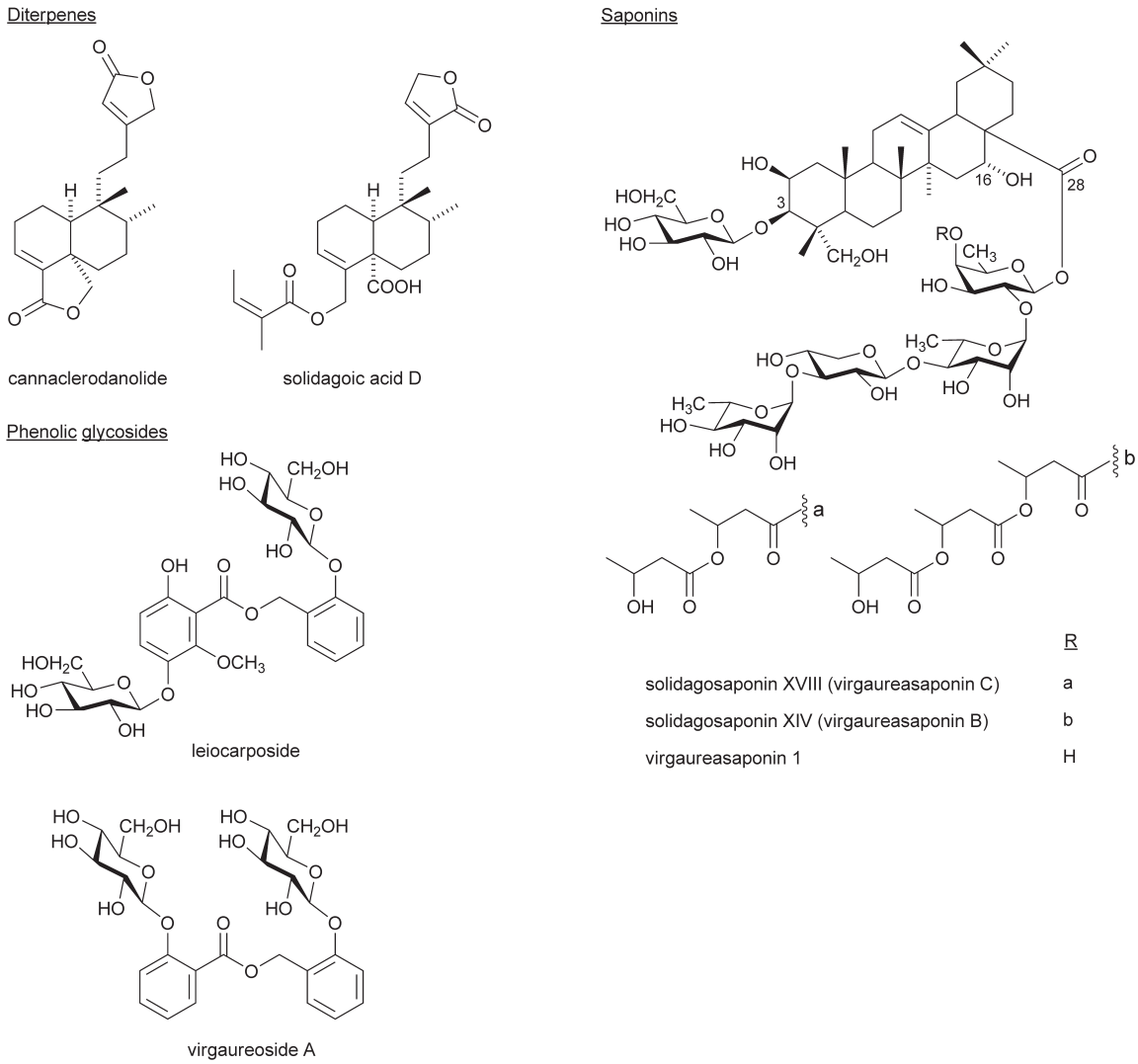

Figure 1 Selected constituents of European Goldenrod.

Food Use

None found.

Herbal Use

European goldenrod is used traditionally as a diuretic,[1, 25–27] and in the treatment of chronic nasopharyngeal catarrh and flatulent dyspepsia.[1]

The European Medicines Agency Committee on Herbal Medicinal Products (HMPC) has adopted a Community Herbal monograph for European goldenrod. Under traditional use, the monograph specifies that it is used 'to increase the amount of urine – as adjuvant in treatment of minor urinary complaints'.[25]

The German Commission E has approved European goldenrod as 'irrigation therapy for inflammatory diseases of the lower urinary tract, urinary calculi and kidney gravel, as proplylaxis for urinary calculi and kidney gravel'.[26]

Dosage

Dosages for oral administration (adults) for traditional uses recommended in standard herbal reference texts are given below:

Comminuted herb 6–12 g daily of herb, or equivalent preparations.[1, 26] 3-5 g, 2-4 times daily as an infusion.[25]

Dried herb 3-4 g, 2-3 times daily as an infusion in 15 mL of water, or equivalent preparations.[27]

Liquid extract 0.5–2.0 mL, 3 times daily.[25]

Tincture 0.5–2 mL, 3 times daily.[25]

Dry extract 350–450 mg, 3 times daily.[25]

Pharmacological Actions

In vitro and animal studies

Antimicrobial activity Ethanolic and methanolic extracts of European goldenrod (plant parts not specified) were found to have antimicrobial activity against *Bacillus subtilis*, *Bacillus pumilis*, *Proteus mirabilis*, *Proteus vulgaris*, *Micrococcus luteus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, and *Aspergillus niger*.[28]

Figure 2 European goldenrod (*Solidago virgaurea*).

Figure 3 European goldenrod – dried drug substance (aerial parts).

Clerodane diterpenes isolated from the aerial parts of European goldenrod were found to have antibacterial activity against *Staphylococcus aureus*.[3]

Antioxidant and anti-inflammatory activity In an *in vitro* study, polyphenolic-polysaccharide conjugates extracted from the flowers of European goldenrod were found to inhibit the peroxynitrite-induced nitration and oxidation of platelet proteins.[29] Ethanolic extracts of European goldenrod (plant parts not specified) were found to have antioxidant activity *in vitro*, with inhibition of lipoxygenase and xanthine oxidase pathways.[30] However, an ethanolic extract of European goldenrod (fresh herb) was found to have no activity on myeloperoxidase *in vitro*.[31]

Aqueous/ethanolic extracts of European goldenrod reduced the intensity of inflammatory effects in arthritis induced by Freund's complete adjuvant in rat paws by almost 40% compared with control rats.[32]

Anti-muscarinic activity Aqueous extracts of European goldenrod leaves inhibited the carbachol-induced contraction of human bladder samples and whole rat bladders transfected with human M2 and M3 muscarinic receptors, in a concentration-dependent manner.[33]

Anti-tumour activity Both aqueous and ethanolic extracts of European goldenrod leaves or flowers (1 mg/mL) had cytotoxic activity against human prostate cancer PC3 cells *in vitro*. Mice pre-injected with the rat prostate cancer cells (AT6.1) were given intraperitoneal, or intraperitoneal and subcutaneous, injections of phosphate-buffered saline extracts of European goldenrod 5 mg/kg every 3 days for 25 days. European goldenrod extracts suppressed tumour growth in these mice compared with control mice.[34]

Diuretic effect Oral administration of an aqueous extract of European goldenrod to rats resulted in an increase in diuresis and elimination of sodium, potassium, and chloride ions.[35] Similar results were found in another study.[36]

Clinical studies

The traditional use of European goldenrod as a diuretic has been well documented but there is a lack of sufficient clinical data to support this use. No constituent with a diuretic action has yet been isolated, or a possible mechanism of action elucidated.[25]

An open multicentre study in 74 female patients with dysuria found that an extract of European goldenrod administrated three times daily for 14 days, decreased the frequency of urination in 69.2% of patients, as well as other symptoms of cystitis in a greater number of patients.[37] In another open multicentre study of 1487 patients, a subgroup of 512 patients with chronic recurrent irritable bladder conditions were given a dry extract of European goldenrod 424.8 mg three times daily; 96% of these patients showed an improvement in the clinical global impression scale.[38]

The EMA assessment report for *Solidago virguarea* L. Herba describes an open multicentre post-marketing study in 53 patients with symptoms of urinary-tract inflammation. Patients were given an ethanolic extract of European goldenrod 64% (v/v) for up to one year; adults were given 100 drops daily, while children under 1 years of age were given 55 drops daily. Clinical improvement, with a reduction in dysuria, pollakiuria, and tenesmus after taking the European goldenrod extract was seen in 65.4% of patients.[39] The EMA assessment report also notes an open post-marketing study in 1487 patients with irritable bladder, urinary-tract infections or renal calculi. Improvement in the clinical global impression scale was seen in 79% of the patients, when an ethanolic extract of European goldenrod was given for an average of 4 weeks.[39]

A case report was also described which states that patients given a dry extract of European goldenrod for 4 weeks after extracorporeal shock wave lithotripsy, required no further spasmolytic treatment.[39]

In an open post-marketing crossover study, 22 healthy subjects given 100 drops daily of an ethanolic extract of European goldenrod 64% (v/v) for 2 days showed an increase in daily urine output of 27% compared with those taking placebo.[39]

Side-effects, Toxicity

There is a lack of clinical safety data and toxicity data for European goldenrod and further investigation of these aspects is required.

Hypersensitivity reactions and mild gastrointestinal disorders have been reported with the use of European goldenrod.[25, 39]

Contra-indications, Warnings

The use of European goldenrod has been contra-indicated in patients with hypersensitivity to *Solidago* spp., or to other plants of the Asteraceae (Compositae) family.[25] The EMEA HMPC monograph for *Solidago virgaurea* L. contra-indicates its use in conditions where a reduced fluid intake is recommended, such as severe cardiac or renal disorders.[25–27] There is a lack of data for the use of European goldenrod in children under the age of 12 years and it is consequently not recommended in this age group.[25]

Advice from a qualified health-care professional should be sought if symptoms such as fever, dysuria, spasms, or haematuria develop while taking European goldenrod.[25]

Pollen from European goldenrod can precipitate allergic reactions One study found that *Hevea brasiliensis* latex and European goldenrod share some cross-reactive allergenic proteins.[40]

Drug interactions None found. However, the potential for preparations of European goldenrod to interact with other medicines administered concurrently, particularly those with similar or opposing effects, should be considered.

Notably, the concurrent use of European goldenrod and diuretics is not recommended.[25]

Pregnancy and lactation In view of the lack of toxicity data, administration of European goldenrod during pregnancy and lactation is not recommended.

Preparations

Single-ingredient Preparations

Germany: Cystinol Long; Nieral; Polbax novo; Solidacur; Solidagoren mono; Solidagoren Uro; Stromic; Urol. *Hungary:* Stromic.

Multi-ingredient Preparations

Australia: Euphrasia Complex; Euphrasia Compound; Phytodolor. *Austria:* Heumann's Blasen- und Nierentee; Phytodolor; Urelium Neu. *Czech Republic:* Epilobin; Urcyston Planta. *France:* Solution Stago Diluée; Tisane de Santé. *Germany:* Aqualibra; BioCyst; Cefasabal; Cystinol N; Dr S.cheffler Bergischer Kräutertee Blasen- und Nierentee; Harntee 400 N; Harntee-Steiner; Heumann Blasen- und Nierentee Solubitrat uro; Nephroselect M; Phytodolor; Prostamed; Solidagoren N. *Hungary:* Herpesil; Prostazyn; Vesevedo; Wörishofener. *Italy:* Flavion. *Malaysia:* Cefasabal. *Poland:* Diuronis; Fitoven; Nefrobonisol; Nefrol; Nefrosept; Prostapol; Reumacor; Urofort; Uroprost. *Russia:* Prostanorm (Простанорм). *Switzerland:* Demonatur Dragées pour les reins et la vessie; Dragées S pour les reins et la vessie; Nephrosolid; Urinex. *Ukraine:* Prostamed (Простамед).

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