Senega

Species (Family)

Polygala senega L. (Polygalaceae) and other closely related species cultivated in western Canada and Japan.

Synonym(s)

Northern Senega (Canada), Polygala, *Polygala senega* var. *latifolia* (Japan), Rattlesnake Root, Snake Root

Part(s) Used

Root, rootstock

Pharmacopoeial and Other Monographs

BHC 1992[G6]
BHP 1996[G9]
BP 2001[G15]
Complete German Commission E[G3]
ESCOP 1997[G52]
Martindale 32nd edition[G43]
PDR for Herbal Medicines 2nd edition[G36]
Ph Eur 2002[G28]

Legal Category (Licensed Products)

GSL[G37]

Constituents[1,G2,G6,G20,G40,G48,G52,G59,G62,G64]

Acids Salicylic acid and its methyl ester 0.1–0.2%; hydroxycinnamic acids (e.g. caffeic acid, ferulic acid, sinapic acid) free or esterified with saponins.[2]

Carbohydrates Arabinose, fructose, glucose, melibiose, raffinose, saccharose, stachyose, sucrose; 1,5-anhydro-D-glucitol and other D-glucitol derivatives;[3,4] trisaccharides; mucilage, pectin. A series of oligosaccharide esters, senegoses A–O, containing acetic, benzoic, *trans*- and *cis*-ferulic acid moieties linked to glucose and fructose.[5,6] Five acylated sucrose glycosides, tenuifolisides A–E, have been isolated from *P. tenuifolia*.[7,8] The esterifying acids are 3,4,5-trimethoxycinnamic, *p*-hydroxybenzoic, sinapic and ferulic.

Terpenoids A complex mixture of bidesmosidic triterpene saponins (6–10%) based on the aglycone presenegin. The total saponin mixture may be referred to as senegin. The saponins of *P. senega* var. *latifolia* are 3-glucosides of presenegin with tetra-, penta- or hexa-glucosyl groups linked at C-28 and including 4″-methoxy-cinnamoyl or 3″,4″-dimethoxycinnamoyl fucosyl resulting in *E*- and *Z*-cinnamoyl isomers of each saponin.[9–11] Senegins I–IV were the first saponins to be characterised and were *E*-isomers.[12,13] *P. tenuifolia* contains similar saponins named onjisaponins A–G.[14,15]

Xanthones A number of xanthones have been isolated from *P. tenuifolia* including 4-C-[β-D-apiofuranosyl-(1→6)-β-D-glucopyranosyl]-1,3,6-trihydroxy-7-methoxyxanthone.[8]

Other constituents Fat, resin, sterols and valeric acid ester.

Other Polygala species *Polygala paniculata* contains coumarins (aurapten, murrangatin, phebalosin and 7-methoxy-8-(1,4-dihydroxy-3-methyl-2-butenyl) coumarin,[16] pyranocoumarin).[17] *Polygala chamaebuxus* (European species) contains hydroxycinnamic acid esters involving acetic, ferulic and sinapic acids as the ester moieties, saponins, tenuifolin (prosapogenin), rutin (flavonoid glycoside), coniferin and syringen (phenolic glycosides).[2]

Other European species (e.g. *Polygala alpestris*, *Polygala comosa*, *Polygala vayredae*) contain complex mixtures of bidesmosidic saponins, tenuifolin (prosapogenin), hydroxycinnimic acid esters similar to those reported for *P. chamaebuxus*.[18] *Polygala triphylla* contains B-ring oxygen-free trioxygenated- and glucosyloxy-xanthones.[19] *Polygala polygama* contains podophyllotoxin and demethylpodophyllotoxin (lignans).[20]

Food Use

Senega is listed by the Council of Europe as a natural source of food flavouring (category N2). This category indicates that senega can be added to foodstuffs in small quantities, with a possible limitation of an

active principle (as yet unspecified) in the final product.[G16]

Herbal Use[G2,G6,G7,G8,G32,G43,G52,G54,G64]

Senega is stated to possess expectorant, diaphoretic, sialogogue and emetic properties. Traditionally, it has been used for bronchitic asthma, chronic bronchitis, as a gargle for pharyngitis, and specifically for chronic bronchitis.

Dosage

Dried root 0.5–1.0 g or by infusion three times daily.[G6,G7]

Senega Liquid Extract (BPC 1968) 0.3–1.0 mL.

Senega Tincture (BPC 1968) 2.5–5.0 mL.

Pharmacological Actions

In vitro and animal studies

Mucosal secretion Polygalic acid and senegin are stated to be irritant to the gastrointestinal mucosa, and to cause a reflex secretion of mucus in the bronchioles.[1,G6,G44,G52] A fluid extract of senega increased respiratory tract fluid secretion in guinea-pig, cat and dog, but not in rabbit.[G52]

CNS-depressant activity CNS-depressant properties in mice (e.g. reduction in spontaneous activity, inhibition of amphetamine stimulation, potentiation of barbiturate-induced sleeping time, and decrease in rectal temperature) have been documented for *Polygala microphylla*.[21] Similar properties have been reported for *Polygala tenuifolia* and have been attributed to the saponin constituents. A methanolic extract of *P. tenuifolia*, various fractions and pure onjisaponins B, F and G prolonged hexobarbital sleeping time in mice.[G52] Onjisaponin F produced sleep times in mice of 33 and 35 minutes for doses of 5 and 20 mg/kg, respectively, compared with 24 minutes for control and 42 minutes for chlorpromazine hydrochloride (2 mg/kg).

Inhibition of alcohol absorption *E,Z*-senegin II and *E,Z*-senagasaponins a and b from *P. senega* var. *latifolia* have potent inhibitory effects on alcohol absorption in rats. *E,Z*-senegasaponins a or b (100 mg/kg) administered orally to rats 1 hour after 20% aqueous ethanol (5 mL/kg, orally) reduced blood alcohol concentrations after 1 hour from 0.5 mg/mL to 0.02 mg/mL.[10] Under similar test conditions, *E,Z*-senegin II administration led to a blood ethanol concentration of 0.09 mg/mL.

Hypoglycaemic activity Senegin II and *E,Z*-senagasaponins a and b have significant hypoglycaemic effects in rodents.[22] Senegin II (2.5 mg/kg, intraperitoneally) reduced blood glucose concentrations in normal mice from 220 mg/dL to 131 mg/dL 4 hours after administration and also significantly lowered blood glucose concentrations in KK-Ay mice from 434 mg/dL to 142 mg/dL under similar test conditions ($p < 0.001$, compared with control, for both studies). In glucose tolerance tests in rats, administration of *E,Z*-senagasaponins a and b (100 mg/kg, orally) resulted in glucose concentrations of 107–123 mg/mL after 30 minutes compared with 156 mg/mL in control animals ($p < 0.01$).[11]

Hypolipidaemic activity Seven hours after administration of an *n*-butanol fraction of a methanolic extract of *P. senega* var. *latifolia* containing senegin II (5 mg/kg, intraperitoneally), the mean (standard deviation) blood triglyceride concentration was 65 (9) mg/100 mL, compared with 152 (17) mg/mL in control animals ($p < 0.05$).[23] The blood triglyceride concentration in cholesterol-fed mice was also significantly reduced ($p < 0.05$) under the similar test conditions. Pure senegin II at a dose of 5 mg/kg was also reported to lower blood triglyceride concentrations in mice.[23]

Other activities Guinea-pig serum taken 2 hours after administration of lyophilised aqueous extract of *P. tenuifolia* (600 mg, intraperitoneally) inhibited the growth of herpes simplex virus type 1 (HSV-1) in Vero cells.[G52] An unspecified senegin from *P. senega* produced a 34% inhibition of influenza virus (A2/Japan 305) at a concentration of 12.5 µg/mL.[G52] An ethanolic extract of *P. senega* has been reported to inhibit growth of a range of fungi.[G52]

Polygala erioptera and *P. paniculata* have exhibited molluscicidal activity, and *P. paniculata* is reported to possess antifungal activity.[17] A butanol extract of *P. tanuifolia* containing onjisaponins (100 µg/mL) inhibited cyclic adenosine monophosphate (cAMP) diesterase by 73%.[G52] Isolated onjisaponins E, F and G inhibited cAMP phosphodiasterase, with IC_{50} values of 3.1, 2.9, and 3.7×10^{-5} mol/L, respectively, being similar in action to papaverine. A total saponin concentration of *P. senega* var. *latifolia* increased rat plasma concentrations of adrenocorticotrophic hormone (ACTH), corticosterone and glucose 30 minutes after intraperitoneal administration (25 mg/kg). Single doses of a dried methanol (50%) extract of *P.*

senega var. *latifolia* and *P. tanuifolia* administered orally (2 g/kg) to rats produced 62% and 100% inhibition, respectively, of congestive oedema.[G52] Under the same conditions, furosemide 100 mg/kg prodced 100% inhibition of concestive oedema.

Clinical studies

A fluid extract of senega root was reported to reduce the viscosity of sputum in patients with bronchiectasis.[G52] A French patent has stated that a triterpenic acid extracted from senega possesses anti-inflammatory activity and is effective against graft rejection, eczema, psoriasis and multiple sclerosis.[24]

Side-effects, Toxicity[G20]

Saponins are generally regarded as irritant to the gastrointestinal mucosa, and irritant properties have been documented for senega plant and for related *Polygala* species.[G51] Large doses of senega are reported to cause vomiting and purging.[G60]

The haemolytic index (HI) of senega saponins is stated to be between 2500 and 4500.[G62] Haemolytic saponins are toxic to mammals when administered intravenously, but have a low toxicity when given orally because they do not cross the gastrointestinal mucosa.[25] Contact with damaged mucosal areas may cause a problem. Toxicity associated with chronic exposure of the gastrointestinal mucosa to haemolytic saponins has not been established. It has been stated that the suitability of saponins for nutritional and pharmacological use requires further investigation: free saponins in the gastrointestinal tract may interact with the mucosal cells, causing a transient increase in the permeability of the small intestine to intraluminal solutes and inhibiting active nutrient absorption.[25] This action may consequently facilitate the entry of antigens and biologically active food peptides into the blood circulation, with adverse systemic effects.[25] Aqueous and methanol extracts of *P. senega* and *P. tenuifolia* were negative in the rec-assay with *Bacillus subtilis* and in the reversion assay with Ames strains TA98 and TA100 of *Salmonella typhimurium*.[G52] A mixture of senegins given to rats (i.p.) gave an LD_{50} value of 3 mg/kg and inhibited the growth of Walker carcinoma in rats with an ED_{50} value of 1.5 mg/kg.[G52]

Cytotoxic lignans have been documented as constituents of a related species, *P. polygama*.[10]

Contra-indications, Warnings

Senega may exacerbate existing gastrointestinal inflammation and excessive doses may cause vomiting. Senega has hypoglycaemic acivity and is contra-indicated in diabetic patients.

Pregnancy and lactation Limited information is available on the chemistry, pharmacology and toxicity of senega. In view of this, and the potential irritant properties of senega, its use during pregnancy and lactation should be avoided.

Pharmaceutical Comment

The chemistry and pharmacology of senega has been extensively investigated but there is only limited clinical data. The activity of the saponins in animals supports the herbal use for bronchitis. In view of the lack of toxicity data and uncertainty regarding the risk associated with chronic ingestion of haemolytic saponins, excessive use of senega should be avoided.

References

See also General References G2, G3, G6, G9, G12, G15, G16, G20, G25, G29, G31, G32, G36, G37, G40, G43, G48, G51, G52, G60, G62 and G64.

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