Gentian

Gentiana lutea

Common names

Common gentian, great yellow gentian, yellow gentian, bitter wort

Family

Gentianaceae (gentian)

Part used

Root

Background and traditional uses

Gentian, also known as common or yellow gentian, is a perennial herb with long, thick cylindrical roots and yellow flowers, growing up to one to two metres high.[1-3] Native to the elevated alpine regions of central and southern Europe and western Asia, the intense bitter taste of gentian is an important characteristic contributing to the herbs traditional uses and current therapeutic effects.[1-3]

Gentian has been used medicinally as far back as the ancient Roman and Greek eras, and the name *Gentiana* originates from Gentius, the king of ancient Illyria (180-167 BCE) who recognised the herbs therapeutic benefits.[3]

Traditionally the roots of gentian have been used as a digestive tonic, bitter and cholagogue for digestive concerns including appetite loss after convalescence, flatulence, bloating, dyspepsia and mild gastrointestinal spasmodic issues.[1-6] Other traditional applications of the herb include for the treatment of dysmenorrhoea, intestinal worms and nausea, to facilitate labour and as an emmenagogue.[2-5] Gentian has also been used traditionally in combination with other bitter and aromatic herbs for digestive complaints.[1]

Actions

Primary:[2,7-9]

- Bitter tonic
- Sialogogue
- Cholagogue
- Spasmolytic

Secondary:[7-9]

- Antioxidant
- Anti-inflammatory
- Antimicrobial
- Cardiotonic

Applications and indications

- Stimulation of appetite and digestion and useful for symptomatic relief of dyspepsia.[10-15]
- Beneficial for the relief of mild digestive symptoms including flatulence, constipation and abdominal pain.[14,15]
- Can help to reduce total daily energy intake and thus may assist weight loss.[16]

Active constituents and pharmacodynamics

The **bitter principles** are the main constituents present in gentian and they are responsible for most of the herbs pharmacological effects.

Primarily found in the root cortex, the **secoiridoid glycosides** have the strongest bitter properties. Gentiopicroside (also called gentiamarine and gentiopicrine) is the principle component of the plant, occurring at concentrations ranging from 2-10%.

Other bitter constituents are swertiamarine, sweroside (0.05-0.08%), and amarogentin (0.03-0.08%), the latter being one of the most bitter substances known.[1-4,17,18] The specific quantities of bitter constituents present in the root is influenced by the season and the age of the plant.[1]

The secoiridoid glycosides, especially amarogentin, stimulate gustatory receptors in the taste buds and mouth, inducing salivary, gastric juice and bile secretion.[1,2] Amarogentin has also been shown to inhibit platelet aggregation.[19]

Gentiopicroside has been observed to have antioxidant[5,20], analgesic[5,21] and smooth muscle relaxant effects.[22,23] Gentiopricroside, swertiamarine and sweroside have demonstrated hepatoprotective[13] and wound healing properties,[18] while sweroside has antimicrobial and antifungal activity.[24]

Trace constituents also found in gentian include volatile oils, phytosterols, triterpenes and tannins.[1,2,5]

Summary of clinical evidence

Gastrointestinal tract and digestion

Several studies have demonstrated the impact of gentian root on the upper gastrointestinal tract that contribute to the herbs beneficial effect on digestion and adverse digestive symptoms.

Gentian root was found to be effective in alleviating dyspeptic symptoms in an open trial involving 205 subjects.[15] Participants were given 120mg dry extract of gentian root capsules (ethanol 53% v/v two to three times daily providing an average dose equivalent to 2.9g gentian) for 15 days. After five days, there was an improvement in symptoms in most patients, and by the end of the study period, the average level of improvement was 68% (symptoms including constipation, flatulence, appetite loss, vomiting, heartburn, abdominal pain and nausea). The interventions efficacy was assessed as excellent (symptom elimination) in 31% of patients, good in 55%, moderate in 9% and inadequate in 5% of patients.[15]

Similar results were observed in a randomised, controlled, clinical trial investigating the effect of a herbal combination including gentian in 359 people with moderate functional gastrointestinal disorders.[14] Subjects were given either placebo, gentian tincture (2%) and *Rheum palmatum* (rhubarb) fluid extract (2%), *Peumus boldus* (boldo) tincture (1%) and *Rhamnus purshiana* (cascara) fluid extract (2%) or a combination of all four herbs for 28 days. Compared with baseline and placebo, the combination of all four herbs resulted in statistically significant improvements in loss of appetite, dyspepsia and constipation ($p<0.001$) while gentian and rhubarb alone improved constipation symptoms ($p<0.001$).[14]

Preliminary evidence also indicates specific effects of gentian on digestive processes. *In vivo* experiments in rabbits observed that direct administration of gentian extract (0.2g/100g ethanol 19% v/v, equiv. to 12.6mg/kg/d dried root) in the stomach of rabbits for three days resulted in secretolytic effects, with production rate levels 37.7% above controls,[12] while an *in vitro* study, found that an aqueous dry extract of gentian added to parietal cells from rat gastric mucosa resulted in direct stimulation of gastric mucosal acid production.[11]

Reducing energy intake

A cross-over, randomised trial investigated the effect of microencapsulated gentian constituents on human appetite and energy intakes in 20 healthy subjects.[16] Subjects were given 100mg of secoiridoids in an ingredient-enriched pudding (ECIP) or a control pudding (CP) on two different days. Blood samples, glycaemia and appetite ratings were collected at baseline and 30, 60, 120 and 180 min after breakfast, plasma gastrointestinal peptides, endocannabinoids (EC) and N-acylethanolamines (NAE) were measured and energy intakes were measured at an ad libitum lunch three hours after breakfast and over the rest of the day.[16] There was no significant difference in the postprandial plasma responses of gastrointestinal hormones, glucose, EC and NAE and appetite between EBIP and CP. However, a trend for a higher response of glucagon-like peptide-1 after EBIP compared with after the CP was observed. EBIP also resulted in a significant 30% lower energy intake over the post-lunch period compared with CP. This study indicates that secoiridoids were effective in reducing daily energy intake in humans.[16]

Antioxidant

Preliminary *in vitro* data has demonstrated that gentian has antioxidant activity. Antioxidant activity was observed in a study that used 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging test and cyclic voltammetry (CV) methods to assess the inhibitory activity of gentian extracts (100% methanol, water and ethanol aqueous solutions [96, 75, 50 and 25%v/v]) on the enzyme myeloperoxidase (MPO).[20] The antioxidant capacity of the 50% ethanol/water extract was the highest in both assay methods, and also showed the best inhibition of MPO activity in comparison with other extracts.

Cardiovascular effects

Animal and *in vitro* evidence has observed that gentian exhibits anti-atherosclerotic, anti-platelet and vascular smooth muscle inhibitory activity.

In rat aortic smooth muscle cells (RASMCs), an aqueous extract of gentian demonstrated several effects, including blocking platelet derived growth factor-BB-induced cell proliferation, preventing S-phase entry of synchronized cells in response to PDGF and blocking PDGF-BB-induced ERK1/2 activation and consequent increase in cellular nitric oxide (NO) levels.[22]

Additional anti-atherosclerotic effects of gentian were also observed in diabetic rats in a separate preliminary study.[22] These mechanisms included blocking leukocyte adhesion, generation of ROS and TNF-alpha induced expression of ICAM-1 and VCAM-1 in human umbilical vein endothelial cells (HUVECs); inhibiting the expression of vascular cell adhesion molecule-1 (VCAM-1), inducible nitric oxide synthase (iNOS), and vascular endothelial cadherin (VE-cadherin) in aortic segments; and decreasing total blood cholesterol and lipid accumulation in aortic tissues.[22]

Other cardiovascular-related properties of gentian constituents were also highlighted in two *in vitro* studies. Gentisin was found to inhibit vascular smooth muscle cell (VSMC) proliferation[26] and amarogentin inhibited platelet aggregation induced by collagen, collagen-induced phosphorylation of phospholipase C (PLC) gamma-2, protein kinase C (PKC), and mitogen-activated protein kinases (MAPKs) and *in vivo* thrombus formation in mice.[19]

Dosage summary

Liquid extract (1:2): 5-15mL weekly[27]
Dried herb equivalent: 1-2g three times daily[7]

Safety information

- Use during pregnancy or lactation is not advised due to insufficient reliable information available about its safety.[1,2,5]
- Safety in children has not been established so is not recommended.[1,2,5]
- Contraindicated in individuals with gastric and duodenal peptic ulcers.[1-3]
- Contraindicated in individuals with stomach irritation, inflammation or hyperacidity.[2,4]

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