Herba Passiflorae

Definition
Herba Passiflorae consists of the dried aerial parts of *Passiflora incarnata* L. (Passifloraceae) (*1–3*).

Synonyms
Granadilla incarnata Medik., *Passiflora kerii* Spreng. (*4*).

Selected vernacular names
Apricot vine, flor de la pasión, Fleischfarbene Passionsblume, fiore della passione, fleur de la passion, grenadille, maracujá, may apple, may flower, may-pop, pasionaria, passiflora, passiflora roja, passiflore, passion vine, rose-coloured passion flower, water lemon, white passion flower, wild passion flower (*2, 4–6*).

Geographical distribution
Indigenous to North America (*5, 7, 8*).

Description
A perennial, creeping herb, climbing by means of axillary tendrils. Leaves alternate, palmately three to five serrate lobes. Flowers large, solitary, with long peduncles, whitish, with a triple purple and pink crown. Fruits are ovate berries containing numerous ovoid, flattened seeds covered with a yellowish or brownish aril (*7*).

Plant material of interest: dried aerial parts
General appearance
Stems lignified, green, greyish-green or brownish, usually less than 5 mm in diameter; rounded, longitudinally striated and often hollow. Leaves alternate with furrowed, often twisted petioles, possessing two extra-floral nectaries at the apex; lamina 6–15 cm long, broad, green to brownish green, palmate with three to five lanceolate lobes covered with fine hairs

on the lower surface; margin serrate. Tendrils borne in leaf axils, smooth, round and terminating in cylindrical spirals. Flowers 5–9 cm in diameter with peduncles up to 8 cm long, arising in leaf axils; five, white, elongated petals; calyx of five thick sepals, upper surface green and with a horn-like extension; involucre of three pointed bracts with papillose margins; five large stamens, joined at the base and fused to the androgynophor; ovary greyish-green, superior; style hairy with three elongated stigmatic branches. Fruits 4–5 cm long, oval, flattened and greenish-brown containing numerous seeds 4–6 mm long, 3–4 mm wide and 2 mm thick, with a brownish-yellow, pitted surface (*2*).

Organoleptic properties

No distinctive odour; taste: bitter (*2*).

Microscopic characteristics

Transverse section of older stem shows epidermis of isodiametric cells with strongly thickened, convex external walls; some cells containing crystals of calcium oxalate, others developing uniseriate trichomes two to four cells long, terminating in a rounded point and frequently hooked; hypodermis consisting of a layer of tangentially elongated cells, outer cortex with groups of collenchyma, containing cells with brown, tanniferous contents; pericycle with isolated yellow fibres and partially lignified walls; inner cortex of parenchymatous cells containing cluster crystals of calcium oxalate; xylem consisting of groups of vessels up to 300 µm in diameter with pitted, lignified tracheids; pith of lignified parenchyma containing numerous starch grains 3–8 µm in diameter, simple or as aggregates. Leaf upper and lower epidermis shows sinuous anticlinal cell walls; numerous anomocytic stomata in the lower epidermis, which also has numerous uniseriate covering trichomes of one to three cells, terminal cells comparatively long, pointed and curved; groups of brown tannin cells occur in the marginal teeth and in the mesophyll; cluster crystals of calcium oxalate 10–20 µm in diameter isolated in the mesophyll or arranged in files associated with the veins. Sepal upper epidermis has large, irregular, polygonal cells with some thickened walls, striated cuticle, rare stomata and numerous small crystals of calcium oxalate; lower epidermis comprises two layers, the outer layer consisting of polygonal cells with numerous stomata and small crystals of calcium oxalate, the inner layer of smaller polygonal cells. Epidermal cells of the petals papillose, especially in the filiform appendices. Pollen grains 65–75 µm in diameter, with a cross-ridged surface and three acuminate germinal pores. Pericarp composed of large cells with few stomata and groups of calcium oxalate crystals; endocarp of thickened, sclerous cells (*2*).

Powdered plant material

Light green and characterized by fragments of leaf epidermis with sinuous cell walls and anomocytic stomata; numerous cluster crystals of calcium oxalate isolated or aligned along the veins; many isolated or grouped fibres from the stems associated with pitted vessels and tracheids; uniseriate trichomes with one to three thin-walled cells, straight or slightly curved, ending in a point or sometimes a hook. If flowers are present, papillose epidermis of the petals and appendages and pollen grains with a reticulate exine. If mature fruits are present, scattered brown tannin cells and brownish-yellow, pitted fragments of the testa (*3*).

General identity tests

Macroscopic and microscopic examinations (*2, 3*), and thin-layer chromatography for the presence of flavonoids (*2, 3, 9*).

Purity tests

Microbiological

Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines on quality control methods for medicinal plants (*10*).

Chemical

Contains not more than 0.01% harman alkaloids (*11*).

Foreign organic matter

Not more than 2% (*3*).

Total ash

Not more than 13% (*3*).

Acid-insoluble ash

Not more than 3.0% (*2*).

Water-soluble extractive

Not less than 15% (*2*).

Loss on drying

Not more than 10% (*3*).

Pesticide residues

The recommended maximum limit for aldrin and dieldrin is not more than 0.05 mg/kg (*12*). For other pesticides, see the *European pharmacopoeia*

(*12*), and the WHO guidelines on quality control methods for medicinal plants (*10*) and pesticide residues (*13*).

Heavy metals

For maximum limits and analysis of heavy metals, consult the WHO guidelines on quality control methods for medicinal plants (*10*).

Radioactive residues

Where applicable, consult the WHO guidelines on quality control methods for medicinal plants (*10*) for the analysis of radioactive isotopes.

Other purity tests

Sulfated ash and alcohol-soluble extractive tests to be established in accordance with national requirements.

Chemical assays

Contains not less than 1.5% of total flavonoids, expressed as vitexin, determined by spectrophotometry (*3*). A high-performance liquid chromatography method for flavonoids is also available (*14*).

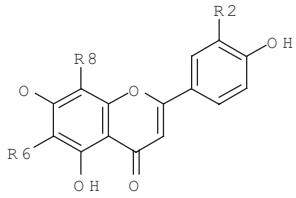
Major chemical constituents

The major constituents are flavonoids (up to 2.5%) with the principal compounds being the *C*-glycosyl of apigenin (R2 = H) and luteolin (R2 = OH), including mono-*C*-glucosyl derivatives isovitexin (up to 0.32%), iso-orientin and their 2''-β-D-glycosides, and di-*C*-glycosyl derivatives schaftoside (up to 0.25%), isoschaftoside (up to 0.15%) and swertisin (*1, 15, 16*). Also found are di-*C*-glucosyl derivatives vicenin-2 and lucenin-2 and small amounts of mono-*C*-glucosyl derivatives orientin and vitexin (*1*). Other chemical constituents include maltol (3-hydroxy-2-methyl-γ-pyrone) (0.05%), chrysin and a cyanogenic glycoside, gynocardin. Traces of the indole (β-carboline) alkaloids (e.g. harman, harmol, harmine) have been reported in the source plants; however, these alkaloids are undetectable in most commercial materials (*4–6, 8, 16*). The structures of the alkaloid harman and characteristic flavonoids are presented below.

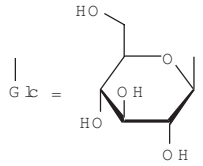
Medicinal uses

Uses supported by clinical data

None.

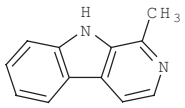


	R2	R6	R8
orientin	OH	H	Glc
iso-orientin	OH	Glc	H
lucenin-2	OH	Glc	Glc
schaftoside	H	Glc	Ara
isoschaftoside	H	Ara	Glc
vicenin-2	H	Glc	Glc
vitexin	H	H	Glc
isovitexin	H	Glc	H

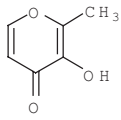


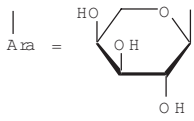
β-D-glucopyranosyl

harman



maltol





α-L-arabinopyranosyl

Uses described in pharmacopoeias and well established documents

Internally as a mild sedative for nervous restlessness, insomnia and anxiety. Treatment of gastrointestinal disorders of nervous origin (*1*, *5*, *11*).

Uses described in traditional medicine

As an anodyne, antispasmodic and mild stimulant (*1*, *6*). Treatment of dysmenorrhoea, neuralgia and nervous tachycardia (*1*).

Pharmacology

Experimental pharmacology

Analgesic and antipyretic activities

Intragastric administration of 5.0 g/kg body weight (bw) of a 60% ethanol extract of Herba Passiflorae per day for 3 weeks to rats did not reduce the pain response as measured in the tail-flick test using radiant heat, and no reductions in body temperature were observed (*17*). Intragastric administration of a 30% ethanol extract of the aerial parts reduced phenylbenzoquinone-induced writhing in mice, median effective dose 1.9 ml/kg bw (*18*).

Anti-inflammatory activity

Intragastric administration of 75.0–500.0 mg/kg bw of an ethanol extract of the aerial parts to rats reduced carrageenan-induced inflammation in the hind-paw model 60 minutes after administration (*19*). Intragastric administration of 500.0 mg/kg bw of the same extract to rats significantly reduced (16–20%; $P < 0.05$–0.001) the weight of granulomas induced by the implantation of cotton pellets (*19*).

Total leukocyte migration into the rat pleural cavity was reduced by approximately 40% in rats with induced pleurisy following intragastric administration of 500.0 mg/kg bw of an ethanol extract of the aerial parts. This effect was due to the suppression of polymorphonuclear and mononuclear leukocyte migration, and the effect was similar to that of 250.0 mg/kg bw of acetylsalicylic acid (*19*).

Antimicrobial activity

A 50% ethanol extract of up to 500.0 mg/ml of the aerial parts did not inhibit the growth of the following fungi: *Aspergillus fumigatus, Botrytis cinerea, Fusarium oxysporum, Penicillium digitatum, Rhizopus nigricans* and *Candida albicans* (*20*). A methanol extract of the aerial parts inhibited the growth of *Helicobacter pylori*, minimum inhibitory concentration 50.0 µg/ml (*21*).

Cardiovascular effects

In vitro perfusion of guinea-pig heart with a 30% ethanol extract of the aerial parts, 0.001%, increased the force of contraction of the heart muscle. Intravenous administration of 0.05 ml/kg bw of the extract had no effect on blood pressure in guinea-pigs or rats (*18*).

Central nervous system depressant activity

Intraperitoneal injection of 25.0 mg/kg bw of an aqueous extract of the aerial parts to mice reduced spontaneous locomotor activity and coordination. However, intraperitoneal administration of the same dose of a fluidextract to mice did not reduce motor activity (*22*). Intraperitoneal or intragastric administration of 60.0–250.0 mg/kg bw of a 30% ethanol or 40% ethanol extract to mice reduced spontaneous locomotor activity. Intragastric administration of 60.0 mg/kg bw of the 40% ethanol extract also potentiated pentobarbital-induced sleeping time, and intraperitoneal administration of 50 mg/kg bw significantly ($P < 0.05$) delayed the onset of pentylenetetrazole-induced seizures (*23*).

The effects of an aqueous or 30% ethanol extract of the aerial parts were assessed in mice using the unconditioned conflict test, the light/dark box choice procedure and the staircase test. The extracts were administered at doses of 100.0 mg/kg bw, 200.0 mg/kg bw, 400.0 mg/kg bw or 800.0 mg/kg bw, while control animals received normal saline. The aqueous extract reduced motor activity in the staircase and free exploratory tests, as measured by the number of rears, steps climbed or locomotor crossings following administration of the 400.0 mg/kg and 800.0 mg/kg doses. The aqueous extract also potentiated pentobarbital-induction of sleep. The 30% ethanol extract was not active in these tests, but appeared

to increase activity of the animals, having an anxiolytic effect at the 400.0 mg/kg dose (*24*).

Intraperitoneal administration of 160.0–250.0 mg/kg bw of an aqueous extract of the aerial parts to mice delayed pentylenetetrazole-induced convulsions, increased pentobarbital-induced sleeping time and reduced spontaneous motor activity (*25*).

Intragastric administration of a 30% ethanol extract of the aerial parts, corresponding to 5.0 g/kg bw, per day for 3 weeks to rats had no effect on body weight, rectal temperature, tail-flick or motor coordination. However, in a one-armed radial maze, the treated animals demonstrated a reduction in motor activity. No changes were observed in electroencephalographic parameters in the treated animals (*17*).

Intragastric administration of 800.0 mg/kg bw of a dried 30% ethanol extract of the aerial parts (containing 2.6% flavonoids) to mice did not affect locomotor activity, but did prolong hexobarbital-induced sleeping time (*26*).

Chrysin displayed high affinity for the benzodiazepine receptors in vitro, and reduced locomotor activity in mice following intraperitoneal administration of 30.0 mg/kg bw (*27, 28*). At the same dose, chrysin also increased pentobarbital-induced hypnosis (*28*).

Uterine stimulant effects

A fluidextract of the aerial parts, 1.0 mol/l, stimulated strong contractions in guinea-pig and rabbit uterus (not pregnant) in vitro (*22*). However, a fluidextract, 1.0–2.0 mol/l, did not stimulate contractions in the isolated uterus from pregnant guinea-pigs (*29*).

Toxicology

The oral median lethal dose of a 30% ethanol extract of the aerial parts in mice was 37.0 ml/kg bw (*18*). Toxicity in mice of an aqueous extract was observed only after intraperitoneal administration of 900.0 mg/kg bw (*25*). No acute toxicity was observed in mice given extracts of the aerial parts at doses of 500.0 mg/kg bw or 900.0 mg/kg bw (*25*, *30*).

Clinical pharmacology

No clinical data available for mono-preparations of Herba Passiflorae.

Adverse reactions

A single case of hypersensitivity with cutaneous vasculitis and urticaria following ingestion of tablets containing an extract of Herba Passiflorae was reported (*31*). In one case, use of the aerial parts was associated with IgE-mediated occupational asthma and rhinitis (*32*). A single case of se-

vere nausea, vomiting, drowsiness, prolonged QT segment and episodes of non-sustained ventricular tachycardia was reported in a female subject after self-administration of a therapeutic dose of the aerial parts (*33*). However, the clinical significance of this reaction has not been evaluated.

Contraindications

Herba Passiflorae has been shown to stimulate uterine contractions in animal models (*22*). Its use is therefore contraindicated during pregnancy.

Warnings

May cause drowsiness. The ability to drive a car or operate machinery may be impaired.

Precautions

Carcinogenesis, mutagenesis, impairment of fertility

A fluidextract of Herba Passiflorae was not genotoxic at concentrations up to 1.3 mg/ml in *Aspergillus nidulans*, as assessed in a plate incorporation assay that permitted the detection of somatic segregation as a result of mitotic crossing-over, chromosome mal-segregation or clastogenic effects. No significant increase in the frequency of segregant sectors per colony were observed at any tested dose (*34*).

Pregnancy: non-teratogenic effects

See Contraindications.

Nursing mothers

Owing to the lack of data concerning its safety and efficacy, Herba Passiflorae should not be used by nursing mothers without consulting a health-care practitioner.

Paediatric use

Owing to the lack of data concerning its safety and efficacy, Herba Passiflora should not be administered to children without consulting a health-care practitioner.

Other precautions

No information available on general precautions or on precautions concerning drug interactions; drug and laboratory test interactions; or teratogenic effects in pregnancy.

Dosage forms

Powdered dried aerial parts, capsules, extracts, fluidextract and tinctures (*5*). Store in a tightly sealed container away from heat and light.

Posology

(Unless otherwise indicated)

Daily dose, adults: as a sedative: 0.5–2.0 g of aerial parts three to four times; 2.5 g of aerial parts as an infusion three to four times; 1.0–4.0 ml tincture (1:8) three to four times; other equivalent preparations accordingly (*2, 11*).

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