



Biotonic – Scientific Validation of Botanical Ingredients

Radix Astragalus (*Astragalus membranaceus*)

Medicinal Actions:

Adaptogenic, antioxidant, cardiotonic, hypotensive, immune enhancing, immunoregulatory, tonic.¹

Traditional Use:

The root of astragalus has been used in traditional Chinese medicine for centuries.¹ Astragalus has been used for health promotion² and to strengthen and tonify the Qi (energy), as well as tonify the blood and the spleen.¹ In clinical practice, astragalus is used as an adaptogenic agent to restore and balance the body's immune response and to increase vitality.²

Scientific Evidence:

The main phytochemical constituents of astragalus include triterpenoid saponins, isoflavonoids and polysaccharides.¹ Astragalus polysaccharides, saponin isolates and flavonoids have been researched in numerous pharmacological studies as water and alcoholic extracts, as well as astragalus injections.¹ The immune modulating activities of astragalus include stimulating macrophage activity, enhancing natural killer (NK) cells and B- and T-cell activity.^{1,2} Based on *in vitro* studies, astragalus has been shown to enhance the growth, metabolism, and longevity of cell cultures. Other *in vitro* effects include reduced oxygen consumption of mitochondrial cells and increased tolerance to stress.^{1,3}

Indications supported by clinical trials include impaired immunity,⁴⁻¹⁰ viral infections,¹¹⁻¹⁴ allergic rhinitis,¹⁵ fatigue,¹⁶ heart conditions,^{17,18} gestational diabetes¹⁹ and as an adjunct in the treatment of cancer.^{20,21}

Safety Summary:

Considered safe and well tolerated with no adverse reaction expected at the dose recommended.¹ Based on traditional considerations, astragalus is contraindicated in acute infections.¹ Considered safe during pregnancy.¹ Exercise caution during breastfeeding as safety has not been scientifically established.¹

Herba Artemesia/Sweet Wormwood (*Artemisia annua*)

Medicinal Actions:

Antiallergic, anticancer, antifungal, antihelmintic, antiinflammatory, antimalarial, antioxidant,²² antiparasitic, antischistosomal,²³ antiviral.^{23,24}

Traditional Use:

In the Traditional Chinese Medicine system, sweet wormwood has been used for centuries for treating "heat" conditions (yang), such as malaria and reliving symptoms of febrile diseases, tidal fever, low grade fever and summer heat stroke due to its cooling nature (yin).²⁵ The leaves are used for colds, flu, malarial fevers, dysentery and diarrhoea, while the seeds are used for night sweats, indigestion and flatulence.²⁴

Scientific Evidence:

The main phytochemical constituents of sweet wormwood include volatile oils, sesquiterpene lactones (artemisinins), phenolic compounds and flavones.²⁶ Artemisinins, the endoperoxide sesquiterpene

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lactones, have been recognized as the major bioactive ingredients responsible for the medicinal properties of sweet wormwood.^{23,27}

There is extensive research *in vitro* and preclinical *in vivo* evidence to support the therapeutic application of artemisinins and sweet wormwood in malarial conditions^{23,28,29} in *Schistosoma haematobium* infection³⁰ and cytomegalovirus infection.³¹

Safety Summary:

Considered safe and well tolerated at the dose recommended.^{23,28,32} May cause allergic reactions or dermatitis (direct contact).²⁴ Avoid during the first trimester of pregnancy due to the artemisinin content which is thought to be teratogenic and may cause foetal resorption.³³

Siberian Ginseng (*Eleutherococcus senticosus*)

Medicinal Actions:

Adaptogen, anticarcinogenic, antifatigue, antiinflammatory, antimicrobial, antioxidant, antistress, antiviral, hepatoprotective, immune modulating, immunoprotective, mild stimulant, neuroprotective, radioprotective,³⁴ tonic.^{1,35}

Traditional Use:

Siberian ginseng has been used for over 2000 years in tradition Chinese medicine. Based on traditional use, Siberian ginseng helps to expel wind dampness in the body, to strengthen bones, and to enhance the flow of Qi and blood. It also helps invigorate and tonify the spleen and kidneys and has tranquilizing actions.¹ Siberian ginseng has been used clinically to prevent respiratory illnesses (colds and influenza), to increase vitality and energy,² to treat oedema, and for joint and back pain. Other indications include insomnia, fatigue, lowered immunity and anorexia.¹

Scientific Evidence:

The key constituents of Siberian ginseng include lignans, phenylpropanoids (eleutherosides), triterpenoid saponins and glycans.¹ Siberian ginseng is primarily known as an adaptogenic herb.³⁶ Based on the writings by Brekhman and colleagues, Siberian ginseng is harmless to the host organism, has broad ranging therapeutic properties, provides non-specific effects in resistance to a wide variety of harmful factors of a physical, chemical or a biological nature, and acts as a normalizing or stabilizing agent.³⁶

Indications supported by clinical trials include improvement of mental³⁷ and physical performance,³⁸⁻⁴⁰ reduction of stress in individuals affected by chronic illness or environmental and occupational stress.^{1,41,42} Siberian ginseng has also been shown to treat fatigue, enhance immune function,⁴³ and act as an adjuvant therapy in dysentery, cancer and convalescence following antibiotic treatment.^{1,44}

Safety Summary:

Considered safe and well tolerated with no adverse reactions expected at the dose recommended.¹ Siberian ginseng is not recommended during the acute phase of infections.¹ In therapeutic doses, it may increase plasma drug levels when used in conjunction with Digoxin.¹ Considered safe with no adverse effects expected during pregnancy and breastfeeding.¹

Radix Polygoni Multiflora (*Polygonum multiflorum*)

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Medicinal Actions:

Antiaging, antialopecia, antibacterial, antidiabetic, antihyperlipidaemic, antiinflammatory, antioxidant, cognition enhancing,⁴⁵ hepatoprotective, immune modulating, neuroprotective.⁴⁶

Traditional Use:

Polygonum has been used in traditional Chinese medicine for centuries as a liver and kidney-tonifying remedy and as an antiaging agent.⁴⁵ It is thought to be preventative in neurodegenerative and cardiovascular diseases.⁴⁶ In clinical practice, polygonum is generally used in combination with other herbs to enhance the therapeutic effects.⁴⁵

Scientific Evidence:

The major phytochemical constituents of polygonum include flavones, quinones, stilbenes, phospholipids and phenolic compounds.⁴⁵

Despite polygonum being one of the most popular traditional Chinese medicines, there have been very few clinical studies conducted to assess the traditional indications or to study the therapeutic potential of its bioactive constituents.⁴⁶

The immune modulating effects of polygonum are due to the polysaccharide and anthraquinone content of the herb.⁴⁵ Based on *in vitro* research, polygonum anthraquinone glycosides are able to enhance T and B lymphocyte proliferation, improve macrophage phagocytosis, increase TNF secretion and enhance the activity of NK cells.⁴⁵

Several *in vivo* and *in vitro* studies have demonstrated the antiinflammatory effects of polygonum and its bioactive constituents. Polygonum works by inhibiting the expression of pro-inflammatory signalling factors such as nuclear factor (NF)-kappa- β , TNF- α , inducible nitric oxide synthase (iNOS), cyclooxygenase-2, chemokines and cytokines.⁴⁶⁻⁵⁰

Safety Summary:

No adverse effects expected at the dose recommended. In therapeutic doses, polygonum administration has been linked to cases of liver damage.⁴⁶ Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.⁵¹

Radix Zingiberis Officinalis (*Zingiber officinale*)

Medicinal Actions:

Antiemetic, antiinflammatory, antiplatelet, carminative, diaphoretic, digestive stimulant, peripheral circulatory stimulant, spasmolytic.¹

Traditional Use:

Traditionally ginger has been used to enhance digestion, to treat digestive problems including colic, flatulent dyspepsia, cramping, peptic ulcer, loss of appetite and gastrointestinal infections.¹ Due to its pungent, sweet and heating properties, ginger has been used for both digestive and respiratory diseases.⁵²

Scientific Evidence:

The key constituents of ginger include monoterpenes (geranial, neral) and sesquiterpenes (zingiberene, beta-bisabolene), essential oils and pungent actives (gingerols, shogaols).^{1,53}



The antiemetic and antinausea activities of ginger have been demonstrated in numerous clinical trials, and assessed in several systematic reviews and meta-analyses.^{1,54-59} Ginger has also been shown to enhance gastric emptying in patients with functional dyspepsia.¹

Animal studies of ginger have also provided supportive evidence for its use in enhancing digestive functions.¹ Ginger was found to stimulate gastric secretion, enhance intestinal lipase activity, increase bile secretion and positively influence gastrointestinal motility.¹

Ginger extract, its main constituents, and essential oil of ginger have also demonstrated antimicrobial activity in both *in vitro* and *in vivo* trials.² Various ginger preparations have documented antibacterial effects against *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Haemophilus influenzae*,⁶⁰ *Penicillium* spp., *Escherichia coli*, *Bacillus subtilis* and *Helicobacter pylori*.²

Safety Summary:

Considered safe and well tolerated at the dose recommended.¹ Contraindicated in therapeutic doses in patients with gallstones.¹ No adverse effects expected during pregnancy and breastfeeding at the dose recommended.⁶¹

Rhizoma Atractylodis Macrocephalae (*Atractylodes lancea*)

Medicinal Actions:

Antiinflammatory, antimicrobial, antioxidant,⁶² antipyretic, antitumor, immunoregulatory.⁶³

Traditional Use:

The rhizome of atractylodes has been used in traditional Chinese medicine as a tonic herb,⁶² for the treatment of rheumatic diseases, digestive disorders, as well as colds and influenza.⁶³ Due to its medicinal properties, atractylodes was used to invigorate the stomach, strengthen the spleen, eliminate dampness, and expel and clear away wind-cold.^{62,63} In Thai traditional medicine, it has been used to treat fever and the common cold. The Thai also utilized atractylodes for the treatment of gastrointestinal disorders including dyspepsia, flatulence, nausea, and non-infectious diarrhoea.⁶³ In Japan, atractylodes was traditionally used to treat gastrointestinal diseases such as nausea, gastroparesis, and gastric atony.⁶⁴

Scientific Evidence:

The major constituents of atractylodes include essential oils (β -eudesmol, hinesol, L-phenylalanine) and esquiterpenoids (atractylenolides and atractylon, atractylodin).^{63,65} Its pharmacological properties have been studied predominantly through *in vitro*, *ex vivo*, and animal trials.⁶³

Atractylodes extract has been shown to delay gastric emptying and stimulate small intestinal motility in mice.⁶⁴ It has also demonstrated antiulcer properties in animal models.^{66,67} In the study by Seo et al., atractylodes isolate, β -eudesmol, has demonstrated antiinflammatory effects by down-regulation of interleukin-6 (IL-6) production and expression, via the modulation of NF-kappa β .⁶⁸ The antimicrobial activity of atractylodes has been demonstrated *in vitro* against *Staphylococcus aureus*, *Escherichia coli*, *Saccharomyces cerevisiae*, *Candida albicans*,⁶⁹ *Rhodotorula glutinis* and *Saprolegnia*.^{63,70}

Safety Summary:

Considered safe and well tolerated with no adverse reactions expected at the dose recommended.⁶⁵ Atractylodes may cause an allergic reaction in individuals with a known sensitivity to plants from the Asteraceae/Compositae family.⁶⁵ Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.⁶⁵

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Wild Yam (*Dioscorea villosa*)

Medicinal Actions:

Antiinflammatory, antioxidant,² antirheumatic, cholagogue, mild diaphoretic, oestrogen-modulating,⁶¹ spasmolytic.⁷¹

Traditional Use:

In traditional Western medicine, wild yam has been used for gastrointestinal disorders including colic, gastrointestinal irritation, spasm, diverticulitis and for neuralgic affection and asthma⁶¹ due to its antispasmodic, antiinflammatory and autonomic nervous system-relaxant properties.² It has also been used for rheumatoid arthritis and hormonal imbalance associated with menopause.⁶¹

Scientific Evidence:

The active constituents of wild yam include phytosterols (β -sitosterol, campesterol, stigmasterol), steroidal saponins (diosgenin, dioscin, dioscornin), alkaloids and flavonoids.⁷¹

To date, wild yam has not been studied under clinical trial conditions, rather evidence is derived mainly from traditional use and *in vitro* and animal studies.² The saponin diosgenin has demonstrated hepatoprotective, antioxidative and hypolipidaemic effects in animal models.⁷² *In vitro* trials with diosgenin have reported antiinflammatory activity through the down-regulation of cyclooxygenase expression.⁷³ Dioscorea saponins have also demonstrated cytotoxic and antifungal activity *in vitro*.⁷⁴

Safety Summary:

Considered safe and well tolerated with no known interactions and contraindications.⁶¹ Due to its saponin content, wild yam may cause irritation of the gastric mucosa and reflux when taken in therapeutic doses.⁶¹ No adverse effects expected during pregnancy and breastfeeding at the dose recommended.⁶¹

Sclerotium Poria Cocos (*Poria cocos*)

Medicinal Actions:

Anticancer,⁷⁵ antifungal, antihyperglycaemic,⁷⁶ antiinflammatory, antioxidant, diuretic immune modulating, sedative.⁷⁷

Traditional Use:

Sclerotium Poria Cocos, also known as poria mushroom, is a saprophytic fungus used in traditional Chinese and Japanese medicine due to its diuretic, sedative, and tonic effects.⁷⁶ It has been used in traditional medicine to treat chronic gastritis, oedema, nephrosis, gastric atony, acute gastroenteric catarrh, dizziness, nausea and emesis.⁷⁵

Scientific Evidence:

The major constituents of poria mushroom include triterpenoids (Lanostane-, Eburicane-, seco-Lanostane and seco-Eburicane-type triterpenes) and polysaccharides.⁷⁶

In vivo administration of polysaccharides isolated from poria mushroom have demonstrated broad-spectrum antiinflammatory activity.⁷⁸ It has been shown to activate macrophages to induce nitric oxide (NO) production and iNOS transcription through the activation of NF-kappa β /Rel.⁷⁸ Treatment of murine

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macrophages has resulted in NF-kappa β /Rel activation and iNOS expression through the p38 kinase pathway and membrane receptors (CD14, Toll-like receptor 4, and CR3), which are critically involved in the signal transduction leading to NF- κ B/Rel activation.⁷⁹

Poria mushroom is known as an immunomodulatory agent that alters the activity of immune function through the dynamic regulation of informational molecules such as cytokines.⁷⁶ Ethanol extracts of poria mushroom have demonstrated immunomodulatory activities *in vitro*.⁷⁷ In human peripheral blood monocytes poria has enhanced the secretion of immune stimulators interleukin (IL)-1 β , IL-6 and TNF- α , and suppressed the secretion of an immune suppressor transforming growth factor- β (TGF- β).⁷⁷

Safety Summary:

Considered safe with no known adverse effects and interactions.⁸⁰ Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.⁸⁰

Radix Codonopsis (*Codonopsis pilosulae*)

Medicinal Actions:

Antifatigue, antimicrobial, antioxidant, antitumor, antiulcer,⁸¹ Immunomodulatory.^{82,83}

Traditional Use:

Codonopsis has been used in traditional Chinese medicine to treat digestive dysfunction and associated symptoms such as poor appetite, dyspepsia, indigestion, loose stools and fatigue.^{83,84} It was also used for pulmonary insufficiencies such as shortness of breath, coughing and wheezing.⁸⁴ Codonopsis exhibits similar therapeutic effects to *Panax ginseng*, and is often used as a substitute for this herb.^{82,84} In traditional Chinese medicine, codonopsis is often used in combination with other herbs to improve Qi deficiency, replenish vital energy and nourish the blood.^{85,86}

Scientific Evidence:

The main constituents of codonopsis include sterols, triterpenes, glycosides, alkaloids and polysaccharides.⁸²

Pharmacological studies on codonopsis have demonstrated its protecting properties against peptic ulceration⁸⁷ and beneficial effects on bowel regulation.⁸⁴ It has also been shown to enhance learning and memory behaviour,^{84,88} increase immunity,^{82,83} and improve chronic obstructive pulmonary disease.⁸⁵

Safety Summary:

Codonopsis is considered safe and well tolerated.⁸⁵ In therapeutic doses, concomitant use may interact with antiplatelet or anticoagulant medications.⁸⁹ Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.⁸⁹

Radix Peony (*Paeonia lactiflora*)

Medicinal Actions:

Anticonvulsant, antiinflammatory, antioxidant, cognition enhancing,⁶¹ muscle relaxant, spasmolytic.⁹⁰

Traditional Use:

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Peony has been used in traditional Chinese medicine to invigorate and cool the blood and clear the liver.⁶¹ Clinically, it is utilized for the treatment of wounds, fungal infections, as well as pain and spasmodic conditions.⁹¹ Peony has also been used in combination with other herbs for the treatment of ovulatory disorders and to promote fertility.⁹²

Scientific Evidence:

The active constituents of peony include glycosides (paeoniflorin), flavonoids, proanthocyanidins, tannins, terpenoids, triterpenoids, and complex polysaccharides.⁹¹

Indications supported by clinical trials include cardiovascular disorders^{93,94} and women's health.⁶¹ Preclinical research also suggests peony has hepatoprotective⁹⁵ and cognition enhancing effects.^{96,97}

Safety Summary:

Considered safe with no adverse effects or interactions expected.⁶¹ No adverse effects expected during pregnancy and breastfeeding at the dose recommended.⁶¹

Tuber Curcumae (*Curcuma longa*)

Medicinal Actions:

Anticarcinogenic, antiinflammatory, antimicrobial, antioxidant, cardioprotective, carminative, cholagogue, choloretic, depurative, hepatoprotective, hypolipidaemic, neuroprotective, radioprotective, vasoprotective.¹

Traditional Use:

Turmeric has a long history of use in Ayurvedic medicine for the treatment of inflammatory conditions, as a tonic, and blood purifying agent. It has also been used for poor appetite and for liver disorders.¹ In traditional Chinese medicine turmeric has been used to invigorate the blood and as a Qi or vital energy stimulant.¹ Other traditional uses include managing abdominal pain, indigestion, and abdominal bloating.⁹⁸

Scientific Evidence:

The main constituents of turmeric include essential oils (sesquiterpene ketones, zingiberene) and curcuminoids (curcumin).¹ The antiinflammatory properties are thought to be related to turmeric's ability to inhibit pro-inflammatory arachidonic acid and neutrophil function during inflammatory episodes.⁹⁹

Research shows that curcumin, the active constituent of turmeric has gastro-protective effects and is beneficial for inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), as well as dyspeptic and biliary-related symptoms.¹ Curcumin has also demonstrated chemopreventative properties against bowel polyps, which may help reduce the of risk of premalignant conditions.¹⁰⁰

In clinical trials, curcumin has demonstrated antioxidant activity¹⁰¹ and gastro protective effects and increased gall bladder contraction in healthy volunteers.^{100,102} It has also been used effectively in post-operative care,¹⁰³ in patients with Crohn disease,¹⁰⁴ ulcerative colitis,¹⁰⁵ and IBS patients.^{1,106}

Safety Summary:

Considered safe and well tolerated with no adverse reaction expected at the recommended dose.¹ Avoid in persons with biliary tract obstruction.¹ Considered safe and well tolerated during pregnancy and breastfeeding.⁵³



Pericarpium Citri Reticulae (*Citrus reticulata*)

Medicinal Actions:

Anticarcinogenic, antiinflammatory, antimicrobial,¹⁰⁷ antioxidant,¹⁰⁸ antiproliferative, antispasmodic, antiviral,¹⁰⁹ vasoprotective.¹⁰⁸

Traditional Use:

Pericarpium citri reticulatae is the dried, ripe fruit peel of *Citrus reticulata*.¹¹⁰ It has been widely used as a herbal medicine in Korea, China, and Japan to treat indigestion and inflammatory disorders of the respiratory tract including bronchitis and asthma.¹¹⁰ The herb is also used for detoxification.¹⁰⁸ In traditional Chinese medicine, *Pericarpium citri reticulatae* has been utilized to eliminate phlegm and strengthen the spleen.¹¹⁰

Scientific Evidence:

The main bioactive constituents of *Pericarpium citri reticulatae* consist of essential oils (D-limonene, α -terpineol, terpinen-4-ol, γ -terpinen, and linalool) and flavonoids (flavone, flavanone and flavonol).^{108,111}

Based on *In vitro* research, flavonoids isolated from *Pericarpium citri reticulatae* have demonstrated antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Salmonella typhi* and *Enterobacter cloacae*.¹⁰⁸ The polymethoxylated flavones extracted from *Citrus reticulata* have also exhibited antifungal activity by inhibiting the growth of *Aspergillus niger*.¹⁰⁸ The volatile constituents of the fruit peel have demonstrated antibacterial activity against *Escherichia coli*, *Staphylococcus aureus*, and antifungal activity against *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus fumigatus* and *Candida albicans*.¹⁰⁷

Safety Summary:

Considered safe at the recommended dose with no known adverse effects.¹¹² In therapeutic doses, *Pericarpium citri reticulatae* may cause hyperkalaemia when used in conjunction with potassium-sparing diuretics.¹¹² Exercise caution during pregnancy and breastfeeding as safety has not been scientifically established during these times.

Glycyrrhizae Uralensis (*Glycyrrhiza uralensis*)

Medicinal Actions:

Adrenal tonic, antibacterial, anticarcinogenic, antiinflammatory, antiviral, demulcent, hepatoprotective, mild laxative, mucoprotective, spasmolytic,¹ antiulcer.¹¹³

Traditional Use:

Glycyrrhiza uralensis also known as Chinese or Ural liquorice is one of the most frequently used herbs in traditional Chinese medicine.¹¹³ It has been used for improving overall health, to lengthen life-span, as a cure for injury and swelling, and also for detoxification.¹¹⁴ In Japan, extract and flavonoid-rich fractions of Chinese liquorice are used for the treatment of gastritis as well as gastric and duodenal ulcers.¹¹⁴

Scientific Evidence:

The key constituents of Chinese liquorice include phenolic compounds,¹¹⁵ pterocarpenes, essential oils, triterpenoids, alkaloids, polyamines and polysaccharides.¹¹³

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Ethanollic extracts and several compounds (pterocarpenes and isoflavanoids) isolated from Chinese liquorice have exhibited strong antibacterial activity against *Streptococcus mutans* (*in vitro* research).¹¹³

Other *in vitro* trials have shown that the flavonoids isolated from Chinese liquorice possess antimicrobial activities against methicillin sensitive *Staphylococcus aureus* (MSSA), methicillin resistant *Staphylococcus aureus* (MRSA), *Micrococcus luteus*, *Bacillus subtilis*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*.¹¹⁴

According to Bone and Mills, the British Pharmacopoeia states that *Glycyrrhiza glabra*, *Glycyrrhiza uralensis* or *Glycyrrhiza inflata* are regarded as being medicinally interchangeable herbs.¹

Indications supported by clinical trials include dyslipidaemia,^{116,117} post-operative recovery,¹¹⁸ gastric ulcer, duodenal ulcer, functional dyspepsia, viral hepatitis and recurrent mouth ulcers.¹

Safety Summary:

Considered safe at the recommended dose.¹ In therapeutic doses, *Glycyrrhiza uralensis* may cause hypertension, sodium and water retention and hypokalaemia.¹ Avoid in therapeutic doses with diuretics and laxative medications.¹ Contraindicated in therapeutic doses in cholestatic liver disorders, liver cirrhosis, hypertension, hyperkalaemia, severe kidney insufficiency, oedema, congestive heart failure and pregnancy.¹ Avoid during pregnancy.¹ Considered safe during breastfeeding.¹

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