

PROFESSIONAL INFORMATION

PILOHERB® tablets

- Complementary Medicine.
- D33.8. Complementary Medicine: Discipline-specific. Other - herbal.
- This unregistered medicine has not been evaluated by the SAHPRA for its quality, safety or intended use.

SCHEDULING STATUS

[S0]

1. NAME OF THE MEDICINE

PILOHERB® tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

| Active ingredients                                                                | Per tablet                                                                 | Per maximum daily dose (9 tablets) |
|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------|------------------------------------|
| Balsamodendron mukul L. (Indian bdeIIium/Sanskrit - guggal) [resin, extract]      | 130 mg                                                                     | 1170 mg                            |
| Triphala [fruit, extracts]                                                        | <i>Embolica officinalis</i> Gaertn. (Indian gooseberry/Sanskrit – amalaki) | 48 mg                              |
|                                                                                   | <i>Terminalia bellerica</i> Roxb. (beleric myrobalan/Sanskrit – bahera)    |                                    |
|                                                                                   | <i>Terminalia chebula</i> Retz. (chebulic myrobalan/Sanskrit – haritaki)   |                                    |
|                                                                                   |                                                                            |                                    |
| <i>Azadirachta indica</i> A. Juss. (Indian lIac/Sanskrit - neem) [leaf, extract]  | 20 mg                                                                      | 180 mg                             |
| <i>Bauhinia variegata</i> L. (orchid tree/Sanskrit – kachnar) [flower, extract]   | 16 mg                                                                      | 144 mg                             |
| <i>Berberis aristata</i> L. (Indian barberry/Sanskrit - daarhadi) [root, extract] | 16 mg                                                                      | 144 mg                             |
| <i>Cassia fistula</i> L. (Indian laburnum/Sanskrit – amaltas) [fruit, extract]    | 10 mg                                                                      | 90 mg                              |
| <i>Tephrosia purpurea</i> L. (wild indigo/Sanskrit - sarphoka) [leaf, extract]    | 6 mg                                                                       | 54 mg                              |
| <i>Curcuma longa</i> L. (turmeric/Sanskrit - haladi) [rhizome, extract]           | 6 mg                                                                       | 54 mg                              |
| <i>Mesua ferrea</i> L. (ironwood tree/Sanskrit – nag kesar) [flower, extract]     | 3 mg                                                                       | 27 mg                              |
| Shilajeet (purified) (natural fulvic acid/Sanskrit - Shilajit) [powder]           | 16 mg                                                                      | 144 mg                             |

Piloherb® tablets is sugar free.

Piloherb® tablets contain a preservative: sodium benzoate 0,37 % m/m.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet, film coated.

Piloherb® tablets are light-brown, round, biconvex, film-coated tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Piloherb® tablets is a herbal supplement that contains ingredients which can assist in the relief of swollen and inflamed veins by reducing inflammation, improving bowel irregularities and supporting healthy blood circulation. Efficacy of support may vary between users.

4.2 Posology and method of administration

The recommended daily dosage and directions for use:

Adults 18 years and older:

Treatment dose:

Two (2) to three (3) tablets, three times per day, after meals with a glass of water, or as directed by a medical practitioner.

Maintenance dose:

Two (2) tablets, twice (2) per day, after meals with a glass of water, for 4 to 6 weeks, or as directed by a medical practitioner.

Advise patients to take 2 hours before or after other medication.

For best results, use with Piloherb® ointment.

If the patient forgets to take Piloherb® tablets

Advise the patient to take the missed dose when they remember. A double dose should not be taken to compensate for forgotten individual doses.

Taking Piloherb® tablets with food, drink and alcohol

There is no known interaction between the contents of Piloherb® tablets and food, drink or alcohol.

4.3 Contraindications

- Must not be given to patients with known hypersensitivity or allergy to any of the ingredients of Piloherb® tablets (see section 6.1 List of excipients).

Patients should be advised to consult their medical practitioner if in doubt.

- Must not be given to patients taking cyclosporin or tacrolimus (see 4.5).

- Must not be given to patients with kidney or liver disorders.

- Must not be given to patients who are pregnant or breastfeeding (see 4.6).

- Patients taking any chronic medication should not use this product without consulting their medical practitioner.

4.4 Special warnings and precautions for use

- Advise patients to consult a healthcare provider or doctor prior to use if they have/are taking:
  - o hypoglycaemia or antidiabetic medication (see 4.5);
  - o a bleeding disorder or blood thinners (anticoagulant/antiplatelet medication) (see 4.5);
  - o an autoimmune disorder or immunosuppressant medication (see 4.5);
  - o a thyroid disorder or thyroid hormone replacement therapy (see 4.5);
  - o (a history of) gallstones or gallbladder disorders as turmeric rhizome may have bile stimulating effects; or
  - o abdominal pain, nausea, fever or vomiting.

- Advise patients to reduce the dose or stop use if laxative effect occurs.

- Advise patients to consult a healthcare provider or doctor if symptom persist or worsen.

- Advise patients to discontinue at least 2 weeks before any surgical procedures.

- Advise patients not to exceed the daily recommended dose.

- Advise patients not to use after the date of expiry.

- Products containing herbal ingredients may interact with some medication.

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*Balsamodendron mukul* (Indian bdeIIium) [resin, extract]

In the Ayurvedic system of medicine, Indian bdeIIium resin is used for the treatment of a variety of ailments, including constipation, haemorrhoids and liver disorders.

The ketonic steroids, Z-guggulsterone and E-guggulsterone, are considered the principle active constituents found in the resin extracts. Several sesquiterpenoids have also been isolated from Indian bdeIIium resin.

Indian bdeIIium resin extracts have shown to have antibacterial activity against both Gram-positive and Gram-negative bacteria. Indian bdeIIium resin extracts also have demonstrated analgesic and anti-inflammatory activity. *In vitro*, guggulsterone has shown to suppress the activation of nuclear factor-kappaB (NF-κB) and downregulate the generation of interleukin (IL)-1beta, IL-2, IL-4, interferon-gamma and nitric oxide.

*Triphala* (Indian gooseberry, beleric myrobalan, chebulic myrobalan) [fruit, extracts]

In Ayurveda, Triphala is used for the relief of occasional constipation and as a rejuvenative and digestive tonic.

Polyphenolic compounds and flavonoids found in Triphala are thought to be responsible for many of its effects. Chebulic myrobalan and beleric myrobalan fruit are reported to have beneficial effects in bowel irregularity and indigestion, which are attributed to their astringent properties. In humans, Indian gooseberry leaf extract has shown to have anti-inflammatory activity by reducing levels of C-reactive protein and has also shown to have gastroprotective properties. The anti-inflammatory effect of Triphala is thought to be via NF-κBp65 and cyclooxygenase (COX) 2 inhibition, whereas the anti-colitis effects are ascribed to its antioxidant properties.

*Azadirachta indica* (Indian lIac) [leaf, extract]

In Ayurveda, Indian lIac extracts are used as a tonic to stimulate appetite, for gastrointestinal disorders and for its hepatoprotective properties, among other indications.

The active phytoconstituents found in Indian lIac leaf are azadirachtin, nimbin and nimbidine.

Nimbin (a triterpene) has shown to have antipyretic, fungicidal and antiseptic properties. The limonoid, azadirachtin, is known as a pain anaesthetiser, speculated to be via activation of endogenous opioid pathways. Indian lIac extracts have also been found to inhibit COX 1 and -2, tumour necrosis factor-α and IL-1. Indian lIac leaf extract has demonstrated to have antidiabetic effects and improve overall pancreatic health, prevent liver and kidney damage and aid recovery in antioxidant systems.

*Bauhinia variegata* (orchid tree) [flower, extract]

In Ayurveda, orchid tree flowers are used for haemorrhoids, rectal prolapse, wound treatment and as a blood purifier .

Orchid tree flower contains an appreciable amount of nerolidol, alpha bisabolol and beta-bisabolen.

Nerolidol has been reported to have antimicrobial, antibiofilm, antioxidant, antinociceptive and anti-inflammatory activity.

*Berberis aristata* (Indian barberry) [root, extract]

In traditional Indian systems of medicines, Indian barberry root is an important ingredient in multiple formulations for the quick healing of wounds, curing haemorrhoids, indigestion and dysentery.

The primary phytoconstituent found in the whole plant is a quaternary protoberberine alkaloid, berberine.

Preliminary and human research suggests that berberine blocks production of the proinflammatory cytokines, decreases the production of IL-8 and selectively inhibits COX-2. Berberine has antimicrobial effects, including activity against *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli*, *Vibrio cholerae*, *Candida albicans* and *Helicobacter pylori*. In animals, berberine has also shown to have hepatoprotective activity. Clinically, berberine has shown to induce peripheral vasodilation.

*Cassia fistula* (Indian laburnum) [fruit, extract]

In Ayurveda, Indian laburnum fruit is used as mild laxative as well as for cardiac conditions and stomach problems.

The ripe fruits of Indian laburnum are source of sennoside B (a laxative in contemporary medicine), Rhein (a major anthraquinone derivative), coumarins, amino acids, (including aspartic acids, glutamic acids and lysine) and micronutrients (including potassium, calcium, iron and manganese).

The purgative action of Indian laburnum is due to the presence of anthraquinones and sennoside B. The fruit has also shown to possess anticandidal activity against *Candida albicans*, *Candida glabrata* and *Candida tropicalis*.

*Tephrosia purpurea* (wild indigo) [leaf, extract]

In Ayurveda, wild indigo leaf extracts are used to treat a variety of ailments, including cirrhosis and jaundice.

Wild indigo leaves contain glycosides (rutin, quercetin and osytrin); retinoids (deguelin, elliptone, rotenone and tephrosin); flavonoids (lanceolatin A, B, C, purpurin, purpurenone, purpuritenin), and sterols (beta sitosterol).

The major biological activities of wild indigo leaves are attributed to the presence of the wide range of flavonoids, speculated to be via membrane stabilising effects and antioxidant properties.

*Curcuma longa* (turmeric) [rhizome, extract]

Turmeric is used in Ayurveda and other traditional Indian medical systems for digestive complaints and for its anti-inflammatory properties. Turmeric contains 3-6 % polyphenolic compounds, collectively known as curcuminoids, which is a mixture of curcumin, demethoxycurcumin and bisdemethoxycurcumin.

In animals, turmeric constituents have been shown to attenuate induced liver damage and fibrosis, possibly due to beneficial effects on the levels and activity of inflammatory cytokines or matrix metalloproteinases. In animals, curcumin has been shown to reduce pain, possibly via inhibition of transient receptor potential vanilloid 1 mediated pain hypersensitivity. Clinically, curcumin has shown to reduce inflammatory markers such as IL-6 and C-reactive protein. In both human and animal research, turmeric has shown to increase bowel motility. In animals, curcumin has shown to improve the activity of digestive enzymes and reduce the incidence of gastrointestinal ulcers, increase intestinal wall mucus and nonprotein sulfhydryl content.

*Mesua ferrea* (ironwood tree) [flower, extract]

In the Ayurvedic system of medicine, ironwood tree flower is mainly used to reduce inflammation and has various uses, including being used for the treatment of bleeding piles and dysentery.

The bud and flower oils contain alpha-opaene and germacrene D, sterols, phenols, flavonoids, saponins, coumarins and aromatics (eugenol and cinnamaldehyde). Recently, 2 new polycyclic polyphenylated acylphloroglucinols, mesuaferroic acid H and taxifloranone were isolated from ironwood tree flower buds which showed excellent antibacterial activity against *Staphylococcus aureus* ATCC25923 and a series of multidrug-resistant Gram positive clinic isolates. The flower buds have also been reported to exhibit antioxidant, hepatoprotective, analgesic, antispasmodic, anti-inflammatory, antitumor and antimicrobial activity.

Shilajeet (natural fulvic acid) [powder]

Shilajeet is a natural substance found mainly in the Himalayas, formed for centuries by the gradual decomposition of certain plants by microorganisms. In Ayurveda, Shilajeet is considered as a rejuvenator and antiaging compound. Shilajeet is used for the treatment of kidney stones, oedema, haemorrhoids, as an internal antiseptic and to reduce anorexia.

Shilajeet is composed mainly of humic substances, including fulvic acid (60-80 %) and digloelements, including selenium.

Several animal studies have shown that fulvic acid exhibits antioxidant, anti-inflammatory, adaptogenic and antidiyslipidemic activities. Fulvic acid has also demonstrated antitumor, anti diarrheal and antiviral activity and is involved in the regulation of immunity and improving microcirculation.

5.2 Pharmacokinetic properties

There is insufficient reliable information available about the pharmacokinetics of Indian bdeIIium resin, Triphala, Indian lIac leaf, orchid tree flower, Indian laburnum fruit, wild indigo leaves and ironwood tree flower.

*Berberis aristata* (Indian barberry) [root, extract]

Absorption: Berberine appears to be a substrate of nuclear transporters such as P-glycoprotein and organic cation transporter, which may limit its oral bioavailability. In animals, time to maximum blood concentration of berberine was 2,4 h.

Metabolism: Berberine appears to undergo phase I hepatic metabolism. Three metabolites - jatrorrhizic-3-sulphate, demethyleberberine-2-sulphate and thalidiflennine-10-sulphate - have been observed in human urine after the use of berberine chloride.

Elimination: Berberine is excreted through urine and faeces.

*Curcuma longa* (turmeric) [rhizome, extract]

Absorption: In humans, the oral bioavailability of curcumin is extremely low. The average peak serum concentrations after taking curcumin 4 g, 6 g and 8 g were 0,51 μmol, 0,63 μmol and 1,77 μmol, respectively. Curcumin absorption appears to increase when taken with food.

Metabolism: Curcumin undergoes significant metabolism in the liver and intestines, contributing to low oral bioavailability. In humans, curcumin is present in the plasma as glucuronide and sulphate conjugates. The half-lives of these conjugates are 6-24 h.

Excretion: In humans, curcumin is present in the faeces following consumption of an extract. In some studies, curcumin was undetectable in the urine following oral intake; however, other studies detected urinary curcumin and its conjugates.

Shilajeet (natural fulvic acid) [powder]

Absorption: After oral administration, fulvic acid is well absorbed.

Elimination: Fulvic acid is eliminated from the body within hours after ingestion.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal silicon dioxide

Crosspovidone

Dicalcium phosphate

Hydroxypropyl methylcellulose

Magn