



EPO SRL - Estratti Piante Officinali
Via Stadera 19, 20141 Milano – Italy
Officina Farmaceutica – GMP Factory



FICUSPHEN®

FICUS CARICA leaves DRY EXTRACT **2,5% polyphenols – 0,1% quercetin**



1- Botanical information: Common Fig or *Ficus carica* L. (fam. Moraceae, mulberry or fig family) is a deciduous shrub or small tree, native to the eastern Mediterranean area and to Asia Minor (from Greece to Afghanistan); it's now commonly grown in all subtropical countries because of its edible, very nutrient fruits (figs).

The tree is often multiple branched. The bark is smooth, silvery gray in color. The coriaceous, dark green leaves are palmate and deeply lobed (3 to 7 lobes) (1); the leaf margin is toothed (1). Leaves contain a sap which is irritant to the skin (2). The pear-shaped fruit, green, yellowish, bronze or purple in color, is actually a false fruit (3), namely an infructescence called syconium, consisting in a hollow floral receptacle with multiple ovaries clustered on the inner wall (1). The tiny, fleshy flowers are therefore not visible externally; in their native habitat, flowers are pollinated by a very specialized wasp, called *Blastophaga psenes*, which enter the fruit by a small orifice, called ostiole, situated at the apex of the syconium (1); the pollinated syconia develop then into a false fruit, containing a sweet, jelly pulp and the real, tiny fruits, some achenes, incorrectly called seeds (3). Without the pollinator insect Fig trees cannot be propagated by seed, but only by vegetative methods (cutting). Many parthenocarpic cultivars have been selected in recent times, meaning they can bear a crop of figs without pollination (sterile fruits without seeds).

Fig trees are very prolific, normally producing two crops per year: a late spring breba crop on last season's branches, and a summer or early fall main crop on new wood; the breba crop is normally inferior to the main crop both in quantity and quality.

The Fig tree requires dry, well drained soils and is drought tolerant; it prefers sunny exposure. It can tolerate moderate salinity (1).

Regarding the etymology, "*Ficus*" is Latin for fig and "*carica*" comes from Caria, a region of Asia minor; the common names are similar in all the European languages: fig (English), higo (Spanish), figue (French), Feige (German), fico (Italian).

Internet: <http://www.eposrl.com> e-mail: epo@eposrl.com

Tel.: ++39.02.89557.1 Fax: ++39.02.89557.490

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2- *Parts used*: fig is a very sweet and highly caloric fruit (200 kcal/100 g) (3); figs can be eaten both fresh or dried; they can be processed too (canned, as jelly etc.); dried cull figs have been roasted and ground as a coffee substitute (1,3).

For medicinal use fruits, leaves, roots and latex have been used. Fruits have laxative properties, due to the high content in sugars, and leaves are regarded as a folk remedy for diabetes in Spain and Southwestern Europe (4); in India the plant has been used as chewed leaves to treat jaundice (5), and also liver and spleen disorders (6). In Indian traditional medicine the roots are used in treatment of leucoderma and ringworms (6). The latex has been used topically to treat warts, insect bites and thorn pricks (2).

3- *Active constituents*: figs contain a high amount (up to 70%) of sugar (glucose and fructose in the same quantity) (3), pectins, flavonoids and vitamins.

Leaves contain phenolic compounds such as **flavonoids** (7), α -tocopherol (8) and 3-O-caffeoylquinic acid (9), with antioxidant capacity (8) and superoxide radical scavenging activity (9). They contain also organic acids, such as oxalic, citric, malic, quinic, shikimic and fumaric acids (9).

In a study (9) comparing the chemical composition and antioxidant potential of three different parts of *Ficus carica* L. (pulp, peels and leaves), leaves were always the most effective part, which seems to be related with phenolic compounds. Leaves contain also steroids, triterpenoids and coumarins (6).

4- *Galenic forms*: decoction of the leaves have been used as a remedy for diabetes (1) and also in the only available study on humans (12): as decoction is a very microbiologically unstable galenic form, a dry powdered extract has been developed by EPO, using ethanol 50% and following the general method of the European Pharmacopoeia 6.1 dated 4/2008; the extract is standardized in polyphenols (min. 2,5 %) and quercetin (min. 0.10 %).

5- *Pharmacology, preclinical and clinical studies*: in spite of the fact that figs are a common folk remedy for constipation, the German Commission E has not approved their use as laxative (3).

Fig **leaves** may have **hypoglycemic effects**, but the mechanism of action is still unknown; some studies suggest facilitation of glucose uptake peripherally (4). Besides, *F. carica* has antioxidant properties (8): a study (10) on streptozotocin-induced diabetic rats showed that antioxidant status is affected in the diabetes syndrome and *F. carica* extracts tend to normalize it.

Hypoglycemic properties have been demonstrated in murine models. In a study (11) the hypoglycemic effect of an aqueous extract of *F. carica* leaves was examined in streptozotocin-diabetic rats. The extract induced a significant hypoglycaemic effect after either oral or intraperitoneal administration; the mechanism involved was not elucidated.

The only available clinical trial investigating the antidiabetic properties of Fig leaves is a small open label, cross over study (12) of fig-leaf decoction (i.e. the traditional galenic form) as a supplement to breakfast for 4 weeks in patients (n=10), aged 22-38 years, with type 1 diabetes mellitus (DM), treated with twice-daily insulin injection and diet. The patients were divided into two groups (n=5) with random allocation and cross-over design. During the first month patients were given a decoction of fig leaves and during the next month a non sweet commercial tea. There was a decrease in postprandial glucose and insulin requirements, but no change in

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fasting glucose when compared with the control commercial tea. No effect was seen in C-peptide level, which may support a non-insulin mediated effect.

Potential **hypolipidemic effects** in diabetic rats have also been demonstrated (13,14). The Authors of a study (15) on hepatic cells have proposed that the flavonoids contained in the Fig leaf aqueous extract may contribute to the hypolipidemic action, as it has been demonstrated that some flavonoids, such as naringenin, inhibit HMG-CoA reductase and ACAT (Acyl-CoA cholesteryl acyl transferase) activities in high cholesterol-fed rats. The same study showed that all the aqueous extracts obtained from *F. carica* leaves could significantly decrease ($p<0.001$) secretion of cholesterol from the liver cell in both stimulated and basal condition which is resemble to the diabetic animals.

An interesting *in vitro* study (16) showed that extracts obtained from *F. carica* leaves can decrease hepatic triglyceride (TG) content, and secretion of TG and total cholesterol (TC) from the liver of roosters. Livers from 8-week-old roosters ($n=24$) with high abdominal fat pad ratios were extracted, sliced and cultured with increasing concentrations of Fig tree leaf extract (FTE), insulin and both of them. While insulin significantly increased TG secretion, TG content and TC secretion above the basal levels, when FTE was added these effects were drastically reduced to the basal levels in a concentration dependent manner ($P<0.001$). The study also showed that FTE modulates the action of insulin, in terms of both TG storage and secretion, when compared to the control and insulin stimulated TG content and secretion. It's well known that insulin acts on TG storage and secretion via acetyl CoA carboxylase, a key enzyme in the biosynthesis of fatty acids; actually this enzyme has become a new, possible target for novel antiobesity drugs. The study doesn't establish whether the FTE effects on the basal and insulin induced lipid changes are due to decreased *de novo* fatty acid synthesis (via acetyl CoA carboxylase) or increased lipolysis of TG; however, the data suggest that FTE administration may be an alternative method to reduce fat mass in roosters, particularly in the **abdominal cavity**, providing increased meat yield and healthier animals.

6-Dosage and cautions: in the only available clinical trial (12) 13 g daily of Fig leaf have been used as a decoction for 4 weeks with no adverse effects.

Because of its hypoglycemic properties, caution is advised in patients with diabetes or hypoglycemia and in those taking drugs, herbs, or supplements affecting blood sugar; patients on diabetic medication should monitor blood sugar and adjust Fig tree leaf extract dosage accordingly (17).

Fig tree extract must be avoided by people with hypersensitivity to Fig tree and other plants in the Moraceae family (17). Excessive sunlight or ultraviolet light exposure should be avoided while using products that contain Fig leaf (17) as it may cause photosensibilization (2).

No data are available about its use during pregnancy, lactation or in paediatric patients.

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