

CRATAEGUS MONOGYNA JACQ. ,
CRATAEGUS LAEVI GATA
(POI RET) DC.
(HAWTHORN)

by Lamberto Monti



Crataegus monogyna

BOTANY: *C. monogyna* and *C. laevigata* (syn.: *C. oxyacantha* L.) are shrubs or small trees about 2 metres tall that are common throughout the temperate regions of the northern hemisphere; the commonest species in Italy is *C. monogyna*. The branches, which are smooth if young, greyish and with thorns if sterile, have leaves, depending on the species, made up of between 3 and 7 shallow and finely serrated lobes. The white or slightly pinkish flowers are in corymbs; the pistil may have from 1 to 3 carpels, depending on the species. The fruits are coral red drupes which can contain, again depending on the species, one or more ovoid seeds. It is represented by the dried roots and rhizomes of *U. dioica* L. and *U. urens* L.; it appears as a mixture of tapering cylindrical rhizomes, at times ramified and brownish-yellow in colour and irregularly brownish-grey twisted roots.

DRUG: A) Italian Pharmacopoeia 10th Ed.: dried leaves and flowering tops of *C. monogyna* and *C. laevigata* which contain not less than 0.7% of flavonoids, calculated as hyperoxide, with reference to the dried drug. B) European Pharmacopoeia 4th Ed.: dried flowering tops of *C. monogyna*, *C. laevigata* or their hybrids, or, more rarely, other European species of hawthorn (*C. pentagyna*, *C. nigra*, *C. azarolus*, etc.) which contain not less than 1.5% of flavonoids calculated as hyperoxide, with reference to the dried drug[§].

CHEMICAL COMPOSITION OF THE DRUG: The drug mainly contains flavonoids (vitexin, vitexin-2"-*O*-alpha-L-ramnoside, hyperoxide, rutin, vicenin-1, orientin), procyanidins resulting from condensation with various degrees of polymerization of catechin and/or epicatechin, triterpenes (ursolic, oleanolic and crataegolic acids), phenolic acids (caffeic acid, chlorogenic acid), biogenic amines (choline, tyramine), xanthine and mineral salts, especially potassium.

PHARMACOLOGY: In many *in vitro* and *in vivo* studies, the extracts of hawthorn leaves and flowers but also fruits, have been shown to increase the contractibility of the cardiac muscle (positive inotropic effect) and the coronary blood flow, probably due to the effects mainly exercised by the procyanidins. An anti-arrhythmic action and a feeble hypotensive action due to the decreased peripheral vascular resistances have also been observed. The action of extracts of hawthorn is attributed to their capacity to inhibit the activity of the enzymes cAMP-phosphodiesterase and Na⁺,K⁺-ATPase. A sedative effect in the mouse induced by hawthorn extract was observed in an old pharmacological study.

TOXICOLOGY: A hydromethanolic extract of leaves and flowers standardized to 18.75% of procyanidins has not caused toxic effects in the mouse and rat up to 3,000 mg/kg given orally; LD50 given interperitoneally has been calculated at 1,170 mg/kg in the mouse and 750 mg/kg in the rat. Toxic effects have not been observed following oral administration to the rat and dog for 26 consecutive weeks of the same extract at daily doses of 30, 90 and 300 mg/kg. In studies on reproductive toxicity, no teratogenous effects have been observed in the rat and rabbit up to the dose of 1.6 g/kg; no signs of peri- and post-natal signs of toxicity and have been found in the rat or in the first-generation offspring, including effects detrimental to fertility.

CLINICAL STUDIES: Many clinical studies have been conducted with hydroalcoholic extracts of hawthorn flowers and leaves standardized in oligomer procyanidins (18.75%) or in flavonoids (2.2%). Both types of preparation administered orally to patients with NYHA class II * cardiac decompensation have generally produced an increase in the tolerance to stress, observed by the decrease in the so-called double product (systolic pressure x heart rate : 100), and a slight decrease in both systolic and diastolic pressure; in some cases an increase in the fraction of left ventricular ejection has been observed. In a recent preliminary study, a tendency towards the reduction of anxious reactions has been observed.

THERAPEUTIC INDICATIONS: Declining cardiac functionality corresponding to NYHA class II; states of nervous excitement.

SIDE EFFECTS, CONTRAINDICATIONS, INTERACTIONS, SPECIAL PRECAUTIONS: No side effects worthy of note, interactions with other drugs or the need to take any special precautions have been reported. For the treatment of cardiac decompensation, medical supervision is recommended; medical assistance is essential if, after taking the product, pain in the chest, in the upper part of the stomach or in the arms or difficulty in breathing appear. In the absence of complete data on reproductive toxicity, hawthorn is not recommended during pregnancy and whilst breastfeeding.

DOSAGES:** 160-900 mg/die of a hydroalcoholic extract (4-7: 1) standardized in procyanidins or in flavonoids; 20 drops of tincture two-three times a day. For sedation, some medicines are available in Italy which contain valerian and/or other plants with hawthorn.

* According to the classification of the functional capacities drawn up by the New York Heart Association, a patient with heart disease is included in class II when suffering from slight limitations in physical activity, reported by a sense of fatigue, palpitations, dyspnoea or anginoid pain, but which are not present at rest.

** ESCOP monographs.

§ The 4th edition of the European Pharmacopoeia also includes the drug made up of the false dried fruit of *C. monogyna* or *C. laevigata* or their hybrids which do not contain less than 1.0% of procyanidins, calculated as cyanidin chloride, with reference to the dried drug.