Hawthorn leaf and flower

Crataegi folium cum flore

DEFINITION
Whole or cut, dried flower-bearing branches of Crataegus monogyna Jacq. (Lindlm.), C. laevigata (Poiret) D.C. (C. oxyacanthoides Thouill.) or their hybrids or, more rarely, other European Crataegus species including C. pentagyna Waldst. et Kt., C. nigra Waldst. et Kit., C. azarolus L.

Content: minimum 1.5 per cent of flavonoids, expressed as hyperoside (C$_{21}$H$_{20}$O$_{12}$; $M$, 464.4) (dried drug).

IDENTIFICATION
A. The stems are dark brown, woody, 1.2-5 mm in diameter, bearing alternate, petiolate leaves with small, often deciduous stipules and coryms of numerous small white flowers. The leaves are more or less deeply lobed with slightly serrate or almost entire margins; those of C. laevigata are pinnately lobed or pinnatisect with 3, 5 or 7 oblong lobes, those of C. monogyna pinnatisect with 5 or 5 acute lobes; the adaxial surface is dark green or brownish-green, the abaxial surface is lighter greyish-green and shows a prominent, dense, reticulate venation. The leaves of C. laevigata, C. monogyna and C. pentagyna are glabrous or bear only isolated trichomes, those of C. azarolus and C. nigra are densely pubescent. The flowers have a brownish-green tubular calyx composed of 5 free, reflexed sepals, a corolla composed of 5 free, yellowish-white or brownish, rounded or broadly ovate and shortly unguiculate petals and numerous stamens. The ovary is fused to the calyx and consists of 15 carpels, each with a long style and containing a single ovule; in C. monogyna there is 1 carpel, in C. laevigata 2 or 3, in C. azarolus 2 or 3, or sometimes only 1, in C. pentagyna 5 or, rarely, 4.

B. Reduce to a powder (355) (2.9.12). The powder is yellowish-green. Examine under a microscope using chloral hydrate solution R. The powder shows the following diagnostic characters: unicellular covering trichomes, usually with a thick wall and wide lumen, almost straight or slightly curved, pitted at the base; fragments of leaf epidermis with cells which have sinuous or polygonal anticlinal walls and with large annomocytic stomata (2.8.3) surrounded by 4-7 subsidiary cells; parenchymatous cells of the mesophyll containing calcium oxalate clusters, usually measuring 10-20 µm.

TESTS
Foreign matter (2.8.2): maximum 5 per cent of deteriorated false fruit and maximum 2 per cent of other foreign matter. It does not contain fruits of other Crataegus species (C. nigra Waldst. et Kit., C. pentagyna Waldst. et Kit. ex Willd., and C. azarolus L.) which are characterised by the presence of more than 3 hard stones.

Loss on drying (2.2.32): maximum 12.0 per cent, determined on 1.000 g of the powdered drug (355) (2.9.12) by drying in an oven at 105 °C for 2 h.

Total ash (2.4.16): maximum 5.0 per cent.

ASSAY
To 2.50 g of the powdered drug (355) (2.9.12) add 30 ml of ethanol (70 per cent V/V) R. Heat under a reflux condenser for 30 min and filter. Wash the residue with 10.0 ml of ethanol (70 per cent V/V) R. Add to the filtrate 15.0 ml of hydrochloric acid R1 and 10.0 ml of water R. Heat under a reflux condenser for 80 min. Allow to cool, filter and wash the residue with ethanol (70 per cent V/V) R until the filtrate is colourless. Dilute the filtrate to 250.0 ml with ethanol (70 per cent V/V) R. Evaporate 50.0 ml of this solution in a round-bottomed flask to about 3 ml and transfer to a separating funnel. Rinse the round-bottomed flask sequentially with 10 ml and 5 ml of water R and transfer to the separating funnel. Shake the combined solution with 3 quantities, each of 15 ml, of butanol R. Combine the organic layers and dilute to 100.0 ml with butanol R.

Measure the absorbance (2.2.25) of the solution at 545 nm. Calculate the percentage content of procyanidins, expressed as cyanidin chloride, using the following expression:

\[
A = \text{mass of the substance to be examined, in grams.}
\]

\[
A \times \frac{500}{75} = m
\]

i.e. taking the specific absorbance of cyanidin chloride to be 75.

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those associated with the veins containing groups of small prism crystals; fragments of petals showing rounded polygonal epidermal cells, strongly papillose, with thick walls, the cuticle of which clearly shows wavy striations; fragments of anthers showing endothecium with an arched and regularly thickened margin; fragments of stems containing collenchymatous cells, bordered pitted vessels and groups of lignified sclerenchymatous fibres with narrow lumina; numerous spherical to elliptical or triangular pollen grains up to 45 µm in diameter, with 3 germinal pores and a faintly granular exine.

Foreign matter (2.8.2): maximum 8 per cent of lignified branches with a diameter greater than 2.5 mm and maximum 2 per cent of other foreign matter.

Loss on drying (2.2.32): maximum 10.0 per cent, determined on 1.000 g of powdered drug (355) (2.9.12) by drying in an oven at 105 °C for 2 h.

Total ash (2.4.16): maximum 10.0 per cent.

ASSAY

Stock solution. Into a 200 ml flask introduce 0.400 g of the powdered drug (250) (2.9.12) and 40 ml of ethanol (60 per cent V/V) R. Heat in a water-bath at 60 °C for 10 min, shaking frequently. Allow to cool and filter through a plug of absorbent cotton into a 100 ml volumetric flask. Transfer the absorbent cotton with the drug residue back into the 200 ml flask, add 40 ml of ethanol (60 per cent V/V) R and heat again in a water-bath at 60 °C for 10 min, shaking frequently. Allow to cool and filter into the same 100 ml volumetric flask. Rinse the 200 ml flask with a further quantity of ethanol (60 per cent V/V) R, filter and transfer to the same 100 ml volumetric flask. Dilute to 100.0 ml with ethanol (60 per cent V/V) R and filter.

Test solution. Introduce 5.0 ml of the stock solution into a round-bottomed flask and evaporate to dryness under reduced pressure. Take up the residue with 8 ml of a mixture of 10 volumes of methanol R and 100 volumes of glacial acetic acid R and transfer into a 25 ml volumetric flask. Rinse the round-bottomed flask with 3 ml of a mixture of 10 volumes of methanol R and 100 volumes of glacial acetic acid R and transfer into the same 25 ml volumetric flask. Add 10.0 ml of a solution containing 25.0 g/l of boric acid R and 20.0 g/l of oxalic acid R in anhydrous formic acid R and dilute to 25.0 ml with anhydrous acetic acid R.

Compensation liquid. Introduce 5.0 ml of the stock solution into a round-bottomed flask and evaporate to dryness under reduced pressure. Take up the residue with 8 ml of a mixture of 10 volumes of methanol R and 100 volumes of glacial acetic acid R and transfer into the same 25 ml volumetric flask. Add 10.0 ml of anhydrous formic acid R and dilute to 25.0 ml with anhydrous acetic acid R.

Measure the absorbance (2.2.25) of the test solution after 30 min at 410 nm, by comparison with the compensation liquid.

Calculate the percentage content of total flavonoids, expressed as hyperoside, using the following expression:

\[
\frac{A \times 1.235}{m}
\]

i.e. taking the value of the specific absorbance of hyperoside to be 405.

\[
A = \text{absorbance at 410 nm},
\]

\[
m = \text{mass of the drug to be examined, in grams.}
\]

HAWTHORN LEAF AND FLOWER DRY EXTRACT

Crataegi folii cum flore extractum siccum

**DEFINITION**
Dry extract produced from *Hawthorn leaf and flower* (1432).

**Content:**
- for aqueous extracts: minimum 2.5 per cent of flavonoids, expressed as hyperoside (C_{21}H_{20}O_{12}; M_r 464.4) (dried extract);
- for hydroalcoholic extracts: minimum 6.0 per cent of flavonoids, expressed as hyperoside (C_{21}H_{20}O_{12}; M_r 464.4) (dried extract).

**PRODUCTION**
The extract is produced from the drug by a suitable procedure using either water or a hydroalcoholic solvent equivalent in strength to a minimum of 45 per cent V/V ethanol.

**CHARACTERS**
**Appearance:** light brown or greenish-brown powder.