

HAWTHORN

This monograph is intended to serve as a guide to industry for the preparation of Product Licence Applications (PLA) and labels for natural health product market authorization. It is not intended to be a comprehensive review of the medicinal ingredient. It is a referenced document to be used as a labelling standard.

Note: Text in parentheses is additional optional information which can be included on the PLA and product label at the applicant's discretion. The solidus (/) indicates that the terms are synonyms or that the statements are synonymous. Either term or statement may be selected by the applicant.

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Table 1: **Proper and common name(s):**

Proper name(s)	Common name(s)
<i>Crataegus laevigata</i> (Poir.) DC. (Rosaceae) (USDA 2007)	Hawthorn (McGuffin et al. 2000) Two-style hawthorn (Wichtl 2004)
<i>Crataegus monogyna</i> Jacq. (Rosaceae) (USDA 2006)	Hawthorn (USDA 2006; McGuffin et al. 2000) One-style hawthorn (Wichtl 2004; McGuffin et al. 2000)

Source material(s):

- ▶ Berry (ESCOP 2009; Barnes 2007; Belz and Loew 2003; Degenring et al. 2003; Mills and Bone 2000; Grieve 1971 [1931])
- ▶ Leaf and flower (Bradley 2006; WHO 1999; ESCOP 2003)

Route(s) of administration: Oral (ESCOP 2009; Bradley 2006; Mills and Bone 2000)

Dosage form(s):

The acceptable pharmaceutical dosage forms include, but are not limited to, chewables (e.g. gummies, tablets), caplets, capsules, strips, lozenges, powders or liquids where the dose is measured in drops, teaspoons or tablespoons.

This monograph is not intended to include foods or food-like dosage forms such as bars, chewing gums or beverages.

Use(s) or Purpose(s):	Statement(s) to the effect of:
Berry:	(Traditionally) used in Herbal Medicine to help maintain and/or support cardiovascular health in adults (ESCOP 2009; Bradley 2006; Wichtl 2004; Degenring et al. 2003; ESCOP 2003; Mills and Bone 2000; WHO 1999; Grieve 1971 [1931]).
Leaf and Flower:	Used in Herbal Medicine to help maintain and/or support cardiovascular health in adults (Bradley 2006; Wichtl 2004; ESCOP 2003; Mills and Bone 2000; WHO 1999).

Dose(s):

Berry:	0.6-3.5 g per day (ESCOP 2009; Bradley 2006; Degenring et al. 2003; Grieve 1971 [1931])
Leaf and Flower:	<ul style="list-style-type: none"> ▶ Preparations equivalent to 1.5-5 g dried leaf and flower, per day (Bradley 2006; ESCOP 2003) ▶ Preparations containing a 4-7:1 dried extract, equivalent to 160-900 mg dried leaf and flower, per day, standardized to 18.75% oligomeric procyanidins, as epi-catechin, and/or 2.2% flavonoids, as hyperoside (Blumenthal et al. 2000; WHO 1999)

See Appendix 1 for examples of appropriate dosage preparations, frequencies of use and directions for use, according to cited references. The purpose of Appendix 1 is to provide guidance to industry.

Duration(s) of use:	Statement(s) to the effect of:
	Use for a minimum of two months to see beneficial effects (Mills and Bone 2000)

Risk information:	Statement(s) to the effect of:
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Caution(s) and warning(s):

- ▶ Consult a health care practitioner if symptoms persist or worsen.
- ▶ Consult a health care practitioner prior to use if you are taking cardiac glycosides such as digitalis/digoxin, or blood pressure medication. (Brinker 2010; Bradley 2006)

Contraindication(s):	No statement required.
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Known adverse reaction(s): No statement required.

Non-medicinal ingredients:

Must be chosen from the current NHPD *Natural Health Products Ingredients Database* and must meet the limitations outlined in the database.

Specifications:

- ▶ The finished product must comply with the minimum specifications outlined in the current NHPD *Compendium of Monographs*.
- ▶ The medicinal ingredient may comply with the specifications outlined in the pharmacopoeial monographs listed in Table 1 below (BP 2008; Ph. Eur. 2007; USP 32).

Table 2: Hawthorn monographs published in British, European and U.S. pharmacopoeiae

Pharmacopoeia	Monograph
British Pharmacopoeia (BP) European Pharmacopoeia (Ph. Eur.)	Hawthorn Berries Hawthorn Leaf and Flower Hawthorn Leaf and Flower Dry Extract Hawthorn Leaf and Flower Liquid Extract, Quantified
US Pharmacopoeia (USP)	Hawthorn Leaf with Flower Powdered Hawthorn Leaf with Flower

References cited:

Belz GG, Loew D. 2003. Dose-response related efficacy in orthostatic hypotension of a fixed combination of D-camphor and an extract from fresh *Crataegus* berries and the contribution of the single components. *Phytomedicine* 10(Supplement 4):61-67.

Blumenthal M, Goldberg A, Brinkmann J, editors. 2000. *Herbal Medicine: Expanded Commission E Monographs*. Boston (MA): Integrative Medicine Communications.

Bradley PR, editor. 2006. *British Herbal Compendium: A Handbook of Scientific Information on Widely Used Plant Drugs, Volume 2*. Bournemouth (GB): British Herbal Medicine Association.

Brinker F. 2010. *Online Updates and Additions to Herb Contraindications and Drug Interactions*, 3rd edition. Sandy (OR): Eclectic Medical Publications. [Updated 2010 February 15; Accessed 2010 March 04]. Available from: <http://www.eclecticherb.com/emp/updatesHCDI.html>

BP 2008: British Pharmacopoeia Commission. *British Pharmacopoeia 2009, Volume III*. London (GB): The Stationary Office on behalf of the Medicines and Healthcare products Regulatory Agency (MHRA).

Degenring FH, Suter A, Weber M, Saller R. 2003. A randomised double blind placebo controlled clinical trial of a standardised extract of fresh *Crataegus* berries (Crataegisan) in the treatment of patients with congestive heart failure NYHA II. *Phytomedicine* 10(5):363-369.

ESCOP 2009: European Scientific Cooperative on Phytotherapy Scientific Committee. ESCOP Monographs: The Scientific Foundation for Herbal Medicinal Products, 2nd edition, Supplement 2009. Exeter (GB): European Scientific Cooperative on Phytotherapy in collaboration with Thieme.

ESCOP 2003: European Scientific Cooperative on Phytotherapy Scientific Committee. ESCOP Monographs: The Scientific Foundation for Herbal Medicinal Products, 2nd edition. Exeter (GB): European Scientific Cooperative on Phytotherapy in collaboration with Thieme.

Grieve M. 1971. *A Modern Herbal*, Volume 1. New York (NY): Dover Publications; [Reprint of 1931 Harcourt, Brace & Company publication].

McGuffin M, Kartesz JT, Leung AY, Tucker AO, editors. 2000. *Herbs of Commerce*, 2nd edition. Silver Spring (MD): American Herbal Products Association.

Mills S, Bone K. 2000. *Principles and Practice of Phytotherapy*. Toronto (ON): Churchill Livingstone.

Ph. Eur. 2007: European Pharmacopoeia Commission. *European Pharmacopoeia* 2008, 6th edition, Volume 2. Strasbourg (FR): Directorate for the Quality of Medicines and HealthCare of the Council of Europe (EDQM).

USDA 2007: United States Department of Agriculture, Agricultural Research Service, National Genetic Resources Program. Germplasm Resources Information Network (GRIN) [online database]. *Crataegus laevigata* (Poir.) DC. Beltsville (MD): National Germplasm Resources Laboratory. [Accessed 2010 March 04]. Available from: http://www.ars-grin.gov/cgi-bin/npgs/html/tax_search.pl

USDA 2006: United States Department of Agriculture, Agricultural Research Service, National Genetic Resources Program. Germplasm Resources Information Network (GRIN) [online database]. *Crataegus monogyna* Jacq. Beltsville (MD): National Germplasm Resources Laboratory. [Accessed 2010 March 04]. Available from: http://www.ars-grin.gov/cgi-bin/npgs/html/tax_search.pl

WHO 2002: World Health Organization. *WHO Monographs on Selected Medicinal Plants*, Volume 2. Geneva (CH): World Health Organization.

Wichtl M, editor. 2004. *Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis*, 3rd edition. Stuttgart (DE): Medpharm GmbH Scientific Publishers.

USP 2009: *The United States Pharmacopeia and the National Formulary* (USP 32/NF 27). Rockville (MD): United States Pharmacopeial Convention, Inc.

References reviewed:

Barnes J, Anderson LA, Philipson JD. 2007. Herbal Medicines, 3rd edition. London (GB): The Pharmaceutical Press.

Brinker F. 2001. Herb Contraindications and Drug Interactions, 3rd edition. Sandy (OR): Eclectic Medical Publications.

Ellingwood F. 1998. American Materia Medica, Therapeutics and Pharmacognosy. Sandy (OR): Eclectic Medical Publications; [Reprint of 1919 original].

Felter HW, Lloyd JU. 1983. King's American Dispensatory, Volume 1, 18th edition. Sandy (OR): Eclectic Medical Publications; [Reprint of 1898 original].

HC 2010. Health Canada. Draft Guidance Document: Schedule A and Section 3 to the Food and Drugs Act. July 23, 2008 [online]. Ottawa (ON): Bureau of Policy, Science and International Programs, Therapeutic Products Directorate; Health Products and Food Branch. [Accessed: 2010 March 04]. Available from: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/draft_shca_ebauche-eng.pdf

Hoffmann D. 2003. Medical Herbalism: The Science and Practice of Herbal Medicine. Rochester (VT): Healing Arts Press.

JC 2008: Department of Justice Canada. Natural Health Products Regulations [online]. Ottawa (ON): Department of Justice Canada. [Accessed 2008 March 28]. Available from: <http://laws.justice.gc.ca/eng/SOR-2003-196/index.html>

McGuffin M, Hobbs C, Upton R, Goldberg A, editors. 1997. American Herbal Products Association's Botanical Safety Handbook. Boca Raton (FL): CRC Press.

Appendix 1: Examples of dosage preparations, frequencies of use and directions for use

BERRY

Powdered:

- ▶ 0.3-1 g, three times per day (ESCOP 2009)

Infusion or decoction:

- ▶ 1.5-3.5 g of dried berry per day (Bradley 2006)

Fluidextract:

- ▶ 0.5-1 g dried equivalent, three times per day (1:1, 25% alcohol, 0.5-1 ml) (ESCOP 2009; Bradley 2006).
- ▶ 0.62-0.92 mg dried equivalent, per day (1:1), 0.62-0.92 ml) (Grieve 1971).

Tincture:

- ▶ 0.2-0.4 g dried equivalent, three times per day (1:5, 45% alcohol, 1-2 ml) (ESCOP 2009)
- ▶ 1.5-3.5 g dried equivalent, per day (1:5, 7.5-17.5 ml) (Bradley 2006)
- ▶ 0.6-1.4 g dried equivalent, per day (1:2, 3-7 ml) (Bradley 2006)

Hydroalcoholic extract:

- ▶ 0.6-2 g dried berry, per day (1:1.3-3.2, 2-2.5 ml) (ESCOP 2009)
- ▶ Dried extract equivalent to 0.69 g fresh berry, per day, (1:3.2, 45% ethanol, 2.5 ml) standardized to contain at least 6.4 mg (0.93%) of active oligomeric procyanidins (OPC) (Degenring et al. 2003)

LEAF AND FLOWER

Infusion or decoction:

- ▶ 1.5-3.5 g dried leaf and flower, daily (Bradley 2006)
- ▶ 1.0-1.5 g comminuted crude herb 3-4 times daily (ESCOP 2003; WHO 1999)
- ▶ 1-1.5 g finely cut dried leaf and flower, 3-4 times daily (Wichtl 2004)
Directions for use: Pour 1 cup (250 ml) of boiling water on dried leaf and flower and steep for 15 minutes (Wichtl 2004).

Standardized Hydroalcoholic extract:

Dried extract equivalent to 160-900 mg dried leaf and flower, per day,

(4-7:1, 45% ethanol) standardized to contain 18.75% oligomeric procyanidins (calculated as epi-catechin) or 2.2% flavonoids (calculated as hyperoside) (Blumenthal et al. 2000; WHO 1999)

Tablets: 1 g leaves and flowers, 2-3 times a day, standardized to 15-20 mg oligomeric procyanidins and 6-7 mg flavonoids (Mills and Bone 2000).

LEAF, FLOWER OR BERRY

Infusion or decoction: 1.5-3.5 g dried leaf, flower or berry, per day (Mills and Bone 2000).