



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

20 November 2019  
EMA/HMPC/509104/2019  
Committee on Herbal Medicinal Products (HMPC)

## List of references supporting the assessment of *Achillea millefolium* L., herba

Draft – Revision 1

**The European Medicines Agency acknowledges that copies of the underlying works used to produce this monograph were provided for research only with exclusion of any commercial purpose.**

Anonymous. Final Report on the Safety Assessment of Yarrow (*Achillea Millefolium*) Extract. *Int J Toxicol* 2001, 20 (Supplement 2): 79–84

Augustin B, Javorka S, Giovannini R, Rom P. Magyar gyógynövények [Hungarian Herbal Drugs] I. Általános és leíró rész (I. General and describing part). Földművelésügyi Minisztérium Budapest, 1948 [Hungarian]

Baggio CH, Otofujii Gde M, Freitas CS, Mayer B, Marques MC, Mesia-Vela S. Modulation of antioxidant systems by subchronic exposure to the aqueous extract of leaves from *Achillea millefolium* L. in rats. *Nat Prod Res* 2015, 30: 613-615

Barnes J, Anderson LA, Philipson JD. Herbal Medicines Third edition. Pharmaceutical Press London, Chicago 2007

Benedek B, Geisz N, Jäger W, Thalhammer T, Kopp B. Choleric effects of yarrow (*Achillea millefolium* s.L.) in the isolated perfused rat liver. *Phytomedicine* 2006, 13(9-10): 702-706

Benedek B, Kopp B, Melzig MF. *Achillea millefolium* L. s.l. - Is the anti-inflammatory activity mediated by protease inhibition? *J Ethnopharmacol* 2007, 113(2): 312-317 Bisset NG, ed. Herbal Drugs and Phytopharmaceuticals: A Handbook for Practice on a Scientific Basis (translated from Wichtl, ed. Teedrogen 2<sup>nd</sup> ed.). Medpharm Scientific Publishers, Stuttgart, 1994, 342-344

Blumenthal M, Busse WR, Goldberg A, Gruenwald J, Hall T, Riggins CW, *et al.* editors. The complete German Commission E monographs. American Botanical Council, Austin Texas 1998, 233-234

Blumenthal M, Goldberg A, Brinckmann J. editors. Herbal medicine, Expanded Commission E monographs. The American Botanical Council, Austin Texas, 2000, 419-423

Boswell-Ruys CL, Ritchie HE, Brown-Woodman PD. Preliminary screening study of reproductive outcomes after exposure to yarrow in the pregnant rat. *Birth Defects Res B Dev* 2003, 68(5): 416-420

---

**Official address** Domenico Scarlattilaan 6 • 1083 HS Amsterdam • The Netherlands

**Address for visits and deliveries** Refer to [www.ema.europa.eu/how-to-find-us](http://www.ema.europa.eu/how-to-find-us)

**Send us a question** Go to [www.ema.europa.eu/contact](http://www.ema.europa.eu/contact) **Telephone** +31 (0)88 781 6000

An agency of the European Union



© European Medicines Agency, 2020. Reproduction is authorised provided the source is acknowledged.

Classified as public by the European Medicines Agency

- Bradley PR editor. British Herbal Compendium. Vol.1. British Herbal Medicine Association, Bournemouth 1992, 227-229
- British Herbal Pharmacopoeia 1974: Section One, Two and Three. Millefolium - *Achillea millefolium*. British Herbal Medicine Association, London 1974
- British Herbal Pharmacopoeia 4<sup>th</sup> ed. Yarrow, *Millefolii herba*. British Herbal Medicine Association, Exeter 1996, 190-191
- Budavari S. (ed.) The Merck Index: an Encyclopedia of Chemicals, Drugs, and Biologicals, 12<sup>th</sup> ed. Whitehouse Station, N.J.: Merck & Co, Inc. 1996 (cited in Blumenthal M et al 2000)
- Candan F, Unlu M, Tepe B, Daferera D, Polissiou M, Sökmen A, Akpulat HA. Antioxidant and antimicrobial activity of the essential oil and methanol extracts of *Achillea millefolium* subsp. *millefolium* Afan. (Asteraceae). *J Ethnopharmacol* 2003, 87(2-3):215-220
- Cavalcanti AM, Baggio CH, Freitas CS, Rieck L, de Sousa RS, Da Silva-Santos JE, Mesia-Vela S, Marques MCA. Safety and antiulcer efficacy studies of *Achillea millefolium* L. after chronic treatment in Wistar rats. *J Ethnopharmacol* 2006, 107:277-284
- Compes E, Bartolome B, Fernandez-Nieto M, Sastre J, Cuesta J. Occupational asthma from dried flowers of *Carthamus tinctorius* (safflower) and *Achillea millefolium* (yarrow). *Allergy* 2006, 61:1239-1240
- Csupor-Löffler B, Hajdú Zs, Zupkó I, Réthy B, Falkay G, Forgo P, Hohmann J. Antiproliferative effect of flavonoids and sesquiterpenoids from *Achillea millefolium* s.l. on cultured human tumour cell lines. *Phytother Res* 2009, 23(5):672-676 (abstract only)
- Dalsenter PR, Cavalcanti AM, Andrade AJ, Araújo SL, Marques MC. Reproductive evaluation of aqueous crude extract of *Achillea millefolium* L. (Asteraceae) in Wistar rats. *Reprod Toxicol* 2004, 18(6):819-823
- de Sant'anna JR, Franco CC, Milyamoto CT, Cunico MM, Miguel OG, Cocco LC, Yamamoto CL, Junoir CC, de Castro-Prado MA. Genotoxicity of *Achillea millefolium* essential oil in diploid cells of *Aspergillus nidulans*. *Phytother Res* 2009, Feb; 23(2):231-235 (abstract only)
- de Souza P, Gasparotto A Jr, Crestani S, Stefanello MÉ, Marques MC, da Silva-Santos JE, Kassuya CA. Hypotensive mechanism of the extracts and artemetin isolated from *Achillea millefolium* L. (Asteraceae) in rats. *Phytomedicine* 2011, 18:819-825
- Deutsches Arzneibuch, 10<sup>th</sup> ed. Schafgarbenkraut – Millefolii herba. Deutscher Apotheker Verlag, Stuttgart, 1997
- Dornberger K, Lich H. Screening nach antimikrobiell sowie potentiell cancerostatisch wirksamen Pflanzeninhaltsstoffen. *Pharmazie* 1982, 37:215-221 (cited in ESCOP Supplement 2009)
- ESCOP Monographs 2<sup>nd</sup> edition Supplement 2009. Millefolii herba – Yarrow. European Scientific Cooperative on Phytotherapy, editor. Thieme, Stuttgart 2009, 175-183
- European Pharmacopoeia 7<sup>th</sup> ed. Yarrow – Millefolii herba. Council of Europe, 07/2014:1382
- Fintelmann V, Weiss RF. Lehrbuch der Phytotherapie 10<sup>th</sup> ed. Dysmenorrhö. Hippokrates Verlag, Stuttgart 2002, 355-356
- Gadgoli C, Mishra SH. Preliminary screening of *Achillea millefolium*, *Cichorium intybus* and *Capparis spinosa* for antihepatotoxic activity. *Fitoterapia* 1995, 66:319-323 (cited in ESCOP 2009)

- German Commission E Monograph. *Achillea millefolium* (Schafgarbe). Bundesanzeiger Nr.22 a vom 01.02.1990 [German]
- Graf U, Moraga AA, Castro R, Díaz Carrillo E. Genotoxicity testing of different types of beverages in the *Drosophila* wing Somatic Mutation and Recombination Test. *Food Chem Toxicol* 1994, 32(5):423-430
- Guin JD. Compositae dermatitis in Childhood, *Arch Dermatol* 1987, 123(4):500-502 (abstract only)
- Haidara K, Zamir L, Shi Q-W, Batist G. The flavonoid Casticin has multiple mechanism of tumor cytotoxicity action. *Cancer Letters* 2006, 242: 180-190
- Hajhashemi M, Ghanbari Z, Movahedi M, Rafieian M, Keivani A, Haghollahi F. The effect of *Achillea millefolium* and *Hypericum perforatum* ointments on episiotomy wound healing in primiparous women. *J Matern Fetal Neonatal Med* 2018, 31:63-69
- Hänsel R, Keller K, Rimpler H, Schneider G, editors. Hagers Handbuch der Pharmazeutischen Praxis. Drogen: A-D. 5<sup>th</sup> ed. Springer-Verlag, Berlin Heidelberg 1992, 48-53
- Hasanzadeh A. K. Hasanzadeh S, Shalizar A. J: Ameliorative effects of *Achillea millefolium* inflorescences alcoholic extract on nicotine-induced reproductive toxicity in male rat: Apoptotic and biochemical evidences. *Veterinary Research Forum*. 2017; 8 (2) 97-104
- Hausen BM, Breuer J, Weglewski J, Rücker G. alpha-Peroxyachifolid and other new sensitizing sesquiterpene lactones from yarrow (*Achillea millefolium* L., Compositae). *Contact Dermatitis* 1991, 24(4):274-280
- Hausen BM. A 6-year experience with compositae mix. *Am J Contact Dermat* 1996, 7(2):94-99 (abstract only)
- Hoerhammer L. Flavone concentration of medicinal plants with regard to their spasmolytic action. *Congr Sci Farm Conf Commun 21<sup>st</sup> Pisa* 1961; 578-588. (cited in Barnes J, Anderson LA, Philipson DJ. Herbal Medicines Third edition. Pharmaceutical Press London, Chicago, 2007)
- Innocenti G, Vegeto E, Dall`Acqua S, Ciana P, Giorgetti M, Agradi E, Sozzi A, Fico G, Tome F. *In vitro* estrogenic activity of *Achillea millefolium* L. *Phytomedicine* 2007, 14:147-152
- Karnick CR. Pharmacopoeial Standards of Herbal Plants Vol. 2. Delhi: Sri Satguru Publications. 1994, 150 (cited in Blumenthal M et 2000)
- Kern W. Hagers Handbuch der Pharmazeutischen Praxis, Substancen and Drogen A-AL Vol 2. 4<sup>th</sup> ed. Springer-Verlag, Berlin, Heidelberg, New York 1969 [German]
- Khan AU, Gilani AH. Blood pressure lowering, cardiovascular inhibitory and bronchodilatory actions of *Achillea millefolium*. *Phytother Res* 2011, 25:577-83
- Lemmens-Gruber R, Marchart E, Rawnduzi P, Engel N, Benedek B and Kopp B. Investigation of the spasmolytic activity of the flavonoid fraction of *Achillea millefolium* s.l. on isolated guinea-pig ilea. *Arzneimittel-Forsch* 2006, 56:582-588
- Lin LT, Liu LT, Chiang LC, Lin CC. *In vitro* anti-hepatoma activity of fifteen natural medicines from Canada. *Phytother Research* 2002, 16(5):440-444 (abstract only)
- Madaus G. Lehrbuch der biologischen Heilmittel. Georg Thieme Verlag, Leipzig, 1938 [German]
- Mahady GB, Pendland SL, Stoia A, Hamill FA, Fabricant D, Dietz BM, Chadwick LR. *In vitro* susceptibility of *Helicobacter pylori* to botanical extracts used traditionally for the treatment of gastrointestinal disorders. *Phytother Res* 2005, 19(11):988-91

Mascolo N, Autore G, Capasso F, Menghini A, Fasulo MP. Biological screening of Italian medicinal plants for anti-inflammatory activity. *Phytother Res* 1987, 1:28–31 (cited in ESCOP 2009)

Mutagenicity study of dry extract from yarrow (70% native) in *Salmonella typhimurium* reverse mutation assay (*in vitro*) - according to Regulation (EC) No. 440/2008 method B.13/14 and OECD Guideline 471 -, LPT Report No. 32134, 2015. Unpublished study provided by Finzelberg GmbH & Co. KG.

Newal AC, Anderson LA, Philipson JD. Herbal Medicines A Guide for Health-care Professionals. The Pharmaceutical Press, London 1996, 271-273

Nilfroushzadeh MA, Shirani-Bidabadi L, Zolfaghari-Baghbaderani A, Saberi S, Siadat AH, Mahmoudi M. Comparison of *Thymus vulgaris* (Thyme), *Achillea millefolium* (Yarrow) and propolis hydroalcoholic extracts versus systemic glucantime in the treatment of cutaneous leishmaniasis in balb/c mice. *J Vector Borne Dis* 2008, 45(4):301-306

Noureddini M, Rasta V. Analgesic Effect of Aqueous Extract of *Achillea Millefolium* L. on Rat's Formalin Test. *Pharmacologyonline* 2008, 3:659-664

O'Donnell SA. 1999. Yarrow: the new cold stopper. *Prevention* 51:44.

Orav A, Arak E, Raal A. Phytochemical analysis of the essential oil of *Achillea millefolium* L. from various European Countries. *Nat Prod Res* 2006, 20(12):1082-1088

Parejo I, Viladomat F, Bastida J, Rosas-Romero A, Flerlage N, Burillo J, Codina C. Comparison between the Radical Scavenging Activity and Antioxidant Activity of Six Distilled and Nondistilled Mediterranean Herbs and Aromatic Plants. *J Agric Food Chem* 2002, 50(23):6882–6890 (abstract only)

Pharmacopoea Hungarica Editio VI. Tomus III. Medicina könyvkiadó, Budapest 1967 [Hungarian]

English version: Hungarian Pharmacopoeia VI<sup>th</sup> ed. Volume III. Akademia Kiadó, Budapest 1970

Polish Herbal Compendium 1978

Rácz G, Rácz-Kotilla E, Laza A. Gyógynövényismeret [Pharmacognosy]. Ceres Könyvkiadó 1984, 95-96 [Hungarian]

Rahchamani R, Mokhberdezfoli MR, Hadjiakhoondi A, Raoofi A, Rezazadeh SH, Banihasan E, Sharifi H, Nazem Bokae Z. Para clinical studies of ethanol extract of *Achillea millefolium* L. on electrocardiogram, cardiac enzymes and serum electrolytes in sheep. *Journal of Medicinal Plants* 2008, 7(26): 63-69+96 (abstract only)

Roncada T, Vicentini VE, Mantovani MS. Possible modulating actions of plant extracts on the chromosome breaking activity of MMC and Ara-C in human lymphocytes *in vitro*. *Toxicol In Vitro* 2004, 18(5):617-622

Sellerberg U, GlasL H. Pharmacognostical examination concerning the hemostyptic effect of *Achillea millefolium* aggregate. *Sci Phar* 2000, 68(2):201-206 (cited in Escop Monograph 2009)

Stojanović G, Radulović N, Hashimoto T, Palić R. *In vitro* antimicrobial activity of extracts of four *Achillea* species: the composition of *Achillea clavennae* L. (Asteraceae) extract. *J Ethnopharmacol* 2005, 101(1-3):185-190

Tadić V, Arsić I, Zvezdanović J, Zugić A, Cvetković D, Pavkov S. The estimation of the traditionally used yarrow (*Achillea millefolium* L. Asteraceae) oil extracts with anti-inflammatory potential in topical application. *J Ethnopharmacol* 2017, 199:138-148

Takzaree N, Mortazavi H, Safaie S, Hosseini SJ. Assessment the effect of *Achillea millefolium* L. extract on spermatogenesis and its reversibility. *Toxicol Lett* 2008, 180 (Sup1) S203-S204

Todd RG editor. Extra Pharmacopoeia Martindale Twenty-fifth edition. The Pharmaceutical Press London 1967

Trouillas P, Calliste C-A, Allais D-P, Simon A, Marfak A, Delage C, Duroux JL. Antioxidant, anti-inflammatory and antiproliferative properties of sixteen water plant extracts used in the Limousin countryside as herbal teas. *Food Chem* 2003, 80(3):399-407

Tunón H, Olavsdotter C, Bohlin L. Evaluation of anti-inflammatory activity of some Swedish medicinal plants. Inhibition of prostaglandin biosynthesis and PAF-induced exocytosis. *J Ethnopharmacol* 1995, 48(2):61-76

WHO monographs on selected medicinal plants. Vol. 4. Herba millefolii. World Health Organisation. Geneva 2009, 179-191

Wren RC. Potter's New Cyclopaedia of Botanical Drugs and Preparations. Completely revised by Williamson EM, Evans FJ. C. W. Daniel Company Ltd, Saffron Walden, Essex 1988, 290

Yaesh S, Jamal Q, Khan AU, Gilani AH. Studies on hepatoprotective, antispasmodic and calcium antagonist activities of the aqueous-methanol extract of *Achillea millefolium*. *Phytother Res* 2006, 20(7):546-551

Zeylstra H. Just Yarrow? *Brit J Phytother* 1997, 4(4):184-189 (cited in Blumenthal M *et al.* 2000)