



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 September 2019
EMA/HMPC/113699/2019
Committee on Herbal Medicinal Products (HMPC)

List of references supporting the assessment of European Union herbal monograph on *Rheum palmatum* L. and *Rheum officinale* Baillon, radix

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.

Bae EA, Han MJ, Kim NJ, Kim DH. Anti-Helicobacter pylori activity of herbal medicines. *Biol Pharm Bull* 1998, 21(9): 990-992

Blaschek W, Ebel S, Hackenthal E, Holzgrabe U, Keller K, Reichling J. editors. HagerROM 2004: Hagers Handbuch der Drogen und Arzneistoffe. Version 4.0. Springer-Verlag, Berlin 2005

Blaszczyk T, Krzyzanowska J, Lamer-Zarawska E. Screening for antimycotic properties of 56 traditional Chinese drugs. *Phytother Research* 2000, 14:210-212

Bright E, Takyi BE. Excretion of drugs in human milk. *J Hosp Pharm* 1970, 28: 317-326

Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM). Bekanntmachung über die Zulassung und Registrierung von Arzneimitteln – Abwehr von Arzneimittelrisiken, Stufe II – Humanarzneimitteln zur innerlichen Anwendung, ausgenommen nach HAB 1 hergestellte homöopathische Arzneimittel, welche Drogen, Drogenzubereitungen oder isolierte Inhaltsstoffe der Anthranoid-(Hydroxyanthracenderivat-) haltigen Pflanzengattungen Andira, Cassia, Rhamnus, Rheum oder Aloe enthalten (German pharmacovigilance actions for anthranoid-containing laxatives) vom 21. Juni 1996, Bundesanzeiger vom 05.07.1996 Nr. 123, Seite 7581

Chirikdjian JJ, Kopp B, Beran H. Über die laxative Wirkung eines neuen Anthrachinonglykosides aus Rhadix Rhei. [The Laxative Action of a New Anthraquinone Glycosides from Rhubarb Roots.] *Planta Med* 1983, 48: 34-37

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

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

An agency of the European Union



Committee for Veterinary Medicinal Products (CVMP). Rhei Radix: Summary Report; EMEA/MRL/648/99-Final, November 1999

Cyong JC, Matsumoto T, Arakawa K, Kiyohara H, Yamada H, Otsuka Y. Anti-Bacteroides fragilis substance from rhubarb. *J Ethnopharmacol* 1987, 19(3): 279-283

De Witte P. Metabolism and pharmacokinetics of anthranoids. *Pharmacology* 1993, 47 (Suppl. 1): 86-97

Engelshowe R. Rhabarber eine alte Droge – noch immer aktuell. *Pharm unser Zeit* 1985, 14: 40–49

ESCOP Monographs 2nd ed. Rhei Radix - Rhubarb. European Scientific Cooperative on Phytotherapy, editor. Thieme Verlag, Stuttgart 2003

European Pharmacopoeia 9th ed. Rhubarb root - Rhei radix. Council of Europe. 1/2008: 0291

Faber P, Strenge-Hesse A. Relevance of rhei excretion into breast milk. *Pharmacology* 1988, 36 (Suppl. 1): 212-220

Fok TF. Neonatal jaundice – traditional Chinese medicine approach. *J Perinatol* 2001, 21 (Suppl. 1): S98-S100

Frerichs G, Arends G, Zörnig H, editors. Hagers Handbuch der Pharmazeutischen Praxis. Vol. 2. Springer-Verlag, Berlin 1927, 563-575

Gordon M, Naidoo K, Akobeng AK, Thomas AG. Cochrane Review: Osmotic and stimulant laxatives for the management of childhood constipation (Review). *E-based Child Health* 2013, 8(1): 57-109

Hänsel R, Keller K, Rimpler H, Schneider G, editors. Hagers Handbuch der Pharmazeutischen Praxis. Drogen P–Z. Vol 6. 5th ed. Springer-Verlag, Berlin 1994, 411-439

Hänsel R, Sticher O, Steinegger E. Pharmakognosie-Phytopharmazie, 6th ed. Springer-Verlag, Berlin-Heidelberg, 1999: 921-923

Harima S, Matsuda H, Kubo M. Study of various rhubarbs regarding the cathartic effect and endotoxin-induced disseminated intravascular coagulation. *Biol Pharm Bull* 1994, 17(11): 1522-1525

Hsiang CY, Hsieh CL, Wu SL, Lai IL, Ho TY. Inhibitory effect of anti-pyretic and anti-inflammatory herbs on Herpes simplex virus replication. *Amer J Chin Med* 2001, 29(3-4): 459-467

Kazuhiro S, Masami M, Sumito O, Satoshi I, Kazuhiro G, Atushi I *et al.* Phytoestrogen activity of emodin, an anthraquinone derivative isolated from rhizomes of *Rheum palmatum*. *Research Commun Pharm Toxicol* 2000, 5(3-4): 179-189

Kommission E. Rhei radix (Rhabarber), Bundesanzeiger Nr. 133 vom 21.07.1993

Kosuge T, Ishida H. Studies on active substances in the herbs used for Oketsu ("Stagnant Blood") in Chinese Medicine. IV. On the anticoagulative principle in Rhei Rhizoma. *Chem Pharm Bull* 1985, 33(4): 1503-1506

Kubo I, Murai Y. Efficient isolation of glycosidase inhibitory stilbene glycosides from *Rheum palmatum*. *J Nat Prod* 1991, 54(4): 1115-1118

Kubo I, Murai Y, Soediro I, Soetarno S, Sastrodihardjo S. Cytotoxic anthraquinones from *Rheum pulmatum*. *Phytochem* 1992, 31(3): 1063-1065

Li LS. Rhubarb in preventing progression of chronic renal disease. *Nephrology* 1996, 2(Suppl. 1): 146-150

Li X, Wang H. Chinese herbal medicine in the treatment of chronic kidney disease. *Adv Chron Kidn Dis* 2005, 12(3): 276-281

Madaus G. Lehrbuch der biologischen Heilmittel. Vol. 1. Thieme Verlag, Leipzig 1938, 2300-2306 (Reprint Georg Olms Verlag, Hildesheim New York 1976)

Mitsuma T, Yokozawa T, Nonakav G-I, Itoh T, Shimada Y, Terasawa K. Differences in cathartic action among different types of the origin drug rhubarb. *J Trad Med* 1998, 15(1): 45-51

Miyazawa M, Minamino Y, Kameoka H. Volatile components of the rhizomes of *Rheum palmatum* L. *Flav Fragr J* 1996, 11: 57-60

NTP Technical Report on the Toxicology and Carcinogenesis Studies of Emodin in F344/N Rats and B6C3F₁ Mice. National Toxicology Program, June 2001, NTP TR 493, NIH Publication No. 01-3952; 1-278

(<https://ntp.niehs.nih.gov/results/pubs/longterm/reports/longterm/tr400499/abstracts/tr493/index.html>)

Oshio H, Imai S, Shoji Fujioka S; Sugawara T, Miyamoto M, Tsukui M. Investigations of Rhubarbs. III. New purgative constituents, sennosides E and F. *ChemPharm Bull* 1974, 22(4): 823-831

Paneitz A, Westendorf J. Anthranoid contents of rhubarb (*Rheum undulatum* L.) and other Rheum species and their toxicological relevance. *Eur Food Res Technol* 1999, 210: 97-101

Peng A, Gu Y, Lin SY. Herbal treatment for renal diseases. *Annals Acad Med Sing* 2005, 34: 44-51

Primschitz E. Screening of Chinese herbs for cholinesterase inhibition and antioxidant activity. Diplomarbeit, Karl-Franzens-University Graz 2005

Sydiskis RJ, Owen DG, Lohr JL, Rosler KH, Blomster RN Inactivation of enveloped viruses by anthraquinones extracted from plants. *Antimicrob Agents Chemother* 1991, 35(12): 2463-2466

Takara K, Horibe S, Obata Y, Yoshikawa E, Ohnishi N, Yokoyama T. Effects of 19 herbal extracts on the sensitivity to paclitaxel or 5-fluorouracil in HeLa Cells. *Biol Pharm Bull* 2005, 28(1): 138-142

Todd RG, editor. Martindale: The Extra Pharmacopoeia. 25th ed. The Pharmaceutical Press, London 1967

Van Os FHL. Anthraquinones derivatives in vegetable laxatives. *Pharmacol* 1976, 14 (Suppl. 1): 7-17

Vyth A and Kamp PE. Detection of anthraquinone laxatives in the urine. *Pharm Weekbl Sci Ed* 1979, 1: 456-459

Wade A, editor. Martindale: The Extra Pharmacopoeia. 27th ed. The Pharmaceutical Press, London 1977: 1341 -1342

Weiss RF. Lehrbuch der Phytotherapie. 3rd ed. Hippokrates-Verlag, Stuttgart 1974: 113-118

Weiss RF. Lehrbuch der Phytotherapie. 7th ed. Hippokrates-Verlag, Stuttgart 1990: 126-128

WHO monographs on selected medicinal plants. Vol. 1. Rhizoma Rhei. World Health Organisation. Geneva 1999: 231-240

Willems M, van Buuren HR, de Krijgera R. Anthranoid self-medication causing rapid development of melanosis coli. *Netherl J Med* 2003, 61(1): 22-24

Yagi T, Yamauchi K, Kuwano S. The synergistic purgative action of aloe-emodin anthrone and rhein anthrone on mice: synergism in large intestinal propulsion and secretion. *J Pharm Pharmacol* 1997, 49: 22-25

Yagi T, Yamauchi K. Synergistic effects of anthraquinones on the purgative activity of rhein anthrone in mice. *J Pharm Pharmacol* 1999, 51: 93-95

Yan M, Zhang LY, Sun LX, Jiang ZZ, Xiao XH. Nephrotoxicity study of total rhubarb anthraquinones on Sprague Dawley rats using DNA microarrays. *J Ethnopharmacol* 2006, 107: 308-311

Yokozawa T, Suzuki N, Zheng PD, Oura H, Nishioka I. Effect of orally administered rhubarb extract in rats with chronic renal failure. *Chem Pharm Bull* 1984, 32(11): 4506-4513

Yokozawa T, Suzuki N, Okuda I, Oura H, Nishioka I. Changes in the urinary constituents in rats with chronic renal failure during oral administration of rhubarb extract. *Chem Pharm Bull* 1985, 33(10): 4508-4514

Yokozawa T, Suzuki N, Oura H, Nonaka G-I, Nishioka I. Effect of extracts obtained from rhubarb in rats with chronic renal failure. *Chem Pharm Bull* 1986, 34(11): 4718-4723

Yokozawa T, Miyakawa S, Suzuki M, Oura H, Kaneko K, Nishioka I. Effect of extract from Rhei rhizoma on dietary hyperazotemia in rats. *Planta Med* 1987, 53(2): 124-127

Yokozawa T, He L-Q, Muto Y, Nagasaki R, Hattori M, Oura H. Effects of rhubarb extract in rats with diabetic nephropathy. *Phytother Res* 1997, 11: 73-75

Yuen MF, Tam S, Fung J, Wong KH, Wong CY, Lai CL. Traditional Chinese medicine causing hepatotoxicity in patients with chronic hepatitis B infection: a 1-year prospective study. *Alim Pharm Therap* 2006, 24: 1179-1186

Zhang TY, Pannell LK, Pu QL, Cai DG, Ito Y. Separation of hydroxyanthraquinone derivatives extracted from rheum with analytical high-speed counter-current chromatography. *J Chromat* 1988, 442: 455-458

Zhang G, Nahas AME. The effect of rhubarb extract on experimental fibrosis. *Nephrol Dial Transplant* 1996, 11: 186-190

Zhou H, Jiao D. 312 cases of gastric and duodenal ulcer bleeding treated with 3 kinds of alcoholic extract rhubarb tablets. *Chin J Mod Devel Trad Med* 1990, 10(3): 150-151, 131-132

Zhu W, Wang XM, Zhang L, Li XY, Wang BX. Pharmacokinetic of rhein in healthy male volunteers following oral and retention enema administration of rhubarb extract: a single dose study. *Amer J Chin Med* 2005, 33(6): 839-850

Zhu YP. Chinese Material Medica. Chemistry, Pharmacology and Applications. CRC Press, Boca Raton 1998, 231-238