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Committee on Herbal Medicinal Products (HMPC)

## List of references supporting the assessment of *Rheum palmatum L.* and *Rheum officinale* Baillon, radix

Final – 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.**

Andersen DO, Weber ND, Wood SG, Hughes BG, Murray BK, North JA. *In vitro* Virucidal Activity of Selected Anthraquinones and Anthraquinone Derivates. *Antiviral Res* 1991, 16:185-96

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 anthranoide-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

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

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- 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 Suppl.* I. 1993, 47:86-97
- Engelshowe R. Rhabarber eine alte Droge – noch immer aktuell. *Pharm unser Zeit* 1985, 14:40-49
- ESCOP Monographs 2<sup>nd</sup> ed. Rhei Radix - Rhubarb. European Scientific Cooperative on Phytotherapy, editor. Thieme Verlag, Stuttgart 2003
- European Pharmacopoeia 9<sup>th</sup> ed. Rhubarb root - Rhei radix. Council of Europe. 1/2008: 0291
- Faber P, Strenge-Hesse A. Relevance of rhein excretion into breast milk. *Pharmacology Suppl.* I. 1988, 36:212-220
- Fok TF. Neonatal jaundice – traditional Chinese medicine approach. *J Perinatol Suppl.* I. 2001, 21: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. 5<sup>th</sup> ed. Springer-Verlag, Berlin 1994, 411-439
- Hänsel R, Sticher O, Steinegger E. Pharmakognosie-Phytopharmazie, 6<sup>th</sup> 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 antraquinone 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 Suppl.* I. 1996, 2:146-150
- 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, Yokozawar 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 B6C3F<sub>1</sub> Mice. National Toxicology Program, June 2001, NTP TR 493, NIH Publication No. 01-3952; 1-278. Available at:

<https://ntp.niehs.nih.gov/results/pubs/longterm/reports/longterm/tr400499/abstracts/tr493/index.htm>  
I

Oshio H, Imai S, Shoji Fujioka S; Sugawara T, Miyamoto M, Tsukui M. Investigations of Rhubarbs. III. New purgative constituents, sennosides E and F. *Chem Pharm 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

Saller R, Büechi S, Meyrat R, Schmidhauser C. Combined herbal preparation for topical treatment. *Forsch Kompl Klass Natur.* 2001, 8(6):373-82

Sydiskis RJ, Owen DG, Lohr JL, Rosler KH, Blomster RN Inactivation of enveloped viruses by anthraquinones extracted from plants. *AntimicrobAgents 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. 25<sup>th</sup> ed. The Pharmaceutical Press, London 1967

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

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. 27<sup>th</sup> ed. The Pharmaceutical Press, London 1977, 1341-1342

Weiss RF. Lehrbuch der Phytotherapie. 3<sup>rd</sup> ed. Hippokrates-Verlag, Stuttgart 1974, 113-118

Weiss RF. Lehrbuch der Phytotherapie. 7<sup>th</sup> ed. Hippokrates-Verlag, Stuttgart 1990, 126-128

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

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

Xiong HR, Luo J, Hou W, Xiao H, Yang ZQ. The effect of emodin, an anthraquinone derivative extracted from the roots of *Rheum tanguticum*, against herpes simplex virus *in vitro* and *in vivo*. *J Ethnopharmacol* 2011, 133(2):718-23

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, Suzukil 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. *Alimt 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