

London, 26 September 2009
Doc. Ref.: EMEA/HMPC/394997/2007

**This document was valid from 14 January 2009 until January 2017.
It is now superseded by a [new version](#) adopted by the HMPC on
31 January 2017 and published on the EMA website.**

Salicis cortex

**Salix [various species including *S. purpurea* L., *S. daphnoides* Vill., *S. fragilis* L.], cortex
(willow bark)**

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

Adamkiewicz et al (1961). Passage of salicin and saligenin across the wall of the rat ileum. *Can J Biochem Physiol* 39: 1097-99.

Akao et al (2002). Evaluation of salicin as an antipyretic prodrug that does not cause gastric injury. *Planta Med* 68: 714-18.

Albrecht et al (1990). Anti-inflammatory activity of flavonol glycosides and salicin derivatives from the leaves of *Populus tremuloides*. *Planta Med* 56: 660.

American Herbal Pharmacopoeia (1999). Willow bark. Scotts Valley, CA, USA.

Aronson (Ed) (2006). Meyler's side effects of drugs. Elsevier Science, Amsterdam, the Netherlands.

Baker et al (1987). Herbal medicine precipitating massive haemolysis [letter]. *Lancet* 1, 1039-40.

Barnes et al (2002) *Herbal Medicines*, 2nd edition. Pharmaceutical Press. London.

Biegert C et al (2004). Efficacy and safety of willow bark extract in the treatment of OA and RA: results of 2 randomised db controlled trials. *J Rheumatol* 31: 2121-30.

Bisset (1994) *Herbal Drugs and Phytopharmaceuticals*. Medpharm Scientific Publishers, Stuttgart.

Blaschek et al (1998) in Hagers Handbuch der Pharmazeutischen Praxis. Folgenband 3. Drogen L-Z. Springer Verlag Berlin Heidelberg, 469-96.

Bogduk (2004). Pharmacological alternatives for the alleviation of back pain. *Expert Opin Pharmacother* 5 (10): 2091-98.

Boullata et al (2003). Anaphylactic reaction to a dietary supplement containing willow bark. *Ann Pharmacotherap* 37: 832-35.

- BHMA (1983). British Herbal Pharmacopoeia. Bournemouth, UK 184-85.
- BHMA (1992). British Herbal Compendium. Bournemouth, UK 224-26.
- Bruneton (2002). Phytothérapie: les données de l'évaluation. Tec et Doc Ed médicales internationales. Paris. 99-100.
- Cheng et al (1994). Anti-inflammatory effectus of tremulacin, a salicin-related substance isolated from *Populus tomentosa* Carr leaves. Phytomedicine 1, 209-11.
- Chrubasik S, Eisenberg E et al (2000). Treatment of low back pain exacerbations with willow bark extract: a randomized double-blind study. Am J Med 109: 9-14.
- Chrubasik S, Kunzel O et al (2001). Treatment of low back pain with a herbal or synthetic anti-rheumatic: a randomized controlled study. Willow bark extract for low back pain. Rheumatology 40:1388-93.
- Chrubasik S, Kunzel O et al (2001). Potential economic impact using a proprietary willow bark extract in outpatient treatment of low back pain: an open non-randomized study. Phytomedicine 8 (4): 241-51.
- Chrubasik et al (2002). Wirksamkeit von Weidenrindenextrakt bei Schmerzen. Z Phytother 23: 263-66.
- Chrubasik S (2003). Effects of willow bark and therapeutic activity. Clin Pharmacol Ther. July (letters to editor) 95.
- Chrubasik JE et al (2007). Evidence of effectiveness of herbal anti-inflammatory drugs in the treatment of painful osteoarthritis and chronic low back pain. Phytother Res 21: 675-83.
- Clauson et al (2005). Evaluation of presence of aspirin-related warnings with willow bark. Ann Pharmacother 39: 1234-37.
- Commission E (1984). *Salicis cortex* (Weidenrinde). BAnz N° 228.
- CPMP/EMEA (1998). Points to consider on clinical investigation of medicinal products used in the treatment of osteoarthritis. CPMP/EWP/784/97.
- CPMP/EMEA (2003). Points to consider on clinical investigation of medicinal products other than NSAIDS for treatment of rheumatoid arthritis. CPMP/EWP/556/95 rev 1.
- DAB 10 (1991) Deutsche Apotheker Verlag, Stuttgart
- DAB 10 (1995). Kommentar. Deutsche Apotheker Verlag, Stuttgart
- Devogelaer et al (2003). Guidelines for clinical studies assessing the efficacy of drugs for the management of acute LBP. Clin Exp Rheumatol 21: 691-94.
- EDQM Willow bark dry extract (2006). Pharmeuropa 18 (1): 158-60.
- EDQM. European Pharmacopoeia 5th edition.
- EDQM. Willow bark (2006). Pharmeuropa 18 (3): 497-99.
- ESCOP (2002). Monographs; second edition: *Salicis cortex* 445-51.

Fiebich et al (2004). Effects of an ethanolic *Salix* extract on the release of selected inflammatory mediators in vitro. *Phytomed* 11: 135-38.

Fötsch et al (1989a). Biotransformation der Phenolglycosid Leiocarposid und Salicin. *Pharmazie* 44: 555-58.

Fötsch et al (1989b) Die Biotransformation der Phenolglycosid Leiocarposid und Salicin – Beispiele für Besonderheiten von Absorption und Metabolismus glycosidischer Verbindungen. *Pharmazie* 44: 710-2.

Fötsch et al (1990). Vergleichende Serumspiegel-untersuchung von Salicylsäure nach oraler Applikation von Salicin bzw Natriumsalicylat in Ratten. *Pharmazie* 45: 535-36.

Gagnier et al (2006). Improving the reporting of randomized controlled clinical trials of herbal medicinal interventions: an elaboration of the CONSORT statement. *Ann Intern Med* 144: 364-67.

Gagnier et al (2007). Herbal medicine for low back pain: a Cochrane Review. *Spine* 32 (1): 82-92.

Gopalan et al (1992). Exolytic hydrolysis of toxic plant glucosides by guinea pig liver cytosolic beta-glucosidase. *J Biol Chem* 267: 14027-32.

Hänsel (1991). Weidenrinde, *Salicis cortex*. In: *Phytopharmaka*, 2nd ed. Berlin-Heidelberg-New York: Springer-Verlag, 96-97.

HagerRom (2001). *Salicis cortex* (*Salix purpurea*-Rinde)

Julkunen-Tiitto et al (1992a). The enzymatic decomposition of salicin and its derivatives obtained from *Salicaceae* species. *J Nat Prod* 55: 1204-12.

Julkunen-Tiitto et al (1992b). Further studies on the drying of willow twigs: the effect of low drying temperature on labile phenolics. *Planta Med* 58: 385-86.

Julkunen-Tiitto et al (2001). Testing the effects of drying methods on willow flavonoids, tannins and salicylates. *J Chem Ecol* 27 (4): 779-89.

Kammerer et al (2005). HPLC-MS/MS analysis of willow bark extracts contained in pharmaceutical preparations. *Phytochem Anal* 16: 470-78.

Kaul et al (1999). Weidenrinde. Renaissance eines Phytoanalgetikums. *Deutsche Apothekerzeitung* 19 (37): 43-50.

Khayyal et al (2005). Mechanisms involved in the anti-inflammatory effect of a standardised willow bark extract. *Arzneim. Forsch / Drug Res* 55 (11): 677-87.

Krivoy et al (2001). Effect of *Salicis cortex* extract on human platelet aggregation. *Planta Med* 67: 209-12.

Kuppsamy et al (1990). Structure-activity studies of flavonoids as inhibitors of hyaluronidase. *Biochem Biophys* 140: 397-401.

Lardos et al (2004). Wirksamkeit und Verträglichkeit eines wässrig ausgezogenen Weidenrindenextraktes bei Patienten mit Hüft-und Kniearthrose. *Z Phytotherap* 25: 275-81.

Leporatti et al (1990). New or uncommon uses of several medicinal plants in some areas of central Italy. *J Ethnopharmacol* 29: 213-23.

März et al (2002). Weidenrindenextract-Wirkungen und Wirksamkeit. Erkenntnisstand zu Pharmakologie, Toxikologie und Klinik. Wien Med Wschr 152: 354-59.

Matsumoto et al (1993). Reduction of erythrocyte membrane permeability and protein binding of LMW drugs following glycoside derivatisation. J Pharm Sci 82: 399-403.

Meier et al (1985a). Identification and determination of 8 phenol glycosides each in *Salix purpurea* and *S. daphnoides* by modern HPLC. Pharm Act Helv 60: 269-75.

Meier et al (1985b). Weidenrinde – Qualität. Gesamtsalicinbestimmung in Weidenrinden und Weidenpräparaten mit HPLC. Deutsche Apoth Ztg 125: 341-47.

Meier et al. (1990). Salizinhaltige pflanzige Arzneimittel. Überlegungen zur Wirksamkeit und Unbedenklichkeit. Z Phytother 11: 50-58.

Mills et al (1996). Effect of a proprietary herbal medicine on the relief of chronic arthritic pain: a double-blind study. Br J Rheumatol 35: 874-78.

Nahrstedt et al (2007). Willow bark extract: the contribution of polyphenols to the overall effect. Wien Med Wochenschr 157 (13-14): 348-51.

Pentz et al (1989). Bioverfügbarkeit von Salicylsäure und Coffein aus einem phytoanalgetischen Kombinationspräparat. Z Phytother 10: 92-96.

Rice-Evans et al (1995). The relative antioxidant activities of plant-derived polyphenolic flavonoids. Free Rad Ser 22 (4): 375-83.

Rohnert et al (1998). Inhibition by Salix-extracts and Phytodolor® of copper-catalyzed oxidative destructions. Z Naturforsch 53: 233-40.

Rotblatt (2002). Evidence-based herbal medicine. Hanley and Belfus, Philadelphia, pp 360-63.

Saller et al (2008). Pain relief with a proprietary extract of willow bark in rheumatology. An open trial. Schweiz Zschr GanzheitsMedizin 20 (3): 156-62.

Samochowiec L. (2001). Efficacy of Cortex Salix Extract (Salix (r)) in patients with arthrosis in double blind, randomized, verum controlled clinical study (unpublished).

Schmid et al (2001 a). Pharmacokinetics of salicin after oral administration of a standardized willow bark extract. Eur J Clin Pharmacol 57: 387-91.

Schmid, Ludtke et al (2001b). Efficacy and tolerability of a standardized willow bark extract in patients with osteoarthritis: randomized placebo-controlled db clinical trial. Phyt Res 15: 344-50.

Schnitzer et al (2004). A comprehensive review of clinical trials on the efficacy and safety of drugs for the treatment of low back pain. Pain Symptom Manage 28: 72-95.

Setty et al (2005). Herbal medications commonly used in the practice of rheumatology: mechanisms of action, efficacy and side effects. Semin Arthritis Rheum 34: 773-84.

Shalansky et al (2007). Risk of warfarin-related bleeding events and supratherapeutic INRs associated with CAM: a longitudinal analysis. Pharmacother 27 (9): 1237-47.

Shrivastava et al (2006). Tanacetum parthenium and *Salix alba* (Mig-RL) combination in migraine prophylaxis. Clin Drug Invest 26 (5), 287-96.

Steele et al (1969). The effect of extraction procedures on the apparent free phenolic glycoside content of *Salix* species. J Chromatog 40: 370-76.

Steinegger et al (1972). Analytische und biologische Untersuchungen an Salicaceen-Wirkstoffen, insbesondere Salicin. Pharm Acta Helv 47: 222-34.

Tunón et al (1995). Evaluation of anti-inflammatory activity of some Swedish medicinal plants. Inhibition of prostaglandin biosynthesis and PAF-induced exocytosis. J Ethnopharmacol 48: 61-76.

Wagner et al (2003a). Influence of willow bark extract on cyclooxygenase activity and on TNF alpha or interleukin 1 beta release in vitro and in vivo. Clin Pharmacol Therap 73 (3): 272-74.

Wagner et al (2003b) Aktuelle Forschungsergebnisse zur Weidenrinde. Pharm. Ztg 138: 21-32.

Wagner et al (2003c). Reply: effects of willow bark. Clin Pharmacol Therap July (letters to editor), 96-97.

Werner et al (2004). Willow bark extract (Assalix ®) for chronic back pain an arthralgia, a post-authorisation study. Phytopharmaka und Phytotherapie 2004 –Forschung und Praxis, Berlin (poster abstract)

Wichtl (ed) (2002). Teedrogen und Phytopharmaka 4th ed, Stuttgart: Wissenschaftliche Verlansgesellschaft, 534-7.

Wurm et al (1982). Beeinflussung des Arachidonsäurestoffwechsels durch Flavanoide. Deutsche Apothekerzeitung 122: 2062-8.

Wuthold et al (2004). TLC and multivariate data analysis of willow bark extracts. J Chromatogr Sci 2004, 42 (6) 306-09.

Wutzke (1991). Radioisotopenmarkierung und Pharmakokinetik von Phenolglycosiden. Dissertation Phillipsuniversität Marburg.