



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

13 January 2021  
EMA/HMPC/509927/2019  
Committee on Herbal Medicinal Products (HMPC)

## List of references supporting the assessment of *Salvia miltiorrhiza* Bunge, radix et rhizoma

Draft

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

Adams JD, Wang R, Yang J, Lien EJ. Preclinical and clinical examinations of *Salvia miltiorrhiza* and its tanshinones in eschemic conditions. *Chin Med* 2006, 23:1-3

Akaberi M, Iranshani M, Mehri S. Molecular Signaling pathways Behind the Biological Effects of *Salvia Species* Diterpenes in Neuropharmacology and Cardiology. *Phytotherapy Research* 2016, 878-893

AHPA (American Herbal Products Association's) Botanical Safety Handbook. 2<sup>nd</sup> edition. Gardener Z, McGuffin M. editors. *Salvia miltiorrhiza*. CRC Press 2013, 767-771

Awaad AS, Govil JN, Sing VK. editors. Recent Progress in Medicinal Plants (RPMP) (27) Drug Plants. Bioactivity of *Salvia miltiorrhiza* and its Constituents. Vol 27. *Stadium Press LLC, U.S.A* 2010, 91-108

Bensky D, Gamble A, Kaptchuk T. Chinese Herbal Medicine: Materia Medica, 1986, published by Eastland Press, U.S.A. 1986, 384-386

Bensky D, Clavey S, Stoger E, Gamble A. Chinese Herbal Medicine: Materia Medica, 2004, 3<sup>rd</sup> edition, published by Eastland Press, U.S.A. 2004

Blaschek W, Hilgenfeld U, Holzgrabe U, Mörike K, Reichling J, Ruth P, editors. HagerROM 2017. Hagers Enzyklopädie der Arzneistoffe und Drogen. *Salvia miltiorrhiza*. *Wissenschaftliche Verlagsgesellschaft Stuttgart* 2017, 8-12

British Herbal Pharmacopoeia. Processed *Salvia Miltiorrhiza* Rhizome and Root. *British Pharmacopoeia Online*, 2014, IV: 1-4

Chan TY. Interaction between warfarin and danshen (*Salvia miltiorrhiza*). *Ann Pharmacother* 2001, 501-504

Chen J, Chen T. Chinese Medical Herbology and Pharmacology. City of Industry: *Art of Medicine Press, U.S.A.* 2004, 636-639

---

**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, 2021. Reproduction is authorised provided the source is acknowledged.

Chen X, Guo J, Bao J, Lu J, Wang Y. The Anticancer properties of *Salvia Miltiorrhiza* Bunge (Danshen): A Systematic Review, *Wiley Online Library* 2013, 768-794

Chen WC, Wu S-Y, Liao P-C, Chou T-C, Chen H-Y, Chiang J-H, et al. Treatment of Urolithiasis with Medicinal Plant *Salvia miltiorrhiza*: A Nationwide Cohort Study. *Evidence-Based Complementary and Alternative Medicine* 2018, Article ID 8403648

Cheng QU, Tang Yu-Ping, Shi Xu-quin, Zhou Gui-sheng, Shang Er-xin, Shang Li-li, et al. comparative study on promoting blood effects of Danshen-Honghua herb pair with different preparations based on chemometrics and multi-attribute comprehensive index methods. *China Journal of Chinese Materia Medica* 2017:3017-3024 (Chinese, only English abstract)

Chinese Pharmacopoeia. Monograph of Radix Salviae Miltiorrhizae. 1963, 50-51

Chinese Pharmacopoeia. Monograph of Radix Salviae Miltiorrhizae. 1977, 114-115

Chinese Pharmacopoeia. Monograph of Radix Salviae Miltiorrhizae. 1985, 58-59

Chinese Pharmacopoeia. Monograph of Radix Salviae Miltiorrhizae. 1990, 62-63

Chinese Pharmacopoeia. Monograph of Radix Salviae Miltiorrhizae. 1995, 62-63

Chinese Pharmacopoeia. Monograph of Radix Salviae Miltiorrhizae. 2000, 57-58

Chinese Pharmacopoeia. Monograph of Radix Salviae Miltiorrhizae. 2005, 52-53

Chinese Pharmacopoeia. Monograph of Salviae Miltiorrhizae Radix et Rhizoma. 2010, 383-384

Chinese Pharmacopoeia. Monograph of Salviae Miltiorrhizae Radix et Rhizoma. 2015, 76-77

Chinese Pharmacopoeia. Monograph of Salvia total phenolic acids and Tanshinones. 2015, 397-399

Dasgupta A, Actor JK, Olsen M, Wells A, Datta P. In vivo digoxin-like immunoreactivity in mice and interference of Chinese medicine danshen in serum digoxin measurement: Elimination of interference by using a chemiluminescent assay. *Clin Chim Acta* 2002, 231-234

Deng S, May BH, Zhang AL, Lu C, Xue C. Phytotherapy in the management of psoriasis: a review of the efficacy and safety of oral interventions and the pharmacological actions of the main plants. *Arch Der Res* 2014, 211-229

Di Cesare Mannelli L, Piccolo M, Maione F, Ferraro MG, Irace C, De Feo V et al. Tanshinones from *Salvia miltiorrhiza* Bunge revert chemotherapy-induced neuropathic pain and reduce glioblastoma cells malignancy. *Biomed Pharmacother* 2018, 1042-1049

European Pharmacopoeia 8.0. *Salvia Miltiorrhiza* root and rhizome. Council of Europe 04/2013, 2663

European Pharmacopoeia 9.1 *Salvia Miltiorrhiza* root and rhizome. Council of Europe 04/2017, 2663

Gao Y, Liu Z, Li G, Li C, Li M, Li B. Acute and subchronic toxicity of danshensu in mice and rats. *Toxicology mechanisms and Methods*. 2009, 363-368

Guo Y, Li Y, Xue L, Severino RP, Gao S, Niu J. *Salvia miltiorrhiza*: an ancient Chinese herbal medicine as a source for anti-osteoporotic drugs. *Journal of Ethnopharmacology*. 2014, 1401-1416

Gruenwald J, Brendler T, Jaenicke C, editors. PDR for Herbal Medicines, 2<sup>nd</sup> ed. *Medical Economics Company U.S.A* 2000, 636-639

Hänsel R, Keller K, Rimpler H, Schneider G. editors. Hagers Handbuch der Pharmazeutischen Praxis (Hager's Handbook of Pharmaceutical Practice for Druggists). *Salvia Miltiorrhiza*. Drogen P-Z. Vol 6. *Springer-Verlag* 1994, 544

- Hellemans R. Chinese Kruidenkunde. Merksem: Institute for Traditional Medicine, 1994, 171
- Hempfen CH, Fischer T. A Materia Medica for Chinese Medicine. Munich: Elsevier, 2009, 570-571
- Hempfen CH, Fischer T. Leitfaden Chinesische Phytotherapie, 2. Auflage, Elsevier, 2018, 580
- Holmes P. The Traditional Chinese Medicine Materia Medica Clinical Reference & Study Guide. Boulder: Snow Lotus Press, U.S.A. 2002, 253
- Hsing-Y C, Yi-Hsuan L, Irene HS, Yu-Chun C, Sien-hung Y, Jiun-liang C. Investigation on Chinese herbal medicine for primary dysmenorrhea: Implication from a nationwide prescription database in Taiwan. *Complementary Therapies in Medicine* 2014, 116-125
- Hou W-C, Tsay H-S, Liang H-J, Lee T-Y, Wang G-J, Liu D-Z. Improving abnormal hemorheological parameters in aging guinea pigs by water soluble extracts of *Salvia miltiorrhiza* Bunge. *J Ethnopharmacol* 2007, 111:483-489
- Hu Y, Ge Y, Zhang Y, Liu J, Xun L, Qiaoping L. Treatment of 100 cases of nerve deafness with injection of radix *salvia miltiorrhiza*. *J Trad Chin Med* 1992, 12:256-258
- Hu Z, Yang X, Ho PCL, Chan SY, Heng PWSH, Chan E, et al. Herb-drug interactions: A literature review. *Drugs* 2005, 65:1239-1282
- Huang KC (editor). The Pharmacology of Chinese herbs. 2<sup>nd</sup> edition. Antianginal herbs. *Tan Seng. CRC Press* Boca Raton, London, New York, Washington, D.C. 1999, 91-94
- Huang YT, Lee T-Y, Lin H-C, Chou T-Y, Yang Y-Y, Hong C-Y. Hemodynamic effects of *Salvia miltiorrhiza* on cirrhotic rats. *Can J Physiol Pharmacol* 2001, 79:566-572
- Izzat MB, Yim AP, El-Zufari MH. A taste of Chinese medicine. *Ann Thorac Surg* 1998, 941-2
- Jiang RW, Lau K-M, Hon P-M, Mak TCW, Woo K-S, Fung K-P. Chemistry and biological activities of caffeic acid derivatives from *Salvia miltiorrhiza*. *Curr Med Chem* 2005, 237-246
- Jinping Q, Peiling H, Yawei L, Abliz Z. Effect of the aqueous extract of *Salvia miltiorrhiza* on the pharmacokinetics of diazepam and on liver microsomal cytochrome P450 enzyme activity in rats. *J Pharm Pharmacol* 2003, 1163-1167
- Kum KY, Booker A, Leon C, Garcia P, Heinrich M. *Salvia miltiorrhiza* (Danshen). An NMR-metabolomic and HPTLC-bases analysis of products quality. *Planta Med* 2016, 381
- Kum KY, Kirchhof R, Luick R, Heinrich M. The quality variation of Danshen – an interdisciplinary approach to studying herbal medicine. *Planta Med* 2019, 1442
- Lam FFY, Yeung JHK, Cheung JHY. Mechanism of the dilator action of danshen on rat isolated femoral artery. *J Cardiovasc Pharmacol* 2005, 361-368
- Lam FFY, Yeung JHK, Cheung JHY, Or MYO. Pharmacological evidence for calcium channel inhibition by danshen (*Salvia miltiorrhiza*) on rat isolated femoral artery. *J Cardiovasc Pharmacol* 2006, 139-145
- Lee CY; Sher H-F, Chen H-W, Liu C-C, Chen C-H, Lin C-S et al. Anticancer effect of tashinone I in human non-small cell lung cancer. *Mol Cancer Ther* 2008, 3527-3538
- Li G, Gao Y, Li S, Li C, Zhu X, Li M, Liu Z. Study on toxicity of danshensu in beagle dogs after 3-month continuous intravenous infusion. *Toxicol Mech Methods*. 2009, 441-446
- Li Z, Xu S, Liu P. *Salvia miltiorrhiza* Burge (Danshen): a golden herbal medicine in cardiovascular therapeutics. *Acta Pharm Sin* 2018, 802-824

- Lin J, Zhu J, Wang Y, Zhang N, Gober HJ, Qiu X, Li D, Wang L. Chinese single herbs and active ingredients for postmenopausal osteoporosis: From preclinical evidence to action mechanism. *BioScience Trends* 2017, 496-506
- List PL, Hörhammer L, Roth HJ, Schmid W. Hagers Handbuch der Pharmazeutischen Praxis (Hager's Handbook of Pharmaceutical Practice for Druggists). Vol 4. *Salvia Miltiorrhiza*. Springer-Verlag 1979, 252
- Lo ACT, Chan K, Yeung JHK, Woo KS. The effects of danshen on pharmacokinetics and pharmacodynamics of warfarin in rats. *Eur. J. Drug Metab. Pharmacokinet Proc.* 1992, 257-262
- Morton JS, Andersson IJ, Cheung PY, Baker P, Davidge T. The Vascular Effects of Sodium Tanshinone IIA Sulphonate in Rodent and Human Pregnancy. *PIOS ONE* 2015, 1-15
- Nizamutdinova IT, Lee G W, Lee JS, Cho MK, Son KH, Jeon SK et al. Tanshinone I suppresses growth and invasion of human breast cancer cells, MDA-MB-231, through regulation of adhesion molecules. *Carcinogenesis* 2008, 1885-1892
- Pang H, Jiang M, Wang Q, Wang X, Gao W, Tian Z, Huang J. Metabolic profile of danshen in rats by HPLC-LTQ-Orbitrap mass spectrometry. *J Zhejiang Univ-Sci B* 2018, 227-244
- Panwar P, Xue L, Soe K, Srivastava K, Law S, Delaisse J-M, Brömme D. An Ectosteric Inhibitor of Cathepsin K Inhibits Bone Resorption in Ovariectomized Mice. *Journal of Bone and Mineral Research* 2017, 2415-2430
- Panwar P, Law S, Jamroz A, Azizi P, Zhang D, Ciufolini M, Brömme D. Tanshinones that selectively block the collagenase activity of cathepsin K provide a novel class of ectosteric antiresorptive agents for bone. *British Journal of Pharmacology* 2018, 902-923
- Paulus E, Ding YH. Handbuch der traditionellen chinesischen Heilpflanzen. *Haug Verlag Heidelberg* 1987, 221-222
- Portert M. Klinische Chinesische Pharmakologie. Heidelberg: Verlag für Medizin Fischer, 1978, 333
- Qiu F, Zhang R, Sun J, Jiye A, Hao H, Peng Y, Ai H, Wang G. Inhibitory effects of seven components of danshen extract on catalytic activity of cytochrome P450 enzyme in human liver microsomes. *Drug Metabolism and Disposition* 2008, 1308-1314
- Qiu F, Wang G, Zhang R, Sun J, Jiang J, Ma Y. Effect of danshen extract on the activity of CYP3A4 in healthy volunteers. *Br J Clin Pharmacol* 2010, 656-662
- Ryu SY, Lee CO, Choi SU. In Vitro Cytotoxicity of Tanshinones from *Salvia miltiorrhiza*. *Planta medica* 1997, 339-342
- Shao H, Li M, Chen F, Chen L, Jiang Z, Zhao L The Efficacy of Danshen Injection as Adjunctive Therapy in Treating Angina Pectoris: A Systematic Review and Meta-Analysis. *Heart Lung Circ*, 2018, 433-442
- Stöger EA. Monographien des Arzneibuches der Volksrepublik China 1985. *DECA* 1989, 1-3
- Stöger EA. Arzneibuch der Chinesischen Medizin. Monographien des Arzneibuches der Volksrepublik China 2000 und 2005. *DAV* 2009, 1-6
- Su C-Y, Ming Q-L, Rahman K, Han T, Qin L-P. *Salvia miltiorrhiza*: Traditional medical uses, chemistry and pharmacology. *Chinese Journal of natural Medicines* 2015, 163-182
- Sun J, Zhan L, Song J, Tian S, Huang C, Feng Z, Yang Lv, Guanghua Du. Pharmacokinetic study of salvianolic acid A in beagle dog after oral administration by a liquid chromatography-mass

- spectrometry method: a study on bioavailability and dose proportionality. *J Ethnopharmacol* 2013, 617-23
- Tam LS, Chan TY, Leung WK, Critchley JA. (1995). Warfarin interactions with Chinese traditional medicines: danshen and methyl salicylate medicated oil. *Aust N Z J Med* 1995, 258
- Tang W. Eisenbrand G. Chinese Drugs of Plant Origin. *Springer Verlag Berlin Heidelberg* 1992, 891-902
- Upton R, Romm A. Botanical Medicine for Women's Health. *Churchill Livingstone, U.S.A.* 2010, 75-96
- Vangermeersch Luc. Phytotherapie Traditionelle Chinoise (陳啟仁中藥案). Brussels, Belgium. S.A.T.A.S. edition. 1986, 197-198
- Van Poppel PCM, Breedveld P, Abbink EK, Roelofs H, van Heerde W, Smits P et al. *Salvia Miltiorrhiza* Root Water-Extract (Danshen) Has No Beneficial Effect on Cardiovascular Risk Factors. A Randomized Double-Blind Cross-Over Trial. 2015, <https://doi.org/10.1371/journal.pone.0128695>
- Wagner H, Bauer R, Melchart D, Xiao P, Staudinger A, editors. Chromatographic Fingerprint Analysis of Herbal Medicines: Thin-Layer and High Performance Liquid Chromatography of Chinese Drugs, 2<sup>nd</sup> ed. Wien: *Springer* 2011, 903-921
- Wang L, Ma R, Liu C, Liu H, Zhu R, Guo S, et al. *Salvia miltiorrhiza*: A Potential Red Light to the Development of Cardiovascular Diseases. *Curr Pharm Design* 2017a, 23, 1-22
- Wang X, Morris-Natschke SL, Lee KH. New developments in the chemistry and biology of the bioactive constituents of danshen. *Med Res Rev* 2007, 133-148 Wu B, Liu M, Zhang S. Danshen agents for acute ischaemic stroke. *Cochrane database Syst Rev* 2007, 1-18
- Wang T, Wang C, Wu Q, Zheng K, Chen J, Lan Y, et al. Evaluation of Tanshinone IIA Developmental Toxicity in Zebrafish Embryos. *Molecules* 2017b, 1-8
- Wu T, Ni J, Wei J. Danshen (Chines medicinal herb) preparations for acute myocardial infarction. *Cochrane database Syst Rev* 2008, 1-27
- Xu X, Lv H, Li X, Su H, Zhang X, Yang J. Danshen attenuates osteoarthritis-related cartilage degeneration through inhibition of NF- $\kappa$ B signaling pathway in vivo and in vitro. *Biochem Cell Biol* 2017, 644-651
- Xu M, Jiang L, Wu T, Chu J, Wei Y, As J, Wang G, Hao H et al. Inhibitory Effects of Danshen components on CYP2C8 and CYP2J2. *Chemico-Biological Interactions* 2018, 15-22
- Yuan SL, Wei Y-Q, Wang X-J, Xiao F, Li S-F, Zhang J. Growth inhibition and apoptosis induction of tanshinone II-A on human hepatocellular carcinoma cells. *World J Gastroenterol* 2004, 2024-2028
- Ye F, Liu Y, Qiu G, Zhao Y, Liu M. Clinical study on treatment on cirrhosis by different dosages of salvia injection. *Zhong yao Cai* 2005, 28:850-854 (Article in Chinese, English abstract)
- Yu CM, Chan JC, Sanderson JE. Chinese herbs and warfarin potentiation by 'danshen'. *J Intern Med* 1997, 337-339
- Zhou L, Zuo Z, Chow MSS. Danshen. An Overview of Its Chemistry, Pharmacology, Pharmacokinetics, and Clinical Use. *J Clin Pharmacol* 2005, 1345-1359
- Zhou L, Chan WK, Xu N, Xiao K, Luo H, Luo KQ et al. Tanshinone IIA, an isolated compound of *Salvia miltiorrhiza* Bunge, induces apoptosis in HeLa cells through mitotic arrest. *Life Sci* 2008, 394-403
- Zhou X, Chan K, Yeung JHK. Herb-drug interactions with Danshen (*Salvia miltiorrhiza*): a review on the role of cytochrome P450 enzymes. *Drug Metabol Drug Interact* 2012, 27:9-18

Zhu YP. Chinese Materia Medica: Chemistry, Pharmacology and Applications. Amsterdam: *Harwood Academic Publishers* 1998, 459-463