



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 January 2017
EMA/HMPC/762955/2015
Committee on Herbal Medicinal Products (HMPC)

List of references supporting the assessment of *Paeonia lactiflora* Pall. and/or *Paeonia veitchii* Lynch, radix (Paeoniae radix rubra)

Final

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.

Abdelhamed S, Yokoyama S, Hafiyani L, Kalauni SK, Hayakawa Y, Awale S, et al. Identification of plant extracts sensitizing breast cancer cells to TRAIL. *Oncol Rep* 2013, 29(5):1991-1998

Abdel-Hafez AA, Meselhy MR, Nakamura N, Hattori M, Watanabe H, Murakami Y, et al. Effects of paeoniflorin derivatives on scopolamine-induced amnesia using a passive avoidance task in mice; Structure-activity relationship. *Biol Pharm Bull* 1998, 21(11):1174-1179

Ahmad F, Tabassum N, Rasool S. Medicinal uses and phytoconstituents of *Paeonia officinalis*. *IRJP* 2012, 3:85-87

Baumgartner RR, Steinmann D, Heiss EH, Atanasov AG, Ganzera M, Stuppner H, et al. Bioactivity-guided isolation of 1,2,3,4,6-Penta-O-galloyl-D-glucopyranose from *Paeonia lactiflora* roots as a PTP1B inhibitor. *J Nat Prod* 2010, 73(9):1578-1581

Blaschek W, Hilgenfeldt U, Holzgrabe U, Reichling J, Ruth P, Schulz V, editors. HagerROM 2013: Hagers Enzyklopädie der Arzneistoffe und Drogen. *Paeonia*. Springer Medizin Verlag, Heidelberg 2013

Bruneton J. Pharmacognosy, phytochemistry, medicinal plants. Lavoisier, Paris 1995, 400-404

Cao BY, Yang YP, Luo WF, Mao CJ, Han R, Sun X, et al. Paeoniflorin, a potent natural compound, protects PC12 cells from MPP+ and acidic damage via autophagic pathway. *J Ethnopharmacol* 2010, 131(1):122-129

Cao C, He X, Wang W, Zhang L, Lin H, Du L. Kinetic distribution of paeoniflorin in cortex of normal and cerebral ischemia-reperfusion rats after intravenous administration of *Paeoniae Radix* extract. *Biomed Chromatogr* 2006, 20(12):1283-1288



- Chang IM et al. Assay of potential mutagenicity and antimutagenicity of Chinese herbal drugs by using SOS Chromotest (*E. coli* PQ37) and SOS UMU test (*S. typhimurium* TA 1535/PSK 1002). Proceedings of the first Korea–Japan Toxicology Symposium, Safety Assessment of Chemicals in Vitro, 1989:236–248
- Chang Y, Wei W, Zhang L, Xu HM. Effects and mechanisms of total glucosides of paeony on synoviocytes activities in rat collagen-induced arthritis. *J Ethnopharmacol* 2009, 121(1):43-48
- Chen C, Xia Z, Wang X. Effect of Radix Paeoniae Rubra on expression of iNOS and eNOS in lipopolysaccharide-induced acute lung injury. *Medical Journal of Wuhan University* 2005, 26(1):35-38
- Chen C, Zhang F, Xia Z-Y, Lin H, Mo A-S. Protective effects of pretreatment with Radix Paeoniae Rubra on acute lung injury induced by intestinal ischemia/reperfusion in rats. *Chinese Journal of Traumatology - English Edition* 2008, 11(1):37-41
- Chen JY, Wu HX, Chen Y, Zhang LL, Wang QT, Sun WY, Wei W. Paeoniflorin inhibits proliferation of fibroblast-like synoviocytes through suppressing G-protein-coupled receptor kinase 2. *Planta Med* 2012, 78(7):665-671
- Chen LC, Lee MH, Chou MH, Lin MF, Yang LL. Pharmacokinetic study of paeoniflorin in mice after oral administration of Paeoniae radix extract. *Journal Chromatogr B: Biomed Sci and Appl* 1999, 735(1):33-40
- Chen LC, Chen YF, Chou MH, Lin MF, Yang LL, Yen KY. Pharmacokinetic interactions between carbamazepine and the traditional Chinese medicine Paeoniae Radix. *Biological & pharmaceutical bulletin* 2002, 25(4):532-535
- Chen LC, Chou MH, Lin MF, Yang LL. Lack of pharmacokinetic interaction between valproic acid and a traditional Chinese medicine, Paeoniae Radix, in healthy volunteers. *J Clin Pharm Ther* 2000, 25(6):453-459
- Chen LC, Chou MH, Lin MF, Yang LL. Effects of Paeoniae Radix, a traditional Chinese medicine, on the pharmacokinetics of phenytoin. *J Clin Pharm Ther* 2001, 26(4):271-278
- Chen T, Guo ZP, Jiao XY, Zhang YH, Li JY, Liu HJ. Protective effects of peoniflorin against hydrogen peroxide-induced oxidative stress in human umbilical vein endothelial cells. *Can J Physiol Pharmacol* 2011, 89(6):445-453
- Chen Y, Wei W, Wu H, Zhang LL, Chen JY. [Effects of paeoniflorin on the level of antibodies and cAMP produced by splenocytes in rats with adjuvant arthritis]. *Acta Pharmaceutica Sinica* 2007, 42(11):1147-1151 [Chinese]
- Chen Z, Li XP, Li ZJ, Xu L, Li XM. Reduced hepatotoxicity by total glucosides of paeony in combination treatment with leflunomide and methotrexate for patients with active rheumatoid arthritis. *Int Immunopharmacol* 2013, 15(3):474-477
- Chinese Pharmacopoeia Commission. Peony Root. Pharmacopoeia of the People's Republic of China 2010, 306-308
- Dai LM, Chen XG, Xu SY. Protective effects of total glucosides of paeony on experimental hepatitis. *Chinese Pharmacological Bulletin* 1993, 9(6):449-453
- Dong Y, Zhang Y, Yang Q, Li Y, Zhu X. [Absorption of extractive Radix Paeoniae Alba in rat everted gut sacs and its interaction with P-glycoprotein]. *China journal of Chinese materia medica* 2009, 34(7):884-888 [Chinese]

- Du JH, Dong BD. [Comparative study on clinical efficacy of using methotrexate singly or combined with total glucosides of Paeony in treating rheumatoid arthritis]. *Chinese journal of integrated traditional and Western medicine* 2005, 25(6):540-542 [Chinese]
- Fang F, Wu YG, Dong J, Ren KJ, Qi XM, Liang C, et al. Protective action of total glucosides of paeony on renal tubulointerstitium and its mechanism in diabetic rats. *Chinese Pharmacological Bulletin* 2008, 24(3):369-373
- Fang S, Zhu W, Zhang Y, Shu Y, Liu P. Paeoniflorin modulates multidrug resistance of a human gastric cancer cell line via the inhibition of NF-kappaB activation. *Mol Med Rep* 2012, 5(2):351-356
- Feng C, Liu M, Shi X, Yang W, Kong D, Duan K, et al. Pharmacokinetic properties of paeoniflorin, albiflorin and oxypaeoniflorin after oral gavage of extracts of Radix Paeoniae Rubra and Radix Paeoniae Alba in rats. *J Ethnopharmacol* 2010, 130(2):407-413
- Frerichs G, Arends G, Zörnig G, editors. Hagers Handbuch der pharmazeutischen Praxis. Bd II. Verlag von Julius Springer, Berlin 1938, 379-380
- Goto H, Shimada Y, Akechi Y, Kohta K, Hattori M, Terasawa K. Endothelium-dependent vasodilator effect of extract prepared from the roots of Paeonia lactiflora on isolated rat aorta. *Planta Med* 1996, 62(5):436-439
- Goto H, Shimada Y, Tanaka N, Tanigawa K, Itoh T, Terasawa K. Effect of extract prepared from the roots of Paeonia lactiflora on endothelium-dependent relaxation and antioxidant enzyme activity in rats administered high-fat diet. *Phytother Res* 1999, 13(6):526-528
- Guo JP, Pang J, Wang XW, Shen ZQ, Jin M, Li JW. In vitro screening of traditionally used medicinal plants in China against enteroviruses. *World J Gastroenterol* 2006, 12(25):4078-4081
- Harada M, Suzuki M, Ozaki Y. Effects of Japanese Angelica root and Peony root on uterine contraction in the rabbit in situ. *J Pharmacobiodyn* 1984, 7(5):304-311
- He DY, Dai SM. Anti-inflammatory and immunomodulatory effects of Paeonia lactiflora Pall., a traditional Chinese herbal medicine. *Frontiers in Pharmacology* 2011, 10(2):1-5
- Herbal Medicines. 4th ed. Peony. Pharmaceutical Press, London 2013, 562-573
- Hoppe HA. Taschenbuch der Drogenkunde. Walter de Gruyter. New York 1981, 200
- Hsiu SL, Lin YT, Wen KC, Hou YC, Chao PD. A deglycosylated metabolite of paeoniflorin of the root of Paeonia lactiflora and its pharmacokinetics in rats. *Planta Med* 2003, 69(12):1113-1118
- Im DY, Lee KI. Tyrosinase inhibitory activity and melanin production inhibitory activity of the extract and fractions from Paeoniae radix. *Korean Journal of Pharmacognosy* 2011, 42(4):323-328
- Im DY, Lee KI. Nitric oxide production inhibitory effect and antibacterial activity of the extract and fractions from Paeoniae radix. *Korean Journal of Pharmacognosy* 2012, 43(2):173-178
- Ishida H, Takamatsu M, Tsuji K, Kosuge T. Studies on active substances in herbs used for Oketsu ('stagnant blood') in Chinese medicine. VI. On the anticoagulative principle in Paeoniae Radix. *Chemical and Pharmaceutical Bulletin* 1987, 35(2):849-852
- Ji Y, Wang T, Wei ZF, Lu GX, Jiang SD, Xia YF, et al. Paeoniflorin, the main active constituent of Paeonia lactiflora roots, attenuates bleomycin-induced pulmonary fibrosis in mice by suppressing the synthesis of type I collagen. *J Ethnopharmacol* 2013, 149(3):825-832

- Jia SJ, Liang GP, Luo SY, Lu QJ, Zhao M. Total glucosides of Paeony regulates cytokines production in lupus CD4+ T cells. 2nd Eastern Asia Dermatology Congress Beijing, China. *Journal of Dermatology* 2012, 39:81
- Jiang B, Qiao J, Yang Y, Lu Y. Inhibitory effect of paeoniflorin on the inflammatory vicious cycle between adipocytes and macrophages. *J Cell Biochem* 2012, 113(8):2560-2566
- Jiang F, Zhao Y, Wang J, Wei S, Wei Z, Li R, et al. Comparative pharmacokinetic study of paeoniflorin and albiflorin after oral administration of Radix Paeoniae Rubra in normal rats and the acute cholestasis hepatitis rats. *Fitoterapia* 2012, 83(2):415-421
- Jin SN, Wen JF, Wang TT, Kang DG, Lee HS, Cho KW. Vasodilatory effects of ethanol extract of Radix Paeoniae Rubra and its mechanism of action in the rat aorta. *J Ethnopharmacol* 2012, 142(1):188-193
- Juan YC, Chang CC, Tsai WJ, Lin YL, Hsu YS, Liu HK. Pharmacological evaluation of insulin mimetic novel suppressors of PEPCK gene transcription from Paeoniae Rubra Radix. *J Ethnopharmacol* 2011, 137(1):592-600
- Juan YC, Tsai WJ, Lin YL, Wang GJ, Cheng JJ, Yang HY, et al. The novel anti-hyperglycemic effect of Paeoniae radix via the transcriptional suppression of phosphoenopyruvate carboxykinase (PEPCK). *Phytomedicine* 2010, 17(8-9):626-634
- Kang SS, Kim JS, Kim EM, Yun-Choi HS. Platelet anti-aggregation of Paeony root. *Korean Journal of Pharmacognosy* 1991, 22(4):215-218
- Kim JY, Yi YS, Lim YH. Biological and antifungal activity of herbal plant extracts against Candida species. *Korean Journal of Microbiology and Biotechnology* 2009, 37(1):42-48
- Kimura M, Kimura I, Nojima H, Takahashi K, Hayashi T, Shimizu M, et al. Blocking effects of a new component, paeoniflorigenone, in paeony root on neuromuscular junctions of frogs and mice. *Jpn J Pharmacol* 1984, 35(1):61-66
- Klein SD, Vanr Zypen D De, Becker S. Prescription patterns of Chinese Medicinal Herbs in Switzerland. *Schweizerische Zeitschrift fur GanzheitsMedizin* 2010, 22(4):226-231
- Kommission E (of Germany). Paeonia. BAnz. Nr. 85 of 05.05.1988
- Kong P, Chi R, Zhang L, Wang N, Lu Y. Effects of paeoniflorin on tumor necrosis factor-alpha-induced insulin resistance and changes of adipokines in 3T3-L1 adipocytes. *Fitoterapia* 2013, 91:44-50
- Koo YK, Kim JM, Koo JY, Kang SS, Bae K, Kim YS, et al. Platelet anti-aggregatory and blood anti-coagulant effects of compounds isolated from Paeonia lactiflora and Paeonia suffruticosa. *Pharmazie* 2010, 65(8):624-628
- Kuo JJ, Wang CY, Lee TF, Huang YT, Lin YL. Paeoniae radix reduces PDGF-stimulated hepatic stellate cell migration. *Planta Med* 2012, 78(4):341-348
- Kwon KB, Park BH, Ryu DG. Chemotherapy through mitochondrial apoptosis using nutritional supplements and herbs: A brief overview. *J Bioenerg Biomembr* 2007, 39(1):31-34
- Landmark CJ, Patsalos PN. Interactions between antiepileptic drugs and herbal medicines. *Bolet N Latinoamericano Y Del Caribe De Plantas Medicinales Y Aromaticas* 2008, 7(N2):108-118
- Lee B, Shin YW, Bae EA, Han SJ, Kim JS, Kang SS, et al. Antiallergic effect of the root of Paeonia lactiflora and its constituents paeoniflorin and paeonol. *Arch Pharm Res* 2008, 31(4):445-450

- Lee KK, Omiya Y, Yuzurihara M, Kase Y, Kobayashi H. Antinociceptive effect of paeoniflorin via spinal alpha2- adrenoceptor activation in diabetic mice. *Eur J Pain* 2011, 15(10):1035-1039
- Lee SC, Kwon YS, Son KH, Kim HP, Heo MY. Antioxidative constituents from *Paeonia lactiflora*. *Arch Pharm Res* 2005, 28(7):775-783
- Lee SM, Li ML, Tse YC, Leung SC, Lee MM, Tsui SK, et al. *Paeoniae Radix*, a Chinese herbal extract, inhibit hepatoma cells growth by inducing apoptosis in a p53 independent pathway. *Life Sci* 2002, 71(19):2267-2277
- Lee SM, Yoon MY, Park HR. Protective effects of *Paeonia lactiflora* pall on hydrogen peroxide-induced apoptosis in PC12 cells. *Biosci Biotechnol Biochem* 2008, 72(5):1272-1277
- Leem K, Kim H, Boo Y, Lee HS, Kim JS, Yoo YC, et al. Effects of *Paeonia lactiflora* root extracts on the secretions of monocyte chemotactic protein-1 and -3 in human nasal fibroblasts. *Phytother Res* 2004, 18(3):241-243
- Li CL, He J, Li ZG, Zheng LW, Hua H. Effects of total glucosides of paeony for delaying onset of Sjogren's syndrome: an animal study. *J Craniomaxillofac Surg* 2013, 41(7):610-615
- Li J, Chen CX, Shen YH. Effects of total glucosides from paeony (*Paeonia lactiflora* Pall) roots on experimental atherosclerosis in rats. *J Ethnopharmacol* 2011, 135(2):469-475
- Li JZ, Wu JH, Yu SY, Shao QR, Dong XM. Inhibitory effects of paeoniflorin on lysophosphatidylcholine-induced inflammatory factor production in human umbilical vein endothelial cells. *Int J Mol Med* 2013, 31(2):493-497
- Li PP, Liu DD, Liu YJ, Song SS, Wang QT, Chang Y, et al. BAFF/BAFF-R involved in antibodies production of rats with collagen-induced arthritis via PI3K-Akt-mTOR signaling and the regulation of paeoniflorin. *J Ethnopharmacol* 2012, 141(1):290-300
- Li R, Guo W, Fu Z, Ding G, Zou Y, Wang Z. Hepatoprotective action of *Radix Paeoniae Rubra* aqueous extract against CCl4-induced hepatic damage. *Molecules* 2011, 16(10):8684-8693
- Li X, Shen J, Zhong Z, Peng J, Wen H, Li J, et al. Paeoniflorin ameliorates schistosomiasis liver fibrosis through regulating IL-13 and its signalling molecules in mice. *Parasitology* 2010, 137(8):1213-1225
- Li X, Shen J, Zhong Z, Wen H, Luo Q, Wei W. Paeoniflorin: a monomer from traditional Chinese medical herb ameliorates *Schistosoma japonicum* egg-induced hepatic fibrosis in mice. *J Parasitol* 2009, 95(6):1520-1524
- Liang J, Xu F, Zhang YZ, Huang S, Zang XY, Zhao X, et al. The profiling and identification of the absorbed constituents and metabolites of *Paeoniae Radix Rubra* decoction in rat plasma and urine by the HPLC-DAD-ESI-IT-TOF-MS(n) technique: a novel strategy for the systematic screening and identification of absorbed constituents and metabolites from traditional Chinese medicines. *J Pharm Biomed Anal* 2013, 83:108-121
- Lin HR. Paeoniflorin acts as a liver X receptor agonist. *J Asian Nat Prod Res* 2013, 15(1):35-45
- Lin J, Xiao L, Ouyang G, Shen Y, Huo R, Zhou Z, et al. Total glucosides of paeony inhibits Th1/Th17 cells via decreasing dendritic cells activation in rheumatoid arthritis. *Cell Immunol* 2012, 280(2):156-163
- Lin TJ, Wang KC, Lin CC, Chiang LC, Chang JS. Anti-viral activity of water extract of *Paeonia lactiflora pallas* against human respiratory syncytial virus in human respiratory tract cell lines. *Am J Chin Med* 2013, 41(3):585-599

- List PH, Hörhammer L in Gemeinschaft mit Roth HJ, Schmid W, editors. Hagers Handbuch der Pharmazeutischen Praxis. Bd. VI. 4th ed. Springer Verlag, Berlin Heidelberg New York 1977, 383-387
- Liu DZ, Xie KQ, Ji XQ, Ye Y, Jiang CL, Zhu XZ. Neuroprotective effect of paeoniflorin on cerebral ischemic rat by activating adenosine A1 receptor in a manner different from its classical agonists. *British journal of pharmacology* 2005, 146(4):604-611
- Liu EH, Qi LW, Li B, Peng YB, Li P, Li CY, et al. High-speed separation and characterization of major constituents in Radix Paeoniae Rubra by fast high-performance liquid chromatography coupled with diode-array detection and time-of-flight mass spectrometry. *Rapid Commun Mass Spectrom* 2009, 23(1): 119-130
- Liu W, Wu H-P, Zhu X-G, Ming L. Protective effect of TGP on complete cerebral ischemia reperfusion injury in rats. *Chinese Pharmacological Bulletin* 2004, 20(2):211-214
- Long J, Gao M, Kong Y, Shen X, Du X, Son YO, et al. Cardioprotective effect of total paeony glycosides against isoprenaline-induced myocardial ischemia in rats. *Phytotherapy: international journal of phytotherapy and phytopharmacology* 2012, 19(8-9):672-676
- Long JW, Wang YY, Pi XM, Tu YT. Clinical observation on the treatment of chronic urticaria with total glucosides of paeony capsule combined with citirizine. *Chin J Integr Med* 2010, 16(4): 353-356
- Lu L, Zhang M, Wang Y, Zhang Y, Zhao X. [Screening and identifying of hepatoprotective compounds in paeoniae radix rubra]. *China journal of Chinese materia medica* 2012, 37(5):597-600 [Chinese]
- Madari H, Jacobs RS. An analysis of cytotoxic botanical formulations used in the traditional medicine of ancient Persia as abortifacients. *J Nat Prod* 2004, 67(8):1204-1210
- Madaus G. Lehrbuch der biologischen Heilmittel, Bd III. Georg Olms Verlag, Hildesheim New York 1976, 2051-2056
- Malviya N, Jain S. Wound healing activity of aqueous extract of Radix paeoniae root. *Acta Pol Pharm* 2009, 66(5):543-547
- Mao QQ, Huang Z, Ip SP, Xian YF, Che CT. Peony glycosides reverse the effects of corticosterone on behavior and brain BDNF expression in rats. *Behav Brain Res* 2012a, 227(1):305-309
- Mao QQ, Ip SP, Ko KM, Tsai SH, Xian YF, Che CT. Effects of peony glycosides on mice exposed to chronic unpredictable stress: further evidence for antidepressant-like activity. *J Ethnopharmacol* 2009, 124(2):316-320
- Mao QQ, Ip SP, Xian YF, Hu Z, Che CT. Anti-depressant-like effect of peony: a mini-review. *Pharm Biol* 2012b, 50(1):72-77
- Ngan LT, Moon JK, Kim JH, Shibamoto T, Ahn YJ. Growth-inhibiting effects of Paeonia lactiflora root steam distillate constituents and structurally related compounds on human intestinal bacteria. *World journal of microbiology & biotechnology* 2012a, 28(4):1575-1583
- Ngan LT, Moon JK, Shibamoto T, Ahn YJ. Growth-inhibiting, bactericidal, and urease inhibitory effects of Paeonia lactiflora root constituents and related compounds on antibiotic-susceptible and -resistant strains of Helicobacter pylori. *J Agric Food Chem* 2012b, 60(36):9062-9073
- Nizamutdinova IT, Jin YC, Kim JS, Yean MH, Kang SS, Kim YS, et al. Paeonol and paeoniflorin, the main active principles of Paeonia albiflora, protect the heart from myocardial ischemia/reperfusion injury in rats. *Planta Med* 2008, 74(1):14-18

- Ohta H, Ni J-W, Matsumoto K, Watanabe H, Shimizu M. Peony and its major constituent paeoniflorin, improve radial maze performance impaired by scopolamine in rats. *Pharmacology Biochemistry and Behavior* 1993, 45(3): 719-723
- Ono K, Sawada T, Murata Y, Saito E, Iwasaki A, Arakawa Y, et al. Pentagalloylglucose, an antisecretory component of *Paeoniae radix*, inhibits gastric H⁺, K⁺-ATPase. *Clin Chim Acta* 2000, 290(2):159-167
- Peony. *Alternative medicine review* 2001, 6(5):495-499
- Pharmeuropa (27.1). Peony root, white. Monograph N.: 2424 (draft)
- Pharmeuropa (27.1). Peony root, white. Monograph N.: 2425 (draft)
- Rawat S, Malviya S. Antipyretic activity of aqueous root extract of *Radix paeoniae*. *Indian Drugs* 2010, 47(5):59-62
- Sung CK, Kang GH, Yoon SS, et al. Glycosidases that convert natural glycosides to bioactive compounds. In Waller G, Yamasaki K, editors. *Saponins Used in Traditional and Modern Medicine*. Plenum Press, New York 1996, 24
- Taiwan Herbal Pharmacopeia. *Paeoniae rubra radix*. Ministry of Health and Welfare Taiwan, Republic of China. 2015, 196-197
- Tang NY, Liu CH, Hsieh CT, Hsieh CL. The anti-inflammatory effect of paeoniflorin on cerebral infarction induced by ischemia-reperfusion injury in Sprague-Dawley rats. *Am J Chin Med* 2010, 38(1):51-64
- Tang W, Eisenbrand G. *Handbook of Chinese Medicinal Plants, Chemistry, Pharmacology, Toxicology*. Vol. 2 Wiley-VCH Verlag, Weinheim 2011, 811-826
- The Society of Japanese Pharmacopoeia. Peony Root. *The pharmacopoeia of Japan XVI*. Tokyo 2011, 1704-1705
- Timmermans MW, Pentinga SE, Rustemeyer T Bruynzeel DP. Contact dermatitis due to *Paeonia* (peony): a rare sensitizer? *Contact dermatitis* 2009, 60(4):232-233
- Tsuboi H, Hossain K, Akhand AA, Takeda K, Du J, Rifa'i M, et al. Paeoniflorin induces apoptosis of lymphocytes through a redox-linked mechanism. *J Cell Biochem* 2004, 93(1):162-172
- Tsuda T, Sugaya A, Ohguchi H, Kishida N, Sugaya E. Protective effects of peony root extract and its components on neuron damage in the hippocampus induced by the cobalt focus epilepsy model. *Exp Neurol* 1997, 146(2):518-525
- Wang C, Yuan J, Yang ZY, Nie XX, Song LH, Wei W. Pharmacokinetics of paeoniflorin microemulsion after repeated dosing in rats with adjuvant arthritis. *Pharmazie* 2012, 67(12):997-1001
- Wang CH, Wang R, Cheng XM, He YQ, Wang ZT, Wu C, et al. Comparative pharmacokinetic study of paeoniflorin after oral administration of decoction of *Radix Paeoniae Rubra* and *Radix Paeoniae Alba* in rats. *J Ethnopharmacol* 2008, 117(3):467-472
- Wang H, Wei W, Wang NP, Wu CY, Yan SX, Yue L, et al. Effects of total glucosides of peony on immunological hepatic fibrosis in rats. *World J Gastroenterol* 2005, 11(14):2124-2129
- Wang R, Xiong AZ, Teng ZQ, Yang QW, Shi YH, Yang L. *Radix Paeoniae Rubra* and *Radix Paeoniae Alba* attenuate CCl₄-induced acute liver injury: An ultra-performance liquid chromatography-mass spectrometry (UPLC-MS) based metabolomic approach for the pharmacodynamic study of traditional chinese medicines (TCMs). *Int J Mol Sci* 2012, 13(11):14634-14647

Wang Y, Xing HY. [Clinical observation on effect of total glucosides of paeony combined with methotrexate on rheumatoid arthritis]. *Chinese journal of integrated traditional and Western medicine* 2007, 27(9):839-840 [Chinese]

Wang YN, Zhang Y, Wang Y, Zhu DX, Xu LQ, Fang H, et al. The beneficial effect of total glucosides of paeony on psoriatic arthritis links to circulating Tregs and Th1 cell function. *Phytother Res* 2014, 28(3):372-381

Wang ZJ, Wan JM, Chen MZ, Xiu SY. Effect of TGP on functions of monocytes and lymphocytes both in normal human and RA patients. *Chinese Pharmacological Bulletin* 1994, 10(3):197-203

Ward T. Safety Concerns Involving Chinese Herbal Medicine. In Mills S, Bone K, editors. *The Essential Guide to Herbal Safety*. Elsevier Churchill Livingstone, Philadelphia 2005, 119-120

Washida K, Itoh Y, Iwashita T, Nomoto K. Androgen modulators from the roots of *Paeonia lactiflora* (paeoniae radix) grown and processed in nara prefecture, Japan. *Chemical & pharmaceutical bulletin* 2009, 57(9):971-974

Wei CC, You FT, Mei LY, Jian S, Qiang CY. Total glucosides of paeony prevents juxta-articular bone loss in experimental arthritis. *BMC Complement Altern Med* 2013, 13:1472-6882

WHO Monographs on Selected Medicinal Plants. Vol 1. Peony. World Health Organization. Geneva 1999

Wu D, Chen J, Zhu H, Xiong XG, Liang QH, Zhang Y, et al. UPLC-PDA determination of paeoniflorin in rat plasma following the oral administration of *Radix Paeoniae Alba* and its effects on rats with collagen-induced arthritis. *Exp Ther Med* 2014, 7(1):209-217

Wu Y, Ren K, Liang C, Yuan L, Qi X, Dong J, et al. Renoprotective effect of total glucosides of paeony (TGP) and its mechanism in experimental diabetes. *J Pharmacol Sci* 2009, 109(1):78-87

Xiao L, Wang YZ, Liu J, Luo XT, Yang Ye, Zhu XZ. Effects of paeoniflorin on the cerebral infarction, behavioral and cognitive impairments at the chronic stage of transient middle cerebral artery occlusion in rats. *Life Sci* 2005, 78(4):413-420

Xu HM, Wei W, Jia XY, Chang Y, Zhang L. Effects and mechanisms of total glucosides of paeony on adjuvant arthritis in rats. *J Ethnopharmacol* 2007, 109(3):442-448

Xu HY, Chen ZW, Wu YM. Antitumor activity of total paeony glycoside against human chronic myelocytic leukemia K562 cell lines in vitro and in vivo. *Medical oncology* 2012, 29(2):1137-1147

Xu W, Zhong W, Liu J, Liu H, Zhu B. Study on anti-tumor effect of total glycosides from *Radix paeoniae rubra* in S180 tumor-bearing mice. *African journal of traditional, complementary, and alternative medicines: AJTCAM / African Networks on Ethnomedicines* 2013, 10(3):580-585

Yang DQ, You LP, Song PH, Zhang LX, Bai YP. A randomized controlled trial comparing total glucosides of paeony capsule and compound glycyrrhizin tablet for alopecia areata. *Chin J Integr Med* 2012, 18(8):621-625

Yang HO, Ko WK, Kim JY, Ro HS. Paeoniflorin: an antihyperlipidemic agent from *Paeonia lactiflora*. *Fitoterapia* 2004, 75(1):45-49

Yang J, Wang J, Feng P, Li Y, Ma C, Xu S. [Protective effect of total paeony glycoside against cerebral ischemia-reperfusion injury in mice]. *Journal of Chinese medicinal materials* 2000a, 23(2):95-97 [Chinese]

- Yang J, Wang J, Liu C. Protective effects of total paeony glycoside on cerebral ischemia mice. *Journal of Chinese medicinal materials* 2001, 24(2):124-126
- Yang J, Wang J, Zhang J-X, Jiang W, Ma C-G, Xu S-Y. Improvement effects of total paeony glycoside on ability of learning and memory in model mice induced by drugs. *Chinese Pharmacological Bulletin* 2000b, 16(1):46-49
- Yang L, Chow YI, Zhu Y. The comparative study on bioactivities of radix paeoniae alba and radix paeoniae Rubra. *Planta Medica* 2013, 79(10)
- Ye J, Duan H, Yang X, Yan W, Zheng X. Anti-thrombosis effect of paeoniflorin: evaluated in a photochemical reaction thrombosis model in vivo. *Planta Med* 2001, 67(8):766-767
- Yu YB, Jeong IY, Park HR, Oh H, Jung U, Jo SK. Toxicological safety and stability of the components of an irradiated Korean medical herb, Paeoniae Radix. *Radiation Physics and Chemistry* 2004, 71(1-2):117-121
- Zhang AP, Chen MZ, Xu SY. Effects of total glucosides of paeony on sleep-waking rhythm in rats. *Chinese Pharmacological Bulletin* 1993, 9(6):454-457
- Zhang CQ, Wu XX, Wu YG, Xu XX, Zhang W, Wang K. Effect of total glucosides of paeony on TLR signal pathway in the kidney from diabetic rats. *Chinese Pharmacological Bulletin* 2014, 30(3):354-359
- Zhang F, Xia ZY, Ouyang JP. Protective effects of pretreatment of Radix Paeoniae Rubra on the acute lung injury induced by intestinal ischemia/reperfusion in rats. *Chinese Journal of Clinical Rehabilitation* 2005, 9(34):119-121
- Zhang HF, Hou P, Xiao WG. [Clinical observation on effect of total glucosides of paeony in treating patients with non-systemic involved Sjögren syndrome]. *Chinese journal of integrated traditional and Western medicine* 2007, 27(7):596-598 [Chinese]
- Zhang HF, Xiao WG, Hou P. [Clinical study of total glucosides of paeony in patients with systemic lupus erythematosus]. *Chinese journal of integrated traditional and Western medicine* 2011, 31(4):476-479 [Chinese]
- Zhang JJ, Li W, Wang LL, Huang YF, Wang C, Wang JX, et al. Varieties, functions and clinical applications of Chishao and Baishao: a literature review. *China journal of Chinese materia medica* 2013a, 38(20):3595-3601
- Zhang JJ, Huang YF, Wang LL, Li W, Wang JX, Wang C, et al. Comparative study on effects of blood enriching on mouse model of blood deficiency syndrome induced by compound method of bleeding, starved feeding and exhausting of Paeoniae Radix Alba and Paeoniae Radix Rubra, paeoniflorin and albiflorin. *China journal of Chinese materia medica* 2013b, 38(19):3358-3362
- Zhang M, Zhu DZ, Li ZS, Zhan XB. Red peony root decoction in treatment of severe acute pancreatitis: a randomized controlled trial. *Journal of Chinese integrative medicine* 2008, 6(6):569-575
- Zhang P, Zhang JJ, Su J, Qi XM, Wu YG, Shen JJ. Effect of total glucosides of paeony on the expression of nephrin in the kidneys from diabetic rats. *Am J Chin Med* 2009, 37(2):295-307
- Zhang W, Dai SM. Mechanisms involved in the therapeutic effects of Paeonia lactiflora Pallas in rheumatoid arthritis. *Int Immunopharmacol* 2012, 14(1):27-31
- Zhang XJ, Chen HL, Li Z, Zhang HQ, Xu HX, Sung JJ, et al. Analgesic effect of paeoniflorin in rats with neonatal maternal separation-induced visceral hyperalgesia is mediated through adenosine A(1) receptor by inhibiting the extracellular signal-regulated protein kinase (ERK) pathway. *Pharmacol Biochem Behav* 2009, 94(1):88-97

- Zhao M, Liang GP, Tang MN, Luo SY, Zhang J, Cheng WJ, et al. Total glucosides of paeony induces regulatory CD4(+)CD25(+) T cells by increasing Foxp3 demethylation in lupus CD4(+) T cells. *Clin Immunol* 2012, 143(2):180-187
- Zhao YX, Liu Y. [Clinical observation on effects of leflunomid and total glucosides of paeony on rheumatoid arthritis]. *Chinese journal of integrated traditional and Western medicine* 2006, 26(4):355-357 [Chinese]
- Zheng LY, Pan JQ, Lv JH. [Effects of total glucosides of paeony on enhancing insulin sensitivity and antagonizing nonalcoholic fatty liver in rats]. *China journal of Chinese materia medica* 2008, 33(20):2385-2390 [Chinese]
- Zheng YQ, Wei W. Total glucosides of paeony suppresses adjuvant arthritis in rats and intervenes cytokine-signaling between different types of synoviocytes. *Int Immunopharmacol* 2005, 5(10):1560-1573
- Zheng YQ, Wei W, Zhu L, Liu JX. Effects and mechanisms of Paeoniflorin, a bioactive glucoside from paeony root, on adjuvant arthritis in rats. *Inflamm Res* 2007, 56(5):182-188
- Zhou Y, Wang H, Li YS, Tao YW, Zhang JY, Zhang ZQ. [Paeoniflorin increases beta-defensin expression and attenuates lesion in the colonic mucosa from mice with oxazolone-induced colitis]. *Acta pharmaceutica Sinica* 2010, 45(1):37-42 [Chinese]
- Zhu HM, Zhu BD. Experimental study on preventive effect of Radix Paeoniae Rubra to restenosis after carotid balloon injury in high fat-diet rabbits. *Chinese journal of integrated traditional and Western medicine* 2004, 24(6):538-540
- Zhu L, Wei W, Zheng YQ. [Effect and mechanism of action of total glucosides of paeony on synoviocytes from rats with collagen-induced arthritis]. *Acta pharmaceutica Sinica* 2006, 41(2):166-170 [Chinese]
- Zhu L, Wei W, Zheng YQ, Jia XY. Effects and mechanisms of total glucosides of paeony on joint damage in rat collagen-induced arthritis. *Inflamm Res* 2005, 54(5):211-220
- Zhu Y, Chow Y, Wu J, Zhang X, Yang L. Comparison of chemical components between Baishao and Chishao water extracts and their effects on proliferation of rat thoracic aorta smooth muscle cells. *Journal of Southern Medical University* 2013, 33(10):1453-1457