



European Medicines Agency
Evaluation of Medicines for Human Use

London, 12 November 2009
Doc. Ref.: EMA/HMPC/101620/2008

COMMITTEE ON HERBAL MEDICINAL PRODUCTS (HMPC)

FINAL

LIST OF REFERENCES SUPPORTING THE ASSESSMENT REPORT ON:

**Hyperici herba
Hypericum perforatum L., herba
(St. John's wort)**

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.

Agostinis, P., Vantieghem, A., Merlevede, W., de Witte P.A.M. Hypericin in cancer treatment: more light on the way. *Int. J. Biochem. Cell Biol.* **34**, 221-241. 2002

Alscher, DM., Klotz, U. Drug interaction of herbal tea containing St. John's wort with cyclosporine. *Transpl Int.* **16**, 543-544. 2003

Andelic, S. Bigeminy – a result fo digoxin and St. John's wort interaction. *Vojnosanit Pregl.* **60**, 361-364. 2003

Anghelescu, I.G., Kohnen, R., Szegedi, A., Klement, S., Kieser, M. Comparison of Hypericum extract WS 5570 and paroxetine in ongoing treatment after recovery from an episode of moderate to severe depression: results from a randomized multicenter study. *Pharmacopsychiatry.* **39**, 213-219. 2006

Arold, G., Donath, F., Maurer, A., Diefenbach, K., Bauer, S., Henneicke-von Zepelin, H.H., Friede, M., Roots, I. No relevant interaction with alprazolam, caffeine, tolbutamide and digoxin by treatment with a low-hyperforin St John's wort extract. *Planta Med.* **71**, 331-337. 2005

Auster, F., Schäfer, J. *Arzneipflanzen.* Georg Thieme Verlag, Leipzig, 1958

Axarlis, S., Mentis, A., Demetzos, C., Skaltsounis, A.L., Marselos, M., Malamas, M. Antiviral in vitro activity of Hypericum perforatum extract on the Human Cytomegalovirus (HCMV). *Phytother Res.* **12**, 507-511. 1998

Barnes, J., Anderson, L.A., Phillipson, J.D. *Herbal medicines.* Second Edition. Pharmaceutical Press, London, 2002

Barnes, J., Barber, N., Wheatley, D., Williamson, E.M. A pilot randomised, open, uncontrolled, clinical study of two dosages of St John's wort (*Hypericum perforatum*) herb extract (LI-160) as an aid to motivational/behavioural support in smoking cessation. *Planta Med.* **72**, 378-382. 2006

- Baureithel, K.K., Berger Bütter, K., Engesser, A., Burkard, W., Schaffner, W. Inhibition of benzodiazepine binding in vitro by amentoflavone, a constituent of various species of *Hypericum*. *Phar Acta Helv.* **72**, 153-157. 1997
- Behnke, K., Jensen, G.S., Graubaum, H.J., Gruenwald, J. *Hypericum perforatum* versus fluoxetine in the treatment of mild to moderate depression. *Adv Ther.* **19**, 43-52. 2002
- Bejjamini, V., Andreatini, R. Effects of *Hypericum perforatum* and paroxetine on rat performance in the elevated T-maze. *Pharmacol Res.* **48**, 199-207. 2003
- Benedi, J., Arroyo, R., Romero, C., Martin-Aragon, S., Villar, AM. Antioxidant properties and protective effects of a standardized extract of *Hypericum perforatum* on hydrogen peroxide-induced oxidative damage in PC12 cells. *Life Sci.* **75**, 1263-1276. 2004
- Bergmann, R., Nüßner, J., Demling, J. Behandlung leichter bis mittelschwerer Depressionen. *TW Neurol Psychiatr.* **7**, 235-240. 1993
- Bernd, A., Simon, S., Ramirez Bosca, A., Kippenberger, S., Diaz Alperi, J., Miquel, J., Villalba Garcia, J.F., Pamies Mira, D., Kaufmann R., Phototoxic effects of *Hypericum* extract in cultures of human keratinocytes compared with those of psoralen. *Photochem Photobiol.* **69**, 218-221. 1999
- Biber, A., Fischer, H., Romer, A., Chatterjee, S.S. Oral bioavailability of hyperforin from *Hypericum* extracts in rats and human volunteers. *Pharmacopsychiatry.* **31**, Suppl 1, 36-43. 1998
- Bjerkensted, L., Edman, G.V., Alken, R.G., Mannel, M. *Hypericum* extract LI 160 and fluoxetine in mild to moderate depression: a randomized, placebo-controlled multi-center study in outpatients. *Eur Arch Psychiatry Clin Neurosci.* **255**, 40-47. 2005
- Bjornsson, T.D., Callaghan, J.T., Einolf, H.J., Fischer, V. et al. The conduct of in vitro and in vivo drug-drug interaction studies: A PhRMA perspective. *J Clin Pharmacol.* **43**, 443-469. 2003
- Bladt, S., Wagner, H. Inhibition of MAO by fractions and constituents of *Hypericum* extract. *J Geriatr Psychiatry Neurol.* **7**, Suppl. 1, 57-59. 1994
- Blaschek, W., Ebel, S., Hackenthal, E., Holzgrabe, U., Keller, K., Reichluing, J., Schulz, V. HagerROM. Springer Verlag, Berlin, Heidelberg, 2008
- Böhme, H. Kommentar zum Europäischen Arzneibuch. Wissenschaftliche Verlagsgesellschaft, Stuttgart, 2006
- Böttcher, M., Mück, W., Ochmann, K., Rohde, G., Unger, S., Hindmarch, I. Investigation of the safety, tolerability, pharmacodynamics and pharmacokinetics of Remotiv (*Hypericum* extract Ze 117). *Eur J Clin Pharmacol.* **56**, A10. 2000
- Bonetto, N., Santelli, L., Battistin, L., Cagnin, A. Serotonin syndrome and rhabdomyolysis induced by concomitant use of triptans, fluoxetine and *Hypericum*. *Cephalgia.* **27**, 1421-1423. 2007
- Borges, L.V., do Carmo Cancino, J.C., Peters, V.M., Las Casas, L., de Oliveira Guerra, M. Development of pregnancy in rats treated with *Hypericum perforatum*. *Phytother Res.* **19**, 885-887. 2005
- Bove, G.M. Acute neuropathy after exposure to sun in a patient treated with St John's wort. *Lancet.* **352**, 1121. 1998
- Bracher, A. Johanniskraut 1 x täglich: Wirkung klinisch belegt. *Ärztliche Praxis extra* 51. 2001

- Bradley, P. British Herbal Compendium. Vol 2. British Herbal Medicine Association, 2006
- Brenner, R., Azbel, V., Madhusoodanan, S., Pawlowska, M. Comparison of an extract of *Hypericum* (LI 160) and sertraline in the treatment of depression: a double-blind, randomized pilot study. *Clin Ther.* **22**, 411-419. 2000
- Butterweck, V., Petereit, F., Winterhoff, H., Nahrstedt, A. Solubilized hypericin and pseudohypericin from *Hypericum perforatum* exert antidepressant activity in the forced swimming test. *Planta Med.* **64**, 291-294. 1998
- Butterweck, V., Jurgenliemk, G., Nahrstedt, A., Winterhoff, H. Flavonoids from *Hypericum perforatum* show antidepressant activity in the forced swimming test. *Planta Med.* **66**, 3-6. 2000
- Butterweck, V., Brockens, T., Korte, B., Wittkowski, W., Winterhoff, H. Long-term effects of St. John's wort and hypericin on monoamine levels in rat hypothalamus and hippocampus. *Brain Res.* **930**, 21-9. 2002
- Butterweck, V., Lieflander-Wulf, U., Winterhoff, H., Nahrstedt, A. Plasma levels of hypericin in presence of procyanidin B2 and hyperoside: a pharmacokinetic study in rats. *Planta Med.* **69**, 189-192. 2003
- Butterweck, V., Nahrstedt, A. Was ist bekannt über Johanniskraut? *Phytochemie und Pharmakologie. Pharmazie in unserer Zeit.* **32**, 212. 2003a
- Cada, A.M, Hansen, D.K, Laborde, J.B, Ferguson, S.A. Minimal effects from developmental exposure to St. John's wort (*Hypericum perforatum*) in Sprague-Dawley rats. *Nutr Neurosci.* **4**, 135-141. 2001
- Caelo 2008: personal communication
- Capasso, R., Borrelli, F., Montanaro, V., Altieri, V., Capasso, F., Izzo, AA. Effects of the antidepressant St. John's wort (*Hypericum perforatum*) on rat and human vas deferens contractility. *J Urol.* **173**, 2194-2197. 2005
- Calapai. G., Crupi. A., Firenzuoli. F., Interrera. G., Squadrito. F., Parisi. A., De Sarro. G., Caputi, A. Serotonin, norepinephrine and dopamine involvement in the antidepressant action of *Hypericum perforatum*. *Pharmacopsychiatry.* **34**, 45-49. 2001
- Catania, M.A., Firenzuoli, F., Crupi, A., Mannucci, C., Caputi, A.P., Calapai, G. *Hypericum perforatum* attenuates nicotine withdrawal signs in mice. *Psychopharmacology.* **169**, 186-189. 2003
- Cervo. L., Roizo. M., Ekalle-Soppo. C.B., Guiso. G., Morazzoni. P., Caccia, S. Role of hyperforin in the antidepressant-like activity of *Hypericum perforatum* extracts. *Psychopharmacology.* **164**, 423-428. 2002
- Chan, L.Y.S., Chiu, P.Y., Lau, T.K. A study of hypericin-induced teratogenicity during organogenesis using a whole rat embryo culture model. *Fertility and Sterility.* **76**, 1073-1074. 2001
- Chatterjee. S.S., Bhattacharya. S.K., Wonnemann. M., Singer, A., Müller, W.E. Hyperforin as a possible antidepressant component of *Hypericum* extracts. *Life Sci.* **63**, 499-510. 1998
- Chen, Y., Ferguson, S.S., Negishi, M., Goldstein, J.A. Induction of human CYP2C9 by rifampicin, hyperforin, and Phenobarbital is mediated by the pregnane x receptor. *J Pharmacol Exp Therapeutics.* **308**, 495-501. 2004
- Chung, D.J., Kim, H.Y., Park, K.H., Jeong, K.A., Lee, S.K., Lee, Y.I., Hur, S.E., Cho, M.S., Lee, B.S., Bai, S.W., Kim, C.M., Cho, S.H., Hwang, J.Y., Park, J.H. Black Cohosh and St. John's Wort (GYNO-Plus(R)) for Climacteric Symptoms. *Yonsei Med J.* **48**, 289-294. 2007

- Commission E monographs. The Complete German Commission E Monographs. American Botanical Council, Austin, 1998
- Coskun, I., Tayfun Uzbay, I., Ozturk, N., Ozturk, Y. Attenuation of ethanol withdrawal syndrome by extract of *Hypericum perforatum* in Wistar rats. *Fundam Clin Pharmacol.* **20**, 481-488. 2006
- DAC, Deutscher Arzneimittel Codex. J010 *Hyperici herba*. Deutscher Apotheker-Verlag, Stuttgart, 1991-1999
- De Vry, J., Maurel, S., Schreiber, R., de Beun, R., Jentsch, KR. Comparison of *Hypericum* extracts with imipramine and fluoxetine in animal models of depression and alcoholism. *Eur Neuropsychopharmacol.* **9**, 461-468. 1999
- Demmling, J.H., Müller, J., Zeller, K. Hoch dosierter Johanniskrautextrakt als tägliche Einmalgabe zur Behandlung von Depressionen. *Nervenheilkunde.* **23**, 160-164. 2004
- Dimpfel W. Electropharmacogram from quercetin is similar to that of moclobemide and other antidepressant drugs. *Z Phytother.* **29**, 6. 2008
- Dinamarca, M.C., Cerpa, W., Garrido, J., Hancke, J.L., Inestrosa, N.C. Hyperforin prevents beta-amyloid neurotoxicity and spatial memory impairments by disaggregation of Alzheimer's amyloid-beta-deposits. *Mol Psychiatry.* **11**, 1032-1048. 2006
- Dingermann, T., Hiller, K., Schneider, G., Zündorfer, I. *Schneider Arzneidrogen*. Elsevier, München, 2004
- Dresser, G.K., Schwarz, U.I., Wilkinson, G.R., Kim, R.B. Coordinate induction of both cytochrome P4503A and MDR1 by St. John's wort in healthy subjects. *Clin Pharmacol Ther.* **73**, 41-50. 2003
- Dugoua, J.J., Mill, E., Perri, D., Koren, G. Safety and efficacy of St. John's wort (*Hypericum*) during pregnancy and lactation. *Can J Clin Pharmacol.* **13**, 268-276. 2006
- Duke, J.A. *Handbook of Medicinal Herbs*. CRP Press LLC, 2002
- Eckert, G.P., Muller, W.E. Effects of hyperforin on the fluidity of brain membranes. *Pharmacopsychiatry.* **34**, 22-25. 2001
- Eich-Höchli, D., Oppliger, R., Powell Golay, K., Baumann, P., Eap, CB. Methadone maintenance treatment and St. John's wort – A case report. *Pharmacopsychiatry.* **36**, 35-37. 2003
- El-Sherbiny, D.A., Khalifa, A.E., Attia, A.S., Eldenshary Eel, D. *Hypericum perforatum* extract demonstrates antioxidant properties against elevated rat brain oxidative status induced by amnestic dose of scopolamine. *Pharmacol Biochem Behav.* **76**, 525-533. 2003
- Ergänzungsbuch zum Deutschen Arzneibuch (Erg.-B6). Deutscher Apotheker-Verlag, Berlin, 1941
- ESCOP Monograph. *HYPERICI HERBA* (St. John's Wort). ESCOP Monographs Second edition. ESCOP 2003
- Evans, R.W. Triptans and serotonin syndrome. *Cephalgia.* **28**, 573-575. 2008
- Fava, M., Alpert, J., Nierenberg, A.A., Mischoulon, D., Otto, M.W., Zajecka, J., Murck, H., Rosenbaum, J.F. A Double-blind, randomized trial of St John's wort, fluoxetine, and placebo in major depressive disorder. *J Clin Psychopharmacol.* **25**, 441-447. 2005
- Fegert, J.M., Kölch, M., Zito, J.M., Glaeske, G., Janhsen, K. Antidepressant use in children and adolescents in Germany. *J Child Adolesc Psychopharmacol.* **16**, 197-206. 2006

- Findling, R.L., McNamara, N.K., O’Riordan, M.A., Reed, M.D., Demeter, C.A., Branicky, L.A., Blumer, J.L. An open-label pilot study of St. John's wort in juvenile depression. *J Am Acad Child Adolesc Psychiatry.* **42**, 908-914. 2003
- Fischer, B., Hartwich, C. *Handbuch der pharmazeutischen Praxis.* Verlag Julius Springer, Berlin, 1902
- Fischer, P. Serotonin syndrome in the elderly patient after antidepressive monotherapy. *J Clin Psychopharmacol.* **15**, 440-442. 1995
- Flamm, S., Kroeber, L., Seel, H. *Pharmakodynamik Deutscher Heilpflanzen.* Hippokrates Verlag, Stuttgart, 1940
- Flausino, O.A. Jr., Zangrossi, H.Jr., Salgado, J.V., Viana, M.B. Effects of acute and chronic treatment with *Hypericum perforatum* L. (LI 160) on different anxiety-related responses in rats. *Pharmacol Biochem Behav.* **71**, 251-257. 2002
- Fox, E., Murphy, R.F., McCully, C.L., Adamson, P.C. Plasma pharmacokinetics and cerebrospinal fluid penetration of hypericin in nonhuman primates. *Cancer Chemother Pharmacol.* **47**, 41-44. 2001
- Frerichs, G., Arends, G., Zörnig, H. *Handbuch der pharmazeutischen Praxis.* Verlag Julius Springer, Berlin, 1938
- Friede, M., Hasenfuss, I., Wüstenberg, P. Alltagssicherheit eines pflanzlichen Antidepressivums aus Johanniskraut. *Fortschr Medizin.* **116**, 131-135. 1998
- Friede, M., Henneicke von Zepelin, H.H., Freudenstein, J. Differential therapy of mild to moderate depressive episodes (ICD-10 F 32.0; F 32.1) with St. John’s wort. *Pharmacopsychiatry.* **34**, 38-41. 2001
- Froestl, B., Steiner, B., Muller, W.E. Enhancement of proteolytic processing of the beta-amyloid precursor protein by hyperforin. *Biochem Pharmacol.* **66**, 2177-2184. 2003
- Gastpar, M., Singer, A., Zeller, K. Efficacy and tolerability of *Hypericum* extract STW3 in long-term treatment with a once-daily dosage in comparison with sertraline. *Pharmacopsychiatry.* **38**, 78-86. 2005
- Gastpar, M., Singer, A., Zeller, K. Comparative efficacy and safety of a once-daily dosage of *Hypericum* extract STW3-VI and citalopram in patients with moderate depression: a double-blind, randomised, multicentre, placebo-controlled study. *Pharmacopsychiatry.* **39**, 66-75. 2006
- Genovese, T., Mazzon, E., Di Paola, R., Muia, C., Crisafulli, C., Menegazzi, M., Malleo, G., Suzuki, H., Cuzzocrea, S. *Hypericum perforatum* attenuates the development of cerulein-induced acute pancreatitis in mice. *Shock.* **25**, 161-167. 2006
- Genovese, T., Mazzon, E., Menegazzi, M., Di Paola, R., Muia, C., Crisafulli, C., Bramanti, P., Suzuki, H., Cuzzocrea, S. Neuroprotection and enhanced recovery with *Hypericum perforatum* extract after experimental spinal cord injury in mice. *Shock.* **25**, 608-617. 2006a
- Gerlach, S. *Hypericum.* PhD Thesis, University Vienna, 2008
- Gibbons, S., Ohlendorf, B., Johnsen, I. The genus *Hypericum* – a valuable resource of anti-Staphylococcal leads. *Fitoterapia.* **73**, 300-304. 2002
- Girzu, M., Carnat, A., Privat, A.M., Fialip, J., Carnat, A.P., Lamaison, J.L. Sedative activity in mice of a hydroalcohol extract of *Hypericum perforatum*. *Phytother Res.* **11**, 395-397. 1997
- Gobbi, M., Moia, M., Pirona, L., Morizzoni, P., Minnini, T. In vitro binding studies with two *Hypericum perforatum* extracts – hyperforin, hypericin and biapigenin-on 5-HT₆, 5-HT₇,

- GABA(A)/benzodiazepine, sigma, NPY-Y1/Y2 receptors and dopamine transporters. *Pharmacopsychiatry*. **34**, Suppl. 1, 45-48. 2001
- Gonzalez, C.L., Christensen, H.D., Rayburn, W.F., Coleman, F.H. Impact of antenatal Hypericum (St. John's wort) exposure on cognition in mice. *Neurobehavioral Teratology Societys abstracts*. 328. 1999
- Gordon, J.B. SSRIs and St. John's wort: possible toxicity? *Am Acad Fam Physician*. **57**, 950. 1998
- Greeson, J.M., Sanford, B., Monti, D.A. St. John's wort (*Hypericum perforatum*): a review of the current pharmacological, toxicological, and clinical literature. *Psychopharmacology*. **153**, 402-414. 2001
- Gregoretti, B., Stebel, M., Candussio, L., Crivellato, E., Bartoli, F., Decorti, G. Toxicity of *Hypericum perforatum* (St. John's wort) administered during pregnancy and lactation in rats. *Toxicol Appl Pharmacol*. **200**, 201-205. 2004
- Grube, B., Grünwald, J., Walper, A., Hopfenmüller, W. Johanniskraut bei leichten temporären Verstimmungen. *Naturamed*. **11**, 21-27. 1996
- Grube, B., Walper, A., Wheatley, D. St. John's Wort extract: efficacy for menopausal symptoms of psychological origin. *Adv Ther*. **16**, 177-186. 1999
- Gruenwald, J., Brendler, T., Jaenicke, C. PDR for Herbal Medicines. Medical Economics Company, Montvale, 1998
- Gruenwald, J., Brendler, T., Jaenicke, C. PDR for Herbal Medicines. Medical Economics Company, Montvale, 2004
- Grundmann, O., Kelber, O., Butterweck, V. Effects of St. John's wort extract and single constituents on stress-induced hyperthermia in mice. *Planta Med*. **72**, 1366-1371. 2006
- Grush, L.R., Nierenberg, A., Keefe, B., Cohen, L.S. St. John's wort during pregnancy. *JAMA*. **280**, 1566. 1998
- Gryzlak, B.M., Wallace, R.B., Zimmermann, M.B., Nisly, N.L. National surveillance of herbal dietary supplements exposures: the poison control center experience. *Pharmacoepidemiol Drug Saf*. **16**, 947-957. 2007
- Gutmann, H., Poller, B., Berger Büter, K., Pfrunder, A., Schaffner, W., Drewe, J. *Hypericum perforatum*: which constituents may induce intestinal MDR1 and CYP3A4 mRNA expression? *Planta Med*. **72**, 685-690: 2006
- Häberlein, H., Prenner, L., Zeller, K. Einfluss von Hyperosid und Hyperforin auf die Regulation und laterale Mobilität von beta1-adrenergen Rezeptoren an lebenden C6-Glioblastomzellen: ein postsynaptischer Ansatz zum Wirkmechanismus von Johanniskraut. *Z Phytother*. **29**, S8, 2008
- Hager, H. Hager's Handbuch der pharmazeutischen Praxis. Verlag Julius Springer, Berlin, 1878
- Hall, S.D., Wang, Z., Huang, S.M., Hamman, M.A., Vasavada, N., Adigun, A.Q., Hilligoss, J.K., Miller, M., Gorski, J.C. The interaction between ST. John's wort and an oral contraceptive. *Clin Pharmacol Ther*. **74**, 525-535. 2003
- Hamacher, H., Wahl, M.A. Selbstmedikation. 10. Ergänzungslieferung, Deutscher Apotheker Verlag Stuttgart, 2006
- Hamacher, H., Wahl, M.A. Selbstmedikation. 8. Ergänzungslieferung, Deutscher Apotheker Verlag Stuttgart, 2001

- Hamacher, H., Wahl, M.A. Selbstmedikation. 9. Ergänzungslieferung, Deutscher Apotheker Verlag Stuttgart, 2003
- Hammerness, P., Basch, E., Ulbricht, C., Barrette, E.P., Foppa, I., Basch, S., Bent, S., Boon, H., Ernst, E. St. John's wort: A systematic review of adverse effects and drug interactions for the consultation psychiatrist. *Psychosomatics*. **44**, 271-282. 2003
- Hänsel, R., Keller, K., Rimpler, H., Schneider, G. Drogen E-O. Springer Verlag, Berlin, 1993
- Hänsel, R., Sticher, O. Pharmakognosie – Phytopharmazie. Springer Medizin Verlag, Heidelberg, 2007
- Hängsen, K.D., Vesper, J., Ploch, M. Multicenter double-blind study examining the antidepressant effectiveness of the Hypericum extract LI 160. *J Geriatr Psychiatr Neurol*. **7**, S15-S18. 1994
- Hängsen, K.D., Vesper, J. Antidepressive Wirksamkeit eines hochdosierten Hypericum-Extrakts. *Münchener Medizinische Wochenschrift*. **138**, 29-33. 1996
- Harrer, G., Hübner W.D., Podzuweit H. Effectiveness and tolerance of the Hypericum extract LI 160 compared to maprotiline: a multicenter double-blind study. *J Geriatr Psychiatr Neurol*. **7**, 24-28. 1994
- Harrer, G., Sohmidt, K., Kuhn, K., Biller, A. Comparison of equivalence between the St. John's wort extract LoHyp-57 and fluoxetine. *Arzneim-Forsch/Drug Res*. **49**, 289-296. 1999
- He, Y.Y., Chignell, C.F., Miller, D.S., Andley, U.P., Roberts, J.E. Phototoxicity in human lens epithelial cells promoted by St. John's Wort. *Photochem Photobiol*. **80**, 583-586. 2004
- Heinrich, M., Barnes, J., Gibbons, S., Williamson, E. Fundamentals of Pharmacognosy and Phytotherapy. Elsevier Science Limited, 2004
- Henderson, L., Yue, Q.Y., Bergquist, C., Gerden, B., Arlett, P. St John's wort (Hypericum perforatum): Drug interactions and clinical outcomes. *Br J Clin Pharmacol*. **54**, 349-356. 2002
- Herberg, K.W. Alternative zu synthetischen Psychopharmaka? *Therapiewoche*. **44**, 704-713. 1994
- Hicks, S.M., Walker, A.F., Gallagher, J., Middleton, R.W., Wright, J. The significance of "nonsignificance" in randomized controlled studies: a discussion inspired by a double-blinded study on St. John's wort (Hypericum perforatum L.) for premenstrual symptoms. *J Altern Complement Med*. **10**, 925-932. 2004
- Hoffmann, J., Kühl, E.D. Therapie von depressiven Zuständen mit Hypericum. *Ztschr Allgmed*. **55**, 776-782. 1979
- Hübner, W.D., Kirste, T. Experience with St John's Wort (Hypericum perforatum) in children under 12 years with symptoms of depression and psychovegetative disturbances. *Phytother Res*. **15**, 367-370. 2001
- Hunt, E.J., Lester, C.E., Lester, E.A., Tackett, R.L. Effect of St. John's wort on free radical production. *Life Sci*. **69**, 181-190. 2001
- Hypericum Depression Trial Study Group. Effect of Hypericum perforatum (St John's wort) in major depressive disorder: a randomized controlled trial. *JAMA*. **287**, 1807-1814. 2002
- Imai, H., Kotegawa, T., Tsutsumi, K., Morimoto, T., Eshima, N., Nakan, S., Ohashi, K. The recovery time-course of CYP3A after induction by St John's wort administration. *Br J Clin Pharmacol*. **65**, 701-707. 2008
- Irion, H. Drogisten-Lexikon. Springer Verlag, Berlin/Göttingen/Heidelberg, 1955

- Ivetic, V., Popovic, M., Mimica-Dukic, N., Barak, O., Pilija, V. St. John's wort (*Hypericum perforatum* L.) and kindling epilepsy in rabbit. *Phytomedicine*. **9**, 496-499. 2002
- Izzo, A.A., Ernst, E. Interactions between herbal medicines and prescribed drugs. An updated systematic review. *Drugs*. **69**, 1777-1798. 2009
- Jang, M.H., Lee, T.H., Shin, M.C., Bahn, G.H., Kim, J.W., Shin, D.H., Kim, E.H., Kim, C.J. Protective effect of *Hypericum perforatum* Linn (St. John's wort) against hydrogen peroxide-induced apoptosis on human neuroblastoma cells. *Neurosci Lett*. **329**, 177-180. 2002
- Johne, A., Brockmüller, J., Bauer, S., Maurer, A., Langheinrich, M., Roots, I. Pharmacokinetic interaction of digoxin with an herbal extract from St. John's wort. *Clin Pharmacol Ther*. **66**, 338-345. 1999
- Johne, A., Brockmüller, J., Bauer S., Mai, I., Schneider, J, Lenzen-Grossimlinghaus, R., Roots, I. St. John's wort extract and liver cirrhosis. *Clin Pharmacol Therap*. **71**, P95. 2002
- Johne, A., Perloff, E.S., Bauer, S., Schmider, J., Mai, I., Brockmoller, J., Roots, I. Impact of cytochrome P-450 inhibition by cimetidine and induction by carbamazepine on the kinetics of hypericin and pseudohypericin in healthy volunteers. *Eur J Clin Pharmacol*. **60**, 617-622. 2004
- Johnson, D., Siebenhüner, G., Hofer, E., Sauerwein-Giese, E., Frauendorf, A. Einfluss von Johanniskraut auf die ZNS-Aktivität. *TW Neurol Psychiatr*. **6**, 436-444. 1992
- Juergenliemk, G., Boje, K., Huewel, S., Lohmann, C., Galla, H.J., Nahrstedt, A. In vitro studies indicate that miquelianin (quercetin 3-O-beta-D-glucuronopyranoside) is able to reach the CNS from the small intestine. *Planta Med*. **69**, 1013-1017. 2003
- Kalb, R., Trautmann-Sponsel, R.D., Kieser, M. Efficacy and tolerability of *Hypericum* extract WS 5572 versus placebo in mildly to moderately depressed patients. A randomized double-blind multicenter clinical trial. *Pharmacopsychiatry*. **34**, 96-103. 2001
- Kaltschmidt, B., Heinrich, M., Kaltschmidt, C. Stimulus-dependent activation of NF-kappaB specifies apoptosis or neuroprotection in cerebellar granule cells. *Neuromolecular Med*. **2**, 299-309. 2002
- Kamuhabwa, A.R., Augustijns, P., de Witte, PA. In vitro transport and uptake of protohypericin and hypericin in the Caco-2 model. *Int J Pharm*. **188**, 81-86. 1999
- Karalapillai, D.C., Bellomo, R. Convulsions associated with an overdose of St. John's wort. *Med J Austr*. **186**, 213-214. 2007
- Kasper, S., Anghelescu, I.G., Szegedi, A., Dienel, A., Kieser, M. Superior efficacy of St John's wort extract WS 5570 compared to placebo in patients with major depression: a randomized, double-blind, placebo-controlled, multi-center trial. *BMC Med*. **4**, 14. 2006
- Kasper, S., Anghelescu, I.G., Szegedi, A., Dienel, A., Kieser, M. Placebo controlled continuation treatment with *Hypericum* extract WS 5570 after recovery from a mild to moderate depressive episode *Wien Med Wochenschr*. **15**, 13-14. 2007
- Kasper, S., Volz, H.P., Moller, H.J., Dienel, A. Kieser, M. Continuation and long-term maintenance treatment with *Hypericum* extract WS 5570 after recovery from an acute episode of moderate depression – A double-blind, randomized, placebo controlled long-term trial. *Eur Neuropsychopharmacol*. **18**, 803-813. 2008
- Kaye, A.D., Clarke, R.C., Sabar, R., Vig, S., Dhawan, K.P., Hofbauer, R., Kaye, AM. Herbal medicines: current trends in anaesthesiology practice – a hospital survey. *J Clin Anesthesia*. **12**, 468-471. 2000

- Khalifa, A.E. Hypericum perforatum as a nootropic drug: enhancement of retrieval memory of a passive avoidance conditioning paradigm in mice. *J Ethnopharmacol.* **76**, 49-57. 2001
- Kientsch. U., Burgi. S., Ruedeberg. C., Probst. S., Honegger, U.E. St. John's wort extract Ze 117 (Hypericum perforatum) inhibits norepinephrine and serotonin uptake into rat brain slices and reduces 3-adrenoceptor numbers on cultured rat brain cells. *Pharmacopsychiatry.* **34**, Suppl 1, 56-60. 2001
- Klier, C.M., Schäfer, M.R., Schmid-Siegel, B., Lenz, G., Mannel, M. St. John's wort (Hypericum perforatum) – is it safe during breastfeeding? *Pharmacopsychiatry.* **35**, 29-30. 2002
- Klier, C.M., Schmid-Siegel, B., Schafer, M.R., Lenz, G., Saria, A., Lee, A., Zernig, G. St. John's wort (Hypericum perforatum) and breastfeeding: plasma and breast milk concentrations of hyperforin for 5 mothers and 2 infants. *J Clin Psychiatry.* **67**, 305-309. 2006
- Klusa, V., Germane, S., Nöldner, M., Chatterjee, SS. Hypericum extract and hyperforin: memory-enhancing properties in rodents. *Pharmacopsychiatry.* **34**, 61-69. 2001
- Köppel, H., Naser, B., Schulz, H.U., Kibbel, T., Schürer, M., Liske, E. Investigation of the effect on phytosensitivity following repeated oral dosing of Hypericum extract in 20 healthy male and female volunteers. *Kongressband Phytopharmaka Phytotherapie.* 26. 2008
- Kumar, V., Jaiswal, A.K., Singh, P.N., Bhattacharya, S.K. Anxiolytic activity of Indian Hypericum perforatum Linn: an experimental study. *Indian J Exp Biol.* **38**, 36-41. 2000
- Kumar, V., Khanna, V.K., Seth, P.K., Singh, P.N., Bhattacharya, S.K. Brain neurotransmitter receptor binding and nootropic studies on Indian Hypericum perforatum Linn. *Phytother Res.* **16**, 210-216. 2002
- Kumar, V., Singh, P.N., Muruganandam, A.V., Bhattacharya, S.K. Effect of Indian Hypericum perforatum Linn on animal models of cognitive dysfunction. *J Ethnopharmacol.* **72**, 119-128. 2000
- Laakmann, G., Schule, C., Baghai, T., Kieser, M. St. John's wort in mild to moderate depression: the relevance of hyperforin for the clinical efficacy. *Pharmacopsychiatry.* **31**, 54-59. 1998
- Laggner, H., Schreier, S., Hermann, M., Exner, M., Muhl, A., Gmeiner, B.M., Kapiotis, S. The main components of St John's Wort inhibit low-density lipoprotein atherogenic modification: a beneficial "side effect" of an OTC antidepressant drug? *Free Radic Res.* **41**, 234-241. 2007
- Länger, R., Kubelka, W., *Phytokodex.* Krause & Pachernegg GmbH, Gablitz, 2001
- Lantz, M.S., Buchalter, E., Giambanco, V. St. John's wort and antidepressant drug interactions in the elderly. *J Geriatr Psychiatry Neurol.* **12**, 7-10. 1999
- Larkin, M. Surgery patients at risk for herb-anaesthesia interactions. *The Lancet.* **354**, 1362. 1999
- Larkin, M. Safe use of herbal products before surgery proposed. *The Lancet.* **358**, 128. 2001
- Lavie, G., Mazur, Y., Lavie, D., Meruelo, D. The chemical and biological properties of hypericin – a compound with a broad spectrum of biological activities. *Med Res Rev.* **15**, 111-119. 1995
- Lecrubier, Y., Clerc, G., Didi, R., Kieser, M. Efficacy of St. John's wort extract WS 5570 in major depression: a double-blind, placebo-controlled trial. *Am J Psychiatry.* **159**, 1361-1366. 2002
- Lee, A., Minhas, R., Matsuda, N., Lam, M., Ito, S. The safety of St. John's wort (Hypericum perforatum) during breastfeeding. *J Clin Psychiatry.* **64**, 966-968. 2003

- Lemmer, W., von den Driesch, V., Klieser, E. Johanniskraut-Spezialextrakt WS 5572 bei leichter bis mittelschwerer Depression. *Fortschr Medizin*. **117**, 143-154. 1999
- Lenoir, S., Degenring, F.H., Saller, R. A double-blind randomised trial to investigate three different concentrations of a standardised fresh plant extract obtained from the shoot tips of *Hypericum perforatum* L. *Phytomedicine*. **6**, 141-146. 1999
- Leuschner, J. Preclinical toxicological profile of *Hypericum* extract LI 160. Abstracts of the 2nd International Conference on Phytomedicine, Munich. SL 80, 1996
- L'homme, R.F.A., Dijkema, T., van der Ven, A.J.A.M., Burger, DM. Enzyme inducers reduce elimination half-life after a single dose of nevirapine in healthy women. *J Acquir Immune Defic Syndr*. **43**, 193-196. 2006
- Linde, K., Berner, M., Egger, M., Mulrow, C. St John's wort for depression: meta-analysis of randomised controlled trials. *Br J Psychiatry*. **186**, 99-107. 2005
- Linde, K. Johanniskraut bei Depression – eine Übersicht der randomisierten Studien bezogen auf einzelne Extrakte. http://www.phytotherapie-komitee.de/Forschung/kfn_hyperic_281206.pdf, 2007
- Linde, K., Berner, M.M., Kriston, L. St. John's wort for major depression (review). *Cochrane Database of Syst Rev* 2008, 4: Art. No. CD000448, DOI: 10.1002/14651858. CD 000448. pub3. 2008
- List, P.H., Hörhammer, L. Hager's Handbuch der pharmazeutischen Praxis. Springer Verlag, Berlin/Heidelberg, 1976
- Lu, Y.H., Du, C.B., Liu, J.W., Hong, W., Wei, DZ. Neuroprotective effects of *Hypericum perforatum* on trauma induced by hydrogen peroxide in PC12 cells. *Am J Chin Med*. **32**, 397-405. 2004
- Lundahl, A., Hedeland, M., Bondesson, U., Knutson, L., Lennernäs, H. The effect of St. John's wort on the pharmacokinetics, metabolism and biliary excretion of finasteride and its metabolites in healthy men. *Eur J Pharm Sci*. **36**, 433-443. 2009
- Madabushi, R., Frank, B., Drewelow, B., Derendorf, H., Butterweck, V. Hyperforin in St. John's wort drug interactions. *Eur J Clin Pharmacol*. **62**, 225-233. 2006
- Madaus, G. Lehrbuch der biologischen Heilmittel. Band II. Georg Thieme Verlag, Leipzig, 1938
- Mai, I., Bauer, S., Perloff, E.S., Johne, A., Uehleke, B., Frank, B., Budde, K., Roots, I. Hyperforin content determines the magnitude of the St. John's wort – cyclosporine drug interaction. *Clin Pharmacol Ther*. **76**, 330-340. 2004
- Maisenbacher, P., Kovar, KA. Analysis and stability of *Hyperici oleum*. *Planta Med*. **58**, 351-354. 1992
- Mannel, M. Drug interactions with St John's wort : mechanisms and clinical implications. *Drug Saf*. **27**, 773-797. 2004
- Mannucci, C., Pieratti, A., Firenzuoli, F., Caputi, A.P., Calapai, G. Serotonin mediates beneficial effects of *Hypericum perforatum* on nicotine withdrawal signs. *Phytomedicine*. **14**, 645-651. 2007
- Martindale. The complete drug references. Pharmaceutical Press, London, 2002
- Meier, B. Vergleichbarkeit von Phytopharmaka am Beispiel von Johanniskraut. In: Loew, D., Blume, H., Dingermann Th. *Phytopharmaka V*, Steinkopff, Darmstadt, 1999
- Mills, E., Montori, V.M., Wu, P., Gallicano, K., Clarke, M., Guyatt, G. Interaction of St John's wort with conventional drugs: systematic review of clinical trials. *BMJ*. **329**, 23-30. 2004

- Misane, I., Ogren, S.O. Effects of *Hypericum perforatum* (St. John's wort) on passive avoidance in the rat: evaluation of potential neurochemical mechanisms underlying its antidepressant activity. *Pharmacopsychiatry*. **34**, Suppl 1, 89-97. 2001
- Mohanasundari, M., Sabesan, M. Modulating effect of *Hypericum perforatum* extract on astrocytes in MPTP induced Parkinson's disease in mice. *Eur Rev Med Pharmacol Sci*. **11**, 17-20. 2007
- Mohanasundari, M., Srinivasan, M.S., Sethuopathy, S., Sabesan, M. Enhanced neuroprotective effect by combination of bromocriptine and *Hypericum perforatum* extract against MPTP-induced neurotoxicity in mice. *J Neurol Sci*. **249**, 140-144. 2006
- Montgomery, S.A., Hübner, W.D., Grigoleit, H.G. Efficacy and tolerability of St. John's wort extract compared with placebo in patients with mild to moderate depressive disorder. *Phytomedicine*. **7**, Suppl 2, 107. 2000
- Moody, D.E. in Mozayani, A., Raymon, L.P. Drug interactions with benzodiazepines. *Handbook of drug interactions: a clinical and forensic guide*. Humana Press, 2004
- Morimoto, T., Kotegawa, T., Tsutsumi, K., Ohtani, Y., Imai, H., Nakano, S. Effect of St. John's wort on the pharmacokinetics of theophylline in healthy volunteers. *J Clin Pharmacol*. **44**, 95-101. 2004
- Moretti, M.E., Maxson, A., Hanna, F., Koren, G. Evaluating the safety of St. John's wort in human pregnancy. *Reprod Toxicol*. **28**, 96-99. 2009
- Mueller, B.M. St. John's wort for depressive disorders: results of an outpatient study with the *Hypericum* extract HYP811. *Adv Ther*. **15**, 109-116. 1998
- Mueller, S.C., Uehleke, B., Woehling, H., Petzsch, M., Majcher-Peszynska, J., Hehl, E.M., Sievers, H., Frank, B., Riethling, A.K., Drewelow, B. Effect of St. John's wort dose and preparations on the pharmacokinetics of digoxin. *Clin Pharmacol Ther*. **75**, 546-557. 2004
- Mueller, S.C., Majcher-Peszynska, J., Uehleke, B., Klammt, S., Mundkowski, R.G., Miekisch, W., Sievers, H., Bauer, S., Frank, B., Kundt, G., Drewelow, B. The extent of induction of CYP3A by St. John's wort varies among products and is linked to hyperforin dose. *Eur J Clin Pharmacol*. **62**, 29-36. 2006
- Mueller, S.C., Majcher-Peszynska, J., Mundkowski, R.G., Uehleke, B., Klammt, S., Sievers, H., Lehnfeld, R., Frank, B., Thurow, K., Kundt, G., Drewelow, B. No clinically relevant CYP3A induction after St. John's wort with low hyperforin content in healthy volunteers. *Eur J Clin Pharmacol*. **65**, 81-87. 2009
- Müller, T., Mannel, M., Murck, H., Rahlfs, VW. Treatment of somatoform disorders with St. John's wort: a randomized, double-blind and placebo-controlled trial. *Psychosom Med*. **66**, 538-547. 2004
- Müller, W.E., Rolli, M., Schäfer, C., Hafner, U. Effects of *Hypericum* extract (LI 160) in biochemical models of antidepressant activity. *Pharmacopsychiatry*. **30**, Suppl 2, 102-107. 1997
- Müller, W.E., Singer, A., Wonnemann, M, Hafner, U. Rolli, M., Schäfer, C. Hyperforin represents the neurotransmitter reuptake inhibiting constituent of *Hypericum* extract. *Pharmacopsychiatry*. **31**, Suppl. 16-21. 1998
- Murck, H., Spitznagel, H., Ploch, M., Seibel, K., Schaffler, K. *Hypericum* extract reverses S-ketamine-induced changes in auditory evoked potentials in humans - possible implications for the treatment of schizophrenia. *Biol Psychiatry*. **59**, 440-445. 2006

- Murphy, P.A., Kern, S.E., Stanczyk, F.Z., Westhoff, C.L. Interaction of St. John's wort with oral contraceptives: effects on the pharmacokinetics of norethindrone and ethinyl estradiol, ovarian activity and breakthrough bleeding. *Contraception*. **71**, 402-408. 2005
- Nebel, A., Schneider, B.J., Baker, R.K., Kroll, D.J. Potential metabolic interaction between St. John's wort and theophylline. *Ann Pharmacother*. **33**, 502. 1999
- Nöldner, M., Schötz, K. Rutin is essential for the antidepressant activity of *Hypericum perforatum* extracts in the forced swimming test. *Planta Med*. **68**, 577-580. 2002
- O'Breasail, A.M., Argouarch, S. Hypomania and St. John's wort. *Can J Psychiatry*. **43**, 746-747. 1998
- Okpanyi, S.N., Lizba, H., Scholl, B.C., Miltenburger, H.G. Genotoxicity of a standardized *Hypericum* extract. *Arzneimittelforschung*. **40**, 851-855. 1990
- Ondrizek, R.R., Chan, P.J., Patton, W.C., King, A. An alternative medicine study of herbal effects on the penetration of zona-free hamster oocytes and the integrity of sperm deoxyribonucleic acid. *Fertil Steril*. **71**, 517-522. 1999
- Ozturk, N., Korkmaz, S., Ozturk Y. Wound-healing activity of St. John's Wort (*Hypericum perforatum* L.) on chicken embryonic fibroblasts. *J Ethnopharmacol*. **111**, 33-39. 2006
- Pal, D., Mitra, A.K. MDR- and CYP3A4-mediated drug-herbal interactions. *Life Sci*. **78**, 2131-2145. 2006
- Panossian, A.G., Gabrielian, E., Manvelian, V., Jurcic, K., Wagner, H. Immunosuppressive effects of hypericin on stimulated human leukocytes: inhibition of the arachidonic acid release, leukotriene B₄ and interleukin-1 α production and activation of nitric oxide formation. *Phytomed*. **3**, 19-28. 1996
- Paulke, A., Nöldner, M., Schubert-Zsilavecz, M., Wurglics, M. St. John's wort flavonoids and their metabolites show antidepressant activity and accumulate in brain after multiple oral dose. *Pharmazie*. **63**, 296-302. 2008
- Perfumi, M., Ciccocioppo, R., Angeletti, S., Cucculelli, M., Massi, M. Effects of *Hypericum perforatum* extraction on alcohol intake in Marchigian Sardinian alcohol-preferring rats. *Alcohol Alcohol*. **34**, 690-698. 1999
- Perfumi, M., Panocka, I., Ciccocioppo, R., Vitali, D., Frolidi, R., Massi, M. Effects of a methanolic extract and a hyperforin-enriched CO₂ extract of *Hypericum perforatum* on alcohol intake in rats. *Alcohol Alcohol*. **36**, 199-206. 2001
- Perfumi, M., Santoni, M., Cippitelli, A., Ciccocioppo, R., Frolidi, R., Massi, M. *Hypericum perforatum* CO₂ extract and opioid receptor antagonists act synergistically to reduce ethanol intake in alcohol-preferring rats. *Alcohol Clin Exp Res*. **27**, 1554-1562. 2003
- Perfumi, M., Mattioli, L., Cucculelli, M., Massi, M. Reduction of ethanol intake by chronic treatment with *Hypericum perforatum*, alone or combined with naltrexone in rats. *J Psychopharmacol*. **19**, 448-454. 2005
- Perfumi, M., Mattioli, L., Forti, L., Massi, M., Ciccocioppo, R. Effect of *Hypericum perforatum* CO₂ extract on the motivational properties of ethanol in alcohol-preferring rats. *Alcohol Alcohol*. **40**, 291-296. 2005a
- Pfrunder, A., Schiesser, M., Gerber, S., Haschke, M., Bitzer, J., Drewe, J. Interaction of St. John's wort with low-dose oral contraceptive therapy: a randomized controlled trial. *Br J Clin Pharmacol*. **56**, 683-690. 2003
- Pharm. Eur.: European Pharmacopoeia, current edition.

Pharm. Helv. 8: Swiss Pharmacopoeia. Eidgenössisches Department des Inneren, Bern, 2001

Philipp, M., Kohnen, R., Hiller, KO. Hypericum extract versus imipramine or placebo in patients with moderate depression: randomised multicentre study of treatment for eight weeks. *BMJ*. **319**, 1534-1538. 1999

Poginsky, B., Westendorf, J., Prosenec, N., Kuppe, M., Marquardt, H. *Dtsch Apoth Ztg*. **128**, 1364-1366. 1988

Randlov, C., Mehlsen, J., Thomsen, CF., Hedman, C., von Fircks, H., Winther, K. The efficacy of St. John's Wort in patients with minor depressive symptoms or dysthymia--a double-blind placebo-controlled study. *Phytomedicin*. **13**, 215-221. 2006

Rayburn, W.F., Christensen, H.D., Gonzalez, C.L. Effect of antenatal exposure to St. John's wort (Hypericum) on neurobehavior of developing mice. *Am J Obstet Gynecol*. **183**, 1225-1231. 2000

Rayburn, W.F., Gonzalez, C.L., Christensen, H.D., Stewart, J.D. Effect of prenatally administered Hypericum (St. John's wort) on growth and physical maturation of mouse offspring. *Am J Obstet Gynecol*. **184**, 191-195. 2001

Rayburn, W.F., Gonzalez, C.L., Christensen, H.D., Harkins, T.L., Kupiec, T.C. Impact of Hypericum (St.-John's-wort) given prenatally on cognition of mice offspring. *Neurotoxicol Teratol*. **23**, 629-637. 2001a

Rengelshausen, J., Banfield, M., Riedel, K.D., Burhenne, J., Weiss, J., Thomsen, T., Walter-Sack, I., Haefeli, W.E., Mikus, G. Opposite effects of short-term and long-term St. John's wort intake on the voriconazole pharmacokinetics. *Clin Pharmacol Ther*. **78**, 25-33. 2005

Rezvani, A.H., Overstreet, D.H., Yang, Y., Clark, E. Jr. Attenuation of alcohol intake by extract of Hypericum perforatum (St. John's Wort) in two different strains of alcohol-preferring rats. *Alcohol Alcohol*. **34**, 699-705. 1999

Röder, C., Schaefer, M., Leucht, S. Meta-analysis of effectiveness and tolerability of treatment of mild to moderate depression with St. John's Wort. *Fortschr Neurol Psychiatr*. **72**, 330-343. 2004

Rychlik, R., Siedentop, H., von den Driesch, V., Kasper, S. St. John's wort extract WS 5572 in minor to moderately severe depression. Effectiveness and tolerance of 600 and 1200 mg active ingredient daily. *Fortschr Med Orig*. **119**, 119-128. 2001

Sanchez-Reus, M.I., Gomez del Rio M.A., Iglesias, I., Elorza, M., Slowing, K., Benedi, J. Standardized Hypericum perforatum reduces oxidative stress and increases gene expression of antioxidant enzymes on rotenone-exposed rats. *Neuropharmacology*. **52**, 606-616. 2007

Sattler, S., Schaefer, U., Schneider, W., Hoelzl, J., Lehr, C.M. Binding, uptake, and transport of hypericin by Caco-2 cell monolayers. *J Pharm Sci*. **86**, 1120-1126. 1997

Schempp, C.M., Ludtke R., Winghofer, B., Simon, J.C. Effect of topical application of Hypericum perforatum extract (St. John's wort) on skin sensitivity to solar simulated radiation. *Photodermatol Photoimmunol Photomed*. **16**, 125-128. 2000

Schempp, C.M., Simon-Haarhaus, B., Simon, J.C. Phototoxic and apoptosis-inducing capacity of pseudohypericin. *Planta Med*. **68**, 171-173. 2002

Schempp, C.M., Windeck, T., Hezel, S., Simon, J.C. Topical treatment of atopic dermatitis with St. John's wort cream--a randomized, placebo controlled, double blind half-side comparison. *Phytomedicine*. **10**, 31-37. 2003

- Schempp, C.M., Winghofer, B., Langheinrich, M., Schopf, E., Simon, J.C. Hypericin levels in human serum and interstitial skin blister fluid after oral single-dose and steady-state administration of *Hypericum perforatum* extract (St. John's wort). *Skin Pharmacol Appl Skin Physiol.* **12**, 299-304. 1999
- Schempp, C.M., Winghofer, B., Ludtke, R., Simon-Haarhaus, B., Schopf, E., Simon, J.C. Topical application of St John's wort (*Hypericum perforatum* L.) and of its metabolite hyperforin inhibits the allostimulatory capacity of epidermal cells. *Br J Dermatol.* **142**, 979-984. 2000
- Schempp, C.M., Winghofer, B., Muller, K., Schulte-Monting, J., Mannel, M., Schopf, E., Simon, J.C. Effect of oral administration of *Hypericum perforatum* extract (St. John's Wort) on skin erythema and pigmentation induced by UVB, UVA, visible light and solar simulated radiation. *Phytother Res.* **17**, 141-146. 2003
- Schey, K.L., Patat, S., Chignell, C.F., Datillo, M., Wang, R.H., Roberts, J.E. Photooxidation of lens alpha-crystallin by hypericin (active ingredient in St. John's Wort). *Photochem Photobiol.* **72**, 200-203. 2000
- Schimmer, O., Krüger, A., Paulini, H., Häfele, E. An evaluation of 55 commercial plant extracts in the Ames Mutagenicity test. *Pharmazie.* **49**, 448-451. 1994
- Schmidt, U. Reactions unaffected by antidepressant treatment with the *Hypericum* preparation LI 160. *Nervenheilkunde.* **10**, 311-312. 1991
- Schmidt, U., Harrer, G., Kuhn, U., Berger-Deinert, W., Luther, D. Interactions of *Hypericum* extract with alcohol. *Nervenheilkunde.* **12**, 324-319. 1993
- Schmitt, L.A., Liu, Y., Murphy, P.A., Petrich, J.W., Dixon, P.M., Birt, D.F. Reduction in hypericin-induced phototoxicity by *Hypericum perforatum* extracts and pure compounds. *J Photochem Photobiol B, Biol.* **85**, 118-130. 2006
- Schmitt, L.A., Liu, Y., Murphy, P.A., Birt, D.F. Evaluation of the light-sensitive cytotoxicity of *Hypericum perforatum* extracts, fractions, and pure compounds. *J Agric Food Chem.* **54**, 2881-2890. 2006a
- Schneider, G. *Arzneidrogen*, Wissenschaftsverlag, Mannheim, 1990
- Schrader, E. Equivalence of St John's wort extract (Ze 117) and fluoxetine: a randomized, controlled study in mild-moderate depression. *Int Clin Psychopharmacol.* **15**, 61-68. 2000
- Schrader, E., Meier, B., Brattström, A. *Hypericum* treatment of mild-moderate depression in a placebo-controlled study. A prospective, double-blind, randomized, placebo-controlled, multicentre study. *Human Psychopharmacology.* **13**, 163-169. 1998
- Schulz, H.U., Schürer, M., Bässler, B., Weiser, D. Investigation of pharmacokinetic data of hypericin, pseudohypericin, hyperforin and the flavonoids quercetin and isorhamnetin revealed from single and multiple oral dose studies with a *Hypericum* extract containing tablet in healthy male volunteers. *Arzneimittelforschung.* **55**, 561-568. 2005a
- Schulz, H.U., Schürer, M., Bässler, B., Weiser, D. Investigation of the bioavailability of hypericin, pseudohypericin, hyperforin and the flavonoids quercetin and isorhamnetin following single and multiple oral dosing of a *Hypericum* extract containing tablet. *Arzneimittelforschung.* **55**, 15-22. 2005b
- Schulz, H.U., Schürer, M., Bässler, D., Weiser, D. Investigation of the effect on photosensitivity following multiple oral dosing of two different *Hypericum* extracts in healthy men. *Arzneimittelforschung.* **56**, 212-221. 2006a
- Schulz, V. Therapierisiken durch Johanniskraut? *Dtsch Apoth Ztg.* **146**, 4280-4291. 2006b

- Schulz, V. Safety of St. John's wort extract compared to synthetic antidepressants. *Phytomed.* **13**, 199-204. 2006c
- Shelton, R.C., Keller, M.B., Gelenberg, A., Dunner, D.L., Herschfeld, R., Thase, M.E., Russell, J., Lydiard, R.B., Crits-Cristoph, P., Gallop, R., Todd, L., Hellerstein, D., Goodnick, P., Keitner, G., Stahl, S.M., Halbreich, U. Effectiveness of St John's wort in major depression: a randomized controlled trial. *JAMA.* **285**, 1978-1986. 2001
- Siepmann, M., Kirch, W., Krause, S., Joraschky, P., Muek-Weymann, M. The effects of St. John's wort extract and amitriptyline on autonomic responses of blood vessels and sweat glands in healthy volunteers. *J Clin Psychopharmacol.* **24**, 79-82. 2004
- Siepmann, M., Krause, S., Joraschky, P., Muck-Weymann, M., Kirch, W. The effects of St John's wort extract on heart rate variability, cognitive function and quantitative EEG: a comparison with amitriptyline and placebo in healthy men. *Br J Pharmacol.* **54**, 272-282. 2002
- Silva, B.A., Dias, A.C., Ferreres, F., Malva, J.O., Oliveira, C.R. Neuroprotective effect of *H. perforatum* extracts on beta-amyloid-induced neurotoxicity. *Neurotox Res.* **6**, 119-130. 2004
- Simbrey, K., Winterhoff, H., Butterweck, V. Extracts of St. John's wort and various constituents affect beta-adrenergic binding in rat frontal cortex. *Life Sci.* **74**, 1027-1038. 2004
- Simeon, J., Nixon, M.K., Milin, R., Jovanovic, R., Walker, S. Open-label pilot study of St. John's wort in adolescent depression. *J Child Adolesc Psychopharmacol.* **15**, 293-301. 2005
- Simmen, U., Schweitzer, C., Burkard, W., Schaffner, W., Lundstrom, K. *Hypericum perforatum* inhibits the binding of μ - and κ -opioid receptor expressed with the Semliki Forest virus system. *Pharm Acta Helv.* **73**, 53-56. 1998
- Singer, A., Schmidt, M., Hauke, W. Vergleich der Relapse- und Rezidivraten nach der Behandlung der mittelschweren Depression mit dem Johanniskrautextrakt STW 3-VI und Citalopram. *Nervenarzt. Suppl.* **4**, 230. 2008
- Sommer, H., Harrer, G., Placebo-controlled double-blind study examining the effectiveness of an *Hypericum* preparation in 105 mildly depressed patients. *J Geriatr Psychiatr Neurol.* **7**, S9-S11. 1994
- Sosa, S., Pace, R., Bornancin, A., Morazzoni, P., Riva, A., Tubaro, A., Della Loggia, R. Topical anti-inflammatory activity of extracts and compounds from *Hypericum perforatum* L. *J Pharm Pharmacol.* **59**, 703-709. 2007
- Stevinson, C., Ernst, E. A pilot study of *Hypericum perforatum* for the treatment of premenstrual syndrome. *BJOG.* **107**, 870-876. 2000
- Stevinson, C., Ernst, E. Can St. John's wort trigger psychoses? *Int J Clin Pharmacol Ther.* **42**, 473-480. 2004
- Szegedi, A., Kohnen, R., Dienel, A., Kieser, M. Acute treatment of moderate to severe depression with *Hypericum* extract WS 5570 (St John's wort): randomised controlled double blind non-inferiority trial versus paroxetine. *BMJ.* **330**, 503-506. 2005
- Teufel-Mayer, R., Gleitz, J. Effects of long-term administration of *Hypericum* extracts on the affinity and density of the central serotonergic 5-HT_{1A} and 5-HT_{2A} receptors. *Pharmacopsychiatry.* **30**, Suppl 2, 113-113. 1997
- Thiede, H.M., Walper, A. Inhibition of MAO and COMT by *Hypericum* extracts and hypericin. *J Geriatr Psychiatry Neurol.* **7**, Suppl 1, 54-56. 1994

- Traynor, N.J., Beattie, P.E., Ibbotson, S.H., Moseley, H., Ferguson, J., Woods, J.A. Photogenotoxicity of hypericin in HaCaT keratinocytes: implications(Auswirkung) for St. John's Wort supplements and high dose UVA-1 therapy. *Toxicol Lett.* **158**, 220-224. 2005
- Trofimiuk, E., Walesiuk, A., Braszko, J.J. St John's wort (*Hypericum perforatum*) counteracts deleterious effects of the chronic restraint stress on recall in rats. *Acta Neurobiol Exp.* **66**, 129-138. 2006
- Trofimiuk, E., Walesiuk, A., Braszko, J.J. St John's wort (*Hypericum perforatum*) diminishes cognitive impairment caused by the chronic restraint stress in rats. *Pharmacol Res.* **51**, 239-246. 2005
- Uebelhack, R., Gruenwald, J., Graubaum, HJ., Busch, R. Efficacy and tolerability of *Hypericum* extract STW 3-VI in patients with moderate depression: a double-blind, randomized, placebo-controlled clinical trial. *Adv Ther.* **21**, 265-275. 2004
- Uebelhack R, Blohmer JU, Graubaum H.J, Busch R, Gruenwald J, Wernecke KD. Black Cohosh and St. John's wort for climacteric complaints. *Obstet Gynecol.* **107**, 247-255. 2006
- Upton, R. St. John's Wort, Monograph of the American Herbal Pharmacopoeia, 1997
- Usai, M., Leggio, B., Grappi, S., Nanni, G., Gambarana, C., Tolu, P., Giachetti, D., De Mortis, M.G. *Hypericum perforatum* subspecies *angustifolium* shows a protective activity on the consequences of unavoidable stress exposure at lower doses than *Hypericum perforatum*. *Pharmacopsychiatry.* **36**, 283-287. 2003
- Uzbay, T.I. *Hypericum perforatum* and substance dependence: A review. *Phytother Res.* **22**, 578-582. 2008
- Van Gorp, G., Meterissian, GB., Haiek, L.N., McCusker, J., Bellavance, F. St John's wort or sertraline? Randomized controlled trial in primary care. *Can Fam Physician.* **48**, 905-912. 2002
- Volz, H.P., Zeller, K. Hochdosierter Johanniskrautextrakt als Einmalgabe: Ergebnisse einer Anwendungsbeobachtung an 11.296 Patienten. *Nervenheilkunde.* **19**, 566-569. 2000
- Volz, H.P., Murck, H., Kasper, S., Moller, H.J. St John's wort extract (LI 160) in somatoform disorders: results of a placebo-controlled trial. *Psychopharmacology.* **164**, 294-300. 2002
- Vorbach, E.U., Arnoldt, K.H., Hubner, W.D. Efficacy and tolerability of St. John's wort extract LI 160 versus imipramine in patients with severe depressive episodes according to ICD-10. *Pharmacopsychiatry.* **30**, Suppl 2, 81-85. 1997
- Wagner, H., Bauer, R. *Arzneidrogen und ihre Inhaltsstoffe. Band 2. Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, 1999*
- Wahlman, J., Hirst, M., Roberts, J.E., Prickett, C.D., Trevithick, J.R. Focal length variability and protein leakage as tools for measuring photooxidative damage to the lens. *Photochem Photobiol.* **78**, 88-92. 2003
- Waksman, J.C., Heard, K., Jolliff, H., Daly, F.F.S., Bogdan, G.M., Dart, R.C. Serotonin syndrome associated with the use of St. John's wort (*Hypericum perforatum*) and paroxetine. *Clin Toxicol.* **38**, 521. 2000
- Wang, Z., Gorski, C., Hamman, M.A., Huang, S.M., Lesko, L.J., Hall, S.D. The effects of St. John's wort (*Hypericum perforatum*) on human cytochrome P450 activity. *Clin Pharmacol Ther.* **70**, 317-326. 2001

- Weber, W., Van der Stoep, A., McCarty, R.L., Weiss, N.S, Biederman, J., McClellan, J. Hypericum perforatum (St John's wort) for attention-deficit/hyperactivity disorder in children and adolescents. *JAMA*. **299**, 2633-2641. 2008
- Wenk, M., Todesco, L., Krahenbuhl, S. Effect of St John's wort on the activities of CYP1A2, CYP3A4, CYP2D6, N-acetyltransferase 2, and xanthine oxidase in healthy males and females. *Br J Clin Pharmacol*. **57**, 495-499. 2004
- Wentworth, J.M., Agostini, M., Love, J., Schwabe, J.W., Chatterjee, V.K.K. St. John's wort, a herbal antidepressant, activates the steroid x receptor. *J Endocrinol*. **166**, R11-R16. 2000
- Werneke, U., Horn, O., Taylor, D.M. How effective is St John's wort? The evidence revisited. *J Clin Psychiatry*. **65**, 611-617. 2004
- Wheatley, D. LI 160, an extract of St. John's wort, versus amitriptyline in mildly to moderately depressed outpatients--a controlled 6-week clinical trial. *Pharmacopsychiatry*. **30**, Suppl 2, 77-80. 1997
- Whitten, D.L., Myers, S.P., Hawrelak, J.A., Wohlmuth, H. The effect of St John's wort extracts on CYP3A: a systematic review of prospective clinical trials. *Br J Clin Pharmacol*. **62**, 512-526. 2006
- WHO monographs. WHO-Monographs on selected medical plants. World Health Organization, Geneva, 2002
- Wichtl, M. Teedrogen. Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, 1984
- Wichtl, M. Teedrogen. Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, 4. Auflage 2002
- Wichtl, M. Herbal Drugs and Phytopharmaceuticals. Medpharm scientific publishers, Stuttgart 2004
- Widy-Tyszkiewicz, E., Piechal, A., Joniec, I., Blecharz-Klin, K. Long term administration of Hypericum perforatum improves spatial learning and memory in the water maze. *Biol Pharm Bull*. **25**, 1289-1294. 2002
- Wielgus, A.R., Chignell, C.F., Miller, D.S., Van Houten, B., Meyer, J., Hu, D.N., Roberts, J.E. Phototoxicity in Human Retinal Epithelial Cells Promoted by Hypericin, a Component of St. John's Wort. *Photochem Photobiol*. **83**, 706-713 2006
- Wilhelm, K.P., Biel, S., Siegers, C.P. Role of flavonoids in controlling the phototoxicity of Hypericum perforatum extracts. *Phytomedicine*. **8**, 306-309. 2001
- Will-Shahab, L., Brattström, A., Roots, I., Bauer, S., Kunter, U., Labes, D., Michler, A. Studie zur Interaktion von Johanniskrautextrakt (Ze117) mit Kontrazeptiva an Probandinnen. Abstract Symposium 'Phytopharmaka VII', 15. 2001
- Woelk, H. Comparison of St John's wort and imipramine for treating depression: randomised controlled trial. *BMJ*. **321**, 536-539. 2000
- Wright, C.W., Gott, M., Grayson, B., Hanna, M., Smith, A.G., Sunter, A., Neill, J.C. Correlation of hyperforin content of Hypericum perforatum (St John's Wort) extracts with their effects on alcohol drinking in C57BL/6J mice: a preliminary study. *J Psychopharmacol*. **17**, 403-408. 2003
- Wurglics, M., Westerhoff, K., Kaunzinger, A., Wilke, A., Baumeister, A., Dressmann, J., Schubert-Zsilavec, M. Comparison of German St. John's wort products according to hyperforin and total hypericin content. *J Am Pharm Ass*. **41**, 560-566. 2001a

- Wurglics, M., Westerhoff, K., Kaunzinger, A., Wilke, A., Baumeister, A., Dressmann, J., Schubert-Zsilavec, M. Batch-to batch reproducibility of St. John's wort preparations. *Pharmacopsychiatry*. **34** Suppl 1, S152-S156. 2001b
- Wurglics, M., Westerhoff, K., Holoubek, G., Schubert-Zsilavec, M., Müller, W.E. Aktuelle Johanniskrautforschung. *Dtsch Apoth Ztg*. **142**, 1153-1175. 2002
- Wurglics, M., Schubert-Zsilavec, M. Johanniskrautextrakt-Präparate im Vergleich. *Pharm Unserer Zeit*. **32**, 236-241. 2003
- Wurglics, M., Schubert-Zsilavec, M. Hypericum perforatum: a 'modern' herbal antidepressant: pharmacokinetics of active ingredients. *Clin Pharmacokinet*. **45**, 449-468. 2006
- Zdunic, G., Godevac, D., Milenkovic, M., Vucicevic, D., Savikin, K., Menkovic, N., Petrovic, S. Evaluation of Hypericum perforatum oil extracts for an antiinflammatory and gatsoprotective activity in rats. *Phytother Res*. **32**, 1559-1564. 2009
- Zhou, S., Chan, E., Pan, S.Q., Huang, M., Lee, E.J. Pharmacokinetic interactions of drugs with St John's wort. *J Psychopharmacol*. **18**, 262-276. 2004
- Zörnig, H. Arzneidrogen. Teil II. Verlag Klinkhardt, Leipzig, 1911
- Zou, Y., Lu, Y., Wei, D. Antioxidant activity of a flavonoid-rich extract of Hypericum perforatum L. in vitro. *J Agric Food Chem*. **52**, 5032-5039. 2004
- Zou, Y., Lu, Y., Wei, D. Hypocholesterolemic effects of a flavonoid-rich extract of Hypericum perforatum L. in rats fed a cholesterol-rich diet. *J Agric Food Chem*. **53**, 2462-2466. 2005