

**ARTEMISININ-COMPOUNDS LITERATURE LIST (2/05)**  
**(cancer-related papers are marked with an asterisk \*)**

Abdin MZ, Israr M, Rehman RU, Jain SK. Artemisinin, a novel antimalarial drug: biochemical and molecular approaches for enhanced production. *Planta Med* 69(4):289-299, 2003.

Ai J, Gao HH, He SZ, Wang L, Luo DL, Yang BF. Effects of matrine, artemisinin, and tetrandrine on cytosolic  $[Ca^{2+}]_i$  in guinea pig ventricular myocytes. *Acta Pharmacol Sin* 22:512-515, 2001.

Akintonwa DA. Theoretical mechanistic basis of the toxic effects and efficacy of AZT in HIV: AIDS. *Med Hypotheses* 59(6):622-625, 2002.

Akompong T, VanWye J, Ghori N, Haldar K: Artemisinin and its derivatives are transported by a vacuolar-network of *Plasmodium falciparum* and their anti-malarial activities are additive with toxic sphingolipid analogues that block the network. *Mol Biochem Parasitol.* 101(1-2):71-79, 1999.

Akompong T, Eksi S, Williamson K, Haldar K: Gametocytocidal activity and synergistic interactions of riboflavin with standard antimalarial drugs against growth of *Plasmodium falciparum* in vitro. *Antimicrob Agents Chemother.* 44(11):3107-3111, 2000.

Aldieri E, Atragne D, Bergandi L, Riganti C, Costamagna C, Bosia A, Ghigo D: Artemisinin inhibits inducible nitric oxide synthase and nuclear factor NF- $\kappa$ B activation. *FEBS Lett* 552(2-3):141-144, 2003.

Alin MH, Bjorkman A, Landberg-Lindgren A, Ashton M: The effect of artemisinin, its derivatives and mefloquine against chloroquine-resistant strains of *Plasmodium falciparum* in vitro. *Trans R Soc Trop Med Hyg* 86:365-397, 1992.

Alin MH, Kihamia CM, Bjorkman A, Bwijo BA, Premji Z, Mtey GJB, Ashton M: Efficacy of oral and intravenous artesunate in male Tanzanian adults with *Plasmodium falciparum* malaria and in vitro susceptibility to artemisinin, chloroquine, and mefloquine. *Am J Trop Med Hyg* 53:639-645, 1995.

Alin MH, Ashton M, Kihamia CM, Mtey GJB, Bjorkman A: Clinical efficacy and pharmacokinetics of artemisinin monotherapy and in combination with mefloquine in patients with *falciparum* malaria. *Br J Clin Pharmacol* 41:587-592, 1996.

Alin MH, Ashton M, Kihamia CM, Mtey GJB, Bjorkman A: Multiple dose pharmacokinetics of oral artemisinin and comparison of its efficacy with that of oral artesunate in *falciparum* malaria patients. *Trans R Soc Trop Med Hyg* 90:61-65, 1996.

Arnold K: Early treatment of malaria in the community using artemisinin- hope or hazard? *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/47-S/49, 1994.

Asawamahasakda W, Benakis A, Meshnick SR: The interaction of artemisinin with red cell membranes. *J Lab Clin Med* 123:757-762, 1994.

Asawamahasakda W, Ittarat I, Chang CC, McElroy P, Meshnick SR: Effects of antimalarials and protease inhibitors on plasmodial hemozoin production. *Mol Biochem Parasitol* 67:183-191, 1994.

Asawamahasakda W, Ittarat I, Pu YM, Ziffer H, Meshnick SR: Reaction of antimalarial endoperoxides with specific parasite proteins. *Antimicrob Agents Chemother* 38:1854-1858, 1994.

Ashton M, Gordi T, Hai TN, Huong NV, Sy ND, Nieu NT, Huong DX, Johansson M, Cong LD: Artemisinin pharmacokinetics in healthy adults after 250, 500 and 1000 mg single oral doses. *Biopharm Drug Dispos* 19:245-250, 1998.

Ashton M, Hai TN, Sy ND, Huong DX, Huong NV, Nieu NT, Cong LD: Artemisinin pharmacokinetics is time-dependent during repeated oral administration in healthy male adults. *Drug Metab Dispos* 26:25-27, 1998.

Ashton M, Johansson L, Thornqvist AS, Svensson USH: Quantitative in vivo and in vitro sex differences in artemisinin metabolism in rat. *Xenobiotica* 29:195-204, 1999.

Ashton M, Sy ND, Huong NV, Gordi T, Hai TN, Huong DX, Nieu NT, Cong LD: Artemisinin kinetics and dynamics during oral and rectal treatment of uncomplicated malaria. *Clin Pharmacol Ther* 63:482-493, 1998.

Augustijns P, D'Hulst A, Van Daele J, Kinget R: Transport of artemisinin and sodium artesunate in Caco-2 intestinal epithelial cells. *J Pharmaceut Sci* 85:577-579, 1996.

Avery BA, Venkatesh KK, Avery MA: Rapid determination of artemisinin and related analogues using high-performance liquid chromatography and an evaporative light scattering detector. *J Chromatogr B: Biomed Sci Appl* 730:71-80, 1999.

Avery MA, Muraleedharan KM, Desai PV, Bandyopadhyaya AK, Furtado MM, Tekwani BL: Structures-activity relationships of the antimalarial agent artemisinin. 8. design, synthesis, and CoMFA studies toward the development of artemisinin-based drugs against leishmaniasis and malaria. *J Med Chem* 46(20):4244-4258, 2003.

Bachi MD, Korshin EE, Hoos R, Szpilman AM, Ploypradith P, Xie S, Shapiro TA, Posner GH: A short synthesis and biological evaluation of potent and nontoxic antimalarial bridged bicyclic beta-sulfonyl-endoperoxides. *J Med Chem* 46(12):2516-2533, 2003.

Bachi MD, Korshin EE, Ploypradith P, Cumming JN, Xie S, Shapiro TA, Posner GH: Synthesis and in vitro antimalarial activity of sulfone endoperoxides. *Bioorg Med Chem*

Lett 8:903-908, 1998.

Bachi MD, Korshin EE, Hoos R, Szpilman AM, Ploypradith P, Xie S, Shapiro TA, Posner GH. A Short Synthesis and Biological Evaluation of Potent and Nontoxic Antimalarial Bridged Bicyclic beta-Sulfonyl-Endoperoxides. *J Med Chem* 46(12):2516-2533, 2003.

Bakhshi HB, Gordi T, Ashton M: In-vitro interaction of artemisinin with intact human erythrocytes, erythrocyte ghosts, haemoglobin and carbonic anhydrase. *J Pharm Pharmacol* 49:223-226, 1997.

Balint GA: Artemisinin and its derivatives: an important new class of antimalarial agents. *Pharmac Therapeut* 90:261-265, 2001.

Bapiro TE, Andersson TB, Otter C, Hasler JA, Masimirembwa CM: Cytochrome P450 1A1/2 induction by antiparasitic drugs: dose-dependent increase in ethoxyresorufin O-deethylase activity and mRNA caused by quinine, primaquine and albendazole in HepG2 cells. *Eur J Clin Pharmacol* 58(8):537-542, 2002.

Batty KT, Ashton M, Ilett KF, Edwards G, Davis TME: The pharmacokinetics of artemisinin (ART) and artesunate (ARTS) in healthy volunteers. *Am J Trop Med Hyg* 58:125-126, 1998.

Batty KT, Ilett KF, Davis TME: Chemical stability of artesunate injection and proposal for its administration by intravenous infusion. *J Pharm Pharmacol* 48:22-26, 1996.

Batty KT, Davis TME, Thu LTA, Binh TQ, Anh TK, Ilett KF: Selective high-performance liquid chromatographic determination of artesunate and  $\alpha$ - and  $\beta$ -dihydroartemisinin in patients with falciparum malaria. *J Chromatogr B: Biomed Appl* 677:345-350, 1996.

Batty KT, Ilett KF, Edwards G, Powell SM, Maggs JL, Park BK, Davis TME: Assessment of the effect of malaria infection on hepatic clearance of dihydroartemisinin using rat liver perfusions and microsomes. *Br J Pharmacol* 125:159-167, 1998.

Batty KT, Thu LTA, Ilett KF, Tien NP, Powell SM, Hung NC, Mai TX, Chon VV, Thien HV, Binh TQ, Kim NV, Davis TME: A pharmacokinetic and pharmacodynamic study of artesunate for vivax malaria. *Am J Trop Med Hyg* 59:823-827, 1998.

Batty KT, Thu LTA, Davis TME, Ilett KF, Mai TX, Hung NC, Tien NP, Powell SM, Thien HV, Binh TQ, Kim NV: A pharmacokinetic and pharmacodynamic study of intravenous vs oral artesunate in uncomplicated falciparum malaria. *Br J Clin Pharmacol* 45:123-129, 1998.

Batty KT, Ilett KE, Powell SM, Martin J, Davis TM. Relative bioavailability of artesunate and dihydroartemisinin: investigations in the isolated perfused rat liver and in

healthy Caucasian volunteers. *Am J Trop Med Hyg* 66(2):130-136, 2002.

\*Beekman AC, Barentsen AR, Woerdenbag HJ, Uden WV, Pras N, Konings AWT, El-Ferally FS, Galal AM, Wikstrom HV: Stereochemistry-dependent cytotoxicity of some artemisinin derivatives. *J Nat Prod* 60:325-330, 1997.

\*Beekman AC, Wierenga PK, Woerdenbag HJ, Uden WV, Pras N, Konings AWT, El-Ferally FS, Galal AM, Wikstrom HV: Artemisinin-derived sesquiterpene lactones as potential antitumour compounds: cytotoxic action against bone marrow and tumour cells. *Planta Med* 64:615-619, 1998.

\*Beekman AC, Woerdenbag HJ, Van Uden W, Pras N, Konings AWT, Wikstrom HV: Stability of artemisinin in aqueous environments: impact on its cytotoxic action to Ehrlich ascites tumour cells. *J Pharm Pharmacol* 49:1254-1258, 1997.

Begum K, Kim HS, Kumar V, Stojilnkovic I, Wataya Y: In vitro antimalarial activity of metalloporphyrins against *Plasmodium falciparum*. *Parasitol Res* 90(3):221-224, 2003.

Benakis A, Paris M, Loutan L, Plessas CT, Plessas ST: Pharmacokinetics of artemisinin and artesunate after oral administration in healthy volunteers. *Am J Trop Med Hyg* 56:17-23, 1997.

Benoit-Vical F, Robert A, Meunier B: In vitro and in vivo potentiation of artemisinin and synthetic endoperoxide antimalarial drugs by metalloporphyrins. *Antimicrob Agents Chemother* 44:2836-2841, 2000.

Berman PA, Adams PA: Artemisinin enhances heme-catalysed oxidation of lipid membranes. *Free Rad Biol Med* 22:1283-1288, 1997.

Bhattacharjee AK, Karle JM: Stereoelectronic properties of antimalarial artemisinin analogues in relation to neurotoxicity. *Chem Res Toxicol* 12:422-428, 1999.

\*Bhisutthibhan J, Philbert MA, Fujioka H, Aikawa M, Meshnick SR: The *Plasmodium falciparum* translationally controlled tumor protein: subcellular localization and calcium binding. *Eur J Cell Biol* 78:665-670, 1999.

Bhisutthibhan J, Meshnick SR. Immunoprecipitation of [(3)H]dihydroartemisinin translationally controlled tumor protein (TCTP) adducts from *Plasmodium falciparum*-infected erythrocytes by using anti-TCTP antibodies. *Antimicrob Agents Chemother*. 45(8):2397-2399, 2001.

Bich NN, De Vries PJ, Van Thien H, Phong TH, Hung LN, Eggelte TA, Anh TK, Kager PA: Efficacy and tolerance of artemisinin in short combination regimens for the treatment of uncomplicated *falciparum* malaria. *Am J Trop Med Hyg*. 55(4):438-443, 1996.

Birku Y, Makonnen E, Bjorkman A: Comparison of rectal artemisinin with intravenous quinine in the treatment of severe malaria in Ethiopia. *East Afr Med J* 76:154-159, 1999.

Bishop LPD, Maggs JL, O'Neill PM, Park BK: Metabolism of the antimalarial endoperoxide Ro 42-1611 (arteflene) in the rat: evidence for endoperoxide bioactivation. *J Pharmacol Exp Ther* 289:511-520, 1999.

Bodley AL, Cumming JN, Shapiro TA: Effects of camptothecin, a topoisomerase I inhibitor, on *Plasmodium falciparum*. *Biochem Pharmacol* 55:709-711, 1998.

Bouwmeester HJ, Wallaart TE, Janssen MHA, van Loo B, Jansen BJ, Posthumus MA, Schmidt CO, De Kraker JW, Konig WA, Franssen MCR: Amorpha-4,11-diene synthase catalyses the first probable step in artemisinin biosynthesis. *Phytochemistry* 52(5):843-854, 1999.

Brewer TG, Peggins JO, Grate SJ, et al: Neurotoxicity in animals due to arteether and artemether. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/33-S1/36, 1994.

Brewer TG, Grate SJ, Peggins JO, Weina PJ, Petras JM, Levine BS, Heiffer MH, Schuster BG: Fatal neurotoxicity of arteether and artemether. *Am J Trop Med Hyg* 51:251-259, 1994.

Brockman A, Price RN, van Vugt M, Heppner DG, Walsh D, Sookto P, Wimonwattrawatee T, Looareesuwan S, White NJ, Nosten F: *Plasmodium falciparum* antimalarial drug susceptibility on the northwestern border of Thailand during five years of extensive use of artesunate-mefloquine. *Trans R Soc Trop Med Hyg* 94:537-544, 2000.

Cazelles J, Robert A, Meunier B: Alkylating capacity and reaction products of antimalarial trioxanes after activation by a heme model. *J Org Chem* 67:609-619, 2002.

Chan KL, Yuen KH, Jinadasa S, Peh KK, Toh WT: A high-performance liquid chromatography analysis of plasma artemisinin using a glassy carbon electrode for reductive electrochemical detection. *Planta Med* 63:66-69, 1997.

Chawira AN, Warhurst DC, Peters W: Qinghaosu resistance in rodent malaria. *Trans R Soc Trop Med Hyg* 80:477-480, 1986.

\*Chen HH, Zhou HJ, Fang X: Inhibition of human cancer cell line growth and human umbilical vein endothelial cell angiogenesis by artemisinin derivatives in vitro. *Pharmacol Res* 48: 231-236, 2003.

\*Chen HH, Zhou HJ, Wu GD, Lou XE. Inhibitory effects of artesunate on angiogenesis and on expressions of vascular endothelial growth factor and VEGF receptor KDR/flk-1. *Pharmacology*. 71(1):1-9, 2004.

\*Chen H-H, Li-Li Y, Shang-Bin L. Artesunate reduces chicken chorioallantoic membrane neovascularisation and exhibits antiangiogenic and apoptotic activity on human microvascular dermal endothelial cell. *Cancer Lett.* 211(2):163-173, 2004.

\*Chen HH, Zhou HJ, Wang WQ, Wu GD. Antimalarial dihydroartemisinin also inhibits angiogenesis. *Cancer Chemother Pharmacol.* 53(5):423-432, 2004.

Chippaux JP, Le Hesran JY, Garcia A, Brasseur P: Recent studies have reported significant toxicity of artemisinin and its derivatives for schistosomula in various *Schistosoma* species. *Am J Trop Med Hyg* 69(1):1;author reply 1-2.

Clark RL, White TE, A Clode S, Gaunt I, Winstanley P, Ward SA. Developmental toxicity of artesunate and an artesunate combination in the rat and rabbit. *Birth Defects Res B Dev Reprod Toxicol.* 71(6):380-394, 2004.

Classen W, Altmann B, Gretener P, Soupart C, Skelton-Stroud P, Krinke G: Differential effects of orally versus parenterally administered qinghaosu derivative artemether in dogs. *Exp Toxic Pathol* 51:507-516, 1999.

Cumming JN, Ploypradith P, Posner GH: Antimalarial activity of artemisinin (qinghaosu) and related trioxanes: mechanism(s) of action. *Adv Pharmacol* 37:253-297, 1997.

Cumming JN, Wang D, Park SB, Shapiro TA, Posner GH: Design, synthesis, derivatization, and structure-activity relationships of simplified, tricyclic, 1,2,4-trioxane alcohol analogues of the antimalarial artemisinin. *J Med Chem* 41:952-964, 1998.

Davidson DE Jr: Role of arteether in the treatment of malaria and plans for further development. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/51-S1/52, 1994.

Davis TME, Phuong HL, Ilett KF, Hung NC, Batty KT, Phuong VDB, Powell SM, Thien HV, Binh TQ: Pharmacokinetics and pharmacodynamics of intravenous artesunate in severe falciparum malaria. *Antimicrob Agent Chemother* 45:181-186, 2001.

Davis TM, Binh TQ, Ilett KF, Batty KT, Phuong HL, Chiswell GM, Phuong VD, Agus C. Penetration of dihydroartemisinin into cerebrospinal fluid after administration of intravenous artesunate in severe falciparum malaria. *Antimicrob Agents Chemother* 47(1):368-370, 2003.

Dayan AD: Neurotoxicity and artemisinin compounds: do the observations in animals justify limitation of clinical use? *Med Trop (Mars)* 58:32-37, 1998.

De Jesus-Gonzalez L, Weathers PJ: Tetraploid *Artemisia annua* hairy roots produce more artemisinin than diploids. *Plant Cell Rep* 21(8):809-813, 2003.

\*Dell'Eva R, Pfeffer U, Vene R, Anfosso L, Forlani A, Albini A, Efferth T. Inhibition of angiogenesis in vivo and growth of Kaposi's sarcoma xenograft tumors by the anti-

malarial artesunate. *Biochem Pharmacol.* 68(12):2359-2366, 2004.

de Vries PJ, Dien TK: Clinical pharmacology and therapeutic potential of artemisinin and its derivatives in the treatment of malaria. *Drugs* 52:818-836, 1996.

de Vries PJ, Khanh NX, Dien TK, Binh LN, Yen NT, Duc DD, van Boxtel CJ, Kager PA: The pharmacokinetics of a single dose of artemisinin in subjects with liver cirrhosis. Bach Mai-Amsterdam Research Group on Artemisinin. *Trop Med Int Health* 2:957-962, 1997.

de Vries PJ, Dien TK, Khanh NX, Binh LN, Yen NT, Duc DD, van Boxtel CJ, Kager PA: The pharmacokinetics of a single dose of artemisinin in patients with uncomplicated falciparum malaria. *Am J Trop Med Hyg* 56:503-507, 1997.

de Vries PJ, Bich NN, Thien HV, Hung LN, Anh TK, Kager PA, Heisterkamp SH: Combinations of artemisinin and quinine for uncomplicated falciparum malaria: efficacy and pharmacodynamics. *Antimicrob Agent Chemother* 44:1302-1308, 2000.

Delhaes L, Blot C, Berry L, Maciejewski LA, Camus D, Brocard JS, Dive D. Novel ferrocenic artemisinin derivatives: synthesis, in vitro antimalarial activity and affinity of binding with ferroprotoporphyrin IX. *Bioorg Med Chem.* 8(12):2739-2745, 2000.

\*Deng DA et al: Derivatives of artemisinin B with antileukemia creativity. *ACTA Pharm Sin* 27:317-320, 1992.

Dhingra V, Rao KV, Narasu ML: Current status of artemisinin and its derivatives as antimalarial drugs. *Life Sci* 66:279-300, 2000.

Dien TK, de Vries PJ, Khanh NX, Koopmans R, Binh LN, Duc DD, Kager PA, van Boxtel CJ: Effect of food intake on pharmacokinetics of oral artemisinin in healthy Vietnamese subjects. *Antimicrob Agents Chemother* 41:1069-1072, 1997.

Dong Y, Vennerstrom JL. Mechanisms of in situ activation for peroxidic antimalarials. *Redox Rep.* 8(5):284-288, 2003.

Dost K, Davidson G: Analysis of artemisinin by a packed-column supercritical fluid chromatography-atmospheric pressure chemical ionisation mass spectrometry technique. *Analyst* 128(8):1037-1042, 2003.

Drobitch RK, Svensson CK: Therapeutic drug monitoring in saliva: an update. *Clin Pharmacokinet* 23:365-379, 1992.

Duarte EC, Fontes CJF, Gyorkos TW, Abrahamowicz M: Randomized controlled trial of artesunate plus tetracycline versus standard treatment (quinine plus tetracycline) for uncomplicated Plasmodium falciparum malaria in Brazil. *Am J Trop Med Hyg* 54:197-202, 1996.

Duc DD, de Vries PJ, Nguyen XK, Le Nguyen B, Kager PA, van Boxtel CJ: The pharmacokinetics of a single dose of artemisinin in healthy Vietnamese subjects. *Am J Trop Med Hyg.* 51(6):785-790, 1994.

Eckstein-Ludwig U, Webb RJ, Van Goethem ID, East JM, Lee AG, Kimura M, O'Neill PM, Bray PG, Ward SA, Krishna S: Artemisinins target the SERCA of *Plasmodium falciparum*. *Nature* 424(6951):957-961, 2003.

Edwards G, Ward S, Breckenridge A: Interaction of arteether with the red blood cell in-vitro and its possible importance in the interpretation of plasma concentrations in-vivo. *J Pharm Pharmacol* 44:280-281, 1992.

Edwards G: Measurement of artemisinin and its derivatives in biological fluids. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/37-S1/39, 1994.

Edwards G: Haem-mediated decomposition of artemisinin and its derivatives: pharmacological and toxicological considerations. *J Pharm Pharmacol* 49 (suppl 2):49-53, 1997.

\*Efferth T, Dunstan H, Sauerbrey A, Miyachi H, Chitambar CR: The anti-malarial artesunate is also active against cancer. *Int J Oncol* 18:767-773, 2001.

Efferth T, Marschall M, Wang X, Huong SM, Hauber I, Olbrich A, Kronschnabl M, Stamminger T, Huang ES.: Antiviral activity of artesunate towards wild-type, recombinant, and ganciclovir-resistant human cytomegaloviruses. *J Mol Med* 80:233-242, 2002.

\*Efferth T, Davey M, Olbrich A, Rucker G, Gebhart E, Davey R.: Activity of drugs from traditional Chinese medicine toward sensitive and MDR1- or MDR1-overexpressing multidrug-resistant human CCRF-CEM leukemia cells. *Blood Cells, Molecules, and Diseases* 28:160-168, 2002.

\*Efferth T, Olbrich A, Bauer R: mRNA expression profiles for the response of human tumor cell lines to the antimalarial drugs artesunate, arteether, and artemether. *Biochem Pharmacol* 64:617-623, 2002.

\*Efferth T, Briehl MM, Tome ME. Role of antioxidant genes for the activity of artesunate against tumor cells. *Int J Oncol.* 23(4):1231-1235, 2003.

\*Efferth T, Sauerbrey A, Olbrich A, Gebhart E, Rauch P, Weber HO, Hengstler JG, Halatsch ME, Volm M, Tew KD, Ross DD, Funk JO. Molecular modes of action of artesunate in tumor cell lines. *Mol Pharmacol.* 64(2):382-394, 2003.

\*Efferth T, Oesch F. Oxidative stress response of tumor cells: microarray-based comparison between artemisinins and anthracyclines. *Biochem Pharmacol.* 68(1):3-10, 2004.



\*Efferth T, Ramirez T, Gebhart E, Halatsch ME. Combination treatment of glioblastoma multiforme cell lines with the anti-malarial artesunate and the epidermal growth factor receptor tyrosine kinase inhibitor OSI-774. *Biochem Pharmacol.* 67(9):1689-1700, 2004.

\*Efferth T, Benakis A, Romero MR, Tomicic M, Rauh R, Steinbach D, Hafer R, Stamminger T, Oesch F, Kaina B, Marschall M. Enhancement of cytotoxicity of artemisinin toward cancer cells by ferrous iron. *Free Radic Biol Med.* 37(7):998-1009, 2004.

Eggelte TA, van Agtmael MA, Vuong TD, van Boxtel CJ: The development of an immunoassay for the detection of artemisinin compounds in urine. *Am J Trop Med Hyg* 61:449-56, 1999.

Ekong R, Warhurst DC: Synergism between arteether and mefloquine or quinine in a multidrug-resistant strain of *Plasmodium falciparum* in vitro. *Trans R Soc Trop Med Hyg* 84:757-758, 1990.

Esimone CO, Adikwu MU, Nwafor SV, Okoli CO, Ndu OO, Nwoke OI. In vitro antimicrobial interactions of artemether with some 4-quinolones. *Boll Chim Farm* 141(5):385-388, 2002.

Ezzet F, Mull R, Karbwang J: Population pharmacokinetics and therapeutic response of CGP 56697 (artemether + benflumetol) in malaria patients. *Br J Clin Pharmacol* 46:553-561, 1998.

Ezzet F, van Vugt M, Nosten F, Looareesuwan S, White NJ: Pharmacokinetics and pharmacodynamics of lumefantrine (benflumetol) in acute falciparum malaria. *Antimicrob Agents Chemother* 44:697-704, 2000.

Farouk ElFeraly, Hala N ElSohly: 4952603 Method for the isolation of artemisinin from *artemisia annua*. *Biotechnol Adv* 9(2):309, 1991.

Fenwick A, Savioli L, Engels D, Robert Bergquist N, Todd MH: Drugs for the control of parasitic diseases: current status and development in schistosomiasis. *Trends Parasitol* 19(11):509-515, 2003.

Ferreira JFS, Janick J: Distribution of artemisinin in *Artemisia annua*. In: J. Janick (ed.) *Progress in new crops*. ASHS Press, Arlington, VA, pp.579-584, 1996.

\*Fishwick J, Edwards G, Ward SA, McLean WG: Binding of dihydroartemisinin to differentiating neuroblastoma cells and rat cortical homogenate. *Neurotoxicology* 19:405-412, 1998.

\*Fishwick J, Edwards G, Ward SA, McLean WG: Morphological and immunocytochemical effects of dihydroartemisinin on differentiating NB2a

neuroblastoma cells. *Neurotoxicology* 19:393-403, 1998.

Fishwick J, McLean WG, Edwards G, Ward SA: The toxicity of artemisinin and related compounds on neuronal and glial cells in culture. *Chem Biol Interact* 96:263-271, 1995.

Foster S: Economic prospects for a new antimalarial drug. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/55-S1/56, 1994.

Gabriels M, Plaizier-Vercammen J: Physical and chemical evaluation of liposomes, containing artesunate. *J Pharm Biomed Anal* 26;31(4):655-667, 2003.

Gabriels M, Plaizier-Vercammen JA: Densitometric thin-layer chromatographic determination of artemisinin and its lipophilic derivatives, artemether and arteether. *J Chromatogr Sci* 41(7):359-366, 2003.

Genovese RF, Newman DB, Li Q, Peggins JO, Brewer TG: Dose-dependent brainstem neuropathology following repeated arteether administration in rats. *Brain Res Bull* 45:199-202, 1998.

Genovese RF, Newman DB, Petras JM, Brewer TG: Behavioral and neural toxicity of arteether in rats. *Pharmacol Biochem Behav* 60:449-458, 1998.

Genovese RF, Newman DB, Gordon KA, Brewer TG: Acute high dose arteether toxicity in rats. *Neurotoxicology* 20:851-860, 1999.

Genovese RF, Newman DB, Brewer TG: Behavioral and neural toxicity of the artemisinin antimalarial, arteether, but not artesunate and artelinate, in rats. *Pharmacol Biochem Behav* 67:37-44, 2000.

Gera R, Khalil A: Artemisinin and its derivatives. *Indian Pediatr* 34:813-816, 1997.

Giao PT, de Vries PJ: Pharmacokinetic interactions of antimalarial agents. *Clin Pharmacokinet.* 40(5): 343-373, 2001.

Girometta MA, Jauch R, Ponelle C, Guenzi A, Wiegand-Chou RC: Animal pharmacokinetics and metabolism of the new antimalarial Ro 42-1611 (arteeflene). *Trop Med Parasitol* 45:272-277, 1994.

Gordi T: Clinical pharmacokinetics of the antimalarial artemisinin based on saliva sampling. *Acta Universitatis Upsaliensis* 250:1-56, 2001.

Gordi T, Hai TN, Hoai NM, Thyberg M, Ashton M: Use of saliva and capillary blood samples as substitutes for venous blood sampling in pharmacokinetic investigations of artemisinin. *Eur J Clin Pharmacol* 56:561-566, 2000.

Gordi T, Huong DX, Hai TN, Nieu NT, Ashton M: Artemisinin pharmacokinetics and efficacy in uncomplicated-malaria patients treated with two different dosage regimens. *Antimicrob Agents Chemother* 46:1026-1031, 2002.

Gordi T, Nielsen E, Yu Z, Westerlund D, Ashton M: Direct analysis of artemisinin in plasma and saliva using coupled-column high-performance liquid chromatography with a restricted-access material pre-column. *J Chromatogr B Biomed Sci Appl* 742:155-162, 2000.

Gordi T, Lepist EI. Artemisinin derivatives: toxic for laboratory animals, safe for humans? *Toxicol Lett.* 147(2):99-107, 2004.

Grace JM, Skanchy DJ, Aguilar AJ: Metabolism of artelinic acid to dihydroqinghaosu by human liver cytochrome P4503A. *Xenobiotica* 29:703-717, 1999.

Green MD, Mount DL, Todd GD, Capomacchia AC: Chemiluminescent detection of artemisinin novel endoperoxide analysis using luminol without hydrogen peroxide. *J Chromatogr A* 695:237-242, 1995.

Green MD, Mount DL, Wirtz RA, White NJ. A colorimetric field method to assess the authenticity of drugs sold as the antimalarial artesunate. *J Pharm Biomed Anal.* 24(1):65-70, 2000.

Green MD, Mount DL, Wirtz RA: Authentication of artemether, artesunate and dihydroartemisinin antimalarial tablets using a simple colorimetric method. *Trop Med International Health* 6:980-982, 2001.

Gu HM, Warhurst DC, Peters W: Rapid action of qinghaosu and related drugs on incorporation of [<sup>3</sup>H]isoleucine by *Plasmodium falciparum* in vitro. *Biochem Pharmacol* 32:2463-2466, 1983.

Guo WZ, Guo XB, Zheng QJ, Tan B, Chen RJ, Ou FZ, Fu LC. [A randomized comparative study of naphthoquine, mefloquine and artesunate in the treatment of *falciparum* malaria] *Zhonghua Yi Xue Za Zhi.* 83(16):1406-1408, 2003. [Article in Chinese]

Gupta S, Svensson USH, Ashton M: In vitro evidence for auto-induction of artemisinin metabolism in the rat. *Eur J Drug Metab Pharmacokinet* 26:173-178, 2001.

Gupta S, Thapar MM, Mariga ST, Wernsdorfer WH, Bjorkman A: *Plasmodium falciparum*: in vitro interactions of artemisinin with amodiaquine, pyronaridine, and chloroquine. *Exp Parasitol* 100:28-35, 2002.

Han J, Lee JG, Min SS, Park SH, Angerhofer CK, Cordell GA, Kim SU: Synthesis of new artemisinin analogues from artemisinic acid modified at C-3 and C-13 and their antimalarial activity. *J Nat Prod* 64(9):1201-1205, 2001.

Haynes RK, Vonwiller SC. Extraction of artemisinin and artemisinic acid: preparation of artemether and new analogues. *Trans R Soc Trop Med Hyg* 88 Suppl 1:S1/23-S1/26, 1994.

Haynes RK: Artemisinin and derivatives: the future for malaria treatment? *Curr Opin Infect Dis* 14:719-726, 2001.

Haynes RK, Monti D, Taramelli D, Basilico N, Parapini S, Olliario P: Artemisinin antimalarials do not inhibit hemozoin formation. *Antimicrob Agents Chemother* 47(3):1175, 2003.

Hien TT, Tam DTH, Cuc NTK, Arnold K: Comparative effectiveness of artemisinin suppositories and oral quinine in children with acute falciparum malaria. *Trans R Soc Trop Med Hyg* 85:210-211, 1991.

Hien TT, White NJ: Qinghaosu. *Lancet* 341:603-608, 1993.

Hien TT: An overview of the clinical use of artemisinin and its derivatives in the treatment of falciparum malaria in Viet Nam. *Trans R Soc Trop Med Hyg* 88 (suppl 1):S1/7-S1/8, 1994.

Hien TT, Day NPJ, Phu NH, Mai NTH, Chau TTH, Loc PP, Sinh DX, van Chuong L, Vinh H, Waller D, Peto TEA, White NJ: A controlled trial of artemether or quinine in Vietnamese adults with severe falciparum malaria. *N Engl J Med* 335:76-83, 1996.

Hien TT, Turner GD, Mai NT, Phu NH, Bethell D, Blakemore WF, Cavanagh JB, Dayan A, Medana I, Weller RO, Day NP, White NJ: Neuropathological assessment of artemether-treated severe malaria. *Lancet* 362(9380):295-296.

Hindley S, Ward SA, Storr RC, Searle NL, Bray PG, Park BK, Davies J, O'Neill PM. Mechanism-based design of parasite-targeted artemisinin derivatives: synthesis and antimalarial activity of new diamine containing analogues. *J Med Chem* 45(5):1052-1063, 2002.

Hofheinz W, Burgin H, Gocke E, Jaquet C, Masciadri R, Schmid G, Stohler H, Urwyler H: Ro 42-1611 (arteflene), a new effective antimalarial: chemical structure and biological activity. *Trop Med Parasitol* 45: 261-265, 1994.

Hong YL, Yang YZ, Meshnick SR: The interaction of artemisinin with malarial hemozoin. *Mol Biochem Parasitol* 63:121-128, 1994.

\*Hu YQ, Tan RX, Chu MY, Zhou J: Apoptosis in human hepatoma cell line SMMC-7721 induced by water-soluble macromolecular components of *Artemisia capillaris* Thunberg. *Jpn J Cancer Res* 91:113-117, 2000.

Hung LN, deVries PJ, Thuy LTD, Lien B, Long HP, Hung TN: Single dose artemisinin-mefloquine versus mefloquine alone for uncomplicated falciparum malaria. *Trans R Soc Trop Med Hyg* 91:191-194, 1997.

Hung LN, Na-Bangchang K, Thuy LTD, Anh TK, Karbwang J: Pharmacokinetics of a single oral dose of dihydroartemisinin in Vietnamese healthy volunteers. *Southeast Asian J Trop Med Public Health* 30:11-16, 1999.

Huang FS, Hu Q, Shi YL: [The inhibitory effects of artemisinin-derivatives on Na<sup>+</sup> and K<sup>+</sup> channels in comparison with those of procaine]. *Sheng Li Xue Bao* 50:145-152, 1998.

Ilett KF, Ethell BT, Maggs JL, Davis TME, Batty KT, Burchell B, Binh TQ, Thu LTA, Hung NC, Pirmohamed M, Park BK, Edwards G: Glucuronidation of dihydroartemisinin in vivo and by human liver microsomes and expressed UDP-glucuronosyltransferases. *Drug Metab Dispos* 30:1005-1012, 2002.

Illapakurthy AC, Sabnis YA, Avery BA, Avery MA, Wyandt CM: Interaction of artemisinin and its related compounds with hydroxypropyl- $\beta$ -cyclodextrin in solution state: experimental and molecular-modeling studies. *J Pharmaceut Sci* 92:649-655, 2003.

Irion A, Felger I, Abdulla S, Smith T, Mull R, Tanner M, Hatz C, Beck HP: Distinction of recrudescences from new infections by PCR-RFLP analysis in a comparative trial of CGP 56 697 and chloroquine in Tanzanian children. *Trop Med Int Health* 3:490-497, 1998.

Ittarat I, Asawamahsakda W, Meshnick SR: The effects of antimalarials on the Plasmodium falciparum dihydroorotate dehydrogenase. *Exp Parasitol* 79:50-56, 1994.

Ittarat W, Pickard AL, Rattanasinganchan P, Wilairatana P, Looareesuwan S, Emery K, Low J, Udomsangpetch R, Meshnick SR: Recrudescence in artesunate-treated patients with falciparum malaria is dependent on parasite burden not on parasite factors. *Am J Trop Med Hyg* 68(2):147-152, 2003.

Ivanovska N, Philipov S: A low dose immunoretorative effect of aporphinoid alkaloid oxoglucine on experimentally immunosuppressed and infected mice. *Meth Find Exp Clin Pharmacol* 19:579-583, 1997.

Janse CJ, Waters AP, Kos J, Lugt CB: Comparison of in vivo and in vitro antimalarial activity of artemisinin, dihydroartemisinin and sodium artesunate in the Plasmodium berghei-rodent model. *Inter J Parasitol* 24:589-594, 1994.

Jaquet C, Stohler HR, Chollet J, Peters W: Antimalarial activity of the bicyclic peroxide Ro 42-1611 (arteflene) in experimental models. *Trop Med Parasitol* 45:266-271, 1994.

\*Jeyadevan JP, Bray PG, Chadwick J, Mercer AE, Byrne A, Ward SA, Park BK, Williams DP, Cosstick R, Davies J, Higson AP, Irving E, Posner GH, O'Neill PM.

Antimalarial and antitumor evaluation of novel C-10 non-acetal dimers of 10beta-(2-hydroxyethyl)deoxoartemisinin. *J Med Chem.*47(5):1290-1298, 2004.

Johann-Liang R, Albrecht R: Safety evaluations of drugs containing artemisinin derivatives for the treatment of malaria. *Clin Infect Dis* 36(12):1626-1627; author reply 1627-1628, 2003.

Jung M, Schinazi RF: Synthesis and in vitro anti-human immunodeficiency virus activity of artemisinin (qinghaosu)-related trioxanes. *Bioorg Med Chem Lett* 4:93-934, 1994.

Jung M, Lee K, Kendrick H, Robinson BL, Croft SL: Synthesis, stability, and antimalarial activity of new hydrolytically stable and water-soluble (+)-deoxoartelinic acid. *J Med Chem* 45:4940-4944, 2002.

Kager PA, Schultz MJ, Zijlstra EE, et al: Arteether administration in humans: preliminary studies of pharmacokinetics, safety and tolerance. *Trans R Soc Trop Med Hyg* 88 (suppl 1):S1/53-S1/54, 1994.

\*Kamchonwongpaisan S, McKeever P, Hossler P, Ziffer H, Meshnick SR: Artemisinin neurotoxicity: neuropathology in rats and mechanistic studies in vitro. *Am J Trop Med Hyg* 56:7-12, 1997.

Kamchonwongpaisan S, Meshnick SR: The mode of action of the antimalarial artemisinin and its derivatives. *Gen Pharmacol* 27:587-592, 1996.

Kapetanaki S, Varotsis C: Fourier transform infrared investigation of non-heme Fe(III) and Fe(II) decomposition of artemisinin and of a simplified trioxane alcohol. *J Med Chem* 44, 3150-3156, 2001.

Karbwang J, Bangchang KN, Thanavibul A, Bunnag D, Chongsuphajaisiddhi T, Harinasuta T: Comparison of oral artemether and mefloquine in acute uncomplicated falciparum malaria. *Lancet* 340:1245-1248, 1992.

Karbwang J, Laothavorn P, Sukontason K, Thiha T, Rimchala W, Na-Bangchang K, Bunnag D: Effect of artemether on electrocardiogram in severe falciparum malaria. *Southeast Asian J Trop Med Public Health* 28:472-475, 1997.

Karbwang J, Na-Bangchang K, Molunto P, Banmairuroi V, Congpuong K.: Determination of artemether and its major metabolite, dihydroartemisinin, in plasma using high-performance liquid chromatography with electrochemical detection. *J Chromatogr B* 690:259-265, 1997.

Karbwang J, Na-Bangchang K, Congpuong K, Molunto P, Thanavibul A: Pharmacokinetics and bioavailability of oral and intramuscular artemether. *Eur J Clin Pharmacol* 52:307-310, 1997.

Karbwang J, Na-Bangchang K, Thanavibul A, Molunto P: Plasma concentrations of artemether and its major plasma metabolite, dihydroartemisinin, following a 5-day regimen of oral artemether, in patients with uncomplicated falciparum malaria. *Ann Trop Med Parasitol* 92:31-36, 1998.

Karbwang J, Na-Bangchang K, Tin T, Sukontason K, Rimchala W, Harinasutl T: Pharmacokinetics of intramuscular artemether in patients with severe falciparum malaria with or without acute renal failure. *Br J Clin Pharmacol* 45:597-600, 1998.

Kayser O, Kiderlen AF, Croft SL: Natural products as antiparasitic drugs. *Parasitol Res* 90 (Supp 2): S1/55-S1/62, 2003.

Khanh NX, de Vries PJ, Ha LD, van Boxtel CJ, Koopmans R, Kager PA: Declining concentrations of dihydroartemisinin in plasma during 5-day oral treatment with artesunate for falciparum malaria. *Antimicrob Agent Chemother* 43:690-692, 1999.

Kim BJ, Sasaki T. Synthesis of O-aminodihydroartemisinin via TMS triflate catalyzed C-O coupling reaction. *J Org Chem.* 69(9):3242-3244, 2004.

\*Kim SH, Kim HJ, Kim TS. Differential involvement of protein kinase C in human promyelocytic leukemia cell differentiation enhanced by artemisinin. *Eur J Pharmacol.* 482(1-3):67-76, 2003.

Klayman DL: Qinghaosu (artemisinin): an antimalarial drug from China. *Science* 228:1049-1055, 1985.

Kohler M, Haerdi W, Christen P, Veuthey JL: Extraction of artemisinin and artemisinic acid from *Artemisia annua* L. using supercritical carbon dioxide. *J Chromatogr A* 785(1-2):353-360, 1997.

Krippner R, Staples J: Suspected allergy to artemether-lumefantrine treatment of malaria. *J Travel Med* 10(5):303-305, 2003.

Krishna S, Planche T, Agbenyega T, Woodrow C, Agranoff D, Bedu-Addo G, Owusu-Ofori AK, Appiah JA, Ramanathan S, Mansor SM, Navaratnam V: Bioavailability and preliminary clinical efficacy of intrarectal artesunate in Ghanaian children with moderate malaria. *Antimicrob Agent Chemother* 45:509-516, 2001.

Krudsood S, Chalermrut K, Pengruksa C, Srivilairit S, Silachamroon U, Treeprasertsuk S, Kano S, Brittenham GM, Looareesuwan S: Comparative clinical trial of two-fixed combinations dihydroartemisinin-naphthoquine-trimethoprim (DNP) and artemether-lumefantrine (Coartem/Riamet) in the treatment of acute uncomplicated falciparum malaria in Thailand. *Southeast Asian J Trop Med Public Health* 34(2):316-321, 2003.

Krudsood S, Wilairatana P, Vannaphan S, Treeprasertsuk S, Silachamroon U, Phomrattanapapin W, Gourdeuk VR, Brittenham GM, Looareesuwan S: Clinical

experience with intravenous quinine, intramuscular artemether and intravenous artesunate for the treatment of severe malaria in Thailand. *Southeast Asian J Trop Med Public Health* 34(1):54-61, 2003.

Krungskrai SR, Yuthavong Y: The antimalarial action on *Plasmodium falciparum* of qinghaosu and artesunate in combination with agents which modulate oxidant stress. *Trans R Soc Trop Med Hyg* 81:710-714, 1987.

\*Lai H, Singh NP: Selective cancer cell cytotoxicity from exposure to dihydroartemisinin and holotransferrin. *Cancer Lett* 91:41-46, 1995.

\*Lai H, Sasaki T, Singh NP, Messay A. Effects of artemisinin-tagged holotransferrin on cancer cells. *Life Sci.* 76(11):1267-1279, 2005.

\*Lai, H and Singh, N.P. Oral artemisinin prevents and delays the development of 7, 12-dimethylbenz(a)anthracene (DMBA)-induced breast cancer in the rat. *Cancer Letters* (In press)

Laughlin JC: Agricultural production of artemisinin- a review. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/21-S1/22, 1994.

\*Lee CH, Hong H, Shin J, Jung M, Shin I, Yoon J, Lee W: NMR studies on novel antitumor drug candidates, deoxoartemisinin and carboxypropyldeoxoartemisinin. *Biochem Biophys Res Comm* 274:359-369, 2000.

Lee P, Ye Z, van Dyke K, Kirk RG: X-ray microanalysis of *Plasmodium falciparum* and infected red blood cells: effects of qinghaosu and chloroquine on potassium, sodium, and phosphorus composition. *Am J Trop Med Hyg* 39:157-165, 1988.

Lefevre G, Bindschedler M, Ezzet F, Schaeffer N, Meyer I, Thomsen MS: Pharmacokinetic interaction trial between co-artemether and mefloquine. *Eur J Pharmaceut Sci* 10:141-151, 2000.

Leo KU, Grace JM, Li Q, Peggins J, Mitchell AL, Aguilar T, Brewer TG: Effects of *Plasmodium berghei* infection on artemether metabolism and disposition. *Pharmacol* 54:276-284, 1997.

Leskovac V, Theoharides AD: Hepatic metabolism of artemisinin drugs--I. Drug metabolism in rat liver microsomes. *Comp Biochem Physiol C* 99:383-390, 1991.

Leskovac V, Theoharides AD: Hepatic metabolism of artemisinin drugs--II. Metabolism of artemether in rat liver cytosol. *Comp Biochem Physiol C* 99:391-396, 1991.

Levander OA, Ager AL, Morris VC, May RG: Qinghaosu, dietary vitamin E, selenium, and cod-liver oil: effect on the susceptibility of mice to the malarial parasite *Plasmodium yoelii*. *Am J Clin Nutr* 50:346-352, 1989.



Li GQ, Guo XB, Fu LC, et al: Clinical trials of artemisinin and its derivatives in the treatment of malaria in china. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/5-S1/6, 1994.

Li QG, Peggins JO, Fleckenstein LL, Masonic K, Heiffer MH, Brewer TG: The pharmacokinetics and bioavailability of dihydroartemisinin, arteether, artemether, artesunic acid and artelinic acid in rats. *J Pharm Pharmacol* 50:173-182, 1998.

Li QG, Peggins JO, Lin AJ, Masonic KJ, Trotman KM, Brewer TG: Pharmacology and toxicology of artelinic acid: preclinical investigations on pharmacokinetics, metabolism, protein and red blood cell binding, and acute and anorectic toxicities. *Trans R Soc Trop Med Hyg* 92:332-340, 1998.

Li QG, Mog SR, Si YZ, Kyle DE, Gettayacamin M, Milhous WK. Neurotoxicity and efficacy of arteether related to its exposure times and exposure levels in rodents. *Am J Trop Med Hyg* 66(5):516-525, 2002.

Li QG, Si YZ, Lee P, Wong E, Xie LH, Kyle DE, Dow GS. Efficacy comparison of intravenous artelinate and artesunate in *Plasmodium berghei*-infected Sprague-Dawley rats. *Parasitology* 126(Pt 4):283-291, 2003.

Li XQ, Bjorkman A, Andersson TB, Gustafsson LL, Masimirembwa CM: Identification of human cytochrome P(450)s that metabolise antiparasitic drugs and predictions of in vivo drug hepatic clearance from in vitro data. *Eur J Clin Pharmacol* 59(5-6):429-442, 2003.

\*Li Y, Shan F, Wu JM, Wu GS, Ding J, Xiao D, Yang WY, Atassi G, Leonce S, Caignard DH, Renard P: Novel antitumor artemisinin derivatives targeting G1 phase of the cell cycle. *Bioorg Med Chem Lett* 11:5-8, 2001.

Li Y, Wu YL: An over four millennium story behind qinghaosu (artemisinin--a fantastic antimalarial drug from a traditional chinese herb). *Curr Med Chem* 10(21):2197-2230, 2003.

Li Y, Wu YL: How Chinese scientists discovered qinghaosu (artemisinin) and developed its derivatives? What are the future perspectives? *Med Trop (Mars)* 58:9-12, 1998.

Li Y, Yang ZS, Zhang H, Cao BJ, Wang FD, Zhang Y, Shi YL, Yang JD, Wu BA: Artemisinin derivatives bearing Mannich base group: synthesis and antimalarial activity. *Bioorg Med Chem* 11(20):4363-4368, 2003.

Li ZL, Gu HM, Warhurst DC, Peters W: Effects of qinghaosu and related compounds on incorporation of [ $G-^3H$ ] hypoxanthine by *Plasmodium falciparum* in vitro. *Trans R Soc Trop Med Hyg* 77:522-523, 1983.

Looareesuwan S: Overview of clinical studies on artemisinin derivatives in Thailand. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/9-S1/11, 1994.

Lou XE, Zhou HJ. [Effects of artesunate on progesterone estrogen content and decidua in rats] *Yao Xue Xue Bao* 36(4):254-257, 2001. [Article in Chinese]

Lou XE, Zhou HJ, Huang HB. [Lipid-peroxidation damage of embryo and placenta induced by artesunate in rats] *Zhejiang Da Xue Xue Bao Yi Xue Ban* 32(1):41-45, 2003. [Article in Chinese]

Lu L. [Study on effect of *Cordyceps sinensis* and artemisinin in preventing recurrence of lupus nephritis] *Zhongguo Zhong Xi Yi Jie He Za Zhi* 22(3):169-171, 2002.

Luo XD, Shen CC: The chemistry, pharmacology, and clinical applications of qinghaosu (artemisinin) and its derivatives. *Med Res Rev* 7:29-52, 1987.

Maono Y, Toyoshima, T, Fujioka H, Ito Y, Meshnick SR, Benakis A, Milhous WK, Aikawa M: Morphologic effects of artemisinin in *Plasmodium falciparum*. *Am J Trop Med Hyg* 49:485-491, 1993.

Martin VJ, Pitera DJ, Withers ST, Newman JD, Keasling JD: Engineering a mevalonate pathway in *Escherichia coli* for production of terpenoids. *Nat Biotechnol* 21(7):796-802, 2003.

McCarty MF: Turning an 'Achilles' Heel' into an asset--activation of HIF-1alpha during angiostatic therapy will increase tumor sensitivity to iron-catalyzed oxidative damage. *Med Hypotheses* 61(4):509-511, 2003.

McGready R, Brockman A, Cho T, Cho D, van Vugt M, Luxemburger C, Chongsuphajaisiddhi, T, White NJ, Nosten F: Randomized comparison of mefloquine-artesunate versus quinine in the treatment of multidrug-resistant *falciparum* malaria in pregnancy. *Trans R Soc Trop Med Hyg* 94:689-693, 2000.

McGready R, Cho T, Cho JJ, Simpson JA, Luxemburger C, Dubowitz L, Looareesuwan S, White NJ, Nosten F: Artemisinin derivatives in the treatment of *falciparum* malaria in pregnancy. *Trans R Soc Trop Med Hyg* 92:430-433, 1998.

McGready R, Cho T, Samuel, Villegas L, Brockman A, van Vugt M, Looareesuwan S, White NJ, Nosten F: Randomized comparison of quinine-clindamycin versus artesunate in the treatment of *falciparum* malaria in pregnancy. *Trans R Soc Trop Med Hyg* 95:651-656, 2001.

\*McLean WG, Ward SA: In vitro neurotoxicity of artemisinin derivatives. *Med Trop (Mars)* 58:28-31, 1998.

Mehra N, Bhasin VK: In vitro gametocytocidal activity of artemisinin and its derivatives in Plasmodium falciparum. Jpn J Med Sci Biol 46:37-43, 1993.

Melendez V, Peggins JO, Brewer TG, Theoharides AD: Determination of the antimalarial arteether and its deethylated metabolite dihydroartemisinin in plasma by high-performance liquid chromatography with reductive electrochemical detection. J Pharmaceut Sci 80:132-138, 1991.

Meshnick SR: Artemisinin and heme. Antimicrob Agents Chemother 47(8):2712;author reply 2712-2713, 2003.

Meshnick SR: Artemisinin antimalarials: mechanisms of action and resistance. Med Trop (Mars) 58:13-17, 1998.

Meshnick SR: Artemisinin: mechanisms of action, resistance and toxicity. Int J Parasitol 32(13):1655-1660, 2002.

Meshnick SR: The mode of action of antimalarial endoperoxides. Trans R Soc Trop Med Hyg 88 (supp 1):S1/31-S1/32, 1994.

Meshnick SR, Taylor TE, Kamchonwongpaisan S: Artemisinin and the antimalarial endoperoxides: from herbal remedy to targeted chemotherapy. Microbiol Rev 60:301-315, 1996.

Meshnick SR, Yang YZ, Lima V, Kuypers F, Kamchonwongpaisan S, Yuthavong Y: Iron-dependent free radical generation from the antimalarial agent artemisinin (qinghaosu). Antimicrob Agents Chemother 37:1108-1114, 1993.

Meyer UA: Overview of enzymes of drug metabolism. J Pharmacokinet Biopharm 24:449-459, 1996.

Miller LG, Panosian CB: Ataxia and slurred speech after artesunate treatment for Falciparum malaria. New England J Med 336:1328-1329, 1997. (Related letters)

Mohanty S, Mishra SK, Satpathy SK, Dash S, Patnaik J:  $\alpha$ ,  $\beta$ -arteether for the treatment of complicated falciparum malaria. Trans R Soc Trop Med Hyg 91:328-330, 1997.

\*Moore JC, Lai H, Li JR, Ren RL, McDougall JA, Singh NP, Chou CK: Oral administration of dihydroartemisinin and ferrous sulfate retarded implanted fibrosarcoma growth in the rat. Cancer Lett 98:83-87, 1995.

Mordi MN, Mansor SM, Navaratnam V, Wernsdorfer WH: Single dose pharmacokinetics of oral artemether in healthy Malaysian volunteers. Br J Clin Pharmacol 43:363-365, 1997.

Mount DL, Todd GD, Navaratnam V: Packed-column supercritical fluid chromatography of artemisinin (qinghaosu) with electron-capture detection. *J Chromatogr B: Biomed Appl* 666:183-187, 1995.

Muellner U, Huefner A, Haslinger E: Behaviour of terpene peroxides from abietic acid in the presence of heme and non-heme iron(II). *Tetrahedron* 56:3893-3899, 2000.

Muhia DK, Thomas CG, Ward SA, Edwards G, Mberu EK, Watkins WM: Ferriprotoporphyryn catalysed decomposition of artemether: analytical and pharmacological implications. *Biochem Pharmacol* 48:889-895, 1994.

Mukanganyama S, Naik YS, Widersten M, Mannervik B, Hasler JA: Proposed reductive metabolism of artemisinin by glutathione transferases in vitro. *Free Radic Res* 35:427-434, 2001.

\*Mukanganyama S, Widersten M, Naik YS, Mannervik B, Hasler JA: Inhibition of glutathione S-transferases by antimalarial drugs possible implications for circumventing anticancer drug resistance. *Int J Cancer* 97:700-705, 2002.

Na-Bangchang K, Karbwang J, Thomas CG, Thanavibul A, Sukontason K, Ward SA, Edwards G: Pharmacokinetics of artemether after oral administration to healthy Thai males and patients with acute, uncomplicated falciparum malaria. *Br J Clin Pharmacol* 37:249-253, 1994.

Na-Bangchang K, Congpoung K, Ubalee R, Thanavibul A, Tan-anya P, Karbwang J: Pharmacokinetics and ex vivo anti-malarial activity of sera following a single oral dose of dihydroartemisinin in healthy Thai males. *Southeast Asian J Trop Med Public Health* 28:731-735, 1997.

Na-Bangchang K, Congpuong K, Hung LN, Molunto P, Karbwang J: Simple high-performance liquid chromatographic method with electrochemical detection for the simultaneous determination of artesunate and dihydroartemisinin in biological fluids. *J Chromatogr B Biomed Sci Appl* 708:201-207, 1998.

Na-Bangchang K, Tippanangkosol P, Ubalee R, Chaovanakawee S, Saengtertsilapachai S, Karbwang J: Comparative clinical trial of four regimens of dihydroartemisinin-mefloquine in multidrug-resistant falciparum malaria. *Trop Med Int Health* 4:602-610, 1999.

Na-Bangchang K, Karbwang J, Palacios PAC, Ubalee R, Saengtertsilapachai S, Wernsdorfer WH: Pharmacokinetics and bioequivalence evaluation of three commercial tablet formulations of mefloquine when given in combination with dihydroartemisinin in patients with acute uncomplicated falciparum malaria. *Eur J Clin Pharmacol* 55:743-748, 2000.

Nagai A, Yokoyama N, Matsuo T, Bork S, Hirata H, Xuan X, Zhu Y, Claveria FG, Fujisaki K, Igarashi I. Growth-Inhibitory Effects of Artesunate, Pyrimethamine, and Pamaquine against *Babesia equi* and *Babesia caballi* in In Vitro Cultures. *Antimicrob Agents Chemother* 47(2):800-803, 2003.

Navaratnam V, Mordi MN, Mansor SM: Simultaneous determination of artesunic acid and dihydroartemisinin in blood plasma by high-performance liquid chromatography for application in clinical pharmacological studies. *J Chromatograph B* 692:157-162, 1997.

Navaratnam V, Mansor SM, Mordi MN, Akbar A, Abdullah MN: Comparative pharmacokinetic study of oral and rectal formulations of artesunic acid in healthy volunteers. *Eur J Clin Pharmacol* 54:411-414, 1998.

Navaratnam V, Mansor SM, Sit NW, Grace J, Li Q, Olliaro P: Pharmacokinetics of artemisinin-type compounds. *Clin Pharmacokinet* 39:255-270, 2000.

Newman RD, Parise ME, Slutsker L, Nahlen B, Steketee RW: Safety, efficacy and determinants of effectiveness of antimalarial drugs during pregnancy: implications for prevention programmes in *Plasmodium falciparum*-endemic sub-Saharan Africa. *Trop Med Int Health* 8(6):488-506, 2003.

Newton P, Suputtamongkol Y, Teja-Isavadharm P, Pukrittayakamee S, Navaratnam V, Bates I, White N: Antimalarial bioavailability and disposition of artesunate in acute *falciparum* malaria. *Antimicrob Agents Chemother* 44:972-977, 2000.

Newton P, Proux S, Green M, Smithuis F, Rozendaal J, Prakongpan S, Chotivanich K, Mayxay M, Looareesuwan S, Farrar J, Nosten F, White NJ: Fake artesunate in southeast Asia. *Lancet* 357(9272):1948-1950, 2001.

Newton PN, van Vugt M, Teja-Isavadharm P, Siriyanonda D, Rasameesorj M, Teerapong P, Ruangveerayuth R, Slight T, Nosten F, Suputtamongkol Y, Looareesuwan S, White NJ: Comparison of oral artesunate and dihydroartemisinin antimalarial bioavailabilities in acute *falciparum* malaria. *Antimicrob Agents Chemother* 46:1125-1127, 2002.

Newton PN, Angus BJ, Chierakul W, Dondorp A, Ruangveerayuth R, Silamut K, Teerapong P, Suputtamongkol Y, Looareesuwan S, White NJ. Randomized comparison of artesunate and quinine in the treatment of severe *falciparum* malaria. *Clin Infect Dis.* 37(1):7-16, 2003.

Ngo T, Duraisingh M, Reed M, Hipgrave D, Biggs B, Cowman AF: Analysis of *pfert*, *pfmdr1*, *dhfr*, and *dhps* mutations and drug sensitivities in *Plasmodium falciparum* isolates from patients in Vietnam before and after treatment with artemisinin. *Am J Trop Med Hyg* 68(3):350-356, 2003.

Nontprasert A, Nosten-Bertrand M, Pukrittayakamee S, Vanijanonta S, Angus BJ, White NJ: Assessment of the neurotoxicity of parenteral artemisinin derivatives in mice. *Am J Trop Med Hyg* 59:519-522, 1998.

Nontprasert A, Pukrittayakamee S, Dondorp AM, Clemens R, Looareesuwan S, White NJ. Neuropathologic toxicity of artemisinin derivatives in a mouse model. *Am J Trop Med Hyg* 67(4):423-429, 2002.

Nosten F: Artemisinin; large community studies. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/45-S1/46, 1994.

Nosten F, van Vugt M, White NJ: Intrarectal artemisinin derivatives. *Med Trop (Mars)* 58:63-64, 1998.

Nosten F, van Vugt M, Price R, Luxemburger C, Thway KL, Brockman A, McGready R, ter Kuile F, Looareesuwan S, White NJ: Effects of artesunate-mefloquine combination on incidence of *Plasmodium falciparum* malaria and mefloquine resistance in western Thailand: a prospective study. *Lancet* 356:297-302, 2000.

\*Oh S, Jeong IH, Shin WS, Lee S: Growth inhibition activity of thioacetal artemisinin derivatives against human umbilical vein endothelial cells. *Bioorg Med Chem Lett* 3(21):3665-3668, 2003.

\*Oh S, Jeong IH, Ahn CM, Shin WS, Lee S. Synthesis and antiangiogenic activity of thioacetal artemisinin derivatives. *Bioorg Med Chem*. 12(14):3783-3790, 2004.

Qiao GF, Yang BF, Li WH, Li BY: Effects of artemisinin on action potentials from C-type nodose ganglion neurons. *Acta Pharmacol Sin* 24(9):937-942, 2003.

Olliaro PL, Nair NK, Sathasivam K, Mansor SM, Navaratnam V: Pharmacokinetics of artesunate after single oral administration to rats. *BMC Pharmac* 1:12-15, 2001.

Olliaro PL, Taylor WR: Antimalarial compounds: from bench to bedside. *J Exp Biol* 206(Pt 21):3753-3759, 2003.

O'Neill PM, Posner GH. A medicinal chemistry perspective on artemisinin and related endoperoxides. *J Med Chem*. 47(12):2945-2964, 2004.

O'Neill PM, Miller A, Bishop LPD, Hindley S, Maggs JL, Ward SA, Roberts SM, Scheinmann F, Stachulski AV, Posner GH, Park BK: Synthesis, antimalarial activity, biomimetic iron(II) chemistry, and in vivo metabolism of novel, potent C-10-phenoxy derivatives of dihydroartemisinin. *J Med Chem* 44:58-68, 2001.

O'Neill PM, Searle NL, Kan KW, Storr RC, Maggs JL, Ward SA, Raynes K, Park BK: Novel, potent, semisynthetic antimalarial carba analogues of the first-generation 1,2,4-trioxane artemether. *J Med Chem* 42:5487-5493, 1999.

\*Opsenica D, Angelovski G, Pocsfalvi G, Juranic Z, Zizak Z, Kyle D, Milhous WK, Solaja BA. Antimalarial and antiproliferative evaluation of bis-steroidal tetraoxanes. *Bioorg Med Chem*. 11(13):2761-2768, 2003.

Orisakwe OE, Oluboyo A, Ofoefule S, Obi E, Ilondu N, Afonne OJ, Agbasi P, Chiroma DH: Adsorption studies of artesunate: evaluation of saline cathartics as additive in management of artesunate poisoning. *J Health Sci* 47:491-494, 2001.

Pandey AV, Babbarwal VK, Okoyeh JN, Joshi RM, Puri SK, Singh RL, Chauhan VS. Hemozoin formation in malaria: a two-step process involving histidine-rich proteins and lipids. *Biochem Biophys Res Commun*. 308(4):736-743, 2003.

Pankova-Kholmyansky I, Dagan A, Gold D, Zaslavsky Z, Skutelsky E, Gatt S, Flescher E. Ceramide mediates growth inhibition of the *Plasmodium falciparum* parasite. *Cell Mol Life Sci* 60(3):577-587, 2003.

Peters W, Robinson BL, Rossiter JC, Misra K, Jefford CW: The chemotherapy of rodent malaria. XLIX. The activities of some synthetic 1,2,4-trioxanes against chloroquine-sensitive and chloroquine-resistant parasites. Part 2: structure-activity studies on cis-fused cyclopenteno-1,2,4-trioxanes (fenzans) against drug-sensitive and drug-resistant lines of *Plasmodium berghei* and *P. yoelii* ssp. NS in vitro. *Ann Trop Med Parasitol* 87:9-16, 1993.

Petras JM, Kyle DE, Gettayacamin M, Young GD, Bauman RA, Webster HK, Corcoran KD, Peggins JO, Vane MA, Brewer TG: Arteether: risks of two-week administration in *Macaca mulatta*. *Am J Trop Med Hyg* 56:390-396, 1997.

Phillips-Howard PA: Regulation of drug use and post-registration surveillance. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/59-S1/62, 1994.

Phillips-Howard PA, ter Kuile FO: CNS adverse events associated with antimalarial agents. *Drug Safty* 12:370-383, 1995.

Phillipson JD: Natural products as drug. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/17-S1/19, 1994.

Phuong CXT, Bethell DB, Phuong PT, Mai TTT, Thuy TTN, Ha NTT, Thuy PTT, Anh NTT, Day NPJ, White NJ: Comparison of artemisinin suppositories, intramuscular artesunate and intravenous quinine for the treatment of severe childhood malaria. *Trans R Soc Trop Med Hyg* 91:335-342, 1997.

Pickard AL, Wongsrichanalai C, Purfield A, Damwendo D, Emery K, Zalewski C, Kawamoto F, Miller RS, Meshnick SR: Resistance to antimalarials in Southeast Asia and genetic polymorphisms in *pfmdrl*. *Antimicrob Agents Chemother* 47(8):2418-2423, 2003.

Pittler MH, Ernst E: Artemether for severe malaria: a meta-analysis of randomized clinical trials. *Clin Infect Dis* 28:597-601, 1999.

Posner GH, Cumming JN, Woo SH, Ploypradith P, Xie S, Shapiro TA: Orally active antimalarial 3-substituted trioxanes: new synthetic methodology and biological evaluation. *J Med Chem* 41:940-951, 1998.

Posner GH, Jeon HB, Ploypradith P, Paik IH, Borstnik K, Xie S, Shapiro TA: Orally active, water-soluble antimalarial 3-aryltrioxanes: short synthesis and preclinical efficacy testing in rodents. *J Med Chem* 45:3824-3828, 2002.

Posner GH, Parker MH, Northrop J, Elias JS, Ploypradith P, Xie S, Shapiro TA: Orally active, hydrolytically stable, semisynthetic, antimalarial trioxanes in the artemisinin family. *J Med Chem* 42:300-304, 1999.

\*Posner GH, Ploypradith P, Parker MH, O'Dowd H, Woo SH, Northrop J, Krasavin M, Dolan P, Kensler TW, Xie S, Shapiro TA: Antimalarial, antiproliferative, and antitumor activities of artemisinin-derived, chemically robust, trioxane dimers. *J Med Chem* 42:4275-4280, 1999.

\*Posner GH, Park IH, Sur S, McRiner AJ, Borstnik K, Xie S, Shapiro TA: Orally active, antimalarial, anticancer, artemisinin-derived trioxane dimers with high stability and efficacy. *J Med Chem* 46:1060-1065, 2003.

Posner GH, O'Neill PM. Knowledge of the proposed chemical mechanism of action and cytochrome p450 metabolism of antimalarial trioxanes like artemisinin allows rational design of new antimalarial peroxides. *Acc Chem Res.* 37(6):397-404, 2004.

\*Posner GH, McRiner AJ, Paik IH, Sur S, Borstnik K, Xie S, Shapiro TA, Alagbala A, Foster B. Anticancer and antimalarial efficacy and safety of artemisinin-derived trioxane dimers in rodents. *J Med Chem.* 47(5):1299-1301, 2004.

Price RN, Nosten F, Luxemburger C, ter Kuile FO, Paiphun L, Chongsuphajaisiddhi T, White NJ: Effects of artemisinin derivatives on malaria transmissibility. *Lancet* 347:1654-1658, 1996.

Price R, Luxemburger C, van Vugt M, Nosten F, Kham A, Simpson J, Looareesuwan S, Chongsuphajaisiddhi T, White NJ: Artesunate and mefloquine in the treatment of uncomplicated multidrug-resistant hyperparasitaemic falciparum malaria. *Trans R Soc Trop Med Hyg* 92:207-211, 1998.

Price R, Van Vugt M, Nosten F, Luxemburger C, Brockman A, Phaipun L, Chongsuphajaisiddhi T, White N: Artesunate versus artemether for the treatment of recrudescence multidrug-resistant falciparum malaria. *Am J. Trop Med Hyg* 59:883-888, 1998.



Price R, Simpson JA, Teja-Isavatharm P, Than MM, Luxemburger C, Heppner DG, Chongsuphajaisiddhi T, Nosten F, White NJ: Pharmacokinetics of mefloquine combined with artesunate in children with acute falciparum malaria. *Antimicrob Agents Chemother* 43:341-346, 1999.

Price RN, Nosten F, Luxemburger C, van Vugt M, Phaipun L, Chongsuphajaisiddhi T, White NJ: Artesunate/mefloquine treatment of multi-drug resistant falciparum malaria. *Trans R Soc Trop Med Hyg* 91:574-577, 1997.

Qiao GF, Yang BF, Li WH, Li BY. Effects of artemisinin on action potentials from C-type nodose ganglion neurons. *Acta Pharmacol Sin.* 24(9):937-942, 2003.

Qinghaosu Antimalaria Coordinating Research Group: Antimalaria studies on qinghaosu. *Chin Med J* 92:811-816, 1979.

Rajanikanth M, Madhusudanan KP, Gupta RC: Liquid chromatographic-mass spectrometric method for the determination of alpha-, beta-artether in rat serum. *J Chromatogr B Analyt Technol Biomed Life Sci* 783(2):391-399, 2003.

\*Reungpatthanapong P, Mankhetkorn S: Modulation of multidrug resistance by artemisinin, artesunate and dihydroartemisinin in K562/adr and GLC/adr resistant cell lines. *Biol Pharm Bull* 25:1555-1561, 2002.

Ribeiro IR, Olliaro P: Safety of artemisinin and its derivatives. A review of published and unpublished clinical trials. *Med Trop (Mars)* 58:50-53, 1998.

Robert A, Coppel Y, Meunier B: Alkylation of heme by the antimalarial drug artemisinin. *Chem Commun (Camb)*:414-415, 2002.

Roche G, Helenport JP: The view of the pharmaceutical industry. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/57-S1/58, 1994.

Rodriguez M, Bonnet-Delpon D, Begue JP, Robert A, Meunier B: Alkylation of manganese(II) tetraphenylporphyrin by antimalarial fluorinated artemisinin derivatives. *Bioorg Med Chem Lett* 24;13(6):1059-1062, 2003.

\*Sadava D, Phillips T, Lin C, Kane SE: Transferrin overcomes drug resistance to artemisinin in human small-cell lung carcinoma cells. *Cancer Lett* 179:151-156, 2002.

Salako LA, walker O, Sowunmi A, et al: Artemether in moderately severe and cerebral malaria in Nigerian children. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/13-S1/15, 1994.

Salako LA, Guiguemde R, Mittelholzer ML, Haller L, Sorenson F, Sturchler D: Ro 42-1611 in the treatment of patients with mild malaria: a clinical trial in Nigeria and Burkina Faso. *Trop Med Parasitol* 45:284-287, 1994.

Schmuck G, Roehrdanz E, Haynes RK, Kahl R: Neurotoxic mode of action of artemisinin. *Antimicrob Agent Chemother* 46:821-827, 2002.

Seguro AC, Campos SB. Diuretic effect of sodium artesunate in patients with malaria. *Am J Trop Med Hyg* 67(5):473-474, 2002.

Selmeçzi K, Robert A, Claparols C, Meunier B. Alkylation of human hemoglobin A0 by the antimalarial drug artemisinin. *FEBS Lett.* 556(1-3):245-248, 2004.

Seo HJ, Surh YJ: Eupatilin, a pharmacologically active flavone derived from *Artemisia* plants, induces apoptosis in human promyelocytic leukemia cells. *Mutat Res* 496:191-198, 2001.

\*Shaikenov TE, Adekenov SM, Williams RM, Prashad N, Baker FL, Madden TL, Newman R: Arglablin-DMA, a plant derived sesquiterpene, inhibits farnesyltransferase. *Oncol Rep* 8:173-179, 2001.

Shrimali M, Bhattacharya AK, Jain DC, Bhakuni RS, Sharma RP: Sodium artelinate: a potential antimalarial. *Ind J Chem* 37B:1161-1163, 1998.

Shukla KL, Gund TM, Meshnick SR: Molecular modeling studies of the artemisinin (qinghaosu)-hemin interaction: docking between the antimalarial agent and its putative receptor. *J Mol Grap* 13:215-222, 1995.

Sibmoo N, Udomsangpetch R, Kijjoa A, Chantharaksri U, Manketkorn S: Redox reaction of artemisinin with ferrous and ferric ions in aqueous buffer. *Chem Pharm Bull* 49:1541-1546, 2001.

Sidhu JS, Ashton M: Single-dose, comparative study of venous, capillary and salivary artemisinin concentrations in healthy, male adults. *Am J Trop Med Hyg* 56:13-16, 1997.

Sidhu JS, Ashton M, Huong NV, Hai TN, Karlsson MO, Sy ND, Jonsson EN, Cong LD: Artemisinin population pharmacokinetics in children and adults with uncomplicated falciparum malaria. *Br J Clin Pharmacol* 45:347-354, 1998.

Simonsson US, Jansson B, Hai TN, Huong DX, Tybring G, Ashton M: Artemisinin autoinduction is caused by involvement of cytochrome P450 2B6 but not 2C9. *Clin Pharmacol Ther* 74(1):32-43, 2003.

\*Singh NP, Lai H: Selective toxicity of dihydroartemisinin and holotransferrin toward human breast cancer cells. *Life Sci* 70:49-56, 2001.

\*Singh NP, Verma KB: Case report of a laryngeal squamous cell carcinoma treated with artesunate. *Arch Oncol* 10:2790280, 2002.

\*Singh NP, Lai HC. Artemisinin induces apoptosis in human cancer cells. *Anticancer Res.* 24(4):2277-2280, 2004.

Smith H, Crandall I, Prudhomme J, Sherman IW: Optimization and inhibition of the adherent ability of *Plasmodium falciparum*-infected erythrocytes. *Mem Inst Oswaldo Cruz* 87 Suppl 3:303-312, 1992.

Smith SL, Fishwick J, McLean WG, Edwards G, Ward SA: Enhanced in vitro neurotoxicity of artemisinin derivatives in the presence of haemin. *Biochem Pharmacol* 53:5-10, 1997.

\*Smith SL, Maggs JL, Edwards G, Ward SA, Park BK, McLean WG: The role of iron in neurotoxicity: a study of novel antimalarial drugs. *Neurotoxicology* 19:557-559, 1998.

Smith SL, Sadler CJ, Dodd CC, Edwards G, Ward SA, Park BK, McLean WG: The role of glutathione in the neurotoxicity of artemisinin derivatives in vitro. *Biochem Pharmacol* 61:409-416, 2001.

Somo-Moyou R, Mittelholzer ML, Sorenson F, Haller L, Sturchler D: efficacy of Ro 42-1611 (arteplene) in the treatment of patients with mild malaria: a clinical trial in Cameroon. *Trop Med Parasitol* 45:288-291, 1994.

Solaja BA, Terzic N, Pocsfalvi G, Gerena L, Tinant B, Opsenica D, Milhous WK. Mixed steroidal 1,2,4,5-tetraoxanes: antimalarial and antimycobacterial activity. *J Med Chem.* 45(16):3331-3336, 2002.

Souret FF, Kim Y, Wyslouzil BE, Wobbe KK, Weathers PJ: Scale-up of *Artemisia annua* L. hairy root cultures produces complex patterns of terpenoid gene expression. *Biotechnol Bioeng* 83(6):653-667, 2003.

Stermitz FR, Scriven LN, Tegos G, Lewis K. Two flavonols from *Artemisia annua* which potentiate the activity of berberine and norfloxacin against a resistant strain of *Staphylococcus aureus*. *Planta Med* 68(12):1140-1141, 2002.

\*Sun WC, Han JX, Yang WY, Deng DA, Yue XF: [Antitumor activities of 4 derivatives of artemisic acid and artemisinin B in vitro]. *Zhongguo Yao Li Xue Bao* 13:541-543, 1992.

Suputtamongkol Y, Newton PN, Angus B, Teja-Isavadharm P, Keeratithakul D, Rasameesoraj M, Pukrittayakamee S, White NJ. A comparison of oral artesunate and artemether antimalarial bioactivities in acute *falciparum* malaria. *Br J Clin Pharmacol.* 52(6):655-661, 2001.

Svensson US, Ashton M: Identification of the human cytochrome P450 enzymes involved in the in vitro metabolism of artemisinin. *Br J Clin Pharmacol* 48:528-535,

1999.

Svensson US, Ashton M, Kai TN, Bertilsson L, Huong DX, Huong NV, Nieu NT, Sy ND, Lykkesfeldt J, Cong LD: Artemisinin induces omeprazole metabolism in human beings. *Clin Pharmacol Ther* 64:160-167, 1998.

Svensson US, Sandstrom R, Carlborg O, Lennernas H, Ashton M: High in situ rat intestinal permeability of artemisinin unaffected by multiple dosing and with no evidence of P-glycoprotein involvement. *Drug Metab Dispos* 27:227-232, 1999.

Svensson US, Maki-Jouppila M, Hoffmann KJ, Ashton M: Characterisation of the human liver in vitro metabolic pattern of artemisinin and auto-induction in the rat by use of nonlinear mixed effects modelling. *Biopharm Drug Dispos* 24(2):71-85, 2003.

Sy ND, Hoan DB, Dung NP, Huong NV, Binh LN, van Son M, Meshnick SR: Treatment of malaria in Vietnam with oral artemisinin. *Am J Trop Med Hyg* 48:398-402, 1993.

Szpilman AM, Korshin EE, Hoos R, Posner GH, Bachi MD: Iron(II)-induced degradation of antimalarial beta-sulfonyl endoperoxides: evidence for the generation of potentially cytotoxic carbocations. *J Org Chem* 66:6531-6540, 2001.

Tang Y, Dong Y, Vennerstrom JL. Synthetic peroxides as antimalarials. *Med Res Rev.* 24(4):425-448, 2004.

Teja-Isavadharm P, Nosten F, Kyle DE, Luxemburger C, ter Kuile F, Peggins JO, Brewer TG, White NJ: Comparative bioavailability of oral, rectal, and intramuscular artesunate in healthy subjects: use of simultaneous measurement by high performance liquid chromatography and bioassay. *Br J Clin Pharmacol* 42:599-604, 1996.

Teja-Isavadharm P, Watt G, Eamsila C, Jongsakul K, Li Q, Keeratithakul D, Sirisopana N, Luesutthiviboon L, Brewer TG, Kyle DE: Comparative pharmacokinetics and effect kinetics of orally administered artesunate in healthy volunteers and patients with uncomplicated falciparum malaria. *Am J Trop Med Hyg* 65:717-721, 2001.

Titulaer HAC, Zuidema J, Kager PA, Wetsteyn JCFM, Lugt CB, Merkus FWHM: The pharmacokinetics of artemisinin after oral, intramuscular and rectal administration to volunteers. *J Pharm Pharmacol* 42:810-813, 1990.

Valecha N, Gupta S, Usha D, Biswas S, Sharma A, Adak T, Asthana OP, Sharma VP: Efficacy of  $\alpha,\beta$ -artesunate in acute uncomplicated *P. falciparum* malaria. *Int J Clin Pharm Res* 17:11-15, 1997.

Valecha N, Tripathi KD. Artemisinin: current status in malaria. *Ind J Pharmacol* 29:71-75, 1997.

van Agtmael MA, Butter JJ, Portier EJG, van Boxtel CJ: Validation of an improved reversed-phase high-performance liquid chromatography assay with reductive electrochemical detection for the determination of artemisinin derivatives in man. *Ther Drug Monit* 20:109-116, 1998.

van Agtmael MA, Cheng-Qi S, Qing JX, Mull R, van Boxtel CJ: Multiple dose pharmacokinetics of artemether in Chinese patients with uncomplicated falciparum malaria. *Int J Antimicrob Agents* 12:151-158, 1999.

van Agtmael MA, Eggelte TA, van Boxtel CJ: Artemisinin drugs in the treatment of malaria: from medicinal herb to registered medication. *Trends Pharmacol Sci* 20:199-205, 1999.

van Agtmael MA, Gupta V, van der Graaf CAA, van Boxtel CJ: The effect of grapefruit juice on the time-dependent decline of artemether plasma levels in healthy subjects. *Clin Pharmacol Ther* 66:408-414, 1999.

van Agtmael MA, Gupta V, van der Wosten TH, Rutten JPB, van Boxtel CJ: Grapefruit juice increases the bioavailability of artemether. *Eur J Clin Pharmacol* 55:405-410, 1999.

van Hensbrook MB, Onyiorah E, Jaffar S, Schneider G, Palmer A, Frenkel J, Enwere G, Forck S, Nusmeijer A, Bennett S, Greenwood B, Kwiatkowski D: A trial of artemether or quinine in children with cerebral malaria. *New England J Med* 335(2):69-75, 1996.

Van Nijlen T, Brennan K, Van den Mooter G, Blaton N, Kinget R, Augustijns P: Improvement of the dissolution rate of artemisinin by means of supercritical fluid technology and solid dispersions. *Int J Pharm* 254(2):173-178, 2003.

van Vugt M, Angus BJ, Price RN, Mann C, Simpson JA, Poletto C, Htoo SE, Looareesuwan S, White NJ, Nosten F: A case-control auditory evaluation of patients treated with artemisinin derivatives for multidrug-resistant *Plasmodium falciparum* malaria. *Am J Trop Med Hyg* 62:65-69, 2000.

van Vugt M, Brockman A, Gemperli B, Luxemburger C, Gathmann I, Royce C, Slight T, Looareesuwan S, White NJ, Nosten F: Randomized comparison of artemether-benflumetol and artesunate-mefloquine in treatment of multidrug-resistant falciparum malaria. *Antimicrob Agents Chemother* 42:135-139, 1998.

van Vugt M, Ezzet F, Nosten F, Gathmann I, Wilairatana P, Looareesuwan S, White NJ: No evidence of cardiotoxicity during antimalarial treatment with artemether-lumefantrine. *Am J Trop Med Hyg* 61:964-967, 1999.

Van Vugt M, Wilairatana P, Gemperli B, Gathmann I, Phaipun L, Brockman A, Luxemburger C, White NJ, Nosten F, Looareesuwan S: Efficacy of six doses of artemether-lumefantrine (benflumetol) in multidrug-resistant *Plasmodium falciparum* malaria. *Am J Trop Med Hyg* 60:936-942, 1999.

- Vattanaviboon P, Siritanaratkul N, Ketpirune J, Wilairat P, Yuthavong Y: Membrane heme as a host factor in reducing effectiveness of dihydroartemisinin. *Biochem Pharmacol* 64:91-98, 2002.
- Vennerstrom JL, Dong Y, Andersen SL, Ager AL, Fu HN, Miller RE, Wesche DL, Kyle DE, Gerena L, Walters SM, Wood JK, Edwards G, Holme AD, McLean WG, Milhous WK: Synthesis and antimalarial activity of sixteen dispiro-1,2,4,5-tetraoxanes: alkyl-substituted 7,8,15,16-tetraoxadispiro[5.2.5.2]hexadecanes. *J Med Chem* 43:2753-2758, 2000.
- Vennerstrom JL, Ager AL Jr, Andersen SL, Grace JM, Wongpanich V, Angerhofer CK, Hu JK, Wesche DL. Assessment of the antimalarial potential of tetraoxane WR 148999. *Am J Trop Med Hyg.* 62(5):573-578, 2000.
- Vennerstrom JL, Arbe-Barnes S, Brun R, Charman SA, Chiu FC, Chollet J, Dong Y, Dorn A, Hunziker D, Matile H, McIntosh K, Padmanilayam M, Santo Tomas J, Scheurer C, Scoreaux B, Tang Y, Urwyler H, Wittlin S, Charman WN. Identification of an antimalarial synthetic trioxolane drug development candidate. *Nature.* 430(7002):900-904, 2004.
- Vinh H, Huong NN, Ha TTB, Cuong BM, Phu NH, Chau TTH, Quoi PT, Arnold K, Hien TT: Severe and complicated malaria treated with artemisinin, artesunate or artemether in Viet Nam. *Trans R Soc Trop Med Hyg* 91:465-467, 1997.
- Vyas N, Avery BA, Avery MA, Wyandt CM: carrier-mediated partitioning of artemisinin into *Plasmodium falciparum*-infected erythrocytes. 46:105-109, 2002.
- Walker DJ, Pitsch JL, Peng MM, Robinson BL, Peters W, Bhisutthibhan J, Meshnick SR: Mechanism of artemisinin resistance in the rodent malaria pathogen *Plasmodium yoelii*. *Antimicrob Agent Chemother* 44:344-347, 2000.
- Wallaart TE, van Uden W, Lubberink HGM, Woerdenbag HJ, Pras N, Quax WJ. Isolation and identification of dihydroartemisinic acid from *Artemisia annua* and its possible role in the biosynthesis of artemisinin. *J Nat Prod* 62(3):430-433, 1999.
- Wallaart TE, Pras N, Quax WJ. Isolation and identification of dihydroartemisinic acid hydroperoxide from *artemisia annua*: A novel biosynthetic precursor of artemisinin. *J Nat Prod* 62(8):1160-1162, 1999.
- Wallaart TE, Pras N, Beekman AC, Quax WJ. Seasonal variation of artemisinin and its biosynthetic precursors in plants of *Artemisia annua* of different geographical origin: proof for the existence of chemotypes. *Planta Med* 66(1):57-62, 2000.
- Wallaart TE, Bouwmeester HJ, Hille J, Poppinga L, Maijers NCA: Amorpho-4,11-diene synthase: cloning and functional expression of a key enzyme in the biosynthetic pathway

of the novel antimalarial drug artemisinin. *Planta* 212:460-465, 2001.

Wang Q, Wu LM, Zhao Y, Zhang XL, Wang NP. [The anticancer effect of artesunate and its mechanism] *Yao Xue Xue Bao* 37(6):477-478, 2002.

\*Wartenberg M, Wolf S, Budde P, Grunheck F, Acker H, Hescheler J, Wartenberg G, Sauer H. The antimalaria agent artemisinin exerts antiangiogenic effects in mouse embryonic stem cell-derived embryoid bodies. *Lab Invest.* 83(11):1647-1655, 2003.

Webster HK, Lehnert EK: Chemistry of artemisinin: an overview. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/27-S1/29, 1994.

Wei N, Sadrzadeh SMH: Enhancement of hemin-induced membrane damage by artemisinin. *Biochem Pharmacol* 48:737-741, 1994.

Weidekamm E, Dumont E, Jaquet C: Tolerability and pharmacokinetics of Ro 42-1611 (arteflene) in man. *Trop Med Parasitol* 45:278-283, 1994.

Wesche DL, DeCoster MA, Tortella FC, Brewer TG: Neurotoxicity of artemisinin analogs in vitro. *Antimicrob Agents Chemother* 38:1813-1819, 1994.

White NJ: Artemisinin: current status. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/3-S1/4, 1994.

White NJ: Assessment of the pharmacodynamic properties of antimalarial drugs in vivo. *Antimicrob Agent Chemother* 41:1413-1422, 1997.

White NJ: Drug resistance in malaria. *Brit Med Bull* 54:703-715, 1998.

White NJ, Olliaro P: Artemisinin and derivatives in the treatment of uncomplicated malaria. *Med Trop (Mars)* 58:54-56, 1998.

White NJ: Clinical pharmacokinetics and pharmacodynamics of artemisinin and derivatives. *Trans R Soc Trop Med Hyg* 88 (supp 1):S1/41-S1/43, 1994.

White NJ, van Vugt M, Ezzet F: Clinical pharmacokinetics and pharmacodynamics and pharmacodynamics of artemether-lumefantrine. *Clin Pharmacokinet* 37:105-125, 1999.

\*Woerdenbag HJ, Merfort I, Passreiter CM, Schmidt TJ, Willuhn G, van Uden W, Pras N, Kampinga HH, Konings AWT: Cytotoxicity of flavonoids and sesquiterpene lactones from *Arnica* species against the GLC4 and the COLO 320 cell lines. *Planta Med* 60:434-437, 1994.

\*Woerdenbag HJ, Moskal TA, Pras N, Malingre TM: Cytotoxicity of artemisinin-related endoperoxides to Ehrlich ascites tumor cells. *J Nat Prod* 56:849-856, 1993.

Woerdenbag HJ, Pras N, van Uden W, Wallaart TE, Beekman AC, Lugt CB: Progress in the research of artemisinin-related antimalarials: an update. *Pharm World Sci* 16:169-180, 1994.

Wong JW, Yuen KH, Nagappan S, Shahul WS, Ho SSD, Gan EK, Toh WT. Therapeutic equivalence of a low dose artemisinin formulation in falciparum malaria patients. *J Pharm Pharmacol* 55:193-198, 2003.

Wongsrichanalai C, Wimonwattrawatee T, Sookto P, Laoboonthai A, Heppner DG, Kyle DE, Wernsdorfer WH: In vitro sensitivity of *Plasmodium falciparum* to artesunate in Thailand. *Bull World Heal Org* 77:392-398, 1999.

\*Wu JM, Shan F, Wu GS, Li Y, Ding J, Xiao D, Han JX, Atassi G, Leonce S, Caignard DH, Renard P: Synthesis and cytotoxicity of artemisinin derivatives containing cyanoarylmethyl group. *Eur J Med Chem* 36:469-479, 2001.

Wu TX, Liu GJ, Zhang MM, Wang Q, Ni J, Wei JF, Zhou LK, Duan X, Chen XY, Zheng J, Qiao JQ. [Systematic review of benefits and harms of artemisinin-type compounds for preventing schistosomiasis] *Zhonghua Yi Xue Za Zhi*. 83(14):1219-1224, 2003. [Article in Chinese]

Wu WM, Chen YL, Zhai Z, Xiao SH, Wu YL: Study on the mechanism of action of artemether against schistosomes: the identification of cysteine adducts of both carbon-centred free radicals derived from artemether. *Bioorg Med Chem Lett* 13(10):1645-1647, 2003.

Wu Y: How might qinghaosu (artemisinin) and related compounds kill the intraerythrocytic malaria parasite? A chemist's view. *Account Chem Res* 35:255-259, 2002.

Wu Y, Liu HH: Probing the possible molecular origin of the highly selective toxicity of antimalarial peroxide qinghaosu (artemisinin). *Chem Res Toxicol* 16(10):1202-1206, 2003.

Wu Y, Yue ZY, Wu YL. Interaction of Qinghaosu (Artemisinin) with Cysteine Sulfhydryl Mediated by Traces of Non-Heme Iron. *Angew Chem Int Ed Engl*. 38(17):2580-2582, 1999.

Wu Y, Yue ZY, Liu HH: New insight into the degradation of qinghaosu (artemisinin) mediated by non-heme-iron chelates, and their relevance to the antimalarial mechanism. *Helvetica Chimica Acta* 84:928-932, 2001.



Xiao SH, You JQ, Gao HF, Mei JY, Jiao PY, Chollet J, Tanner M, Utzinger J. *Schistosoma japonicum*: effect of artemether on glutathione S-transferase and superoxide dismutase. *Exp Parasitol* 102(1):38-45, 2002.

Xiao SH, Wu YL, Tanner M, Wu WM, Utzinger J, Mei JY, Scorneaux B, Chollet J, Zhai Z. *Schistosoma japonicum*: in vitro effects of artemether combined with haemin depend on cultivation media and appraisal of artemether products appearing in the media. *Parasitol Res* 89(6):459-466, 2003.

\*Yamachika E, Habte T, Oda D. Artemisinin: an alternative treatment for oral squamous cell carcinoma. *Anticancer Res.* 24(4):2153-2160, 2004.

Yang YZ, Asawamahasakda W, Meshnick SR: Alkylation of human albumin by antimalarial artemisinin. *Biochem Pharmacol* 46: 336-339, 1993.

Yang YZ, Little B, Meshnick SR: Alkylation of proteins by artemisinin. Effects of heme, pH, and drug structure. *Biochem Pharmacol* 48:569-573, 1994.

Zhan JX, Zhang YX, Guo HZ, Han J, Ning LL, Guo DA: Microbial metabolism of artemisinin by *Mucor polymorphosporus* and *Aspergillus niger*. *J Nat Prod* 65(11):1693-1695, 2002.

Zhang F, Gosser DK, Jr., Meshnick SR: Hemin-catalyzed decomposition of artemisinin (qinghaosu). *Biochem Pharmacol* 43:1805-1809, 1992.

Zhang SQ, Hai TN, Ilett KF, Huong Dx, Davis TME, Ashton M: Multiple dose study of interactions between artesunate and artemisinin in healthy volunteers. *Br J Clin Pharmacol* 52:377-385, 2001.

Zhao YH, Wang JY [Neurotoxicity of artemisinin antimalarials and its mechanism] *Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi* 20(1):49-51, 2002.

Zhao KC, Xuan WY, Zhao Y, Song ZY: [The pharmacokinetics of a transdermal preparation of artesunate in mice and rabbits]. *Yao Xue Xue Bao* 24:813-816, 1989.

\*Zheng GQ: Cytotoxic terpenoids and flavonoids from *Artemisia annua*. *Planta Med* 60:54-57, 1994.

Ziffer H, Highet RJ, Klayman DL: Artemisinin: an endoperoxidic antimalarial from *Artemisia annua* L. *Fortschr Chem Org Naturst* 72:121-124, 1997.