

LITERATURE CITED

- Alam, M. T., H. Bora, P. K. Bharti, M. A. Saifi, M. K. Das, V. Dev, A. Kumar, N. Singh, A. P. Dash, B. Das, S. Wajihullah and D. Yagya. 2007. Similar trends of pyrimethamine resistance-associated mutations in *Plasmodium vivax* and *P. falciparum*. **Antimicrob. Agents. Chemother.** 51(3): 857-863.
- Alker, A. P., V. Mwapasa and R. Meshnick. 2004. Rapid Real-time PCR Genotyping of Mutations Associated with Sulfadoxine-Pyrimethamine Resistance in *Plasmodium falciparum*. **Antimicrob. Agents. Chemother.** 48(8): 2924-2929.
- Avery, M. A., K. M. Muraleedharan, P. V. Desai, A. K. Bandyopadhyaya, M. M. Furtado and B. L. Tekwani. 2003. Structure-activity relationships of the antimalarial agent artemisinin. design, synthesis, and CoMFA studies toward the development of artemisinin-based drugs against leishmaniasis and malaria. **J. Med. Chem.** 46(20): 4244-4258.
- Avery, M. A., M. Alvim-Gaston, C. R. Rodrigues, E. J. Barreiro, F. E. Cohen, Y. A. Sabnis and J. R. Woolfrey. 2002. Structure-activity relationships of the antimalarial agent artemisinin. The development of predictive in vitro potency models using CoMFA and HQSAR methodologies. **J. Med. Chem.** 45(2): 292-303.
- Basco, L. K., P. E. Pecoulas, C. M. Wilson, J. L. Bras and A. Mazabraud. 1995. Point mutations in the dihydrofolate reductase-thymidylate synthase gene and pyrimethamine and cycloguanil resistance in *Plasmodium falciparum*. **Mol. Biochem. Parasitol.** 69: 135-138.
- Botelho, A. 1971. Chemotherapy of malaria. Short historical review. **Anais da Escola Nacional de Saude Publicaede Medicina Tropical, Lisbon.** 5(1/2): 99-114.

- Boys, S. F. and F. Bernardi. 1970. The calculations of small molecular interaction by the difference of separate total energies some procedures with reduced error. **Mol. Phys.** 19: 553-566.
- Brobey, R. K. B., G. Sano, F. Itoh, K. Aso, M. Kimura, T. Mitamura and T. Horii. 1996. Recombinant *Plasmodium falciparum* dihydrofolate reductase-based in vitro screen for antifolate antimalarials. **Mol. Biochem. Parasitol.** 81: 225-237.
- Brown, R.D. and Y.C. Martin. 1997. The information content of 2D and 3D structural descriptors relevant to ligand-receptor binding. **J. Chem. Inf. Comput. Sci.** 37: 1-9.
- Bush, B. L. and R. B. Jr. Nachbar. 1993. Sample-distance Partial Least Squares: PLS optimized for many variables, with application to CoMFA. **J. Comput. Aided Mol. Des.** 7: 587-619.
- Case, D. A., T. A. Darden, III. T. E. Cheatham, C. L. Simmerling, J. Wang, R. E. Duke, R. Luo, K. M. Merz, D. A. Pearlman, M. Crowley, R. C. Walker, W. Zhang, B. Wang, S. Hayik, A. Roitberg, G. Seabra, K. F. Wong, F. Paesani, X. Wu, S. Brozell, V. Tsui, H. Gohlke, L. Yang, C. Tan, J. Mongan, V. Hornak, G. Cui, P. Beroza, D. H. Mathews, C. Schafmeister, W. S. Ross and P. A. Kollman. 2006. **AMBER9.0**.
- Collins W. E., and G. M. Jeffery. 2007. *Plasmodium malariae*: parasite and disease. **Clin. Microbiol. Rev.** 20(4): 579-592.
- Cramer, R. D. III, D. E. Patterson and J. D. Bunce. 1988. Comparative Molecular Field Analysis CoMFA: 1. Effect of shape on binding of steroids to carrier proteins. **J. Am. Chem. Soc.** 110: 5959-5967.

- Cramer, R. D. III, D. E. Patterson and J. D. Bunce. 1989. Recent advances in comparative molecular field analysis (CoMFA). **Prog. Clin. Biol. Res.** 291: 161-165.
- Cheng, F., J. Shen, X. Luo, W. Zhu, J. Gu, R. Ji, H. Jiang and K. Chen. 2002. Molecular docking and 3D-QSAR studies on the possible antimalarial mechanism of artemisinin analogues. **Bioorg. Med. Chem.** 10: 2883-2891.
- Chusacultanchai, S., P. Thiensathit, B. Tarnchompoo, W. Sirawaraporn and Y. Yuthavong. 2002. Novel antifolate resistant mutations of *Plasmodium falciparum* dihydrofolate reductase selected in Escherichia coli. **Mol. Biochem. Parasitol.** 120: 61-72.
- Cho, S. J. and A. Tropsha. 1995. Cross-Validated R²-Guided Region Selection for Comparative Molecular Field Analysis: A Simple Method To Achieve Consistent Results. **J. Med. Chem.** 38: 1060-1066.
- Clark, D.E. and D.R. Westhead. 1996. Evolutionary algorithms in computer-aided molecular design. **J. Comput. Aided Mol. Des.** 4: 337-358.
- Clark, M. and R. D. III. Cramer. 1993. The Probability of Chance Correlation Using Partial Least Squares (PLS). **Quant. Struct.-Act. Relat.** 12(2): 137-145.
- Cody, V. and C. H. Schwalbe. 2006. Structural characteristics of antifolate dihydrofolate reductase enzyme interactions. *Crystallog. Rev.* 12 (4), 301-333.
- Cornell, W. D., P. Cieplak, C. I. Bayly and P. A. Kollman. 1993. Application of RESP Charges to Calculate Conformational Energies, Hydrogen-bond Energies, and Free-energies of Solvation, **J. Am. Chem. Soc.** 115, 9620-9631.

- Cui, Z., L. Zhang and R. Li. 1997. Studies on synthesis of lipophilic antifolate 2,4-diamino-5-methyl-6-(substituted benzylamino) quinazoline compounds with methods of 2D- and 3D-QSAR. **J. Chin. Pharm. Sci.** 6(2): 113-114.
- Cui, Z., W. Zhao and R. Li. 1999. 3D-QSAR study on lipophilic antifolates quinazolines. **Prog. Nat. Sci.** 9(7): 516-519.
- Cummins, P. L., K. Ramnarayan, U. C. Singh and J. E. Gready. 1991. Molecular dynamics/free energy perturbation study on the relative affinities of the binding of reduced and oxidized NADP to dihydrofolate reductase. **J. Am. Chem. Soc.** 113(22): 8247-8256
- Czaplinski, K-H., W. Hansel, M. Wiese and JK. Seydel. 1995. New benzylpyrimidines: inhibition of DHFR from various species. QSAR, CoMFA and PC analysis. **Eur. J. Med. Chem.** 30: 779-787.
- Dapprich, S., I. Komaromi, K. S. Byun, K. Morokuma and M. J. Frisch. 1999. A new ONIOM implementation in Gaussian98. partI. The calculation of energies, gradients, vibrational frequencies and electric field derivatives. **J. Mol. Struct. (Theochem)** 461-462: 1-21.
- Dasgupta, T. and K. S. Anderson. 2008. Probing the Role of Parasite-Specific, Distant Structural Regions on Communication and Catalysis in the Bifunctional Thymidylate Synthase- Dihydrofolate Reductase from *Plasmodium falciparum*. **Biochemistry** 47(5): 1336-1345.
- Delfino, R. T., O. A. Santos-Filho and J. D. Figueroa-Villar. 2002. Molecular modeling of wild-type and antifolate resistant mutant *Plasmodium falciparum* DHFR. **Biophys. Chem.** 98: 287-300.
- Delfino, R. T., O. A. Santos-Filho and J. D. Figueroa-Villar. 2002. Type 2 antifolates in the chemotherapy of *falciparum* malaria. **J. Braz. Chem. Soc.** 13: 727-741.

- Edstein, M. D., A. E. T. Yeo, G. D. Shanks and K. H. Rieckmann. 1997. Ex vivo antimalarial activity of proguanil combined with dapson against cycloguanil-resistant *Plasmodium falciparum* isolates. **Acta Tropica**. 66: 127-135.
- Fidock, D. A., T. Nomura and T. E. Wellems. 1998. Cycloguanil and its parent compound proguanil demonstrate distinct activities against *Plasmodium falciparum* malaria parasites transformed with human dihydrofolate reductase. **Mol. Pharmacol.** 54(6): 1140-1147.
- Fogel, G. B., M. Cheung, E. Pittman and D. Hecht. 2008. Modeling the inhibition of quadruple mutant *Plasmodium falciparum* dihydrofolate reductase by pyrimethamine derivatives. **J. Comput. Aided. Mol. Des.** 22: 29–38.
- Frisch, M. J., G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Jr. Montgomery, T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople. 2003. **Gaussian 03**, revision B.05;Gaussian, Inc.: Pittsburgh.
- Gatton, M. L. and Q. Cheng. 2006. *Plasmodium falciparum* infection dynamics and transmission potential following treatment with sulfadoxine- pyrimethamine. **J. Antimicrob. Chemoth.** 58(1): 47-51.

- Golbraikh, A. and A. Tropsha. 2002. Beware of q^2 !. **J. Mol. Graph. Mod.** 20: 269-276.
- Golbraikh, A., P. Bernard and J. R. Chretien. 2000. Validation of protein-based alignment in 3D quantitative structure-activity relationship with CoMFA models. **Eur. J. Med. Chem.** 35: 123-136.
- Gregson, A. and C.V. Plowe. 2005. Mechanisms of Resistance of Malaria Parasites to Antifolates. **Pharmacol. Rev.** 57, 117-145.
- Hansch, C. and A. Leo. 1995. Exploring QSAR. Fundamentals and Applications in Chemistry and Biology. *American Chemical Society, Washington, DC.*
- Hansch, C and T. Fujita. 1964. A method for the correlation of biological activity and chemical structure. **J. Am. Chem. Soc.** 86: 161-1626.
- Hannongbua, S., K. Nivesanond, L. Lawtrakul, P. Pungpo and P. Wolschann. 2001. 3D-Quantitative Structure-Activity Relationships of HEPT Derivatives as HIV-1 Reverse Transcriptase Inhibitors, Based on Ab Initio Calculations. **J. Chem. Inf. Comput. Sci.** 41: 848-855.
- Haraldson, C. A., J. M. Karle, S. G. Freeman, R. K. Duvadie and M. A. Avery. 1997. The synthesis of 8,8-disubstituted tricyclic analogs of artemisinin. **Bioorgan. Med. Chem. Lett.** 7(18): 2357-2362.
- Hastings, I. M. and M. J. Donnelly. 2005. The impact of antimalarial drug resistance mutations on parasite fitness, and its implications for the evolution of resistance. **Drug Resist. Updat.** 8: 43-50.

- Hekmat-Nejad, M. and P. K. Rathod. 1997. *Plasmodium falciparum*: kinetic interactions of WR99210 with pyrimethamine-sensitive and pyrimethamine-resistant dihydrofolate reductase. **Exp. Parasitol.** 87: 222-228.
- Jung, M. and H. Kim. 2001. CoMFA of artemisinin derivatives: effect of location and size of lattice. **Bioorg. Med. Chem. Lett.** 11: 2041-2044.
- Kamchonwongpaisan, S., R. Quarrell, N. Charoensetakul, R. Ponsinet, T. Vilaivan, J. Vanichtanankul, B. Tarnchompoo, W. Sirawaraporn, G. Lowe and Y. Yuthavong. 2004. Inhibitors of multiple mutants of *Plasmodium falciparum* dihydrofolate reductase and their antimalarial activities. **J. Med. Chem.** 47: 673-680.
- Kim, K. H., G. Greco and E. Novellino. 1998. A Critical Review of Recent CoMFA Applications. **Perspect. Drug Discov. Des.** 257-315.
- Kokpol, S.K., S.V. Hannongbua, N. Thongrit, S. Polman, B.M. Rode and M.G. Schwendinger. 1988. Analysis of structure-activity relation for primaquine antimalarial drugs by a quantum pharmacological approach. **Anal. Sci.** 4: 565-568.
- Kubinyi, H. 1993. QSAR: Hansch Analysis and Related Approaches; *VCH: Weinheim*.
- Kubinyi, H., G. Flokers and Y. C. Martin. 1998. 3D QSAR in Drug Design: Ligand-Protein Interactions and Molecular Similarity. **Perspect. Drug Discov. Des.** 3-398.
- Kuno, M., R. Hongkengkai and S. Hannongbua. 2006. ONIOM-BSSE scheme for H- π system and applications on HIV-1 reverse transcriptase. **Chem. Phys. Lett.** 424: 172-177.

- Kuno, M., S. Hannongbua and K. Morokuma. 2003. Theoretical investigation on nevirapine and HIV-1 reverse transcriptase binding site interaction, based on ONIOM method. **Chem. Phys. Lett.** 380: 456–463.
- Krudsood, S., S. N. Patel, N. Tangpukdee, W. Thanachartwet, W. Leowattana, K. Pornpininworakij, A. K. Boggild, S. Looareesuwan and K. C. Kain. 2007. Efficacy of atovaquone- proguanil for treatment of acute multidrug-resistant *Plasmosium falciparum* malaria in Thailand. **Am. J. Trop. Med. Hyg.** 76(4): 655-658.
- Leartsakulpanich, U., M. Imwong, S. Pukrittayakamee, N. J. White, G. Snounou, W. Sirawaraporn and Y. Yuthavong. 2002. Molecular characterization of dihydrofolate reductase in relation to antifolate resistance in *Plasmodium vivax*. **Mol. Biochem. Parasitol.** 119: 63-73.
- Liu, M., P. Wilairat, S. L. Croft, A. L-C. Tan and M-L. Go. 2003. Structure-activity relationships of antileishmanial and antimalarial chalcones. **Bioorgan. Med. Chem.** 11(13): 2729-2738.
- Marbiah, N. T., E. Petersen, K. David, E. Magbity, J. Lines and D. J. Bradley. 1998. A Controlled Trial of Lambda-cyhalothrin-impregnated Bed Nets and/or Dapsone/Pyrimethamine for Malaria Control in Sierra Leone. **Am. J. Trop. Med. Hyg.** 58(1): 1-6.
- Marshall, G. R. and R. D. III, Cramer. 1988. Three-dimensional structure-activity relationships. **Trends Pharmacol. Sci.** 9(8): 285-289.
- Martin, S. 2007. Malaria Chemotherapeutics Part I: History of Antimalarial Drug Development, Currently Used Therapeutics and Drugs in Clinical Development. **ChemMedChem**, 2(7): 944-986.

- Matsika-Claquin, M. D., D. Menard, A. L. Fontanet, A. Ngwhotue, J. Sarda and A. Talarmin. 2006. Efficacy of chloroquine- proguanil malaria prophylaxis in a non-immune population in Bangui, Central African Republic: a case-control study. **Trop. Med. Hyg.** 100(4): 381-386.
- Matsubara, T., M. Dupuis and M. Aida. 2007. The ONIOM molecular dynamics method for biochemical applications: Cytidine deaminase. **Chem. Phys. Lett.** 437: 138–142.
- Mattioni, B. E. and P. C. Jurs. 2003. Prediction of dihydrofolate reductase inhibition and selectivity using computational neural network and linear discriminant analysis. **J. Mol. Graph. Model.** 21: 391-419.
- Militello, K., M. Dodge, L. Bethke and D. F. Wirth. 2004. Identification of regulatory elements in the *Plasmodium falciparum* genome. **Mol. Biochem. Parasitol.** 134: 75-88.
- Meshnick, S. R. and M. J. Dobson. 2001. The history of antimalarial drugs. **Antimalarial Chemoth.** 15-25.
- Morokuma, K., Q. Wang and T. Vreven. 2006. Performance Evaluation of the Three-Layer ONIOM Method: Case Study for a Zwitterionic Peptide. **J. Chem. Theory Comput.** 2(5): 1317-1324.
- Nakato, H., R. Vivancos and P. R. Hunter. 2007. A systematic review and meta-analysis of the effectiveness and safety of atovaquone- proguanil (Malarone) for chemoprophylaxis against malaria. **J. Antimicrob. Chemoth.** 60(5): 929-936.
- Nilsson, J., S. De Jong and A. K. Smilde. 1997. Multilinear PLS analysis application to 3D QSAR data set. **J. Chemometrics.** 11: 511-524.

- Nosten, F., R. McGready, U. Alessandro, A. Bonell, F. Verhoeff, C. Menendez, M. Clara, T. Mutabingwa and B. Brabin. 2006. Antimalarial drugs in pregnancy: a review. **Curr. Drug Safety**. 1(1): 1-15.
- Nunriem, P., M. Kuno, S. Saen-oon and S. Hannongbua. 2005. Particular interaction between efavirenz and the HIV-1 reverse transcriptase binding site as explained by the ONIOM2 method. **Chem. Phys. Lett.** 405: 198–202.
- Nzila, A. 2006. Inhibitors of De-novo Folate Enzymes in *Plasmodium falciparum*. **Drug Discov. Today**. 11(19-20), 936-944.
- Nzila, A. 2006. The Past, Present and Future of Antifolates in the Treatment of *Plasmodium falciparum* Infection. **J. Antimicrob. Chemother.** 57, 1043-1054.
- Olliaro, P. L. and Y. Yuthavong. 1999. An overview of chemotherapeutic targets for antimalarial drug discovery. **Pharmacol. Ther.** 81: 91-110.
- Onefelt, A., S. Hellberg and W. Svante. 1986. Relationships between induction of anesthesia and mitotic spindle disturbances studied by means of principal component analysis. **Mutat. Res. Lett.** 174(2), 109-13.
- Parenti, M. D., S. Pacchioni, A. M. Ferrari, and G. Rastelli. 2004. Three-Dimensional Quantitative Structure-Activity Relationship Analysis of a Set of *Plasmodium falciparum* Dihydrofolate Reductase Inhibitors Using a Pharmacophore Generation Approach. **J. Med. Chem.** 47: 4258-4267.
- Peterson, D. S., W. K. Milhous and T. E. Wellems. 1990. Molecular basis of differential resistance to cycloguanil and pyrimethamine in *Plasmodium falciparum* malaria. **Proc. Natl. Acad. Sci. U.S.A.** 87: 3018-3022.

- Polhemus, M. E., S. Remich, B. Ogutu, J. Waitumbi, M. Lievens, W. R. Ballou and D. G. Jr. Heppner. 2008. Malaria treatment with atovaquone- proguanil in malaria-immune adults: implications for malaria intervention trials and for pre-exposure prophylaxis of malaria. **Antimicrob. Agents Chemoth.** 52(4): 1493-1495.
- Prapunwattana, P., W. Sirawaraporn, Y. Yuthavong and D. V. Santi. 1996. Chemical synthesis of the *Plasmodium falciparum* dihydrofolate reductase-thymidylate synthase gene. **Mol. Biochem. Parasitol.** 83: 93-106.
- Rastelli, G., S. Sirawaraporn, P. Sompornpisut, T. Vilaivan, S. Kamchonwongpaisan, R. Quarrell, G. Lowe, Y. Thebtaranonth and Y. Yuthavong. 2000. Interaction of pyrimethamine, cycloguanil, WR99210 and their analogues with *Plasmodium falciparum* dihydrofolate reductase: structural basis of antifolate resistance. **Bioorg. Med. Chem.** 8: 1117-1128.
- Redl, G., R. D. III. Cramer and C. E. Berkoff. 1974. Quantitative drug design. **Chem. Soc. Rev.** 3(3): 273-292.
- Saadat, F., M. R. Khorramizadeh and A. Mirshafiey. 2005. Chemoprevention by pyrimethamine. **Immunopharm. Immunot.** 27(2): 233-240.
- Saen-oon, S., M. Kuno and S. Hannongbua. 2005. Binding Energy Analysis for Wild-type and Y181C Mutant HIV-1 RT/8-Cl TIBO Complex Structures: Quantum Chemical Calculations Based on the ONIOM Method. **PROTEINS: Structure, Function, and Bioinformatics.** 61: 859-869.
- Saen-oon, S., O. Aruksakunwong, K. Wittayanarakul, P. Sompornpisut and S. Hannongbua. 2007. Insight into Analysis of Interactions of Saquinavir with HIV-1 Protease in Comparison between the Wild-type and G48V and G48V/L90M Mutants Based on QM and QM/MM Calculations. **J. Mol. Graph. Model.** 26: 720-727.

- Santos-Filho, O. A., R. K. Mishra and A. J. Hopfinger. 2001. Free energy force field (FEFF) 3D-QSAR analysis of a set of *Plasmodium falciparum* dihydrofolate reductase inhibitors. **J. Comput. Aided Mol. Des.** 15: 787–810.
- Sao, S. S. and M. Karplus. 2001. Evaluation of designed ligands by a multiple screening method: Application to glycogen phosphorylase inhibitors constructed with a variety of approaches. **J. Comput. Aided Mol. Des.** 15: 613-647.
- Schlitzer, M. 2007. Malaria chemotherapeutics. Part I: History of antimalarial drug development, currently used therapeutics, and drugs in clinical development. **ChemMedChem.** 2(7): 944-986.
- Sirawaraporn, W., T. Sathitkul, R. Sirawaraporn, Y. Yuthavong and D.V. Santi. 1997. Antifolate-resistant mutants of *plasmodium falciparum* dihydrofolate reductase. **Proc. Natl. Acad. Sci.** 94: 1124-1129.
- Sirawaraporn, S., R. Sirawaraporn, S. Yongkiettrakul, A. Anuwatwora, G. Rastelli, S. Kamchonwongpaisan and Y. Yuthavong. 2002. Mutational analysis of *Plasmodium falciparum* dihydrofolate reductase: the role of aspartate 54 and phenylalanine 223 on catalytic activity and antifolate binding. **Mol. Biochem. Parasitol.** 39: 127-34.
- Sirawaraporn, W., S. Yongkiettrakul, R. Sirawaraporn, Y. Yuthavong and D. V. Santi. 1997. *Plasmodium falciparum*: asparagine mutant at residue 108 of dihydrofolate reductase is an optimal antifolate-resistant single mutant. **Exp. Parasitol.** 87: 245-252.

- Sirichaiwat, C., C. Intaraudom, S. Kamchonwongpaisan, J. Vanichtanankul, Y. Thebtaranonth and Y. Yuthavong. 2004. Target guided synthesis of benzyl-2,4-diaminopyrimidines: their antimalarial activities and affinities to wild type and mutant dihydrofolate reductases from *plasmodium falciparum*. **J. Med. Chem.** 47: 345-354.
- Snow, R. W., C. A. Guerra, A. M. Noor, H. Y. Myint and S. I. Hay. 2005. Estimating Clinical Episodes of Malaria. **Nature.** 434: 214-217.
- Sowunmi, A., B. A. Fateye, A. A. Adedeji, G. O. Gbotosho, T. C. Happi, A. E. Bamgboye, O. M. Bolaji and A. M. J. Oduola. 2006. Predictors of the Failure of Treatment with Pyrimethamine-sulfadoxine in Children with Uncomplicated Falciparum Malaria. **Acta Trop.** 98: 6-14.
- Svante, W. and M. Sjoestroem. 1986. Linear free energy relationships. Local empirical rules - or fundamental laws of chemistry. A reply to Kamlet and Taft. **Acta Chemica Scandinavica, Series B: Organic Chemistry and Biochemistry.** B40(4): 270-7.
- SYBYL Molecular Modelling Softwares, Version 7.0, Tripos Associates, Inc., St. Louis, MO, 63144, USA, 1998.
- Tonmunphean, S., V. Parasuk and S. Kokpol. 2000. QSAR study of antimalarial activities and artemisinin-heme binding properties obtained from docking calculations. **Quant. Struct. -Act. Relat.** 19: 475-483.
- Tonmunphean, S., S. Kokpol, V. Parasuk, P. Wolschann, R. H. Winger, K. R. Liedl and B. M. Rode. 1998. Comparative molecular field analysis of artemisinin derivatives: ab initio versus semiempirical optimized structures. **J. Comput. Aided Mol. Des.** 12(4): 397-409.

- Tschumpera, G. S. and K. Morokuma. 2002. Gauging the applicability of ONIOM (MO/MO) methods to weak chemical interactions in large systems: hydrogen bonding in alcohol dimers. **J. Mol. Struct. (Theochem)** 592: 137–147.
- Uhlemann, A. C., Y. Yuthavong and D. A. Fidock. 2005. Mechanisms of Antimalarial Drug Action and Resistance. **Mol. Arch. Malaria**. 429-461.
- Verloop, A., W. Hoogenstraaten and J. Tipfer. 1976. Development and application of new steric substituent parameters. **Drug Design**. 7: 165-207.
- Vilaivan, T., N. Saesaengseerung, D. Jarprung, S. Kamchonwongpaisan, W. Sirawaraporn and Y. Yuthavong. 2003. Synthesis of solution-phase combinatorial library of 4,6-diamino-1,2-dihydro-1,3,5-triazine and identification of new leads against A16V + S108T mutant dihydrofolate reductase of *Plasmodium falciparum*. **Bioorg. Med. Chem.** 11: 217-224.
- Vreven, T. and K. Morokuma. 1999. The accurate calculation and prediction of the bond dissociation energies in a series of hydrocarbons using the IMOMO (integrated molecular orbital + molecular orbital) methods. **J. Chem. Phys.** 111(19): 8799-8803.
- Vreven, T. and K. Morokuma. 2000. On the application of the IMOMO (integrated molecular orbital + molecular orbital) method. **J. Com. Chem.** 21(16): 1419-1432.
- Vreven, T. and K. Morokuma. 2006. Hybrid methods: ONIOM(QM:MM) and QM/MM. **Annu. Rep. Com. Chem.** 2: 35-51.
- Vreven, T., K. S. Byun, I. Komaromi, S. Dapprich, J. A. Jr. Montgomery, K. Morokuma and M. J. Frisch. 2006. Combining Quantum Mechanics Methods with Molecular Mechanics Methods in ONIOM. **J. Chem. Theory Comput.** 2(3): 815-826.

- Warhurst, D. C. 2002. Resistance to antifolates in *Plasmodium falciparum*, the causative agent of tropical malaria. **Sci. Prog.** 85: 89-111.
- Walliker, D., P. Hunt and H. Babiker. 2005. Fitness of drug-resistant malaria parasites. **Acta Trop.** 94: 251-259.
- Wattananarangsarn, J., S. Chusacultachai, J. Yuvaniyama, S. Kamchonwongpaisan and Y. Yuthavong. 2003. Effect of N-terminal truncation of *Plasmodium falciparum* dihydrofolate reductase on dihydrofolate reductase and thymidylate synthase activity. **Mol. Biochem. Parasitol.** 126: 97-102.
- Winter, G., Q. Chen and M. Wahlgren. 2004. Meeting report: the molecular background of severe and complicated malaria. **Mol. Biochem. Parasitol.** 134: 37-41.
- Yeo, A. E. T., M. D. Edstein and K. H. Rieckmann. 1997. Antimalarial activity of the triple combination of proguanil, atovaquone and dapsone. **Acta Trop.** 67(3): 207-214.
- Yuthavong, Y. 2002. Basic for antifolate action and resistance in malaria. **Microbes Infect.** 4: 175-182.
- Yuthavong, Y., J. Yuvaniyama, P. Chitnumsub, J. Vanichtanankul, S. Chusacultachai, B. Tarnchompoo, T. Vilaivan and S. Kamchonwongpaisan. 2005. Malarial (*Plasmodium falciparum*) dihydrofolate reductase-thymidylate synthase: structural basis for antifolate resistance and development of effective inhibitors. **Parasitol.** 130: 249-259.
- Yuthavong, Y., S. Kamchonwongpaisan, U. Leartsakulpanich and P. Chitnumsub. 2006. Folate Metabolism as a Source of Molecular Targets for Antimalarials. **Future Microb.** 1(1): 113-125.

- Yuthavong, Y., T. Vilaivan, N. Chareonsethakul, S. Kamchonwongpaisan, W. Sirawaraporn, R. Quarrell and G. Lowe. 2000. Development of a lead inhibitor for the A16V+S108N mutant of dihydrofolate reductase from the cycloguanil-resistant strain (T9/94) of *plasmodium falciparum*. **J. Med. Chem.** 43: 2738-2744.
- Yuvaniyama, J., P. Chitnumsub, S. Kamchonwongpaisan, J. Vanichtanankul, S. Sirawaraporn, P. Taylor, M. D. Walkinshaw and Y. Yuthavong. 2003. Insights into antifolate resistance from malarial DHFR-TS structures. **Nat. Struct. Biol.** 10: 357-365.
- Zongo, I., G. Dorsey, N. Rouamba, C. Dikomajilar, M. Lankoande, J-B. Ouedraogo and P. J. Rosenthal. 2005. Amodiaquine, sulfadoxine-pyrimethamine, and combination therapy for uncomplicated *falciparum* malaria: a randomized controlled trial from Burkina Faso. **Am. J. Trop. Med. Hyg.** 73(5): 826-832.