

## REFERENCES

### Thai

- จารีย์ บันสิทธิ์. เปรริบเนื้อบักน้ำพุกยาศาสตร์ของสูกใต้ใบ-หญ้าใต้ใบ สกุล *Phyllanthus* ในภาคกลางของไทย. วารสารกรมวิทยาศาสตร์การแพทย์ 33(4)(2534): 155-168.
- ชัยวัฒน์ ต่อสกุลแก้ว. ศรีร่วมทางเดินอาหาร. พิมพ์ครั้งที่ 1. กรุงเทพฯ: เท็กซ์ แอนด์ เจอร์นัล พับพิเช่น. 2541.
- นิจศิริ เรืองรังษี และพยอน ตันติวัฒน์. พืชสมุนไพร. กรุงเทพฯ: โรงพยาบาลรามคำแหงมหาวิทยาลัย, 2532.
- นุญมี สัญญาสุจารี. การทดสอบหน้าที่ของตับและโรคตับในสัตว์ (Liver function tests and liver diseases in animals). เอกสารประกอบการสอนวิชาพยาธิทั่วไปทางสัตวแพทย์. พิมพ์ครั้งที่ 1. ภาควิชาพยาธิวิทยา คณะสัตวแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, 2544.
- ป่าไม้, กรม. สำนักวิชาการป่าไม้, ส่วนพุกยาศาสตร์ป่าไม้. ชื่อพรรณไม้แห่งประเทศไทย. พิมพ์ครั้งที่ 2. กรุงเทพฯ: ประชาชน, 2544.
- พิศมัย เหล่าภารเกณ, วีรพล คุ่งวิริยพันธุ์, ปราโมทย์ ทองกระจา, และนังอร ศรีพาณิชกุลชัย. การศึกษาฤทธิ์ต้านไวรัสตับอักเสบและต้านพิษต่อตับของสูกใต้ใบและหญ้าใต้ใบ. รายงานการวิจัย, คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น. 2544.
- มหาวิทยาลัยมหิดล, คณะเภสัชศาสตร์. สมุนไพรสวนสิริรุกขชาติ. กรุงเทพฯ: ออมรินทร์พรินติ้งกรุ๊ฟ, 2535: 160.
- วันดี อุดมอักษร, สถาพร พฤติพรวรษ, มาลินี วงศ์นาวา, อనุพงษ์ นิติเรืองจรัส, นุชรัตน์ วรรณพงษ์, และ นิรชา บันเย่ยม. ฤทธิ์ของสูกใต้ใบต่อพิษของพาราเซตามอลในตับหนูขาว. วารสารกรมวิทยาศาสตร์การแพทย์ 42(2)(2543): 119-132.
- วิญญา มิตรานันท์. พยาธิวิทยาภาษาบวก. กรุงเทพฯ: ไอเอส พรินติ้งเฮาส์. 2538.
- ศุภลักษณ์ โรมรัตนพันธุ์. เทคนิคทางเนื้อเยื่อวิทยา. กรุงเทพฯ: สำนักพิมพ์มหาวิทยาลัยเกษตรศาสตร์, 2539.
- ศูนย์วิชาการเพื่อป้องกันแก้ไขปัญหาสุรา (ศวส.). สถานการณ์ปัญหาระบิโภคสุรา. เข้าถึงได้จาก: URL:<http://www.cas.or.th/howto.htm> [เข้าถึงเมื่อ 27 ธันวาคม 2547].
- สำนักงานกองทุนสนับสนุนการสร้างเสริมสุขภาพ (สสส.). การบริโภคเครื่องดื่มแอลกอฮอล์. เข้าถึงได้จาก: URL:<http://www.thaihealth.or.th> [เข้าถึงเมื่อ 27 ธันวาคม 2547].
- วิจิตร บรรคุณารา. พยาธิวิทยาของเซลล์: การเปลี่ยนแปลงแนวดำเนินอลิซีน. ใน อนุเทพ รังสีพิพัฒน์ (บรรณาธิการ). ตำราพยาธิวิทยาทั่วไปทางสัตวแพทย์, พิมพ์ครั้งที่ 3. หน้า 35-66 กรุงเทพฯ: ปอยท์ กราฟิก, 2548.

### English

- Adachi, M. and Ishii, H. Role of mitochondria in alcohol liver injury. Free Radical Biology & Medicine 36(6)(2002): 487-491.
- Adedapo, A.A., Adegbayibi, A.Y. and Emikpe, B.O. Some clinico-pathological changes associated with the aqueous extract of the leaves of *Phyllanthus amarus* in rats. Phytotherapy Research 19(11)(2005): 971-976.
- Adedapo, A.A., Abatan, M.O., Akinloye, A.K., Idowa, S.U. and Olorunsogo, O.O. Morphometric and Histopathological studies on the effect of some chromatographic fractions of *Phyllanthus amarus* and *Euphorbia hirta* on the male reproductive organs of rats. Journal of Veterinary Science 4(2) 2003: 181-185.
- Arteel, G.E. Oxidation and Antioxidants in Alcohol-Induced Liver Disease. Gastroenterology 124(2003): 778 -790.
- Ballantyne, B., Marrs, T., and Syversen T. General and Applied Toxicology. 2 nd ed. London: Maemillan Reference. 2000.
- Barros, M.E., Schor, N. and Boim, M.A. Effect of an aqueous extract from *Phyllanthus niruri* on calcium oxalate crystallization in vitro. Urological Research 30(2003): 374-379.
- Bautista, A.P. and Spitzer, J.J. Role of kupffer cells in the ethanol induced oxidative stress in the liver. Frontiers in Bioscience 4(1999): 589-595.
- Boelsterli, U.A. Mechanistic toxicology: the molecular basis of how chemical disrupts biological targets. 1 st ed. London: Taylor & Francis, 2003.
- Bouneva, I., Abou-assi, S., Heuman, D.M., and Mihas, A.A. Alcohol Liver Disease. Hospital Physician 2003: 31-38.
- Buege, J.A. and Aust, S.D. Microsomal Lipid Peroxidation. Method in Enzymology (1978): 302-310.
- Campos, A.H. and Schor, N. *Phyllanthus niruri* inhibits calcium oxalate endocytosis by renal tubular cells: its role in urolithiasis. Nephron 81(4) (1999): 393-397.
- Colorado State University. Regeneration of the liver, Phathophysiology of the digestive system. Available from URL:<http://www.arbl.cvmbs.colostate.edu/hbooks/pathphys/digestion/liver/regen.html>. [Cited 2006 March 2].

- Deleve, L.D. and Kaplowitz, N. Glutathione metabolism and its role in hepatotoxicity. Pharmac Ther 52(1991): 287-305.
- Dickinson, D.A. and Forman, H.J. Cellular glutathione and thiols metabolism. Biochemical Pharmacology 64(2002): 1019-1026.
- Eaton, S., Record, C.O. and Bartlett. Multiple biochemical effects in the pathogenesis of alcoholic fatty liver. European Journal of Clinical Investigation 27(1997): 719-722.
- Ellman, G.L. Tissue sulhydryl groups. Archives of Biochemistry and Biophysics 82(1959): 70-77.
- Eriksson, C.J. The role of acetaldehyde in the actions of alcohol (update 2000). Alcoholism, Clinical and Experimental Research 25(2001): 15S-32S.
- Flora, K., Hahn, M., Rosen, H., and Benner, K. Milk Thistle (*Silybum marianum*) for the therapy of liver disease. The American Journal of Gastroenterology 93(2) (1998): 139-143.
- Ford, M.D., Delancy, K.A., Ling, L. and Erickson, T. Clinical Toxicology. 1 st ed Philadelphia: WB saunders, 2001.
- Freitas, A.M., Schor, N. and Boim, M.A. The effect of *Phyllanthus niruri* on urinary inhibitors of calcium oxalate crystallization and other factors associated with renal stone formation. BJU International. 89(9)(2002): 829-834.
- Gitnick, G., Labrecque, D.R. and Moody, F.G. Diseases of the liver and biliary tract. Missouri: Mosby, 1991.
- Gowrishankar, B. and Vivekanandan, O.S. Invivo studies of a crude extract of *Phyllanthus amarus* L. In modifying the genotoxicity induced in Vicia faba L. by tennery effluents. Mutation Research 322(3)(1994): 185-192.
- Harish, R. and Shivanandappa, T. Antioxidant activity and Hepatoprotective potential of *Phyllanthus niruri*. Food Chemistry 95(2006): 180-185.
- Hodgson, E. and Smart, R.C. Introduction to Biochemical toxicity. 3 rd ed. New York: Wiley Interscience, 2001.
- Jardao, A.A., Chiarello, P.G., Arantes, M.R. Meirelles, M.S. Vannucchi, H. Effect of an acute dose of ethanol on lipid peroxidation in rats: action of vitamin E. Food and Chemical Toxicology 42(2004): 459-464.

- Jagatia, G.C. and Baliga, M.S. The evaluation of nitric oxide scavenging activity of Certain Indian Medicinal Plant in vitro: a preliminary study. Journal of Medicinal Food 7(3)(2004): 343-348.
- Jarvelainen, H.A., Fang, C., Sundberd, M.I. and Lindros, K.O. Effect of chronic coadministration of endotoxin and ethanol on rat liver pathology and proinflammatory and anti-inflammatory cytokines. Hepatology 29(5)(1999): 1503-1510.
- Jarvelainen, H. Inflammatory responses in alcoholic liver disease. Helsinki: National public health institute, 2000.
- Jeena, K.J., Joy, K.L. and Kuttan, R. Effect of *Emblica officinalis*, *Phyllanthus amarus* and *Picrorrhiza kurroa* on N-nitrosodimethylamine induced hepatocarcinogenesis. Cancer Letters 136(1999): 11-16.
- Jollow, D.J., Kocsis J.J., Snyder, R., and Vainio, H. Biochemical aspects of toxic metabolites: formation, detoxication, and covalent binding. Biological Reactive Intermediates (1977): 42-59.
- Jose, C., Checa, F., and Kaplowitz N. Hepatic mitochondrial glutathione: Transport and role in disease and toxicity. Toxicity and Applied Pharmacology 204(2005): 263-273.
- Junqueira, L.C. and Carneiro, J. Basic histology. 4<sup>th</sup> ed. pp. 347-362. California: Lange Medical Publications, 1983.
- Kang, J.J., Joen, Y.T., Park, S.K., Yang, K.H., and Kim, H.M. Protective against lipopolysaccharide-induced sepsis and inhibition of interleukin-1 $\beta$  and prostaglandin E<sub>2</sub> synthesis by silymarin. Biochemical Pharmacology 67(2004): 175-181.
- Kassuya, C.A.L., Silvastre, A.A., Rehder, V.L.G. and Calixto, J.B. Anti-allodynic and anti-oedematogenic properties of the extract and lignans from *Phyllanthus amarus* in models of persistent inflammatory and neuropathic pain. European Journal of Pharmacology 478 (2003): 145-153.
- Kernsakphai J, Sukchotiratana M, Buddhasukh D, Apisariyakul A. Inhibitory effect of some medicinal plant used by the Hilltribe against diarrhoeal bacteria. 1998 Available from URL: <http://www.grad.cmu.ac.th/abstract/1998/sci/abstract/sci980352.html>. [Cited 2006 March 2].

- Keshavarzian, A., Choudhary, S., Holmes, E.W., Yong, S., Banan, A., Jakate, S., et al. Preventing gut leakiness by Oats supplementation ameliorates alcoholic induced liver damage in rats. The Journal of Pharmacology and Experimental Therapeutics 299(2)(2001): 442-448.
- Khanna, A.K., Rizvi, F. and Chandar, R. Lipid lowering activity of *Phyllanthus niruri* in hyperlipemic rats. Journal of Ethnopharmacology 82(1)2002: 19-22.
- Khare, C.P. Indian herbal remedies: rational western therapy, ayurvedic and other traditional used, botany, p. 358. Berlin: Springer, 2004.
- Khatoon, S., Rai, V., Rawat, A.K.S. and Mehrotra, S. Comparative pharmacognostic studies of three *Phyllanthus* species. Journal of Ethnopharmacology 104(2006): 79-86.
- Kiemer, A.K., Hartung, T., Huber, C. and Vollmar, A.M. *Phyllanthus amarus* has anti-inflammation potential by inhibition of iNOS, COX-2 and cytokine via The NF-kappa B pathway. Journal of Hepatology 38(3)(2003): 289-297.
- Klaassen, C.D. Casarett and Doull's Toxicology: the basic science of poisons. 6 st ed. New York: McGraw Hill, 2001.
- Kloucek, P., Polesny, Z., Svobodova, B., Vikova, E., and Kokoska, L. Antibacterial screening of some Peruvian medicinal plants use in Calleria District. Journal of Ethnopharmacology 99(2005): 309-312.
- Kongstan, N. Effect of *Phyllanthus amarus* on Hepatotoxicity induced by Galactosamine in rats. Master's thesis, Department of Toxicology, Faculty of Science, Mahidol University. 2000.
- Kosem, N., Moongkarndi, P., Luanratana, O., Pongtan, N. and Tongplod, S. Inhibitory effect of madicinal plant on cancer cell perliferation. Report of the Faculty of Pharmacy, Mahidol University, 2000.
- Kumar, K.B.H. and Kuttan, R. Protective effect of an extract of *Phyllanthus amarus* against radiation induced damage in mice. Journal of Radiation Research 45(2004): 133-139
- Kumar, K.B.H. and Kuttan, R. Chemoprotective activity of an extract of *Phyllanthus amarus* against cyclophosphamide induced toxicity in mice. Phytomedicine 12(2005): 494-500.

- Kumaran, A. and Karunakaran, R.J. In vitro antioxidant activities of methanol extracts of five *Phyllanthus* species from India. LWT-Food Science and Technology In Press, Corrected Proof(2005).
- Kwon, H.J., Kim, Y.Y. and Choung, S.Y. Effect of natural product extract on the fatty liver induced by alcohol diet in rats. Journal of Health Science 50(5)(2004): 466-473.
- Lamp, R.G., Wood, C.K. and Fallon,H.J. The effect of acute and chronic ethanol intake on hepatic glycerolipid biosynthesis in the hamster. Journal of Clinical Investigation 63(1979): 14-20.
- Lee, H.C. and Wei, Y.H. Mitochondrial role in life and death of the cell. Journal of Biomedical Science 7(2000): 2-15.
- Lieber, C.S. Alcoholic liver disease: new insights in pathogenetic lead to new treatments. Journal of Hepatology 32 (1) (2000a): 113-128.
- Lieber, C.S. Alcohol and the liver: metabolism of alcohol and its role in hepatic and extrahepatic disease. The Mount Sinai Journal of Medicine 67(1)(2000b): 84-94.
- Lieber, C.S. Alcoholic fatty liver: its pathogenesis and mechanism of progression to inflammation and fibrosis. Alcohol 34(2004): 9-19.
- Liebert, J.J., Matlawska, I., Bylka, W. and Murias, M. Protective effect of *Aquilegia vulgaris* on APAP-induced oxidative stress in rats. Journal of Ethnopharmacology 97(2005): 351-358.
- Lodish, H, Berk, A, Zipursky, S.L., Matsudaira, P, Baltimore, D and Darnell, J. Molecular cell biology. 4 th ed., p. 1045. New York: W.H. Freeman and Company, 2000.
- Luczaj, W. and Skrzydlewski, E. Antioxidant properties of black tea in alcohol intoxication. Food and Chemical Toxicology 42(2004): 2045-2051.
- Mahendran, P. and Shyamala Devi, C.S. The modulating effect of *Garcinia Cambogia* extract on ethanol induced peroxidative damage in rats. Indian Journal of Pharmacology 33(2001): 87-91.
- Mannan, A. and Ahmad, K. Preliminary study of sex hormones of medical importance in Bangladesh plants. Bangladesh Medicinal Research Council Bulletin 4(2)1978: 78-85.

- McClain, C.J., Shedlofsky, S., Barve, S., and Hill, D.B. Cytokine and alcoholic liver disease. *Alcohol health & Research world*. 21(4)(1997): 317-320.
- Mckim, S.E., Gabele, E., Isayawa, F., Lambert, J.C., Tucker, L.M., Wheeler, M.D., et al. Inducible nitric oxide synthase is required in alcohol-induced liver injury: studies with knockout mice. *Gastroenterology* 125(2003):1834-1844.
- Moshi, M.J., Lutale, J.J.K., Rimoy, G.H., Abbas, Z.G., Josiah, R.M. and Swai, A.B.M. The effect of *Phyllanthus amarus* aqueous extract on blood glucose in non-insulin dependent diabetic patients. *Phytotherapy Research* 15(2001): 577-580.
- Moshi, M.J., Uiso, F.C., Mahunnah, R.L.A., Malele, R.S. and Swai, A.B.M. A study of the effect of *Phyllanthus amarus* extract on blood glucose in rabbits. *Int J Phamacog* 37(1997): 167-173.
- Nagy, L.E. Recent insights into the role of the innate immune system in the development of alcoholic liver disease. *Experimental Biology and Medicine* 2003: 882-890.
- Niemela, O. Distribution of ethanol induced protein adduct in vivo: relationship to tissue injury. *Free radical Biological & Medicine* 31(12)(2001): 1531-1538.
- Nishiura, J.L., Campos, A.H., Boim, M.A., Heilberg, I.P. and Schor, N. *Phyllanthus niruri* normalizes elevated urinary calcium levels in calcium stone forming (CSF) patients. *Urological Research* 32(2004): 362-366
- Odetola, A.A. and Akojenu, S.M. Anyi-diarrhoeal and gastro-intestinal potentials of the aqueous extract of *Phyllanthus amarus* (Euphorbiaceae). *The African Journal of Medical Science* 29(2)2000: 119-122.
- Oh, S.I., Kim, C.I., Chun, H.J., Park, S.C. Chronic ethanol consumption affects glutathione status in rat liver. *The Journal of Nutrition* 128(4)(1998): 758-763.
- Onocha, P.A., Opegbemi, A.O., Kadri, Ao., Ajayi, K.M. and Okorie, D.A. Antimicrobial evaluation of Nigerian Euphorbiaceae plant: *Phyllanthus amarus* and *Phyllanthus muellerianus* leaf extracts. *Nigerian Journal of Natural Products and Medicine* 7(2003): 9-12.
- Ostrowska, J., Luczaj, W., Kasacka, I., Rozanski, A. and Skrzypidenska, E. Green tea protects against ethanol-induced lipid peroxidation in rat organs. *Alcohol* 32(2004): 25-32.

- Palmes, D. and Spiegel, H.U. Animal models of liver regeneration. Biomaterials 25(2004): 1601-1611.
- Papas, A.M. Antioxidant status, Diet, Nutrition, and Health. New York: CRC Press LLC. 1999.
- Poggi, M. and Di Luzio, N.R. The role of liver and adipose tissue in the pathogenesis of the ethanol-induced fatty liver. Journal of lipid Research 5(1964): 427-441.
- Prakash, A., Satyan, K.S., Wahi, S.P., and Singh, R.P. Comparative Hepatoprotective Activity of three *Phyllanthus* species, *P. urinaria*, *P. amarus* and *P. simplex* on Carbon Tetrachloride induced liver injury in the rats. Phytotherapy Research 9(1995): 594-596.
- Pramyothisin, P., Udomuksorn, W., Poungshompoon, S. and Chaichantipyuth, C. Hepatoprotective effect of *Andrographis paniculata* and its constituent, Andrographalide, on ethanol hepatotoxicity in rats. Asia Pacific Journal of Pharmacology 9(1994): 73-78.
- Rai, V., Khatoon, S., Bisht, S.S. and Mehrotra, S. Effect of cadmium on growth, ultramorphology of leaf and secondary metabolites of *Phyllanthus amarus* Schum. and Thonn. Chemosphere 61(2005): 1644-1650.
- Rajeshkumar, N.V., and Kuttan, R. *Phyllanthus amarus* extract administration increase the life span of rats with hepatocellular carcinoma. Journal of Ethnopharmacology 73(2000): 215-219.
- Rajeshkumar, N.V., Joy, K.L., Kuttan, G., Ramasewak, R.S., Nair, M.G. and Kuttan, R. Antitumour and anticarcinogenic activity of *Phyllanthus amarus* extract. Journal of Ethnopharmacology 81(2002): 17-22.
- Rao, M.V. and Alice, K.M. Contraceptive effect of *Phyllanthus amarus* extract in female mice (*Mus musculus*). Phytotherapy Research 15(2001): 265-267.
- Rao, M.V., Shah, K.D. and Rajani, M. Contraceptive effect of *Phyllanthus amarus* extract in male mouse (*Mus musculus*). Phytotherapy Research 11(1997): 594-596.
- Raphael, K.R., Ajith, T.A., Joseph, S. and Kuttan, R. Anti-mutagenic activity of *Phyllanthus amarus* Schum. et. Thonn. in vitro as well as in vivo. Teratogenesis, Carcinogenesis, and Mutagenesis 22(4)(2002): 285-291.

- Raphael, K.R. and Kuttan, R. Inhibition of experimental gastric lesion and inflammation of *Phyllanthus amarus* extract. Journal of Ethnopharmacology 87(2003): 193-197.
- Raphael, K.R., Suba, M.C. and Kuttan R. Hypoglycemic effect of methanol extract of *Phyllanthus amarus* Schum. et. Thonn. On alloxan induced diabetes mellitus in rats and its relation with antioxidant potential. Indian Journal of Experimental Biology 40(8)2002: 905-909.
- Ravikumar, V., Shivashangari, K.S. and Devaki, T. Hepatoprotective activity of *Tridax procumbens* against D-galactosamine/lipopolysaccharide-induced hepatitis in rats. Journal of Ethnopharmacology 101(2006): 55-60.
- Rotblatt, M and Ziment, I. Evidence-based herbal medicine. Philadelphia: Hanley & Belfus, 2002.
- Saravanan, R., Visvanathan, P. and Pugalendi, K.V. Protective effect of ursolic acid on ethanol mediated experimental liver damage in rats. Life Science 78 (2006): 713-718.
- Sanmugapriya, E. and Venkataraman, S. Studies on hepatoprotective and oxidant actions of *Strychnos potatorum* Linn. seed on CCl<sub>4</sub> induced acute hepatic injury in experimental rats. Journal of Ethnopharmacology 105(2006): 154-160.
- Saraswat, B., Visen, P.K.S., Patnaik, G.K. and Dhawan B.N. Ex vivo and in vivo investigations of *Picrorhiza kurroa* in an alcohol intoxication model in rats. Journal of Ethnopharmacology 66(1999): 263-269.
- Santos, A.R.S., De Campos, R.O.P., Miguel, O.G., Filho, V.C., Siani, A.C., Yunes, R.A., et al. Antinociceptive properties of extract of new species of plants of the genus *Phyllanthus* (Euphorbiaceae). Journal of Ethnopharmacology 72(2000): 229-238.
- Santos, A.R.S., Filho, V.C., Niero, R., Viana, A.M., Moreno, F.N., Campos, M.M., et al. Analgesic effect of culture extracts from selected species of *Phyllanthus* in mice. The Journal of Pharmacy and Pharmacology 46(9) (1994): 755-759.
- Siler, S.Q., Neese, R.A., Parks, E.J. and Hellerstein, M.K. VLDL-triglyceride production after alcohol ingestion, studied using [2-<sup>13</sup>C] glycerol. Journal of Lipid Research 39(1998): 2319-2328.

- Saravanan, R., Viswanathan, P. and Pugalendi K.V. Protective effect of ursolic acid on ethanol-mediated experimental liver damage in rats. Life Science 78 (2006): 713-718.
- Sripanidkulchai, B., Tattawasart, U., Laupatarakasem, P., Vinitketkumneun, U., Sripanidkulchai, K., Furihata, C., et al. Antimutagenic and anticarcinogenic effect of *Phyllanthus amarus*. Phytomedicine 9(2002): 26-32.
- Sridhya, N. and Periwal, S. Diuretic, hypotensive and hypoglycaemic effect of *Phyllanthus amarus*. Indian Journal of Experimental Biology 33(11)(1995): 861-864.
- Song, Z., Deaciuc, I., Song, M., Lee, D.Y.W., Liu, Y., Ji, X., et al. Silymarin protects against acute ethanol induced hepatotoxicity in mice. Alcoholism: Clinical and Experimental Research 30(3)(2006): 407-412.
- Subeki, N., Matsuura, H., Takahashi, K., Yamasaki, M., Yamato, O., Maede, Y., et al. Anti-babesial and Anti-plasmodial Compounds from *Phyllanthus niruri*. Journal of Natural Products 68(2005): 537-539.
- Shimizu, M., Horie, S., Terashima, S., Ueno, H., Hayashi, T., Arisawa, M., et al. Studies on aldose reductase inhibitors from natural products II. Active components of Paraguayan cude drug “Paraparai mi”, *Phyllanthus niruri*. Chemical & Pharmaceutical Bulletin 37(9) (1989): 2531-2532.
- Syamasundar, K.V., Singh, B., Thakor, R.S., Husain, A., Kiso, Y., and Hikino, H. Antihepatotoxic principle of *Phyllanthus niruri* herbs. Journal of Ethno-pharmacology 14(1)(1985): 41-44.
- Teerasukaporn, P. Development of method for isolation and purification of Phyllanthin from Phyllanthus amarus Schum. & Thonn. Master's thesis, Faculty of Pharmacy, Mahidol University. 1998.
- Teare, J.P., Greenfield, S.M., Watson, D., Punchard, N.A., Miller, N., Rice-Evan, C.A., et al. Lipid peroxidation in rats chronically fed ethanol. Gut 35(11) (1994): 1644-1647.
- Tilg, H. and Diehl, A.M. Cytokine in alcoholic and non alcoholic steatohepatitis. The New England Journal of Medicine 343(20)(2000): 1467-1476.

- Tona, L., Cimanga, R.K., Mesia, K., Musuamba, C.T., Bruyne, T.D., Apers, S. *et al.* In vitro antiplasmodial activity of extracts and fractions from seven medicinal plants used in the Democratic Republic of Congo. *Journal of Ethnopharmacology* 93(2004): 27-32.
- Tona, L., Mesia, K., Ngimbi, N.P., Chrimwami, B., Okond, A., Cimanga, R.K., *et al.* In vivo antimalarial activity of *Cassia occidentalis*, *Morinda morindoides* and *Phyllanthus niruri*. *Annals of Tropical Medical and Parasitology* 95(1) (2001): 47-57.
- Tona, L., Ngimbi, N.P., Tsakala, M., Mesia, K., Cimanga, R.K. and Apers, S. Antimalarial activity of 20 crude extracts from nine African medicinal plants used in Kinshasa, Congo. *Journal of Ethnopharmacology* 68(1999):193-203.
- Tuma, D. J. Role of malondialdehyde-acetaldehyde adducts in liver injury. *Free Radical Biology & Medicine* 32(4)(2002): 303-308.
- Ueno, H., Horie, S., Nishi, Y., Shogawa, H., Kawasaki, M., Suzuki, S., *et al.* Chemical and Pharmaceutical studies on medicinal plants in Paraguay. Geraniin, an angiotensin-converting enzyme inhibitor from “paraparai mi”, *Phyllanthus niruri*. *Journal of Natural Products* 51(2)(1988): 357-359.
- Umarani, D., Devaki, T., Govindaraju, P., and Shanmugasundaram, K.R. Ethanol induced metabolic alteration and effect of *Phyllanthus niruri* in their reversal. *Ancient Science Life* 4(3)(1985): 174-180.
- Venkatesan, P., Satyan, K.S., Kumar, M.S., and Prakash, A., Protective Effect by aqueous Extract of *Phyllanthus amarus*, Phyllanthin and Nirocil against Carbontetrachloride induced liver and brain toxicity. *Indianpharma* 2003. Available from: URL: <http://www.Indianpharma.org/journal/index.php/2003/3May%20-%20June/22.htm>. [Cited 2005 Jan 31].
- Walaiphachara, N. *Effect of Phyllanthus amarus on Carbon Tetrachloride(CCl<sub>4</sub>)-induced Hepatotoxicity in Rats*. Master's thesis, Department of Pathobiology, Faculty of Science, Mahidol University. 1994.
- Wheeler, M.D., Kono, H., Yim, M., Nakagami, M., Uesugi, T., Arteel, G.E., *et al.* The role of Kupffer cell oxidant production in early ethanol-induced liver disease. *Free Radical Biology & Medicine* 31(12) (2001): 1544-1549.
- Wong, F.K. *Medicinal plants southeast asia*. 2 nd ed., pp. 167-168. Selanger: Prentice Hall Pearson Malaysia, 2002.

- Wongnava, M., Taina, P., Bumrungwong, N., Nitiruangjaras, A., Muso, A., and Prasartthong V. Effect of the aqueous extract from *Phyllanthus amarus* Schum. et Thonn. and its hepatoprotective mechanism on paracetamol hepatotoxicity in rats. Rasearch report. Available from: URL: <http://www.psu.ac.th> [Cited 2004 Oct 20].
- Zimmerman, H.J. Hepatotoxicity: the adverse effects of drug and other chemicals on the liver. 2 nd ed. Philadelphia: Lippincott Williams & wilkins, 1999.

## **APPENDIX**

Table 17. Summary of clinical chemistry values and histopathological grading in effect of PA extract given 24 hours before single oral dose of ethanol (5 g/kg) (acute toxicity study) (n=6).

Groups	ALT (U/L)	AST (U/L)	STg (mg/dl)	HTg (mg/g liver)	GSH (μmol/g liver)	MDA (nmol/g liver)	TNF-α (pg/ml)	IL-1β (pg/ml)	Histopath grading
Control (distilled water)	17.24 ± 1.50	44.40 ± 1.93	82.75 ± 12.49	22.94 ± 3.90	6.78 ± 0.68	8.60 ± 0.43	44.85 ± 8.84	53.96 ± 5.41	0
Ethanol 5 g/kg	26.37 ± 1.24*	76.88 ± 6.46*	111.55 ± 11.39	25.17 ± 5.06	6.47 ± 0.48	9.64 ± 0.24	68.69 ± 23.46	60.63 ± 8.74	+1
PA 25 mg/kg	26.47 ± 1.62*	57.68 ± 3.82 <sup>#</sup>	107.23 ± 14.43	20.83 ± 3.43	6.37 ± 0.28	9.10 ± 0.74	52.93 ± 5.45	45.33 ± 6.79	+1
PA 50 mg/kg	22.59 ± 1.45	51.87 ± 1.34 <sup>#</sup>	113.57 ± 15.31	33.09 ± 4.68	6.57 ± 0.31	9.92 ± 0.71	53.44 ± 10.61	55.33 ± 5.57	0
PA 75 mg/kg	19.10 ± 0.66 <sup>#</sup>	50.02 ± 2.89 <sup>#</sup>	121.06 ± 6.78	28.84 ± 1.82	6.23 ± 0.10	9.61 ± 0.75	49.97 ± 9.84	46.90 ± 5.74	0
SL 5 mg/kg	19.97 ± 0.86 <sup>#</sup>	52.35 ± 2.36 <sup>#</sup>	113.74 ± 10.46	19.45 ± 3.94	6.04 ± 0.28	9.51 ± 0.41	49.98 ± 9.50	36.90 ± 8.22	0

Results are expressed as mean ± SEM and grading (0 = normal, +1 = mild, +2 = moderate and +3 = severe).

\* Significant difference from control group (p<0.05).

# Significant difference from ethanol group (p<0.05).

Table 18. Summary of clinical chemistry values and histopathological grading in effect of PA extract given 7 days after administration of ethanol (4 g/kg/day) for 21days (sub-acute toxicity study)(n=8).

Groups	ALT (U/L)	AST (U/L)	STg (mg/dl)	HTg (mg/g liver)	GSH (μmol/g liver)	MDA (nmol/g liver)	TNF-α (pg/ml)	IL-1β (pg/ml)	Histopath grading
Control (distilled water)	18.03 ± 0.49	40.94 ± 0.89	57.40 ± 7.85	21.30 ± 3.49	5.64 ± 0.27	10.15 ± 0.27	42.35 ± 6.43	36.71 ± 6.75	0
Ethanol 4 g/kg	27.41 ± 1.78 *	56.64 ± 2.74 *	120.90 ± 23.29	37.43 ± 4.65 *	5.95 ± 0.25	13.95 ± 0.61*	101.48 ± 26.11*	74.50 ± 9.68*	+3
Ethanol + self recovery	19.85 ± 1.16 #	45.30 ± 2.85 #	88.50 ± 30.13	28.44 ± 2.58	5.25 ± 0.18	11.48 ± 0.57#	62.09 ± 9.09	46.26 ± 6.77	+2
Ethanol + PA 75 mg/kg	19.71 ± 0.87#	47.26 ± 2.33#	53.51 ± 8.09	22.36 ± 2.31 #	5.47 ± 0.16	10.24 ± 0.28#	48.69 ± 6.84#	46.12 ± 7.57	+1
Distilled water + PA 75 mg/kg	17.52 ± 1.23 #	41.52 ± 1.51#	60.73 ± 11.71	20.95 ± 2.90 #	5.17 ± 0.14	9.65 ± 0.15#	37.54 ± 4.62#	50.24 ± 4.59	0
Ethanol + SL 5 mg/kg	18.69 ± 0.97 #	44.28 ± 1.83#	66.46 ± 8.50	29.57 ± 3.47	5.37 ± 0.13	10.62 ± 0.31#	41.58 ± 7.50#	42.88 ± 5.66#	0

Results are expressed as mean ± SEM and grading (0 = normal, +1 = mild, +2 = moderate and +3 = severe).

\* Significant difference from control group (p<0.05).

# Significant difference from ethanol group (p<0.05).

Table 19. Clinical chemistry values of each rats in control and ethanol (5g/kg) groups (acute toxicity study, n=6).

Groups	Rats	ALT (U/L)	AST (U/L)	STg (mg/dl)	HTg (mg/g liver)	GSH (μmol/g liver)	MDA (nmol/g liver)	TNF-α (pg/ml)	IL-1β (pg/ml)
Control (distilled water)	1	14.54	41.29	54.75	41.62	5.09	7.88	56.00	51.41
	2	11.50	38.97	97.77	22.67	5.77	8.03	43.69	37.29
	3	20.36	43.04	58.10	21.59	5.20	10.02	36.00	51.41
	4	16.87	43.04	60.90	17.79	7.96	9.50	43.69	70.24
	5	19.20	48.28	132.69	18.96	7.56	7.28	77.54	69.06
	6	20.94	51.77	92.31	15.00	9.10	8.87	12.15	44.35
Ethanol 5 g/kg	1	27.92	59.91	124.02	22.80	6.62	9.87	46.00	34.94
	2	30.25	94.23	120.14	12.73	6.61	8.61	185.23	54.94
	3	24.43	91.32	95.83	21.68	5.71	10.31	43.69	73.76
	4	22.10	87.25	64.58	47.41	4.62	9.99	39.08	49.06
	5	25.01	68.06	119.23	16.41	7.93	9.40	57.54	96.12
	6	28.50	60.49	145.51	29.96	7.33	9.68	40.62	54.94

Table 20. Clinical chemistry values of each rats in PA 25 and 50 mg/kg groups (acute toxicity study, n=6).

Groups	Rats	ALT (U/L)	AST (U/L)	STg (mg/dl)	HTg (mg/g liver)	GSH (μmol/g liver)	MDA (nmol/g liver)	TNF-α (pg/ml)	IL-1β (pg/ml)
PA 25 mg/kg	1	28.50	57.00	156.94	20.50	6.51	11.44	49.08	39.65
	2	31.99	67.47	73.61	16.69	6.51	9.69	59.08	49.06
	3	20.36	42.46	94.70	16.90	6.10	9.76	57.54	38.47
	4	24.43	51.77	77.74	37.48	5.69	9.59	39.85	33.76
	5	25.59	62.82	94.87	18.89	5.81	7.86	38.31	33.76
	6	27.92	64.57	145.51	14.52	7.59	6.24	73.69	77.29
PA 50 mg/kg	1	18.61	50.02	126.50	22.27	6.19	10.88	79.08	58.47
	2	23.26	54.09	142.50	54.39	6.34	11.89	27.54	70.24
	3	18.03	46.53	57.95	25.80	6.47	11.65	39.08	62.00
	4	26.18	55.26	81.41	32.29	6.89	8.53	49.85	37.29
	5	23.27	51.19	116.03	35.74	7.89	8.36	91.38	39.65
	6	26.18	54.10	157.05	28.05	5.64	8.21	33.69	64.35

Table 21. Clinical chemistry values of each rats in PA 75 mg/kg and SL 5 mg/kg groups (acute toxicity study, n=6).

Groups	Rats	ALT (U/L)	AST (U/L)	STg (mg/dl)	HTg (mg/g liver)	GSH (μmol/g liver)	MDA (nmol/g liver)	TNF-α (pg/ml)	IL-1β (pg/ml)
PA 75 mg/kg	1	20.94	52.93	96.65	34.77	6.39	9.59	87.54	42.00
	2	20.36	45.37	132.16	28.87	6.44	11.98	37.54	30.24
	3	17.45	43.04	109.54	21.35	6.28	11.50	26.00	42.00
	4	20.35	47.70	119.43	31.50	5.89	9.15	43.69	47.88
	5	18.03	62.82	125.00	27.63	5.98	8.02	71.38	46.71
	6	17.45	48.28	143.59	28.91	6.38	7.42	33.69	72.59
SL 5 mg/kg	1	21.52	54.68	92.95	10.15	5.43	8.40	90.62	27.88
	2	20.94	53.51	108.97	14.71	5.07	8.34	21.38	26.71
	3	19.20	54.68	83.33	9.66	6.70	9.21	46.00	14.94
	4	20.08	42.46	128.62	23.97	6.04	10.01	36.77	33.76
	5	16.29	49.44	113.78	34.26	6.19	10.61	56.77	72.59
	6	21.92	59.33	154.77	23.96	6.81	10.48	48.31	45.53

Table 22. Clinical chemistry values of each rats in control and ethanol 4 g/kg/day groups (sub-acute toxicity study, n=8).

Groups	Rats	ALT (U/L)	AST (U/L)	STg (mg/dl)	HTg (mg/g liver)	GSH (μmol/g liver)	MDA (nmol/g liver)	TNF-α (pg/ml)	IL-1β (pg/ml)
Control (distilled water)	1	19.20	40.14	42.24	15.10	6.64	10.97	33.69	23.18
	2	18.61	38.97	55.47	31.39	6.39	10.12	13.69	26.71
	3	18.03	40.14	29.01	17.06	6.35	10.23	43.69	23.18
	4	16.29	44.21	39.19	36.40	4.95	10.91	78.31	73.76
	5	16.28	41.30	77.86	30.31	5.36	10.31	47.54	37.29
	6	16.87	37.23	50.38	12.75	4.42	10.30	37.54	44.35
	7	19.78	44.79	69.21	10.15	5.48	9.83	48.31	50.24
	8	19.20	40.72	95.80	17.21	5.50	8.52	36.00	14.94
Ethanol 4 g/kg	1	22.69	47.70	91.32	56.81	6.80	13.20	75.23	73.76
	2	25.01	51.19	150.14	24.74	6.45	12.77	241.38	138.47
	3	25.59	54.68	126.61	26.64	5.98	12.62	33.69	69.06
	4	23.27	50.61	73.39	20.47	6.13	17.88	154.46	72.59
	5	31.99	69.80	91.88	46.26	5.61	13.26	43.69	65.53
	6	31.41	65.73	107.00	48.35	6.68	13.51	82.92	58.47
	7	36.06	59.33	267.59	44.04	4.84	14.94	147.54	71.41
	8	23.27	54.10	59.28	32.10	5.12	13.43	32.92	46.71

Table 23. Clinical chemistry values of each rats in ethanol (self recovery) and PA 75 mg/kg treatment groups (sub-acute toxicity study, n=8).

<b>Groups</b>	<b>Rats</b>	<b>ALT (U/L)</b>	<b>AST (U/L)</b>	<b>STg (mg/dl)</b>	<b>HTg (mg/g liver)</b>	<b>GSH (μmol/g liver)</b>	<b>MDA (nmol/g liver)</b>	<b>TNF-α (pg/ml)</b>	<b>IL-1β (pg/ml)</b>
Ethanol + self recovery	1	18.03	44.79	44.28	31.82	5.05	11.46	56.00	49.06
	2	23.27	55.84	52.84	34.52	4.16	10.43	91.38	31.41
	3	17.45	43.63	42.75	34.29	5.26	11.25	40.62	69.06
	4	22.69	48.86	103.31	22.67	5.76	8.50	64.46	32.59
	5	18.61	52.93	290.08	17.84	5.56	11.47	103.69	47.88
	6	14.54	30.25	48.18	36.38	5.65	12.85	48.31	20.82
	7	20.36	38.97	93.00	30.38	5.55	13.97	26.00	42.00
	8	23.85	47.12	33.59	19.60	5.03	11.92	66.00	77.29
Ethanol + PA 75 mg/kg	1	22.69	51.77	48.35	19.69	5.13	10.09	74.46	52.59
	2	21.52	45.37	37.66	11.26	5.21	10.53	56.77	36.12
	3	16.29	54.10	39.19	30.66	5.50	10.54	69.08	27.88
	4	20.36	39.55	102.29	19.88	4.89	9.27	32.92	38.47
	5	16.87	36.65	46.54	23.29	6.17	9.67	39.85	43.18
	6	21.52	52.35	64.82	29.25	5.66	10.54	22.92	34.94
	7	17.45	52.93	29.36	17.66	6.04	11.76	62.15	96.12
	8	20.94	45.37	59.83	27.21	5.18	9.53	31.38	39.65

Table 24. Clinical chemistry values of each rats in PA 75 mg/kg alone and SL 5 mg/kg treatment groups (sub-acute toxicity study, n=8).

Groups	Rats	ALT (U/L)	AST (U/L)	STg (mg/dl)	HTg (mg/g liver)	GSH (μmol/g liver)	MDA (nmol/g liver)	TNF-α (pg/ml)	IL-1β (pg/ml)
Distilled water + PA 75 mg/kg	1	17.45	45.37	83.97	26.49	4.92	9.35	24.46	54.94
	2	17.45	41.88	52.42	19.93	5.40	9.21	29.85	52.59
	3	23.27	48.86	40.71	19.78	5.71	9.86	29.08	32.59
	4	15.12	38.39	44.78	21.61	5.13	9.49	64.46	51.41
	5	19.20	40.14	132.32	8.28	4.53	10.04	42.15	60.82
	6	18.61	40.14	59.03	10.86	5.35	10.38	45.23	27.88
	7	18.03	42.46	43.26	29.78	5.51	9.59	36.77	62.00
	8	11.05	34.90	29.36	30.83	4.78	9.25	28.31	59.65
Ethanol + SL 5 mg/kg	1	15.12	43.04	105.85	25.28	4.90	9.49	53.69	42.00
	2	19.78	52.93	52.93	49.37	4.93	11.58	15.23	26.71
	3	16.87	44.21	53.94	26.37	5.32	9.64	46.00	19.65
	4	23.27	38.97	45.29	28.10	5.66	10.96	18.31	32.59
	5	18.03	45.95	101.79	24.11	5.60	10.03	38.31	60.82
	6	15.71	47.70	55.40	21.03	5.34	10.27	25.23	47.88
	7	20.36	36.06	68.14	39.59	5.21	11.14	61.38	47.88
	8	20.36	45.37	48.35	22.69	5.99	11.85	74.46	65.53

**CURRICULUM VITAE**

Mr. Chanon Ngamtin was born on September 14, 1981 in Bangkok. He received his Bachelor of Science in Public Health (second class honours) from Faculty of Public Health, Khon Kaen University in 2004 and then studied a Master of Science in Pharmacology, Graduate School, Chulalongkorn University.