

Isolation and identification of antiplatelet aggregatory principles from the leaves of *Piper lolot*

Li C.-Y., Tsai W.-J., Damu A.G., Lee E.-J., Wu T.-S., Nguyen X.D., Tran D.T., Thanh L.

Department of Chemistry, National Cheng Kung University, Tainan, Taiwan; National Research Institute of Chinese Medicine, Taipei, Taiwan; Neurophysiology Laboratory, Department of Surgery and Anesthesiology, National Cheng Kung University Medical Center and Medical School, Tainan, Taiwan; Faculty of Chemistry, College of Natural Sciences, Hanoi National University, 19-Le Thanh Tong Street, Hanoi, Viet Nam; Faculty of Chemistry, Vinh University, 182-Le Duan, Vinh City, Nghean Province, Viet Nam; Faculty of Chemistry, Hue University, 47-Le Loi Street, Hue, Viet Nam

Abstract: The methanolic extract of *Piper lolot*, having shown potent inhibitory activity on platelet aggregation induced by arachidonic acid (AA) and platelet activating factor (PAF), was subjected to activity-guided isolation to yield twelve new amide alkaloids, piperlotine A-L (1-12), along with twenty-nine known compounds. Their structures were elucidated on the basis of spectroscopic analysis. The isolated compounds were tested for their inhibitory activity on the rabbit platelet aggregation. The compounds piperlotine A (1), piperlotine C (3), piperlotine D (4), piperlotine E (5), 3-phenyl-1-(2,4,6-trihydroxyphenyl)propan-1-one (21), 3-(4-methoxyphenyl)-1-(2,4,6-trihydroxyphenyl)propan-1-one (22), 1-trans-cinnamoylpyrrolidine (24), sarmentine (26), pellitorine (27), methyl 3-phenylpropionate (32), and (10S)-10-hydroxypheophorbide a methyl ester (40) showed potent antiplatelet aggregation activity. © 2007 American Chemical Society.

Author Keywords: Antiplatelet aggregation; *Piper lolot*; Piperaceae; Piperlotine

Index Keywords: alkaloid; antithrombocytic agent; animal; article; chemistry; drug effect; isolation and purification; Piperaceae; plant leaf; rabbit; thrombocyte aggregation; Alkaloids; Animals; Piper; Plant Leaves; Platelet Aggregation; Platelet Aggregation Inhibitors; Rabbits; *Oryctolagus cuniculus*; *Piper lolot*; Piperaceae

Year: 2007

Source title: Journal of Agricultural and Food Chemistry

Volume: 55

Issue: 23

Page : 9436-9442

Cited by: 2

Link: Scopus Link

Chemicals/CAS: Alkaloids; Platelet Aggregation Inhibitors

Correspondence Address: Wu, T.-S.; Department of Chemistry, National Cheng Kung University, Tainan, Taiwan; email: tswu@mail.ncku.edu.tw

ISSN: 218561

CODEN: JAFCA

DOI: 10.1021/jf0719631

PubMed ID: 17941696

Language of Original Document: English

Abbreviated Source Title: Journal of Agricultural and Food Chemistry

Document Type: Article

Source: Scopus

Authors with affiliations:

- Li, C.-Y., Department of Chemistry, National Cheng Kung University, Tainan, Taiwan
- Tsai, W.-J., National Research Institute of Chinese Medicine, Taipei, Taiwan
- Damu, A.G., Department of Chemistry, National Cheng Kung University, Tainan, Taiwan
- Lee, E.-J., Neurophysiology Laboratory, Department of Surgery and Anesthesiology, National Cheng Kung University Medical Center and Medical School, Tainan, Taiwan
- Wu, T.-S., Department of Chemistry, National Cheng Kung University, Tainan, Taiwan, National Research Institute of Chinese Medicine, Taipei, Taiwan
- Nguyen, X.D., Faculty of Chemistry, College of Natural Sciences, Hanoi National University, 19-Le Thanh Tong Street, Hanoi, Viet Nam
- Tran, D.T., Faculty of Chemistry, Vinh University, 182-Le Duan, Vinh City, Nghean Province, Viet Nam
- Thanh, L., Faculty of Chemistry, Hue University, 47-Le Loi Street, Hue, Viet Nam

References:

- Davies, M.J., Thomas, M.B., Thrombosis and acute coronary lesions in sudden cardiac ischemic death (1984) *N. Engl. J. Med.*, 310, pp. 1137-1140
- Fuster, V.F., Badimon, J.J., Chesebro, J.H., Mechanisms of disease: The pathogenesis of coronary artery disease and the acute coronary syndromes (1992) *N. Engl. J. Med.*, 326, pp. 242-250
- Wu, T.S., Kao, M.S., Wu, P.L., Lin, F.W., Shi, L.S., Teng, C.M., Antiplatelet principles from the root of *Petasites formosanus* (2000) *Phytochemistry*, 52, pp. 901-905
- Wu, T.S., Shi, L.S., Wang, J.J., Iou, S.C., Chang, H.C., Chen, Y.P., Kuo, Y.H., Teng, C.M., Cytotoxic and antiplatelet aggregation principles of *Ruta graveolens* (2001) *J. Chin. Chem. Soc.*, 50, pp. 171-178
- Wu, T.S., Tsang, Z.J., Wu, P.L., Lin, F.W., Li, C.Y., Teng, C.M., Lee, K.H., New constituents and antiplatelet aggregation and anti-HIV principles of *Artemisia capillaries* (2001) *Bioorg. Med. Chem.*, 9, pp. 77-83
- Liou, M.J., Teng, C.M., Wu, T.S., Constituents from *Rubia ustulata* Diels and *R. yunnanensis* Diels and their antiplatelet aggregation activity (2002) *J. Chin. Chem. Soc.*, 49, pp. 1025-1030
- Shultes, R.E., Raffauf, R.F., (1990) *The Healing Forest: Medicinal and Toxic Plants of the Northwest Amazonia*
- Historical, Ethno- & Economic Botany, 2, pp. 362-368. , Dioscoride Press: Portland, OR
- Iwashita, M., Saito, M., Yamaguchi, Y., Takagaki, R., Nakahata, N., Inhibitory effect of ethanol extract of *Piper longum* L. on rabbit platelet aggregation through antagonizing thromboxane A2 receptor (2007) *Biol. Pharm. Bull.*, 30, pp. 1221-1225
- Chen, Y.C., Liao, C.H., Chen, I.S., Lignans, an amide and anti-platelet activities from *Piper philippinum* (2007) *Phytochemistry*, 68, pp. 2101-2111
- Tripathi, A.K., Jain, D.C., Kumar, S., Secondary metabolites and their biological and medicinal activities of *Piper* species plants (1996) *J. Med. Aromat. Plant Sci.*, 18, pp. 302-321
- Kiuchi, F., Nakamura, N., Tsuda, Y., Kondo, K., Yoshimura, H., Studies on crude drugs effective on visceral larva migrans. IV. Isolation and identification of larvicidal principles in pepper (1988) *Chem. Pharm. Bull.*, 36, pp. 2452-2465
- Park, I.K., Lee, S.G., Shin, S.C., Park, J.D., Ahn, Y.J., Larvicidal activity of isobutylamides identified in *Piper nigrum* fruits

- against three mosquito species (2002) *J. Agric. Food Chem*, 50, pp. 1866-1870
- Truyen, L.V., Chau, N.G., (1999) *Selected Medicinal Plants in Vietnam*, pp. 182-184. , Science and Technology Publishing House: Hanoi, Vietnam
 - Parmar, V.S., Jain, S.C., Bisht, K.S., Jain, R., Taneja, P., Jha, A., Tyagi, O.D., Boll, P.M., *Phytochemistry of the Genus Piper* (1997) *Phytochemistry*, 46, pp. 597-673
 - Luger, P., Weber, M., Dung, N.X., Luu, V.T., Rang, D.D., Tuong, D.T., Ngoc, P.H., The crystal structure of 3-(4'-methoxyphenyl)propanoyl pyrrole of Piper lolot C. DC from Vietnam (2002) *Cryst. Res. Technol*, 37, pp. 627-633
 - Singh, S. K.
 - Prasad, A. K.
 - Olsen, C. E.
 - Jha, A.
 - Jain, S. C.
 - Parmar, V. S.
 - Wengel, J. Neolignans and alkaloids from Piper argyrophyllum. *Phytochemistry* 1996, 43, 1355-1360 Dharmaratne, H.R.W., Nanayakkara, N.P.D., Khan, I.A., Kavalactones from Piper methysticum, and their ¹³C NMR spectroscopic analyses (2002) *Phytochemistry*, 59, pp. 429-433
 - Ekundayo, O., Laakso, I., Adegbola, R.M., Oguntimein, B., Sofowora, A., Hiltunen, R., Essential oil constituents of Ashanti pepper (*Piper guineense*) fruits (Berries) (1988) *J. Agric. Food Chem*, 36, pp. 880-882
 - Tsai, W.J., Hsieh, H.T., Chen, C.C., Kuo, Y.C., Chen, C.F., Characterization of the antiplatelet effect of (2S)-5-methoxy-6-methylflavan-7-ol from *Draconis Resina* (1998) *Eur. J. Pharmacol*, 346, pp. 103-110
 - Hung, C.C., Tsai, W.J., Yang, L.M., Kuo, Y.H., Evaluation of caffeic acid amide analogues as anti-platelet aggregation and anti-oxidative agents (2005) *Bioorg. Med. Chem*, 13, pp. 1791-1797
 - Hsu, H. C.
 - Yang, W. C.
 - Tsai, W. J.
 - Chen, C. C.
 - Huang, H. Y.
 - Tsai, Y. C. α -Bulnesene, a novel PAF receptor antagonist isolated from *Pogostemon cablin*. *Biochem. Biophys. Res. Commun.* 2006, 345, 1033-1038
 - Ishihara, H., Hori, K., Sugihara, H., Ito, Y.N., Katsuki, T., Highly diastereo- and enantioselective aziridination of α,β -unsaturated amides with diaziridine and mechanistic consideration on its stereochemistry (2002) *Helv. Chim. Acta*, 85, pp. 4272-4286
 - Cerbai, G., Dipaco, G.F., Dell'Omodarme, G., Neurosedative and hypotensive activity in a series of acyl derivatives of certain heterocyclic bases (1962) *Boll. Chim. Farm*, 101, pp. 211-214
 - Bruening, C. H.
 - Darling, C. M.
 - Magarian, R. A.
 - Nobles, W. L. Use of N-methyltetrahydrofurfurylamine in the Mannich reaction. *J. Pharm. Sci.* 1965, 54, 1537-1539
 - Soloshonok, V.A., Cai, C., Hruby, V.J., Rational design of highly diastereoselective, organic base-catalyzed, room-temperature Michael addition reactions (2000) *J. Org. Chem*, 65, pp. 6688-6696
 - Sibi, M.P., Liu, M., N-Benzylhydroxylamine addition to β -aryl enoates. Enantioselective synthesis of β -aryl- β -amino acid precursors (2000) *Org. Lett*, 2, pp. 3393-3396

- Priestap, H.A., Seven aristololactams from *Aristolochia argentina* (1985) *Phytochemistry*, 24, pp. 849-852
- Achari, B., Chakrabarty, S., Bandyopadhyay, S., Pakrashi, S.C., A new 4,5-dioxoaporphine and other constituents of *Aristolochia indica* (1982) *Heterocycles*, 19, pp. 1203-1206
- Kojima, H., Sato, N., Hatano, A., Ogura, H., Sterol glucosides from *Prunella vulgaris* (1990) *Phytochemistry*, 29, pp. 2351-2355
- Bohlmann, F., Abraham, W.R., Neue diterpene aus *Helichrysum acutatum* (1979) *Phytochemistry*, 18, pp. 1754-1756
- Ishihara, H., Hori, K., Sugihara, H., Ito, Y.N., Katsuki, T., Highly diastereo- and enantioselective aziridination of alpha, beta-unsaturated amides with diaziridine and mechanistic consideration on its stereochemistry (2002) *Helv. Chim. Acta*, 85, pp. 4272-4286
- Li, C.Y., Lee, E.J., Wu, T.S., Antityrosinase principles and constituents of the petals of *Crocus sativus* (2004) *J. Nat. Prod.*, 67, pp. 437-440
- Teresa, J.D.P., Urones, J.G., Marcos, I.S., Núñez, L., Basabe, P., Diterpenoids and flavonoids from *Cistus palinhæ* (1983) *Phytochemistry*, 22, pp. 2805-2808
- Crosignani, S., White, P.D., Lindau, B., Polymer-supported O-alkylisoureas: Useful reagents for the O-alkylation of carboxylic acids (2004) *J. Org. Chem.*, 69, pp. 5897-5905
- Yang, D., Wong, M.K., Yan, Z., Regioselective intramolecular oxidation of phenols and anisoles by dioxiranes generated in situ (2000) *J. Org. Chem.*, 65, pp. 4179-4184
- Kai, H., Baba, M., Okuyama, T., Two new megastigmanes from the leaves of *Cucumis sativus* (2007) *Chem. Pharm. Bull.*, 55, pp. 133-136
- Duan, H., Takaishi, Y., Momota, H., Ohmoto, Y., Taki, T., Immunosuppressive constituents from *Saussurea medusa* (2002) *Phytochemistry*, 59, pp. 85-90
- Hernandez, L.R., Riscala, E.C., de Catalan, C.A.N., Diaz, J.G., Herz, W., Sesquiterpene lactones and other constituents of *Stevia maimarensis* and *Synedrellopsis grisebachii* (1996) *Phytochemistry*, 42, pp. 681-684
- Lin, C.H., Li, C.Y., Kuoh, C.S., Wu, T.S., Constituents of the leaves of *Petasites formosanus* and their antioxidative activity (2003) *Heterocycles*, 60, pp. 1881-1890
- Gupta, M.M., Verma, R.K., Akhila, A., Oxo acids and branched fatty acid esters from rhizomes of *Costus speciosus* (1986) *Phytochemistry*, 25, pp. 1899-1902
- Hanahan, D.J., Platelet activating factor: A biologically active phosphoglyceride (1986) *Annu. Rev. Biochem.*, 55, pp. 483-509