

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:

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

References:

1. 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
2. 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
3. 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
4. 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.*, 48, pp. 171-178
5. 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
6. 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
7. Shultes, R.E., Raffauf, R.F., (1990) *The Healing Forest: Medicinal and Toxic Plants of the Northwest Amazonia*
8. Historical, Ethno- & Economic Botany, 2, pp. 362-368. , Dioscoride Press: Portland, OR
9. 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
10. 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
11. 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
12. 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

13. 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
14. Truyen, L.V., Chau, N.G., (1999) Selected Medicinal Plants in Vietnam, pp. 182-184. , Science and Technology Publishing House: Hanoi, Vietnam
15. 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
16. 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
17. Singh, S. K.
18. Prasad, A. K.
19. Olsen, C. E.
20. Jha, A.
21. Jain, S. C.
22. Parmar, V. S.
23. Wengel, J. Neolignans and alkaloids from *Piper argyrophyllum*. *Phytochemistry* 1996, 43, 1355-1360Dharmaratne, 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
24. Ekundayo, O., Laakso, I., Adegbola, R.M., Oguntiemein, B., Sofowora, A., Hiltunen, R., Essential oil constituents of Ashanti pepper (*Piper guineense*) fruits (Berries) (1988) *J. Agric. Food Chem.*, 36, pp. 880-882
25. Tsai, W.J., Hsieh, H.T., Chen, C.C., Kuo, Y.C., Chen, C.F., Characterization of the antiplatelet effect of (2 5)-5-methoxy-6-methylflavan-7- ol from *Draconis Resina* (1998) *Eur. J. Pharmacol.*, 346, pp. 103-110
26. 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
27. Hsu, H. C.
28. Yang, W. C.
29. Tsai, W. J.
30. Chen, C. C.
31. Huang, H. Y.
32. Tsai, Y. C. ?-Bulnesene, a novel PAF receptor antagonist isolated from *Pogostemon cablin*. *Biochem. Biophys. Res. Commun.* 2006, 345, 1033-1038Ishihara, H., Hori, K., Sugihara, H., Ito, Y.N., Katsuki, T., Highly diastereoselective and enantioselective aziridination of ?,- unsaturated amides with diaziridine and mechanistic consideration on its stereochemistry (2002) *Helv. Chim. Acta*, 85, pp. 4272-4286
33. 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
34. Bruening, C. H.
35. Darling, C. M.
36. Magarian, R. A.
37. Nobles, W. L. Use of N-methyltetrahydrofurfurylamine in the Mannich reaction. *J. Pharm. Sci.* 1965, 54, 1537-1539Soloshonok, 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
38. Sibi, M.P., Liu, M., N-Benzylhydroxylamine addition to ?-aryl enoates. Enantioselective synthesis of ?-aryl-?-amino acid

- precursors (2000) *Org. Lett.*, 2, pp. 3393-3396
- 39. Priestap, H.A., Seven aristololactams from *Aristolochia argentina* (1985) *Phytochemistry*, 24, pp. 849-852
 - 40. 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
 - 41. Kojima, H., Sato, N., Hatano, A., Ogura, H., Sterol glucosides from *Prunella vulgaris* (1990) *Phytochemistry*, 29, pp. 2351-2355
 - 42. Bohlmann, F., Abraham, W.R., Neue diterpene aus *Helichrysum acutatum* (1979) *Phytochemistry*, 18, pp. 1754-1756
 - 43. 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
 - 44. 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
 - 45. Teresa, J.D.P., Urones, J.G., Marcos, I.S., N??ez, L., Basabe, P., Diterpenoids and flavonoids from *Cistus paliniae* (1983) *Phytochemistry*, 22, pp. 2805-2808
 - 46. 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
 - 47. 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
 - 48. Kai, H., Baba, M., Okuyama, T., Two new megastigmanes from the leaves of *Cucumis sativus* (2007) *Chem. Pharm. Bull.*, 55, pp. 133-136
 - 49. Duan, H., Takaishi, Y., Momota, H., Ohmoto, Y., Taki, T., Immunosuppressive constituents from *Saussurea medusa* (2002) *Phytochemistry*, 59, pp. 85-90
 - 50. 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 *Synedrellaopsis grisebachii* (1996) *Phytochemistry*, 42, pp. 681-684
 - 51. 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
 - 52. 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
 - 53. Hanahan, D.J., Platelet activating factor: A biologically active phosphoglyceride (1986) *Annu. Rev. Biochem.*, 55, pp. 483-509