

Crotonkinins A and B and related diterpenoids from *Croton tonkinensis* as anti-inflammatory and antitumor agents

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Abstract: Cytotoxicity-guided phytochemical investigation of a methanolic extract of *Croton tonkinensis* afforded two new kaurane diterpenoids (1, 2) and 10 known ent-kaurane-type diterpenoids (3-12). The structures of 1 and 2 were based on analysis of spectroscopic and mass spectral data. Compounds 3-12 were identified by comparison of their spectroscopic and physical data with those reported in the literature. Selected compounds from this plant were examined for cytotoxic and anti-inflammatory activities. Compounds 4 and 9 showed the highest cytotoxic activity against the tested tumor cell lines. Compounds 3, 4, 6, 8, 9, and 11 had IC_{50} values less than 5 μ M and were more potent than the nonspecific NOS inhibitor L-NAME in inhibiting LPS-induced NO production. © 2007 American Chemical Society and American Society of Pharmacognosy.

Index Keywords: *Croton tonkinensis* extract; crotonkinin a; crotonkinin b; diterpenoid; ent 18 acetoxy 7 α ,14 β dihydroxykaur 16 en 15 one; ent 18 acetoxy 7 β hydroxykaur 15 one; ent 18 acetoxykaur 16 en 15 one; ent 18 hydroxykaur 16 en 15 one; ent 1 β acetoxy 7 α ,14 β dihydroxykaur 16 en 15 one; ent 7 α ,14 β dihydroxykaur 16 en 15 one; ent 7 β hydroxy 15 oxokaur 16 en 18 ol; ent 7 β hydroxy 15 oxokaur 16 en 18 yl acetate; ent 7 β hydroxy 16 kauren 15 one; ent kaur 16 en 15 one 18 oic acid; kaurane derivative; lipopolysaccharide; methanol; n(g) nitroarginine methyl ester; nitric oxide; plant extract; unclassified drug; animal cell; antiinflammatory activity; antineoplastic activity; article; controlled study; *Croton tonkinensis*; cytotoxicity; drug isolation; drug structure; Euphorbia; human; human cell; mass spectrometry; medicinal plant; nonhuman; nuclear magnetic resonance spectroscopy; tumor cell; Anti-Inflammatory Agents, Non-Steroidal; Antineoplastic Agents, Phytogetic; Croton; Diterpenes; Drug Screening Assays, Antitumor; Humans; Inhibitory Concentration 50; Lipopolysaccharides; Molecular Structure; NG-Nitroarginine Methyl Ester; Nitric Oxide; Plants, Medicinal; Vietnam; *Croton tonkinensis*

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References:

- Hsieh, C.F., (1993) Flora of Taiwan, 3, p. 454. , Epoch: Taiwan
- Vo, V.C., (1997) Dictionary of Vietnamese Medicinal Plants
- Publishing House Medicine: Ho Chi Minh City, pp. 622-623
- (1999) Selected Medicinal Plants in Vietnam, 1, pp. 260-262. , Publishing House Science and Technology: Hanoi
- Do, T.L., (2001) Medicinal Plants and Remedies of Vietnam, p. 826. , Publishing House Medicine: Hanoi
- Son, P.T., Giang, P.M., Taylor, W.C., (2000) Aust. J. Chem, 53, pp. 1005-1003
- Minh, P.T.H., Ngoc, P.H., Quang, D.N., Hashimoto, T., Takaoka, S., Asakawa, Y., (2003) Chem. Pharm. Bull, 51, pp. 590-591
- Giang, P.M., Jin, H.Z., Son, P.T., Lee, J.H., Hong, Y.S., Lee, J.J., (2003) J. Nat. Prod, 66, p. 1220

- Minh, P.T.H., Ngoc, P.H., Taylor, W.C., Cuong, N.M., (2004) *Fitoterapia*, 75, pp. 556-552
- Giang, P.M., Son, P.T., Lee, J.H., Otsuka, H., (2004) *Chem. Pham. Bull*, 52, pp. 882-879
- Giang, P.M., Son, P.T., Hamada, Y., Otsuka, H., (2005) *Chem. Pham. Bull*, 53, pp. 296-300
- Lorimer, S.D., Weavers, R.T., (1987) *Phytochemistry*, 26, pp. 3215-3207
- Buchanan, M.S., Connolly, J.D., Kadir, A.A., Rycroft, D.S., (1996) *Phytochemistry*, 42, pp. 1641-1646
- Asakawa, Y., Takikawa, K., Toyota, M., Ueda, A., Tori, M., Kumar, S.S., (1987) *Phytochemistry*, 26, pp. 1019-1022
- Fraga, B.M., Gonzalez, P., Guillermo, R., Hernandez, M.G., (1996) *Tetrahedron*, 52, pp. 13767-13782
- Perry, N.B., Burgess, E.J., Baek, S.H., Weavers, R.T., Geis, W., Mauger, A.B., (1999) *Phytochemistry*, 50, pp. 423-433
- Waiss Jr., A.C., Elliger, C.A., Haddon, W.F., Benson, M., (1993) *J. Nat. Prod*, 56, pp. 1365-1372
- Lee, K.H., Huang, E.S., Piantadosi, C., Pagano, J.S., Geissman, T.A., (1971) *Cancer Res*, 31, pp. 1649-1654
- Lee, K.H., Hall, I.S., Mar, E.C., Starnes, C.O., ElGebaly, S.A., Waddell, T.G., Hadgraft, R.I., Weidner, I., (1977) *Science*, 196, pp. 533-535
- Dringen, R., (2005) *Antioxid. Redox Signaling*, 7, pp. 1233-1223
- Li, J., Baud, O., Vartanian, T., Volpe, J.J., Rosenberg, P.A., (2005) *Proc. Natl. Acad. Sci. U.S.A*, 102, pp. 9936-9941
- Pacher, P., Beckman, J.S., Liaudet, L., (2007) *Physiol. Rev*, 87, pp. 315-424
- Wang, Y.H., Wang, W.Y., Chang, C.C., Liou, K.T., Sung, Y.J., Liao, J.F., Chen, C.F., Shen, Y.C., (2006) *J. Biomed. Sci*, 13, pp. 127-141
- Di Rosa, M., Radomski, M., Carnuccio, R., Moncada, S., (1990) *Biochem. Biophys. Res. Commun*, 172, pp. 1246-1252
- Van den Worm, E., Beukelman, C.J., Van den Berg, A.J., Kroes, B.H., Labadie, R.P., Van Dijk, H., (2001) *Eur. J. Pharmacol*, 433, pp. 225-230
- Lin, L.C., Wang, Y.H., Hou, Y.C., Chang, S., Liou, K.T., Chou, Y.C., Wang, W.Y., Shen, Y.C., (2006) *J. Pharm. Pharmacol*, 58, pp. 129-135
- Liou, K.T., Shen, Y.C., Chen, C.F., Tsao, C.M., Tsai, S.K., (2003) *Eur. J. Pharmacol*, 475, pp. 19-27
- Cheng, M.J., Lee, S.J., Chang, Y.Y., Wu, S.H., Tsai, I.L., Jayaprakasam, B., Chen, I.S., (2003) *Phytochemistry*, 63, pp. 603-608
- Wang, X., Bastow, K.F., Sun, C.M., Lin, Y.L., Yu, H.J., Don, M.J., Wu, T.S., Lee, K.H., (2004) *J. Med. Chem*, 47, pp. 5816-5819