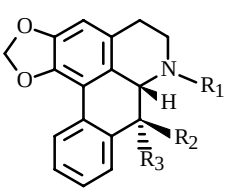
# CHEMICAL CONSTITUENTS FROM THE LEAVES OF *Michelia alba*

**C. Y. Chen,[1*] L. Y. Huang,[2] L. J. Chen,[2] W. L. Lo,[1]**
**S. Y. Kuo,[1] Y. D. Wang,[2] S. H. Kuo,[1] and T. J. Hsieh [1]**

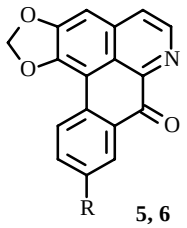
UDC 547.945:972

The genus *Michelia* (Magnoliaceae) consists of about 30 species. *Michelia alba* is an evergreen tree, especially distributed in Taiwan and China. *Michelia* species have been used by indigenous peoples for the treatment of cancer. For example, *Michelia champaca* has been used in India for the treatment of abdominal tumors and *M. hypoleuca* and *M. officinalis* for carcinomatous sores and leukemia, respectively, in China [1]. Previous phytochemical studies on this species isolated, from the roots and flowers of *M. alba*, ushinsunine, oxoushinsunine, salicifoline, michelalbine, limonene, benzyl acetate, linalool, nerol, hydroxycitronellal, benzaldehyde, benzyl benzoate, and methyl eugenol [2, 3]. To further understand the chemotaxonomy and to continue searching for novel agents from Magnoliaceous plants, the leaves of *M. alba* were chosen for the first time for phytochemical investigation. In this paper, we report the isolation of 21 pure substances. The compounds included four aporphines, (-)-anonaine (**1**) [4], (-)-norushinsunine (**2**) [5], (-)-ushinsunine (**3**) [5], and (-)-*N*-acetylanonaine (**4**) [6]; two oxoaporphines, liriodenine (**5**) [5] and oxoxylopine (**6**) [7]; three sesquiterpene lactones, michelenolide (**7**) [8], costunolide (**8**) [8], and 11,13-dehydrolanuginolide (**9**) [9]; one amide, *N-trans*-feruloyltyramine (**10**) [10]; one lignan, (+)-syringaresinol (**11**) [11]; three benzenoids, 4-hydroxybenzaldehyde (**12**) [12], 4-hydroxybenzoic acid (**13**) [12], and methylparaben (**14**) [12]; two steroids, $\beta$-sitosterol and stigmasterol [13]; three aliphatic compounds, palmitic acid [14], stearic acid [15], and linoleic acid [16]; and two chlorophylls, pheophorbide a [17] and aristophyll-C [18]. In addition to **3** and **5**, all of these compounds were isolated for the first time from this source.



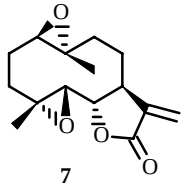
**1 - 4**

**1:** $R_1 = R_2 = R_3 = H$
**2:** $R_1 = R_2 = H$, $R_3 = OH$
**3:** $R_1 = CH_3$, $R_2 = H$, R = OH
**4:** R = $COCH_3$, $R_2 = R_3 = H$

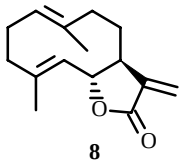


**5, 6**

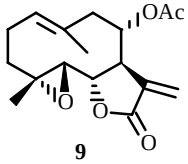
**5:** R = H
**6:** R = OH



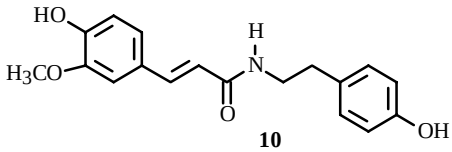
**7**



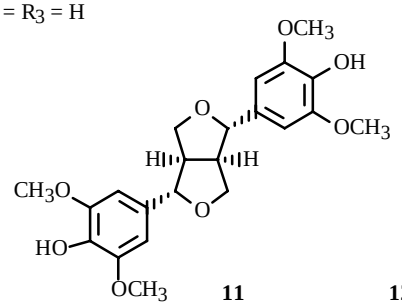
**8**



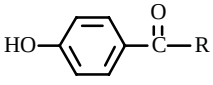
**9**



**10**



**11**



**12 - 14**

**12:** R = H; **13:** R = OH; **14:** R = $OCH_3$

The leaves of *M. alba* were collected from Fooyin University, Kaohsiung County, Taiwan in March, 2005. A voucher specimen (Michelia 2) was characterized by Dr. Yen-Ray Hsui of the Division of Silviculture, Taiwan Forestry Research

1) School of Medicine and Health Sciences, Fooyin University, Kaohsiung County 831, Taiwan, tel: +886-7-7811151-6200, fax: +886-7-7863667, e-mail: xx377@mail.fy.edu.tw; 2) Department of Medical Technology, Fooyin University, Kaohsiung County 831, Taiwan. Published in Khimiya Prirodnykh Soedinenii, No. 1, pp. 105-106, January-February, 2008. Original article submitted November 8, 2006.

0009-3130/08/4401-0137 

Institute, Taipei, Taiwan and deposited in the Basic Medical Science Education Center, Fooyin University, Kaohsiung County, Taiwan. The air-dried leaves of *M. alba* (6.0 kg) were extracted with MeOH (70 L × 6) at room temperature, and a MeOH extract (367.8 g) was obtained upon concentration under reduced pressure. The MeOH extract, suspended in $H_2O$ (1 L), was partitioned with $CHCl_3$ (2 L × 5) to give fractions soluble in $CHCl_3$ (154.3 g) and $H_2O$ (144.1 g). The $CHCl_3$-soluble fraction was chromatographed over silica gel (800 g, 70-230 mesh) using *n*-hexane/$CHCl_3$/MeOH mixtures as eluents to produce five fractions. Part of fraction 1 (43.12 g) was subjected to silica gel chromatography by eluting with *n*-hexane-EtOAc (5:1) and enriched gradually with EtOAc to furnish five fractions (1-1-1-4). Fraction 1-1 (12.89 g) was further purified on a silica gel column using *n*-hexane/EtOAc mixtures to obtain palmitic acid (52 mg), stearic acid (27 mg), and linoleic acid (37 mg).

Fraction 1-2 (6.23 g) was further purified on a silica gel column using *n*-hexane/EtOAc mixtures to obtain pheophorbide a (25 mg) and aristophyll-C (51 mg). Fraction 1-3 (15.31 g) was further purified on a silica gel column using *n*-hexane/EtOAc/MeOH mixtures to obtain a mixture of *β*-sitosterol and stigmasterol (144 mg). Fraction 1-4 (4.11 g) was further purified on a silica gel column using *n*-hexane/EtOAc/MeOH mixtures to obtain methylparaben (**14**) (15 mg). Part of fraction 2 (9.21 g) was subjected to silica gel chromatography by eluting with *n*-hexane-EtOAc (1:1) enriched with EtOAc to furnish five further fractions (2-1-2-4). Fraction 2-2 (1.43 g) was purified on a silica gel column (200 g, 230-400 mesh) using $CHCl_3$/MeOH mixtures to obtain 4-hydroxybenzaldehyde (**12**) (21 mg) and 4-hydroxybenzoic acid (**13**) (18 mg). Part of fraction 3 (13.25 g) was subjected to silica gel chromatography by eluting with *n*-hexane-EtOAc (1:1) and enriched gradually with EtOAc to furnish five fractions (3-1-3-3). Fraction 3-1 (5.53 g) was further purified on a silica gel column using *n*-hexane/EtOAc mixtures to obtain michelenolide (**7**) (12 mg). Fraction 3-3 (4.87 g) was further purified on a silica gel column using *n*-hexane/EtOAc mixtures to obtain 11,13-dehydrolanuginolide (**9**) (34 mg). Part of fraction 4 (38.54 g) was subjected to silica gel chromatography by eluting with $CHCl_3$-MeOH (40:1), enriched with MeOH to furnish five fractions (4-1-4-5). Fraction 4-1 (3.02 g) was subjected to further silica gel chromatography by eluting with $CHCl_3$-MeOH (100:1) and enriched gradually with MeOH to obtain four fractions (4-1-1-4-1-4). Fraction 4-1-1 (0.52 g) was further purified by passage over another silica gel column using *n*-hexane/EtOAc mixtures to obtain costunolide (**8**) (11 mg). Fraction 4-1-2 (0.74 g), eluted with *n*-hexane-EtOAc (1:7), was further separated using silica gel column chromatography and preparative TLC ($CHCl_3$-MeOH (100:1) and gave (+)-syringaresinol (**11**) (15 mg). Fraction 4-2 (5.73 g) was subjected to further silica gel chromatography by eluting with $CHCl_3$-MeOH (100:1) and enriched gradually with MeOH, to obtain four fractions (4-2-1-4-2-3). Fraction 4-2-1 (2.11 g) was further purified by passage over another silica gel column using EtOAc/MeOH mixtures to obtain liriodenine (**5**) (25 mg). Fraction 4-2-2 (0.44 g), eluted with EtOAc/MeOH (20:1), was further separated using silica gel column chromatography and preparative TLC (EtOAc-MeOH (100:1) and gave oxoxylopine (**6**) (5 mg). Fraction 4-3 (15.12 g) was subjected to further silica gel chromatography by eluting with $CHCl_3$-MeOH (50:1) and enriched gradually with MeOH to obtain three fractions (4-3-1-4-3-3). Fraction 4-3-2 (3.15 g), eluted with $CHCl_3$-MeOH (100:1), was further separated using silica gel column chromatography and preparative TLC ($CHCl_3$-MeOH (100:1) and gave (-)-*N*-acetylanonaine (**4**) (14 mg). Fraction 4-3-3 (7.75 g), eluted with $CHCl_3$-MeOH (40:1), was further separated using silica gel column chromatography and gave (-)-anonaine (**1**) (46 mg). Fraction 4-5 (8.74 g) was subjected to further silica gel chromatography by eluting with $CHCl_3$-MeOH (80:1) and enriched gradually with MeOH to obtain four fractions (4-5-1-4-5-5). Fraction 4-5-2 (4.13 g) was further purified on a silica gel column using $CHCl_3$/MeOH mixtures to obtain (-)-norushinsunine (**2**) (48 mg). Fraction 4-5-4 (1.27 g) was further purified on a silica gel column using $CHCl_3$/MeOH mixtures to obtain (-)-ushinsunine (**3**) (58 mg). Part of fraction 5 (15.01 g) was subjected to silica gel chromatography by eluting with $CHCl_3$-MeOH (50:1) and enriched gradually with MeOH, to furnish five fractions (5-1-5-4). Fraction 5-2 (4.07 g) was further purified on a silica gel column using $CHCl_3$/MeOH mixtures to obtain *N-trans*-feruloyltyramine (**10**) (26 mg).

**ACKNOWLEDGMENT**

This investigation was supported by a grant from the National Science Council of the Republic of China NSC-95-2320-B-242-004 (C.-Y. Chen).

**REFERENCES**


1. J. L. Hartwell, *Lloydia*, **33**, 97 (1970).
2. T. H. Yang, *J. Pharm.*, **82**, 804 (1962).
3. D. J. Wang, *Sci. Dev.*, **7**, 1036 (1979).
4. W. L. Lo, Y. C. Wu, T. J. Hsieh, S. H. Kuo, H. C. Lin, and C. Y. Chen, *Chin. Pharm. J.*, **56**, 69 (2004).
5. C. Y. Chen, F. R. Chang, and Y. C. Wu, *J. Chin. Chem. Soc.*, **44**, 313 (1997).
6. M. K. Pyo, H. S. Yun-Choi, and Y. J. Hong, *Planta Med.*, **69**, 267 (2003).
7. S. K. Talapatra, A. Patra, and B. Talapatra, *Chem. Ind.*, 1056 (1969).
8. M. Ogura, G. A. Cordell, and N. R. Farnsworth, *Phytochemistry*, **17**, 957 (1978).
9. S. K. Talapatra, A. Patra, and B. Talapatra, *Phytochemistry*, **12**, 1827 (1973).
10. C. Y. Chen, F. R. Chang, H. F. Yen, and Y. C. Wu, *Phytochemistry*, **49**, 1443 (1998).
11. C. Y. Chen, T. Y. Wu, F. R. Chang, and Y. C. Wu, *J. Chin. Chem. Soc.*, **45**, 629 (1998).
12. C. Y. Chen, F. R. Chang, C. M. Teng, and Y. C. Wu, *J. Chin. Chem. Soc.*, **46**, 77 (1999).
13. Y. H. Kuo and M. H. Yeh, *J. Chin. Chem. Soc.*, **44**, 379 (1997).
14. I. Addae-Mensah and H. Achenbach, *Phytochemistry*, **24**, 1817 (1985).
15. M. P. Dupont, G. Llabres, C. Delaude, L. Tchissambou, and J. P. Gastmans, *Planta Med.*, **63**, 282 (1997).
16. I. L. Tsai, Y. F. Jeng, B. Jayaprakasam, and I. S. Chen, *Chin. Pharm. J.*, **53**, 291 (2001).
17. Y. Nakatani, G. Ourisson, and J. P. Beck, *Chem. Pharm. Bull.*, **29**, 2261 (1981).
18. Y. Y. Chan, Y. L. Leu, and T. S. Wu, *Chem. Pharm. Bull.*, **47**, 887 (1999).