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CHEMICAL COMPOUNDS FROM THE BARK OF *Cratoxylum formosum* ssp. *pruniflorum*

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Cratoxylum formosum ssp. *pruniflorum* is a valuable species distributed in Yunnan and Guangxi Provinces of China. Thirteen compounds have been isolated from the bark of *C. formosum* ssp. *pruniflorum*. Their structures were identified on the basis of spectroscopic analysis and chemical evidence: epifriedelinol (**2**), vismiaquinone B (**3**), 3,8-dihydroxy-1,2,4-trimethoxyxanthone (**5**), methyl-2,6-dihydroxy-3,4-dimethylbenzoate (**6**), 1,7-dihydroxy-4-methoxyxanthone (**7**), 11-hydroxy-5-methoxy-2,2,9-trimethyl-2*H*-naphtho[1,2-b]pyran-7,12-dione (**8**), physcion (**9**), 1,8-dihydroxy-2-methoxyxanthone (**10**), vismione B (**11**), neriifolone C (**12**), and 1,7-dihydroxyxanthone (**13**). Compounds **1** and **4** were identified by direct comparison with authentic samples as β-sitosterol and friedelin, respectively. Among them, compounds **1**, **2–6**, **10**, **11**, and **13** were isolated from *C. formosum* ssp. *pruniflorum* for the first time.

The air-dried and powdered bark of *Cratoxylum formosum* ssp. *pruniflorum* (7.0 kg) were extracted with 95% aqueous ethanol and filtered at room temperature. The filtrate was concentrated and extracted with petroleum ether, then extracted by ethyl acetate. The petroleum ether extract (100 g) was subjected to silica gel column chromatography eluted with a petroleum ether–EtOAc (90:10→40:60) gradient system to furnish six fractions, G1–G6. All fractions were collected and combined by monitoring with TLC. Fraction G2 (21 g) was further chromatographed over RP-18 (MeOH–H_2O 70:30→100:0) to provide subfractions G2a–G2c. Subfraction G2a was further chromatographed over silica gel using acetone–petroleum ether (10%) to give compounds **1** (7 mg) and **2** (20 mg). Then, in the same way, G2b and G2c were further separated to give compounds **3** (15 mg), **4** (17 mg), **5** (12 mg), **6** (10 mg), and **7** (10 mg). Subfraction G4 was treated in the same way to give compound **11** (11 mg).

The ethyl acetate (250 g) extract was subjected to silica gel column chromatography eluted with a methanol–chloroform (100:1→5:1) gradient system to furnish five fractions, F1–F5. All fractions were collected and combined by monitoring with TLC. Fraction F3 was further chromatographed over RP-18 (MeOH–H_2O 60:40→100:0) to provide subfractions F3a–F3b. The F3a part was further purified by Sephadex LH-20 (MeOH) to obtain compounds **6** (7 mg), **7** (13 mg), and **12** (15 mg). Then, in the same way, F3b was further separated to give compounds **8** (14 mg), **9** (13 mg), **10** (17 mg), and **13** (13 mg).

Epifriedelinol (2), colorless amorphous powder, $C_{30}H_{52}O$. ESI-MS *m/z* 429 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [1].

Vismiaquinone B (3), yellow amorphous powder, $C_{21}H_{20}O_6$. ESI-MS *m/z* 369 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [2].

3,8-Dihydroxy-1,2,4-trimethoxyxanthone (5), yellow amorphous powder, $C_{16}H_{14}O_7$. ESI-MS *m/z* 319 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [3].

Methyl 2,6-dihydroxy-3,4-dimethylbenzoate (6), colorless amorphous powder, $C_{10}H_{12}O_4$. ESI-MS *m/z* 197 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [4].

7-Dihydroxy-4-methoxyxanthone (7), yellow amorphous powder, $C_{14}H_{10}O_5$. ESI-MS *m/z* 259 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [5].

11-Hydroxy-5-methoxy-2,2,9-trimethyl-2*H*-naphtho[1,2-b]pyran-7,12-dione (8), yellow amorphous powder, $C_{21}H_{18}O_5$. ESI-MS *m/z* 351 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [6].

Physcion (9), yellow amorphous powder, $C_{16}H_{12}O_5$. ESI-MS *m/z* 285 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [7].

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TABLE 1. Cytotoxic Activities of Compounds **8–12** (IC_{50}, μM)

Compound	HL-60	SMMC-7721	A-549	MCF-7	SW480
8	> 40	> 40	> 40	> 40	> 40
9	> 40	> 40	> 40	> 40	> 40
10	> 40	> 40	> 40	> 40	> 40
11	19.02	19.18	11.38	38.10	12.19
12	5.60	27.08	16.43	22.91	28.60
cis-Platin	2.48	12.83	10.58	20.81	11.04
Taxol	< 0.008	< 0.008	< 0.008	< 0.008	< 0.008

1,8-Dihydroxy-4-methoxyxanthone (10), yellow amorphous powder, $C_{14}H_{10}O_5$. ESI-MS *m/z* 259 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [8].

Vismione B (11), brown amorphous powder, $C_{21}H_{22}O_5$. ESI-MS *m/z* 355 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [9].

Neriifolone C (12), yellow amorphous powder, $C_{18}H_{16}O_6$. ESI-MS *m/z* 329 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [10].

1,7-Dihydroxyxanthone (13), yellow amorphous powder, $C_{13}H_8O_4$. ESI-MS *m/z* 229 $[M + H]^+$. The MS and NMR spectral data were consistent with those reported [11].

Compounds **1** and **4** were identified by direct comparison with authentic samples as β-sitosterol and friedelin, respectively [12, 13]. The cytotoxic activity of compounds **8–12** against HL-60, SMMC-7721, A-549, MCF-7, and SW480 cell lines was studied by MTT [3-(4,5)-dimethylthiazol-2-yl)-3,5-diphenyltetrazolium bromide] assay [14]. The biological activity test results are summarized in Table 1. Both compounds **11** and **12** showed moderate cytotoxic activity against HL-60, SMMC-7721, A-549, MCF-7, and SW480 cell lines.

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REFERENCES

1. M. Sainsbury, *Phytochemistry,* **9**, 2209 (1970).
2. M. do Carmo, M. Miraglia, A. A. L. Mesquita, M. de Jesus, C. Varejao, O. R. Gottlieb, and H. E. Gottlieb, *Phytochemistry,* **20**, 2041 (1981).
3. A. Kijjoa, M. J. Gonzalez, M. M. M. Pinto, A. M. S. Silva, C. Anantachoke, and W. Herz, *Phytochemistry*, **55**, 833 (2000).
4. D. H. R. Barton, S. V. Ley, P. D. Magnus, and M. N. Rosenfeld, *J. Chem. Soc., Perkin Trans. 1*, 567 (1977).
5. Y. H. Duan, Y. Dai, G. H. Wang, X. Zhang, H. F. Chen, J. B. Chen, X. S. Yao, and X. K. Zhang, *J. Nat. Prod.,* **73**, 1283 (2010).
6. N. Boonnak, C. Karalai, S. Chantrapromma, C. Ponglimanont, A. Kanjana-Opas, K. Chantrapromma, and H. K. Fun, *Can. J. Chem. -Rev. Can. Chim.,* **85**, 341 (2007).
7. J. A. Pedersen, *J. Chem. Soc., Faraday Trans.,* **88**, 3423 (1992).
8. E. Wijeratne, T. J. Turbyville, A. Fritz, L. Whitesell, and A. Gunatilaka, *Bioorg. Med. Chem.,* **14**, 7917 (2006).
9. B. Botta, F. Delle Monache, G. Delle Monache, G. B. Marini Bettolo, and J. U. Oguakwa, *Phytochemistry,* **22**, 539 (1983).
10. W. Nuangnaowarat, W. Phupong, and M. Isaka, *Heterocycles,* **81**, 2335 (2010).
11. L. Kato, C. M. A. de Oliveira, I. Vencato, and C. Lauriucci, *J. Chem. Crystallogr.,* **35**, 23 (2005).
12. Q. F. Fan, Z. Na, H. B. Hu, Y. K. You, and T. Tang, *Chin. Trad. Herb. Drugs*, **43,** 436 (2012).
13. T. Akihisa, K. Yamamoto, T. Tamura, Y. Kimura, T. Iida, T. Nambara, and F. C. Chang, *Chem. Pharm. Bull*., **40**, 789 (1992).
14. L. G. Chen, L. L. Yang, and C. C. Wang, *Food Chem. Toxicol.,* **46**, 688 (2008).