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Lignans and diterpenes isolated from *Tirpitzia ovoidea* and their biological activities

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[ABSTRACT] A new lignan, tirpitzin A (**17**) together with 20 known compounds (**1**−**16**, and **18**−**21**) were isolated from the ethyl acetate soluble fraction of ethanol extract of the aerial parts of *Tirpitzia ovoidea*. The structure of new compound was elucidated by means of spectroscopic analysis. Of the known compounds, **7**−**21** were isolated from Linaceae family for the first time. The pharmacological activity of the crude extracts was tested using a mouse inflammation model induced by dimethyl benzene. The results demonstrated that the ethyl acetate soluble fraction had anti-inflammatory activity. Moreover, the cytotoxic and anti-inflammatory activities of some compounds were studied. The new compound **17** showed moderate cytotoxic effect against BxPC-3 cell line (IC_{50} = 19.51μmol·L^{-1}) and Compound **10** showed significant cytotoxicity against HepG2, HL-60, U87 and BxPC-3 cell lines with IC_{50} values in the range 4.2-8.3μmol·L^{-1}. Additionally, Compounds **2**, **10**, **11,** and **13** exhibited potent inhibitory effects on LPS-induced nitric oxide production in RAW 264.7 macrophages at the concentration of 50μmol·L^{-1}.

[KEY WORDS] *Tirpitzia ovoidea;* Linaceae; Lignans; Diterpenes; Cytotoxic activity; Anti-inflammatory activity

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Introduction

The stems, branches, and leaves of *Tirpitzia ovoidea* Chun et How ex Sha (Linaceae) have been used for the treatment of bruises sprains, rheumatoid arthritis, infection, sores furuncle, the adjunctive therapy of liver cancer and chronic hepatitisin Guangxi for a long time [1-3]. However, there are few reports about the chemical constituents and pharmacological effects of *T. ovoidea*. Our previous studies have revealed 18 diterpenes from the petroleum ether fraction of *T. ovoidea* [4]. In the present study, the cytotoxic and anti-inflammatory activities of different polar parts extracted from *T. ovoidea* were evaluated. As part of an ongoing study for the discovery of active constituents, a new neolignan, together with 14 known lignans and 6 known diterpenes, was obtained from the ethyl acetate fraction of *T. ovoidea*. Structures of the new compound **17** were elucidated applying 1D, 2D NMR, HRESIMS, and CD spectra. In addition, the cytotoxic effects of compounds **7**−**17** against HepG2, HL-60, U87, and BxPC-3 cell lines and the inhibitory effect of Compounds **2**−**14** and **17**−**20** against LPS-induced NO production of RAW 264.7 macrophages were also determined.

Results and Discussion

Chemistry

Compound **17** obtained as transparent oil was assigned as $C_{22}H_{26}O_7$ from its HR-ESI-MS data (*m/z* 425.1574 $[M + Na]^+$). The ^{13}C NMR, DEPT and HSQC showed 22 carbon signals: 12 phenyl carbons, 2 olefinic carbons, 4 methoxy carbons, and 4 aliphatic carbons. The above information showed the presence of a ring structure, 1 double bond, and 2 benzene ring in the structure of compound **17**.

Accronding to the ^{1}HNMR and ^{1}H-^{1}H COSY spectra, signals observed at δ_H 6.64 (s, 2H), 6.89 (s, 2H), 6.56 (d, *J* = 15.9 Hz, 1H), and 6.16 (dt, *J*=15.9, 6.2 Hz, 1H) were assigned to 4 phenyl protons and 2 alkenyl protons; δ_H 3.86 (s, 6H), 3.90 (s, 3H), and 3.39 (s, 3H) were assigned to protons of 4

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methoxy. δ_H 6.56 (d, J = 15.9 Hz, 1H) / 6.16 (dt, J = 15.9, 6.2 Hz, 1H) / 4.08 (d, J = 6.2 Hz, 2H), indicated the presence of Ar-CH=CH-CH_2-O; δ_H 5.57 (d, J = 7.4 Hz, 1H) / 3.63 (m, 1H) / 3.93−4.02 (m, 2H) indicated the presence of Ar-CH-CH-CH_2-O; According to the above information, we deduced that **17** is 4′, 7-epoxy-8, 3′-neolignan.

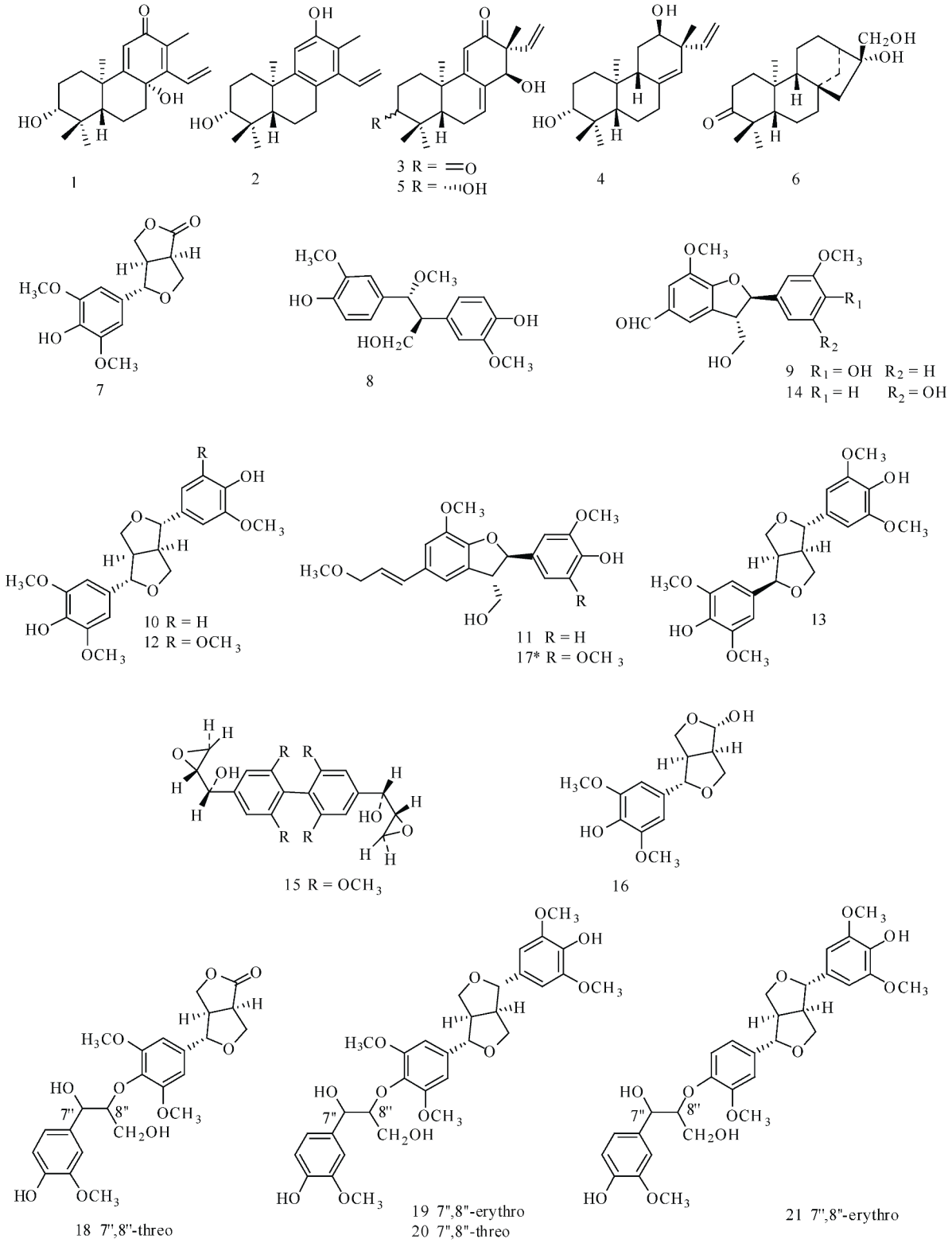

Fig. 1 Structures of compounds 1-21 from *Tirpitzia ovoidea*