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Chemical constituents of the fruits of *Artocarpus altilis*

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1. Subject and source

There are approximately 50 species of plants in the genus *Artocarpus* (Moraceae) distributed in tropical Asia. *Artocarpus altilis* (Parkinson) Fosberg, a tree of moderate size, is widely cultivated in tropics for a staple crop, construction material and animal feed, and its leaves have been used traditionally for the treatment of liver cirrhosis, hypertension and diabetes (Wang et al., 2007). The fruits of *A. altilis* were collected from the central province of Sri Lanka in February 2004 and identified by the comparison with the herbarium specimen (No. 2090) available at the National Herbarium, Peradeniya, Sri Lanka.

2. Previous work

Phytochemical studies on the leaves (Wang et al., 2007), heartwood (Shimizu et al., 2000) and bud covers (Patil et al., 2002) of this plant have revealed the presence of phenolic compounds such as stilbenes, chalcones and flavones. Cycloartane triterpenes and α-amyrin were isolated from the fruits of *A. altilis* (Altman and Zito, 1976).

3. Present study

The dried powdered whole fruit of *A. altilis* (900 g) was defatted with *n*-hexane and extracted with ethyl acetate and methanol at room temperature using a sonicator. Evaporation of ethyl acetate under reduced pressure gave a brown colored residue (4.7 g) and evaporation of methanol gave a dark brown solid (65 g). Methanol extract was partitioned with *n*-butanol and water. The *n*-butanol extract was evaporated under reduced pressure to yield a brown solid (10.6 g). The ethyl acetate and *n*-butanol extracts were combined and chromatographed over a column of silica gel (Merck Art. 7734) using *n*-hexane, ethyl acetate and methanol to give 12 fractions (F_1–F_{12}). F_5, F_6 and F_7, showed antifungal activity, were combined and further purified over a combination of chromatographic techniques [silica gel, sephadex

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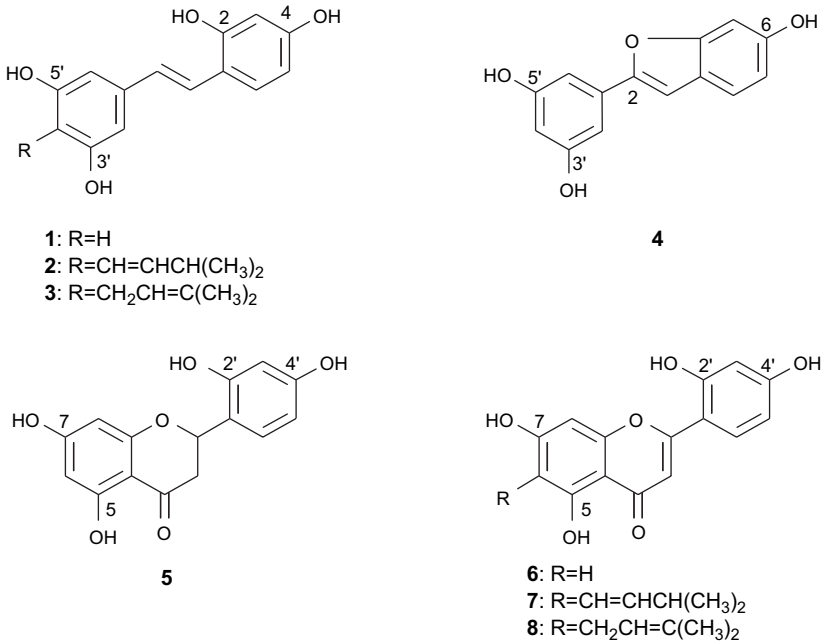
LH-20, reverse phase silica (C_{18}), reverse phase HPLC (STR prep ODS 20 × 250 mm column, 5 ml/min, 30–40% H_2O/MeOH, UV detection 254 nm)] to yield (*E*)-2,3′,4,5′-stilbenetetrol (oxyresveratrol) (**1**, 4 mg; Djapic et al., 2003), 4′-[3-methyl-1(*E*)-butenyl]-(*E*)-2,3′,4,5′-stilbenetetrol (artoindonesianin F) (**2**, 6 mg; Jayasinghe et al., 2004), (3-methyl-2-butenyl)-(*E*)-2,3′,4,5′-stilbenetetrol (**3**, 11 mg; Jayasinghe et al., 2004), 3′,5′,6-trihydroxy-2-phenylbenzofuran (moracin M) (**4**, 25 mg; Zhou et al., 1999), 2′,4′,5,7-tetrahydroxyflavanone (norartocarpanone) (**5**, 18 mg; Shimizu et al., 1998), 2′,4′,5,7-tetrahydroxyflavone (norartocarpetin) (**6**, 12 mg; Radhakrishnan et al., 1965), 2′,4′,5,7-tetrahydroxy-6-[3-methyl-1(*E*)-butenyl]flavone (isoartocarpesin) (**7**, 8 mg; Shimizu et al., 1998), 2′,4′,5,7-tetrahydroxy-6-(3-methyl-2-butenyl)flavone (**8**, 38 mg; Kijjoa et al., 1996), 3β-acetoxyolean-12-en-11-one (**9**, 12 mg; Wahlberg et al., 1972), cycloartenyl acetate (**10**, 46 mg; Pavanasasivam and Sultanbawa, 1973), sitosterol (**11**, 28 mg) and sitosterol β-D-glucopyranoside (**12**, 8 mg). Identification of the compounds isolated was done by means of spectroscopic methods (EI- or FAB-MS, ^1H, ^{13}C NMR) and comparison with literature data (Scheme 1).

Compounds **1**–**4** exhibited significant antifungal activity against *Cladosporium cladosporioides* by TLC bioautography method (Homans and Fuchs, 1970) with MIC values at 20, 10, 10 and 15 μg/spot, respectively, and strong antioxidant activity against DPPH (2,2′-diphenyl-1-picrylhydrazyl) radical by spectrophotometric method (Burtis and Bucar, 2000) at IC_{50} values 3.5, 10, 4 and 2 ppm, respectively (IC_{50} value of a positive control, ascorbic acid, 4 ppm). Compound **4** showed cytotoxicity against *Artemia salina* (McLaughlin et al., 1998) with LC_{50} at 25 ppm and the phytotoxicity against *Lactuca sativa* (100% shoot growth inhibition at 250 ppm).

4. Chemotaxonomic significance

The present study reported the isolation of stilbenes (**1**–**3**), arylbenzofuran (**4**), flavanone (**5**), flavones (**6**–**8**), triterpenes (**9** and **10**) and sterols (**11** and **12**) from the fruits of *A. altilis*. Compounds **2**, **6**, **9** and **12** are reported from this plant for the first time. Compound **1** has been previously reported from several genera in the family Moraceae, including *Artocarpus* (Likhitwitayawuid et al., 2005), and a few other families. Compounds **2** and **3** have been isolated from the genera *Artocarpus* (Jayasinghe et al., 2004; Boonlaksiri et al., 2000; Shimizu et al., 2000). Compound **4** has been reported from *Artocarpus dadah* (Su et al., 2002) and several *Morus* species (Sun et al., 2001). Compound **5** has been previously isolated from the family Moraceae, including from the heartwood of *A. altilis* (Shimizu et al., 2000), besides two other families. Compound **6** has been reported from several *Artocarpus* species (Likhitwitayawuid et al.,



Scheme 1. Structure of compounds **1**–**8**.

2000; Soekamto et al., 2003; Su et al., 2002; Lin et al., 1995) and *Cudrania* (Young et al., 1989) in the family Moraceae, besides two genera of the family Leguminosae. Compound **7** has been isolated from the heartwood of this plant (Shimizu et al., 1998). Compound **8** has been obtained from several genera in the Moraceae family, including *Artocarpus* (Shimizu et al., 1998; Kijjoa et al., 1996; Radhakrishnan et al., 1965).

It is documented that the genus *Artocarpus* is a rich source of prenylated phenolic compounds such as geranylated flavones (Hakim et al., 2006). One of the benzene rings in these phenolics often has a unique 2,4-di- or 2,4,5-trioxygenation pattern as exemplified by 2′,4′-dihydroxyflavones. Compounds **1**–**8** isolated from the fruits of *A. altilis* in the present study all possess the characteristic 2,4-dioxygenation pattern. Hence, compounds **1**–**8** can be used as taxonomic markers for the family Moraceae, especially, the genus *Artocarpus*.

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