Cytotoxicity of Neolignans from *Magnolia obovata* Fruits

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**Abstract** Repeated SiO$_2$ and octadecyl silica gel (ODS) column chromatographies of the EtOAc fraction from *Magnolia obovata* fruits, 10 neolignans, named magnolol (1), honokiol (2), isoobovatol (3), isomagnolol (4), obovatol (5), obovatal (6), 9-methoxyobovatol (7), magnobovatol (8), obovaaldehyde (9), and 2-hydroxyobovaaldehyde (10) were isolated and identified. All isolated compounds were evaluated for in vitro cytotoxicity against seven human cancer cell lines.

**Keywords** cancer cell · cytotoxicity · honokiol · *Magnolia obovata* · magnolol · neolignan

*Magnolia obovata* Thunb. is a deciduous tree that is distributed throughout Korea, China, and Japan. This plant has been used for the treatment of fever, headache, diarrhea, anxiety, and relief of asthma in Chinese medicine. *M. obovata* has been reported to have anti-platelet (Pyo et al., 2002a; 2002b), anti-gastritic (Cho et al., 2008), anti-inflammatory (Tzeng and Liu, 2004; Seo et al., 2013) and cytotoxic (Min et al., 2008; Youn et al., 2008) activities. So far, magnolol, honokiol, and obovatol have been reported to show cytotoxic activities against human cancer cells (Kim and Ryu, 1999; Lin et al., 2001; Yang et al., 2003; Youn et al., 2008; Patrick et al., 2011). However cytotoxic effects of neolignans from *M. obovata* fruits have never been reported. Therefore, in the present study, the neolignans from *M. obovata* fruits were evaluated for cytotoxic effects against human cancer cell lines in vitro using the micro culture tetrazolium (MTT) assay. We isolated 10 neolignans from *M. obovata* fruits using SiO$_2$ and octadecyl silica gel (ODS) column chromatography and their phytochemical structures were identified using spectroscopic methods.

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Repeated SiO$_2$ and ODS column chromatographies for the EtOAc fraction of the MeOH extract yielded 10 neolignans, which were identified as magnolol (1), honokiol (2), isobovatol (3), isomagnolol (4), obovatol (5), obovatal (6), 9-methoxyobovatol (7), magnobovatol (8), obovaldehyde (9), and 2-hydroxyobovaaldehyde (10) (See et al. 2013). Thus, the isolated compounds were tested for their cytotoxic activity against seven human cancer cell lines in vitro by the modified MTT assay method (Fig. 1). Compound 1 showed cytotoxicity with IC$_{50}$ values of 39.2 μM (SK-MEL-5), 39.5 μM (MCF-7), 41.4 μM (SK-BR-3), 42.8 μM (HeLa), and 44.6 μM (HCT-116). Compound 2 showed IC$_{50}$ values of 13.3 μM (SK-BR-3), 13.5 μM (MCF-7), 15.5 μM (SK-MEL-5), 15.6 μM (SK-OV-3), 17.1 μM (HCT-116), 17.1 μM (HeLa), and 20.3 μM (HepG2). Compound 4 showed IC$_{50}$ values of 44.6 μM for HeLa, and moderate cytotoxicity with IC$_{50}$ values over 70 μM for other cancer cell lines. Compound 5 showed cytotoxicity against all cancer cells except for HepG2 with IC$_{50}$ values of 42.8-74.1 μM. Compound 8 showed IC$_{50}$ values of 30.2 μM (SK-BR-3), 42.5 μM (HCT-116), 57.8 μM (SK-MEL-5), and 61.4 μM (SK-OV-3). Compound 9 showed IC$_{50}$ values of 40.7 μM (SK-MEL-5), 44.5 μM (HCT-116), 46.1 μM (MCF-7), 46.3 μM (SK-OV-3), HeLa 63.1 μM (HeLa), and 87.1 μM (SK-BR-3). Compounds 3, 6–7, and 10 showed no cytotoxic activities against the seven cell lines even at 100 μM. Even though the tested neolignans have similar chemical structure, they showed different cytotoxicity according to a few variance in structure. The inactive neolignans such as compounds 3–10 have the ether bond

Fig. 1 The cytotoxicity of neolignans 1–10 isolated from the fruits of Magnolia obovata Thunb. against HCT-116, MCF-7, SK-BR-3, SK-OV-3, HeLa, HepG2, and SK-MEL-5 cancer cell lines.
between monomer phenylpropanoids, while active ones such as compounds 1 and 2 have C-C bond. Therefore, the distance between two phenylpropanoid moieties could be a conclusive factor to show the cytotoxicity (Park et al. 2011; Lee et al. 2010). Magnolol (1), honokiol (2), and obovatol (5) were reported to show cytotoxic activity against the HeLa and HCT-116 cancer cell lines with IC50 values ranging from 8.6±1.4 to 16.4±1.7 μg/mL (Youn et al., 2008). However, the structures of isolated neolignans from M. obovata fruits are very similar, they showed different cytotoxic potencies on the cancer cells used in this study.

References