Antifungal Activity of Modified Hederagenin Glycosides from the Leaves of *Kalopanax pictum* var. *chinense*

Min-Won Lee,*[,a] Sung Uk Kim,[b] and Dug-Ryoung Hahn[a]

College of Pharmacy, Chung Ang University,[a] 221 Huksuk-dong Dong Jak-Ku Seoul 156–756, Korea, Antibiotics Research Lab., Korea Research Institute of Bioscience and Biotechnology,[b] P. O. Box 115, Yusung, Taejon 305–333, Korea.
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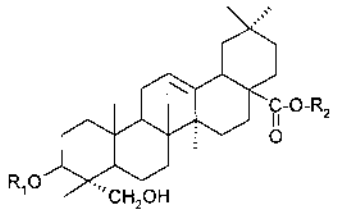
Monodesmosides which were obtained from the partial degradation of hederagenin bisdesmosides exhibited significant antifungal effect against *Microsporum canis*, *Coccidioides immitis*, *Trichophyton mentagrophytes*, *Cryptococcus neoformans*, and *Candida albicans* at the minimal inhibitory concentrations of 6.25—25 μg/ml. The hederagenin glycosides were isolated from the leaves of *Kalopanax pictum* var. *chinense*.

Key words hederagenin glycoside; triterpenoid; antifungal activity; *Kalopanax pictum* var. *chinense*; Araliaceae

The barks of *Kalopanax* spp.(Araliaceae) have been used as a Korean traditional medicine for the remedies of paralysis, rheumatic arthritis, tonics and cutaneous fungal infection.[1)] Several triterpene glycosides were isolated as main components of Kalopanax plants sources.[2—4)] Noticeable biological effects of triterpene glycosides are not known yet but some saponin is known to have fungitoxic activity.[5)] It has been also reported that the antifungal and molluscidal saponins have monodesmoside form[6)] and hereragenin glycoside with a free carboxyl group at C-28 show antifungal activity against yeast.[7)] Recently, it was reported that monodesmosides from *Kalopanax pictum* inhibited the human pathogenic fungi significantly.[8)] But it was known that the contents of hederagenin glycoside with monodesmoside form in the kalopanax plant were low as compared with those of bisdesmoside.[9)]

We have attempted proving the antifungal activities of the monodesmosides obtained by alkali hydrolysis (ester degradation) of the bisdesmosides, penta (kalopanax saponin B, **1**), hexa (kalopanax saponin H, **2**) and hepta [3-*O*-β-D-glucopyranosyl (1—4)-β-D-xylopyranosyl (1—3)-α-L-rhamnopyranosyl (1—2)-α-L-arabinopyranosyl-23-hydroxyolean-12-en-28-*O*-α-L-rhamnopyranosyl (1—4)-β-D-glucopyranosyl (1—6)-β-D-glucopyranosyl ester, **3**] glycosides of hederagenin (see Chart 1) which were isolated from the leaves of *Kalopanax pictum* var. *chinense*, one of the kalopanax species growing in Korea. The partial hydrolysis of **1**, **2** and **3** by 0.5 N-KOH produced compounds **4**, **5** and **6** which were identified as α-hederin, sapindoside B and C respectively by comparison with published spectral data and authentic samples.[3,4)] All these bisdesmosides did not show anti-fungal activity but the monodesmosides (compounds **4**, **5**, **6**) obtained by partial hydrolysis of C-28 ester likage of **1**, **2** and **3**, exhibited antifungal activity against *Microsporum canis*, *Coccidioides immitis*, *Trichophyton mentagrophytes*, *Cryptococcus neoformans* and *Candida albicans* at the minimal inhibitory concentrations of 6.25—25 μg/ml (Table 1). These results suggest that α-hederin, sapindosides B and C obtained by partial degradation of bisdesmosides are shown to be antifungal agents. The inactive bisdesmosides, major ingredients of *Kalopanax pictum* var. *chinense*, might be sources of fungicidal agent.



	R_1	R_2
1 :	α -L-ara[2]-α -L-rha	β -D-glc[6]-β -D-glc[4]-α -L-rha
2 :	α -L-ara[2]-α -L-rha[3]-β -D-xyl	β -D-glc[6]-β -D-glc[4]-α -L-rha
3 :	α -L-ara[2]-α -L-rha[3]-β -D-xyl[4]-β -D-glc	β -D-glc[6]-β -D-glc[4]-α -L-rha
4 :	α -L-ara[2]-α -L-rha	H
5 :	α -L-ara[2]-α -L-rha[3]-β -D-xyl	H
6 :	α -L-ara[2]-α -L-rha[3]-β -D-xyl[4]-β -D-glc	H

Chart 1

Table 1. Antifungal Activities of the Hederagenin Glycosides (Bisdesmosides and Monodesmosides) against Human Pathogenic Fungi

Fungi	Compound						
	1	2	3	4	5	6	Nystatin[a)]
Candida albicans ATCC 10231	>100	>100	>100	100	25	100	3.125
Microsporum canis ATCC 11622	>100	>100	>100	12.5	12.5	50	ND[b)]
Trichophyton mentagrophytes ATCC9533	100	100	100	50	6.25	6.25	25
Cryptococcus neoformans ATCC 36556	>100	100	100	50	50	50	1.56
Coccidioides immitis ATCC 34020	100	100	50	25	50	50	3.125

MIC : μg/ml. *a*) Nystatin: Positive control. *b*) ND: Not determined.

* To whom correspondence should be addressed. e-mail: mwlee@cau.ac.kr
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MATERIALS AND METHODS

Materials Extraction and isolation of the compounds from the leaves of *Kalopanax pictum* var. *chinense* were carried out as described previously.[9] Bisdesmosides, compounds **1** and **2** were elucidated by comparison with reported values and authentic standards.[3,4] Compound **3** was isolated from the same plant previously.[4]

Production of the monodesmosides; 100 mg of **1** was dissolved with 0.5 N KOH 100 ml and heated in water bath for 1 h. The reaction mixture was diluted with water and neutralized by 0.5 N HCl and extracted with organic solvent (EtOAc : *n*-BuOH=2 : 1) 2 times. The organic layer was concentrated to syrup, which was subjected to a column of silica gel. Elution with $CHCl_3$–MeOH–H_2O (70 : 30 : 4) afforded **4** (40 mg). As using the same method, compounds **5** (45 mg) and **6** (35 mg) were obtained from compounds **2** and **3**.

Antifungal Activity Minimum inhibitory concentrations (MIC) were determined by the two-fold serial agar dilution method.[10] Human pathogenic fungi were grown on Sabouraud's agar medium. Antifungal activity was observed after 24 h incubation at 30 °C for yeasts and 48 h incubation for fungi at 25 °C.

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