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## Phytochemicals and Their Pharmacological Aspects of *Acanthopanax koreanum*

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### 1. Introduction

Botanical medicines have been applied for the treatment of various human diseases with thousands of years of history all over the world. In some Asian and African countries, 80 % of population depends on traditional medicine in primary health care. On the other hand, in many developed countries, 70 % to 80 % of the population has used some forms of alternative or complementary medicine. The long tradition of using plants for medicine, supplemented by pharmaceutical research, has resulted in many plant-based Western medicines. Traditional medicine has provided Western medicine with over 40 % of all pharmaceuticals (Samuelsson & Bohlin, 2004). In the past decades, therefore, research has been focused on scientific evaluation of traditional drugs of plant origin.

*Acanthopanax* species (Araliaceae) are widely distributed in Asia, Malaysia, Polynesia, Europe, North Africa and the America. There are about 40 species of *Acanthopanax* to be found in over the world. *Acanthopanax* species have traditionally been used as a tonic and sedative as well as in the treatment of rheumatism, and diabetes. *A. koreanum* Nakai is an indigenous plant prevalently distributed throughout South Korea. It is deciduous shrub with upright to slightly arching stems, small, fresh green, trilobed to palmately divided leaves and several axillary as well as terminal round clusters of decorative, bluish black berries in late summer and autumn. Extensive investigation of chemical components in *A. koreanum* has been reported by many researchers in the worldwide. Several types of compounds have been isolated from this plant. Major active constituents are reported as lupanes and their glycosides, diterpenes, monoterpenes, lignans, phenylpropanoids, flavonoids from whole parts of *A. koreanum*. Of these, lupane triterpenes were reported as major components of leaves and *ent*-kauranes are main components of the roots of *A. koreanum*. They showed significant biological effects by several bioassay systems such as 1) anti-inflammatory activities: inhibit lipopolysaccharide (LPS)-stimulated TNF- $\alpha$ , IL-6, and IL-12 p40 productions in bone marrow-derived dendritic cells, decrease the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) proteins, and reduce iNOS and COX-2 mRNA in a dose-dependent pattern, 2) anticancer, and 3) anti-osteoporosis by effects on the differentiation of osteoblastic MC3T3-E1 cells. The desired target of this chapter is to introduce explanations of structures and pharmacological activities of novel compounds, which have been isolated and identified from *A. koreanum* since 1985. Those studies have reported and focused on bioactivities of unambiguous

compounds from *A. koreanum*, therefore we discuss new pharmacological findings on these compounds.

The depth and breadth of research involving this plant has been organized into easily accessible and comparable information. Using Chemical Abstracts, Scifinder Scholar, and BIOSIS databases, relevant research papers were selected by based on pertinence and specificity to ethnopharmacology and phytochemistry, as well as readability. This collection was then carefully reviewed, extracted, and corroborated with available characterization data from other sources.

## 2. Phytochemistry and pharmacology of *A. koreanum*

### 2.1 Lupane aglycones

Impressic acid (**1**) was isolated for the first time from *Schefflera impressa* by (Srivastava, 1992) and it was found in the roots (Cai et al., 2004b) and the leaves (Kim et al., 2010) of *A. koreanum*. Impressic acid exhibited potently NFAT inhibitory activity with IC<sub>50</sub> value of 12.6  $\mu$ M. In the studies of (Kim et al., 2010), impressic acid (**1**) and (20*R*)-3 $\alpha$ -hydroxy-29-dimethoxylupan-23,28-dioic acid (**4**) showed significantly anti-inflammatory activities by inhibiting TNF- $\alpha$ , IL-6, and IL-12 p40 productions in bone marrow-derived dendritic cells with LPS-stimulated. Furthermore, impressic acid was found to inhibit TNF- $\alpha$ -induced NF- $\kappa$ B activity by inhibiting the induction of COX-2 and iNOS in HepG2 cells. Impressic acid also up-regulated the transcriptional activity of PPAR by elevating the expression of PPAR $\gamma$ 1, PPAR $\gamma$ 2, and SREBF-2, and by suppressing the expression of Insig-2 (Kim et al., 2011). One new norlupane, 3 $\alpha$ ,11 $\alpha$ -dihydroxy-20,23-dioxo-30-norlupane-28-oic acid (**2**) as well as two known lupane aglycones, impressic acid (**1**), 3 $\alpha$ ,11 $\alpha$ -dihydroxy-lup-20(29)-en-23-al-28-oic acid (**3**) were isolated and determined by (Park et al., 2010). They were evaluated for the differentiation of osteoblastic MC3T3-E1 cells. Among of them, compound **1** significantly increased osteoblastic cell growth and differentiation as assessed by MTT assay and collagen content. Compound **2** significantly increased the growth of MC3T3-E1 cells and caused a significant elevation of osteoblastic cell differentiation as assessed by the alkaline phosphatase activity (Park et al., 2010). Other compounds, 3 $\alpha$ ,11 $\alpha$ -dihydroxy-lup-20(29)-en-23-al-28-oic acid, 3 $\alpha$ -hydroxylup-20(29)-en-23,28-dioic acid (**5**), and 3 $\alpha$ ,11 $\alpha$ ,23-trihydroxy-lup-20(29)-en-28-oic acid (**6**) were also isolated from steamed leaves (Kim et al., 2010). However, they showed weak anti-inflammatory activity. 3 $\alpha$ -Hydroxylup-20(29)-en-23,28-dioic acid (**5**) possessed broader antiviral activity against respiratory syncytial, influenza (H1N1), coxsackie B3, and herpes simplex virus type 1 viruses with IC<sub>50</sub> values of 6.2, 25.0, 12.5, and 18.8  $\mu$ g/mL, respectively (Li et al., 2007).

### 2.2 Lupane-triterpene glycosides

Up to date, eighteen lupane-type triterpene glycosides have been isolated from this plant and almost of them from the leaves of *A. koreanum*. They are main saponin components of the leaves of *A. koreanum*. The first lupane triterpene glycoside, acantrifoside A (**1**) was isolated from both *A. koreanum* and *A. trifoliatum* in a year of 1998 by (Yook et al., 1998). And then, two new saponins, acankoreoside A (**10**) and acankoreoside B (**11**) were isolated from the leaves of this plant (Chang et al., 1998). Our group reported seven new lupane-type triterpene glycosides, acankoreosides I-O. Their biological activities were evaluated for

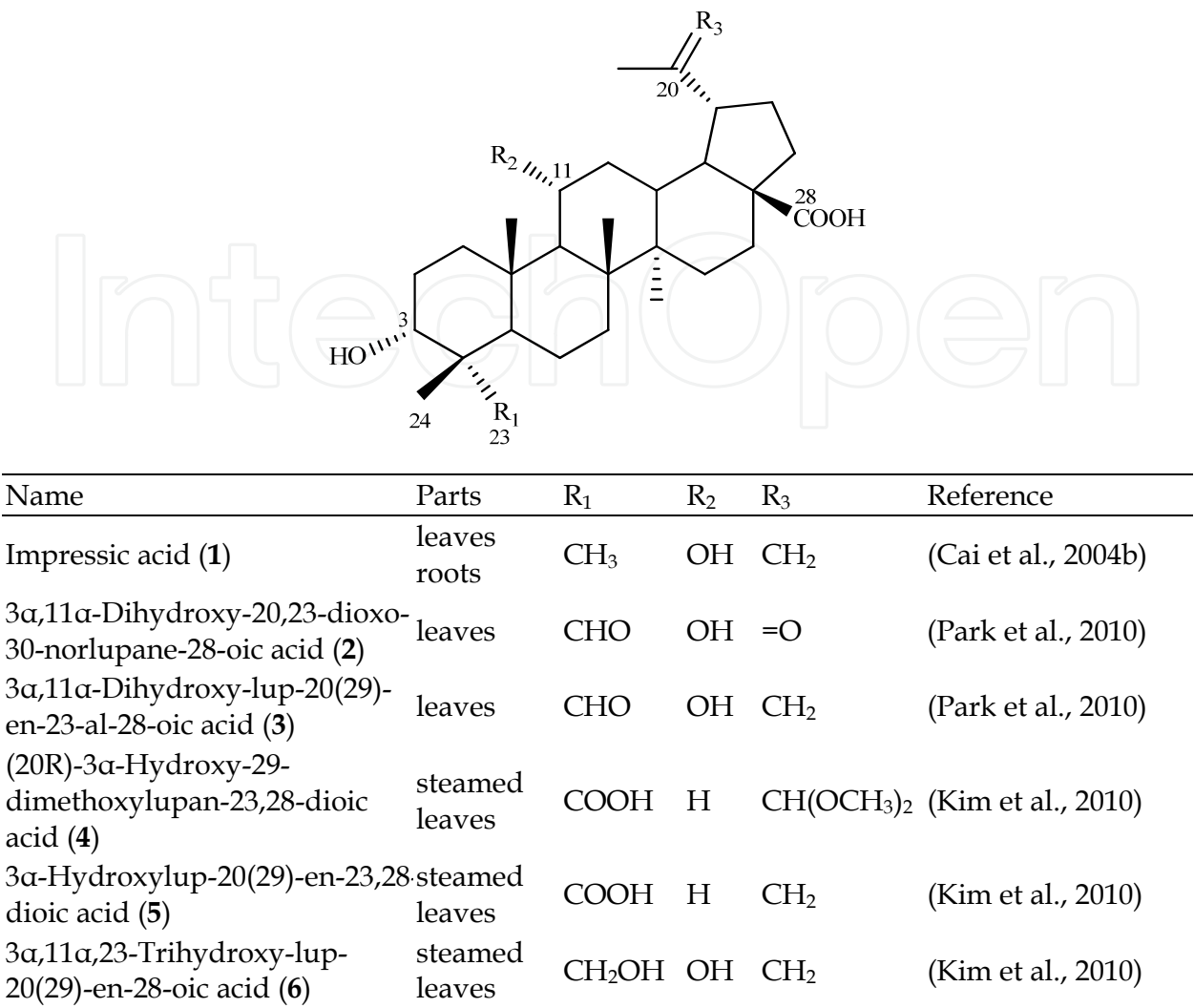


Fig. 1. Structures of main lupane-type triterpenes isolated from *Acanthopanax koreanum*

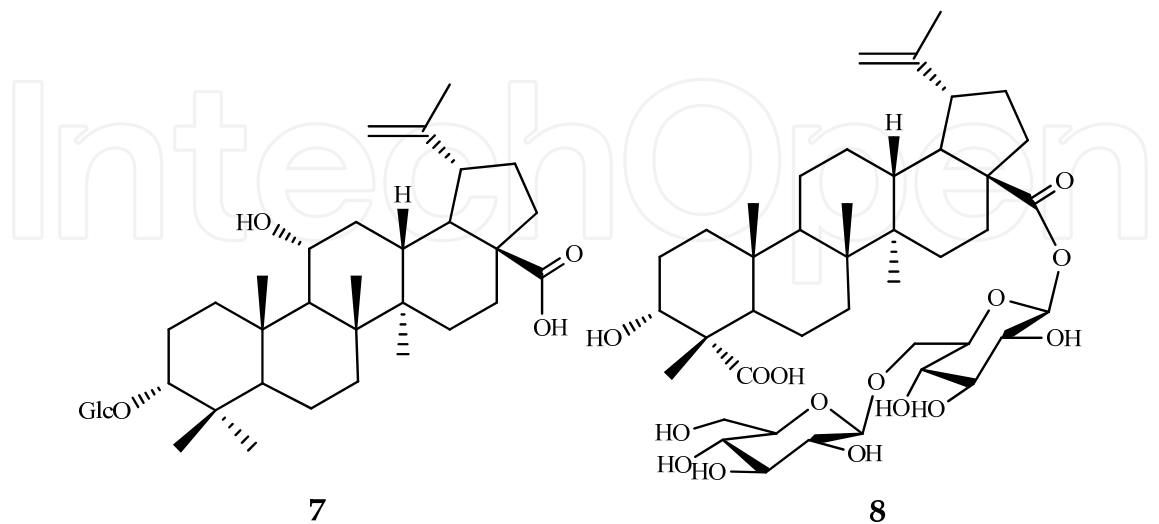


Fig. 2. 3-O-β-D-glucopyranosyl 3α,11α-dihydroxylup-20(29)-en-28-oic acid (7) and 3α-hydroxylup-20(29)-en-23,28-oic acid 28-O-[β-D-Glucopyranosyl-(1→6)-β-D-Glucopyranosyl] ester (8) (Kim et al., 2010)

cytotoxic activities including A549 (lung), HL-60 (acute promyelocytic leukemia), MCF-7 (breast), U937 (leukemia) cancer cell lines; immune enhancement activity (INF- $\gamma$  and IL-2 release in spleen cells); anti-inflammatory (inhibitory TNF- $\alpha$ , IL-6, and IL-12 p40 productions in bone marrow-derived dendritic cells with LPS-stimulated, and RAW 264.7). Searching for anticancer activities from natural compounds, several acankoreosides showed significantly cytotoxic activities in various cancer cell lines (A549, HL-60, MCF-7, and U937). The effects of three new lupane glycosides, acankoreosides F-H (**13**, **14**, and **21**) on the LPS-induced production of nitric oxide and prostaglandin E<sub>2</sub> were evaluated in RAW 264.7 macrophages. Among of them, acankoreoside F (**13**) showed the most potent inhibitory PGE<sub>2</sub> (59.0 %) and NO (42.0 %) production at concentration of 200.0  $\mu$ M. Furthermore, eleven lupane triterpene glycosides from *A. koreanum*, including three new compounds acankoreoside M-O (**16**, **24**, and **25**) were evaluated for Con A-induced splenolytic production of IL-2 and IFN- $\gamma$ . The results indicated that acankoreosides A (**10**), D (**12**), L (**24**), and acantrifoside A (**9**)

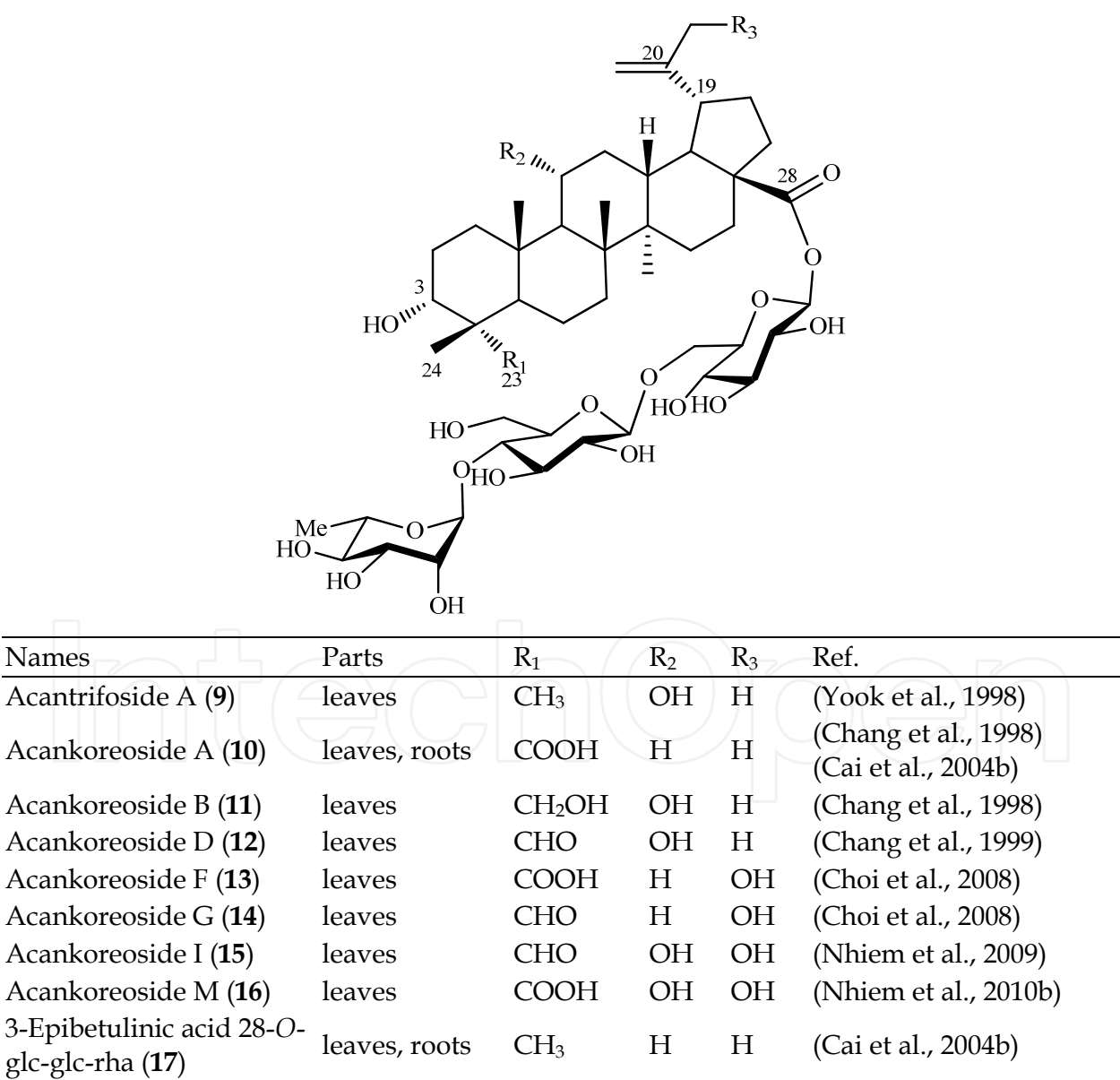
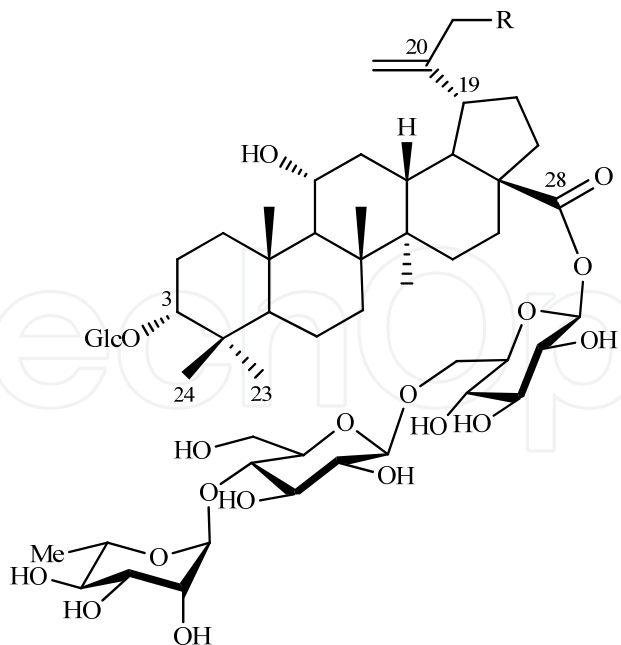
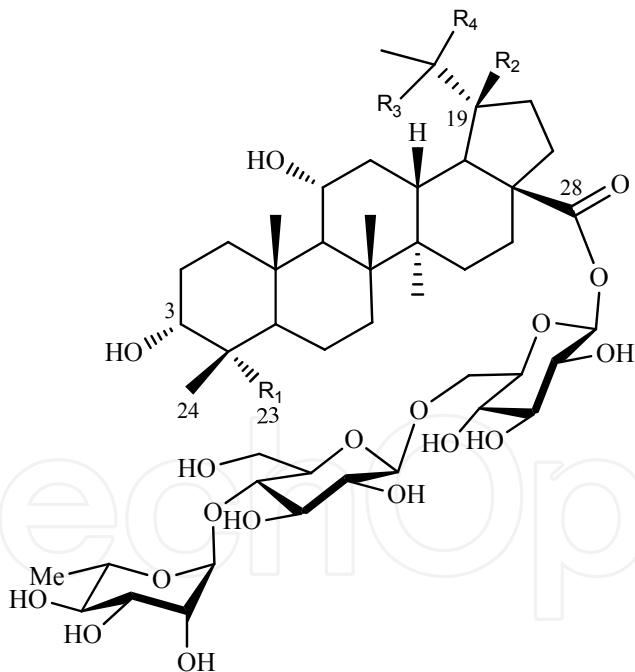


Fig. 3. Structures of lupane-type triterpene glycosides from *A. koreanum*



Name	Part	R	Reference
Acankoreoside C (18)	leaves	H	(Chang et al., 1999)
Acankoreoside N (19)	leaves	OH	(Nhiem et al., 2010b)



Name	Part	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	Reference
Acankoreoside E (20)	leaves	COOH	H	H	CHO	(Park et al., 2005)
Acankoreoside H (21)	leaves	CHO	H	H	COOH	(Choi et al., 2008)
Acankoreoside J (22)	leaves	COOH	H	=O	-	(Nhiem et al., 2010a)
Acankoreoside K (23)	leaves	COOH	H	OH	Me	(Nhiem et al., 2010a)
Acankoreoside L (24)	leaves	COOH	H	OH	CH <sub>2</sub> OH	(Nhiem et al., 2010a)
Acankoreoside O (25)	leaves	COOH	OH	H	CH <sub>3</sub>	(Nhiem et al., 2010b)

Fig. 3. Structures of lupane-type triterpene glycosides from *A. koreanum* (continued)



significantly increased both IL-2 and IFN- $\gamma$ . The structure-activity relationship of these compounds was also discussed. Moreover, lupane aglycones and lupane glycosides were assayed for LPS-stimulated pro-inflammatory cytokine production. These results suggested lupane aglycone inhibited pro-inflammatory cytokine production stronger than lupane glycosides (Kim et al., 2010). This was further confirmed by the study of (Cai et al., 2004b).

2.3 Pimarane-type diterpenes

A number of pimarane-type diterpenes have been isolated and associated with significant biological activity. There are seven pimarane-type diterpenes from *A. koreanum*. All of them were isolated from the roots. Acanthoic acid was presented in roots and leaves of this plant, and was one of compounds having potent anti-inflammatory activity. Acanthoic acid, a pimarane diterpene ((-)-pimara-9(11),15-dien-19-oic acid), was isolated for the first time from *A. koreanum* in a year of 1988 by (Kim et al., 1988b) and was proved with high content of this plant. Acanthoic acid has widely exhibited of biological activities. In study of (Kang et al., 1996), acanthoic acid has potent anti-inflammatory effects by reducing the production of proinflammatory cytokines such as IL-1 and TNF- $\alpha$ . It was also effective in supressing experimental silicosis and cirrhosis. Furthermore, acanthoic acid was found to suppress TNF- $\alpha$  gene expression (Kang et al., 1998) and TNF- $\alpha$ -induced IL-8 production in a dose-dependent manner. Acanthoic acid also inhibited TNF- $\alpha$ -induced MAPKs activation, I $\kappa$ B degradation, NF- $\kappa$ B nuclear translocation, and NF- $\kappa$ B/DNA binding activity (Kim et al., 2004). Furthermore, acanthoic acid significantly inhibited production of both TNF- $\alpha$  and tryptase in trypsin-stimulated human leukemic mast cell-1 at concentrations of 10 and 100  $\mu$ g/mL with a dose-dependent manner. Acanthoic acid inhibited ERK phosphorylation and NF- $\kappa$ B activation induced by trypsin treatment without blocking of trypsin activity even though 100  $\mu$ g/mL. These results suggested that acanthoic acid may inhibit the production of inflammatory mediators through inhibition of ERK phosphorylation and NF- $\kappa$ B activation pathway in human mast cells (Kang et al., 2006).

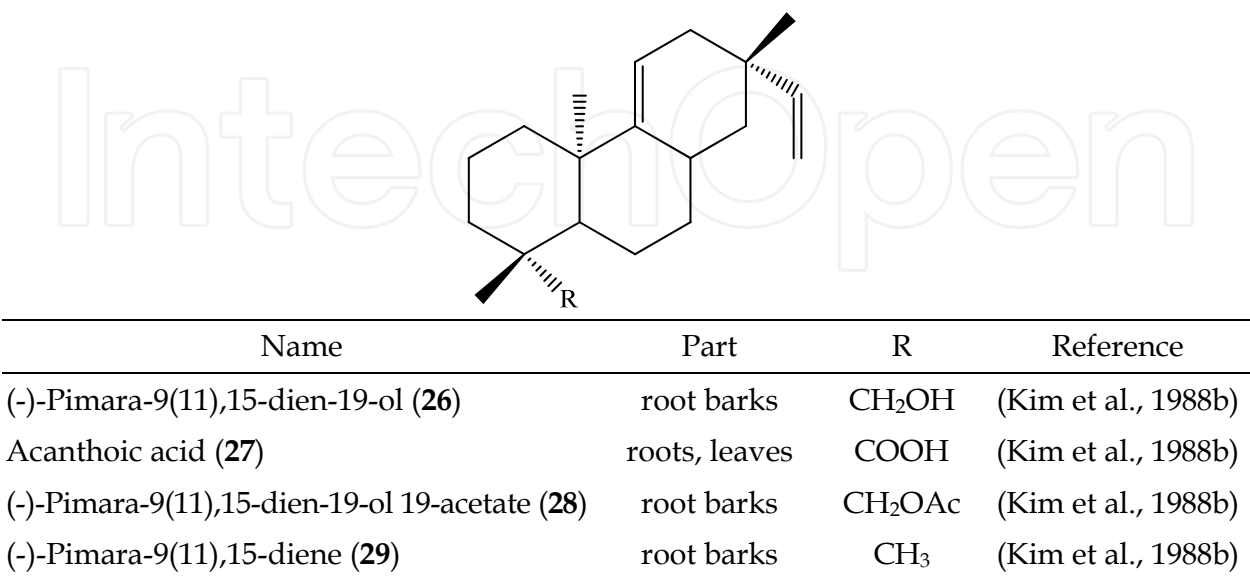
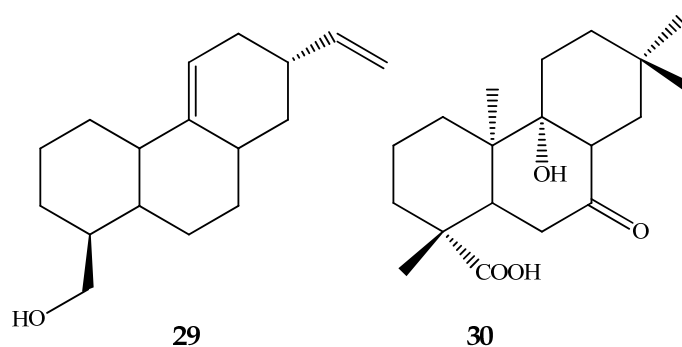
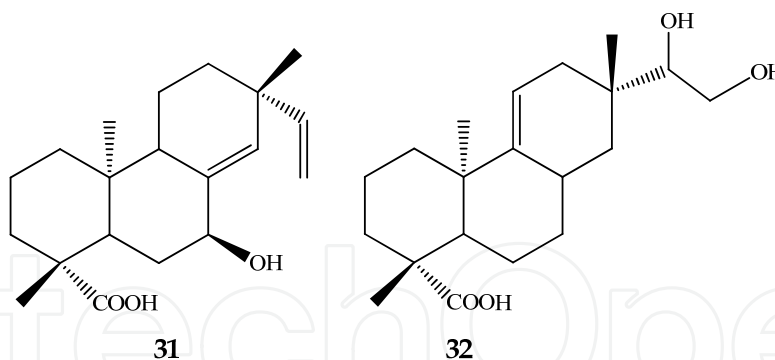


Fig. 4. Structures of pimarane-type diterpenes from *A. koreanum*

The hepatoprotective effects of acanthoic acid were evaluated in a D-galactosamine/lipopolysaccharide-induced fulminant hepatic failure mouse model. The effects were likely associated with a significant decrease in serum TNF- $\alpha$  levels, which are correlated not only with those of alanine aminotransferase and aspartate aminotransferase but also with the reduced number of apoptotic hepatocytes in the liver as confirmed using the terminal deoxynucleotidyl transferase-mediated (dUTP) nick end-labeling method and DNA fragmentation assay (Nan et al., 2008). The protective effect of acanthoic acid was investigated in acetaminophen-induced hepatic toxicity. These results indicated that acanthoic acid protected liver tissue from oxidative stress elicits by acetaminophen-induced liver damage (Wu et al., 2010). Acanthoic acid markedly suppressed the protein expression of TNF- $\alpha$ , COX-2, NF- $\kappa$ B and chymase as well as the mRNA expression of TNF- $\alpha$  and COX-2 (Kang et al., 2010).



Isopimara-9(11),15-dien-19-ol (29)	roots	(Chung & Kim, 1986)
Acanthokoreoic acid A (30)	roots	(Cai et al., 2003a)



7 $\beta$ -Hydroxy-ent-pimara-8(14),15-dien-19-oic acid (31)	roots	(Cai et al., 2004a)
Sumogaside (32)	roots	(Cai et al., 2004a)

Fig. 4. Structures of pimarane-type diterpenes from *A. koreanum* (continued)

In study of (Cai et al., 2003a), a new compound, acanthokoreoside acid A (30) as well as acanthoic acid (27), (-)-pimara-9(11),15-dien-19-ol (26), and sumogaside (32) were isolated from CH<sub>2</sub>Cl<sub>2</sub> fraction of *A. koreanum* roots. They were evaluated for inhibitory activity on IL-8 secretion in TNF- $\alpha$ -stimulated HT-29 and TNF- $\alpha$  secretion in trypsin-stimulated HMC-1. In the TNF- $\alpha$ -stimulated HT-29, acanthoic acid and sumogaside significantly inhibited IL-8 secretion at concentrations of 1, 10, and 100  $\mu$ M and at concentrations of 10 and 100  $\mu$ M, respectively.



2.4 *ent*-Kaurane-type diterpenes

*ent*-Kaurane, a tetracyclic diterpene, has been proven to exert various biological activities like cytotoxicity, anti-inflammation, and so on. From the roots of *A. koreanum*, (Kim et al., 1988b) and (Cai et al., 2003b) isolated six *ent*-kaurane-type diterpenes, including *ent*-kaur-16-en-19-oic acid (33), 16 $\alpha$ -hydroxy-*ent*-kauran-19-oic acid (34), paniculose IV (35), 16 $\alpha$ H,17-isovaleryloxy-*ent*-kauran-19-oic acid (36), 16 $\alpha$ -hydroxy-17-isovaleryloxy-*ent*-kauran-19-oic acid (37), and 16 $\alpha$ ,17-dihydroxy-*ent*-kauran-19-oic acid (38). (Cai et al., 2003b) evaluated five *ent*-kauranes for TNF- $\alpha$  secretion from HMC-1, a trypsin-stimulated human leukemic mast cell line. The results indicated that 16 $\alpha$ H,17-isovaleryloxy-*ent*-kauran-19-oic acid (36) exhibited potently an inhibitory activity with IC<sub>50</sub> value of 16.2  $\mu$ M. Furthermore, these compounds were assayed for their inhibitory effect against NFAR transcription factor and 16 $\alpha$ -hydroxy-17-isovaleryloxy-*ent*-kauran-19-oic acid (37) was found to significantly inhibit NFAT transcription factor with IC<sub>50</sub> of 6.7  $\mu$ M (Cai et al., 2004a). The authors also found that remain compounds containing a hydroxyl group at C-16 or a glycoside at C-4 showed no activity.

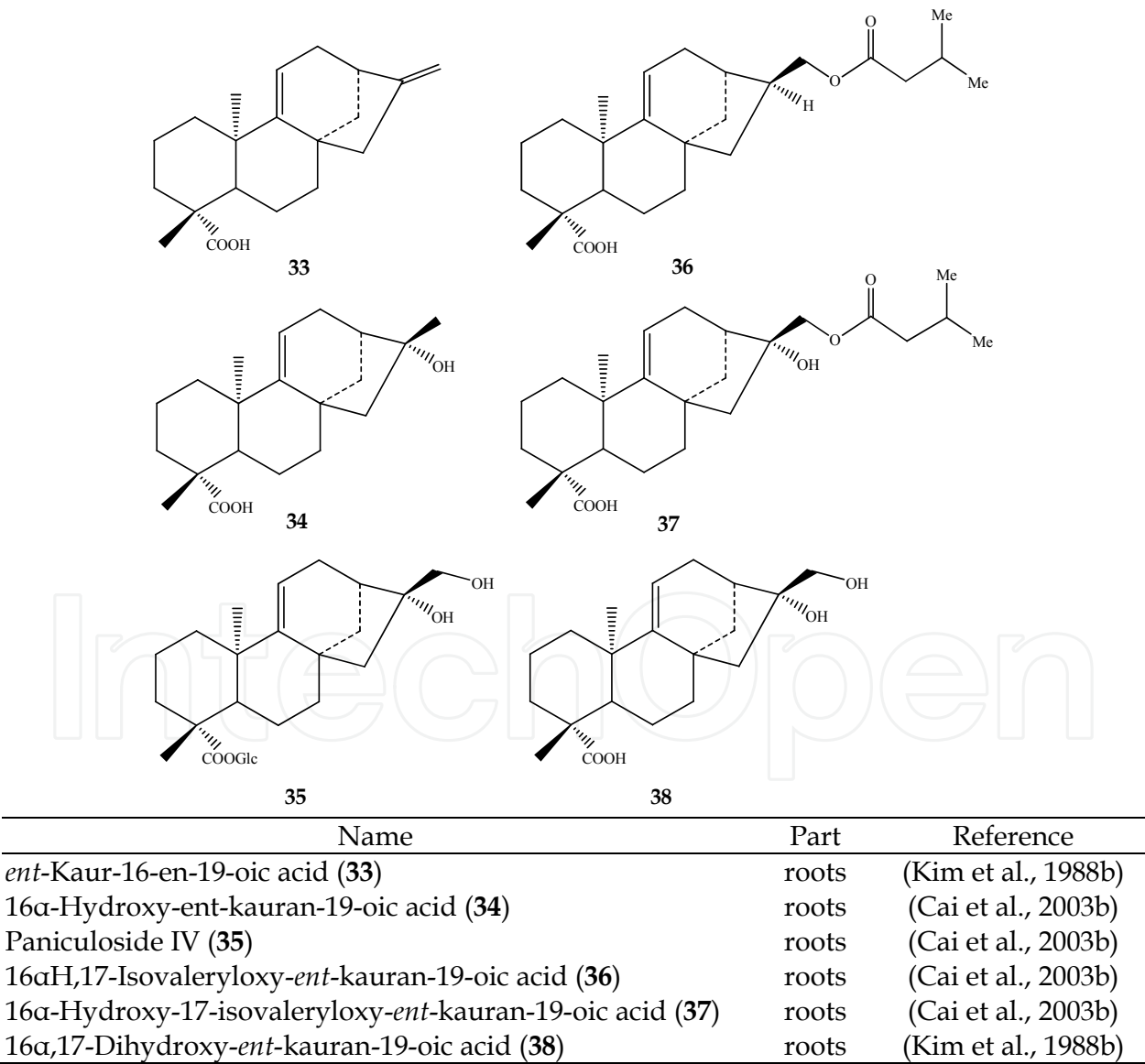


Fig. 5. Structures of *ent*-kaurane-type diterpenes from *A. koreanum*

## 2.5 Other class compounds

Two lignans were found from the roots of *A. koreanum*. Those were acanthoside D (**39**) (Hahn et al., 1985) and ariensin (**40**) (Kim et al., 1988a). Beside these lignans, the first

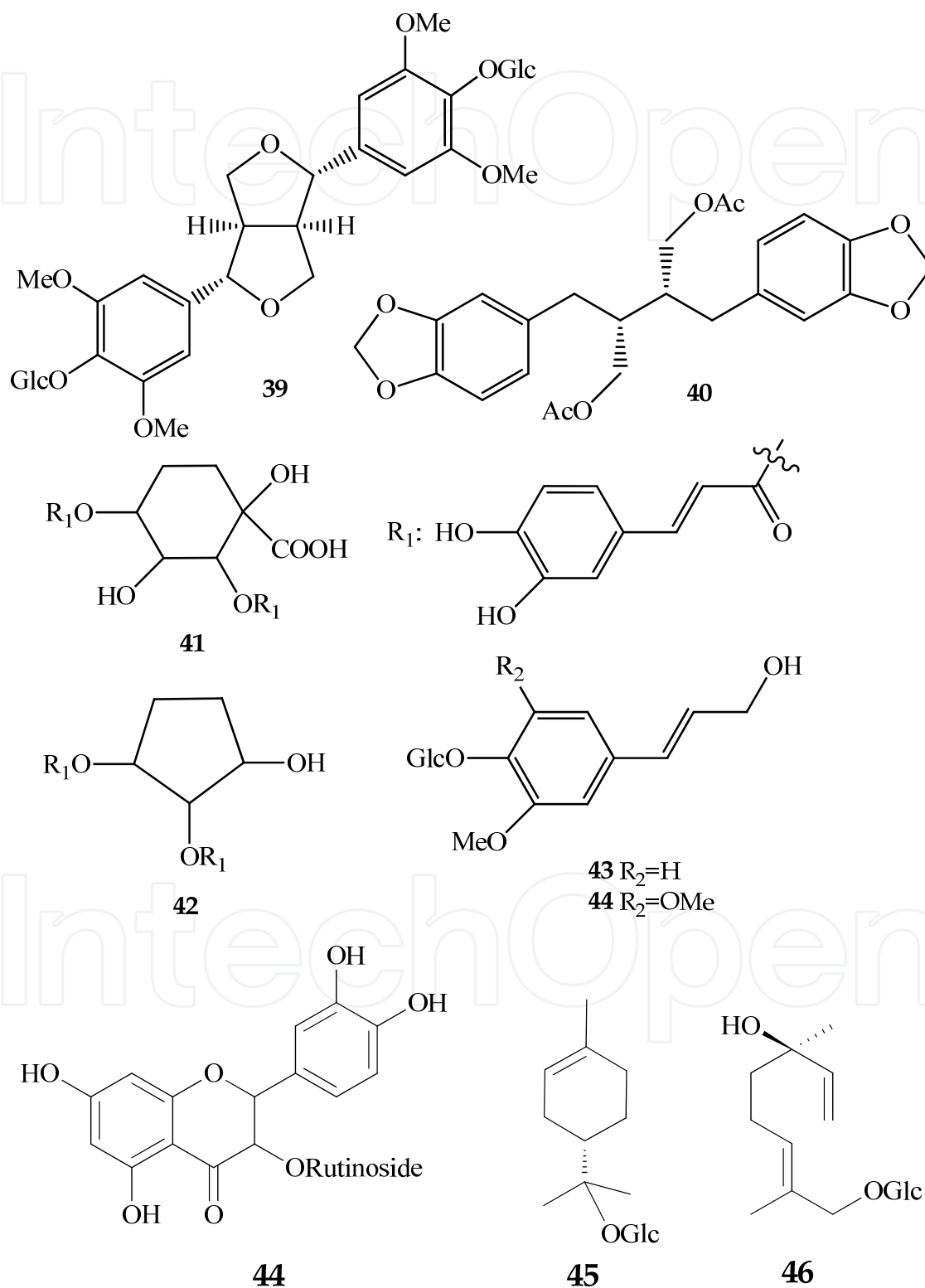


Fig. 6. Structures of compounds isolated from *A. Koreanum*

Pos.	1	2	3	4	5	6	7	8	9	10	11	12
1	35.8	35.7	35.1	32.8	32.6	35.9	36.2	33.1	36.2	33.1	35.9	34.9
2	26.8	26.9	25.5	26.0	25.9	27.1	21.9	26.2	26.9	26.2	27.1	26.8
3	74.8	73.7	75.8	72.8	72.7	75.9	81.5	71.5	75.3	73.0	75.7	72.7
4	38.4	53.5	37.7	51.8	51.7	41.2	37.9	51.9	38.5	52.8	41.1	52.6
5	49.4	44.4	48.8	44.7	44.8	43.9	50.6	45.3	49.6	45.0	43.8	43.9
6	19.2	21.8	19.3	21.6	21.0	18.3	18.4	21.7	18.6	21.8	18.3	21.0
7	36.0	35.7	35.4	23.8	34.5	35.6	35.7	34.6	35.7	34.6	35.4	35.2
8	42.7	43.2	42.2	41.6	41.5	42.8	42.7	41.8	42.8	42.8	42.7	42.4
9	55.9	56.2	55.6	50.7	50.8	56.2	55.9	51.0	56.2	51.2	55.6	55.6
10	39.8	39.6	39.1	38.2	37.2	39.6	39.7	37.4	39.9	37.6	39.6	38.7
11	69.8	70.7	70.4	21.1	21.5	69.9	69.9	20.9	69.8	21.2	69.8	69.4
12	38.4	39.4	37.7	27.7	25.8	38.4	38.3	26.0	38.3	26.0	38.3	37.8
13	37.5	37.5	37.2	28.6	38.4	37.6	37.7	38.4	37.4	38.4	37.4	37.0
14	42.9	44.1	42.6	43.0	42.7	42.8	42.9	42.9	43.0	43.0	42.9	43.0
15	29.9	30.6	29.5	30.2	30.0	30.1	30.2	30.1	30.0	30.1	30.0	29.6
16	32.8	32.7	32.0	34.7	32.8	32.8	32.9	32.2	32.3	32.4	32.2	31.9
17	56.5	57.1	56.2	56.7	56.4	56.5	56.6	57.0	56.9	57.7	56.9	56.6
18	47.5	50.0	46.6	49.1	49.5	49.4	49.4	49.8	49.5	49.7	49.4	49.1
19	49.4	52.5	48.6	43.7	47.5	47.5	47.5	47.4	47.2	47.5	47.1	46.8
20	151.0	215.0	149.7	37.6	151.1	150.8	150.9	150.9	150.4	151.0	150.4	150.1
21	31.0	29.4	30.5	24.6	30.9	31.2	31.3	30.8	30.9	30.9	30.9	30.6
22	37.5	37.7	36.8	37.2	37.3	37.4	37.4	36.9	36.8	37.2	36.7	36.4
23	29.6	210.9	28.7	178.9	179.6	71.9	29.9	181.3	29.8	179.0	71.9	209.7
24	22.7	15.1	22.2	17.8	17.7	18.3	23.0	18.1	22.9	18.0	18.3	14.6
25	18.0	17.2	17.3	16.6	16.5	17.0	16.8	16.8	16.9	16.8	17.1	16.5
26	17.4	17.8	16.2	16.6	16.5	17.7	17.6	16.7	17.7	16.6	17.7	17.4
27	14.4	15.0	14.6	14.5	14.6	14.8	14.8	14.8	14.8	14.8	14.8	14.4
28	179.2	179.4	181.5	179.4	178.6	178.8	178.9	175.0	175.0	175.9	175.0	174.6
29	110.0	30.0	110.2	107.8	109.7	110.0	110.1	110.0	110.2	110.0	110.0	109.9
30	19.2		17.9	16.4	19.2	19.5	19.6	19.4	19.5	19.3	19.5	19.2
Solv.	a	a	b	a	a	a	a	a	a	a	a	a

<sup>a</sup> recorded in pyridine-*d*<sub>5</sub>, <sup>b</sup> recorded in methanol-*d*<sub>4</sub>.  
Note: NMR data were obtained from **1**: (Srivastava, 1992); **2**, **3** (Park et al., 2010); **4**, **8**: (Kim et al., 2010); **5**, **6**, **10**, **11**: (Chang et al., 1998); **7**, **12**: (Chang et al., 1999)

Table 1. <sup>13</sup>C-NMR data of lupane aglycone moieties

Pos.	13	14	15	16	17	18	19	20	21	22	23	24	25
1	33.2	33.1	35.9	35.5	36.5	36.1	36.7	33.3	33.1	34.0	34.2	33.9	34.5
2	26.1	26.7	27.0	26.4	26.6	21.8	19.2	26.1	26.7	26.1	26.1	26.1	26.1
3	72.8	73.0	73.8	73.8	73.5	81.3	82.4	72.7	73.0	73.4	73.3	73.6	73.3
4	51.8	52.5	53.7	53.0	40.3	37.8	38.5	51.7	52.5	52.2	52.1	52.3	52.1
5	45.4	44.0	44.5	45.4	49.9	50.5	51.0	45.6	44.0	46.6	46.9	46.2	47.4
6	21.7	20.9	22.0	22.6	19.2	18.4	22.2	21.7	21.1	22.2	22.2	22.3	22.2
7	34.5	34.1	36.2	36.1	36.3	35.4	36.4	34.6	34.1	35.1	35.5	35.3	35.5
8	41.8	41.8	41.6	43.5	43.4	42.6	43.5	41.7	41.8	42.5	43.0	42.6	43.1
9	51.0	50.6	56.3	56.7	50.2	55.8	56.3	50.6	50.2	51.9	52.0	51.7	52.0
10	37.4	36.9	38.2	40.0	38.3	39.6	40.4	37.4	36.9	38.2	38.1	38.1	38.2
11	21.0	21.0	71.1	71.1	24.2	69.7	71.2	20.9	20.8	22.0	22.4	22.0	22.2
12	27.1	27.0	38.3	39.4	26.5	38.1	39.5	26.9	26.9	28.5	29.8	28.3	26.1
13	38.3	38.3	39.5	38.2	38.2	37.3	38.3	38.2	38.2	38.6	39.5	39.4	39.1
14	42.8	42.8	44.3	44.3	43.8	42.9	44.0	43.0	43.0	43.6	44.5	44.0	44.3
15	30.2	30.1	30.8	30.8	31.6	30.0	30.9	30.0	30.0	30.9	31.2	30.9	30.9
16	32.2	32.1	32.8	32.9	32.8	32.2	32.9	32.0	32.1	32.4	33.1	32.9	34.5
17	57.0	56.9	57.9	57.9	57.9	56.8	58.0	57.0	57.3	58.0	60.1	58.0	59.4
18	50.2	50.2	50.9	50.9	50.1	49.4	51.0	48.5	48.9	50.8	49.5	49.7	50.4
19	43.2	43.2	43.7	43.7	48.2	47.1	43.8	37.3	40.6	52.8	45.7	39.3	85.4
20	156.5	156.5	155.9	155.9	151.3	150.4	156.0	50.1	42.1	215.4	76.1	39.5	36.8
21	32.7	32.7	33.5	33.6	30.6	30.8	33.6	24.6	25.0	29.3	28.8	24.38	34.5
22	36.8	36.7	37.3	37.4	37.5	36.7	37.4	37.4	37.3	37.6	37.5	38.3	37.2
23	181.2	209.8	211.2	180.6	29.5	29.8	29.8	181.8	209.9	183.4	184.2	181.8	185.2
24	18.2	14.6	15.2	18.2	23.0	23.0	23.3	18.3	14.6	18.3	18.4	18.2	18.6
25	16.8	16.4	17.2	17.5	17.8	16.8	17.3	16.8	16.3	17.2	17.4	17.2	17.4
26	16.7	16.5	18.3	18.1	17.0	17.6	18.0	16.6	16.5	16.9	17.2	17.0	17.1
27	14.9	14.8	15.1	15.1	14.9	14.7	15.2	14.7	14.9	15.2	15.6	15.1	15.5
28	175.1	175.0	176.3	176.3	176.2	174.8	176.4	175.0	174.9	176.2	177.0	176.4	176.7
29	106.1	106.1	107.7	107.7	110.8	110.1	107.6	204.6	180.0	29.9	71.2	8.9	21.9
30	64.3	64.3	65.5	65.5	19.6	19.6	65.6	7.0	10.0		19.6	110.3	27.0
Solv.	<i>a</i>	<i>a</i>	<i>b</i>	<i>b</i>	<i>b</i>	<i>a</i>	<i>b</i>	<i>a</i>	<i>a</i>	<i>b</i>	<i>b</i>	<i>b</i>	<i>b</i>

<sup>a</sup> recorded in pyridine-*d*<sub>5</sub>, <sup>b</sup> recorded in methanol-*d*<sub>4</sub>.  
Note: NMR data were obtained from **13**, **14**, **21**: (Choi et al., 2008); **15**: (Nhiem et al., 2009) (Cai et al., 2004b), **16**, **19**, **25**: (Nhiem et al., 2010b); **17**: (Cai et al., 2004b); **18**: (Chang et al., 1999), **20**: (Park et al., 2005); **21**: (Choi et al., 2008); **22**, **23**, **24**: (Nhiem et al., 2010a).

Table 1. <sup>13</sup>C-NMR data of lupane aglycone moieties (continued)

phenylpropanoid, syringoside (**44**) were isolated from the roots of *A. koreanum* by (Hahn et al., 1985) and then was ariensin (**43**) (Kim et al., 1988a). In study antioxidant activity of chemical components from the leaves of this plant, (Nhiem et al., 2011) isolated one new phenylpropanoid named acanthopanic acid and one known 1,2-O-dicaffeoylcyclopenta-3-ol. These compounds showed significantly antioxidant activity by the intracellular ROS radical scavenging DCF-DA assay with IC<sub>50</sub> values of 3.8 and 2.9  $\mu$ M, respectively. Until now, only rutin (**45**), a quercetin glycoside was isolated from this plant with large amount. Rutin is used in many countries as medication for blood vessel protection and are ingredients of numerous multivitamin preparations and herbal remedies. Rutin has various biological activities that are beneficial to human health such as antioxidant effect (Nhiem et al., 2011), protective effect against hepatotoxicity, and anti-inflammatory effect. On the other hand, from the leaves of *A. koreanum*, two monoterpenoids, 4S)- $\alpha$ -terpineol O- $\beta$ -D glucopyranoside (**46**) (Nhiem et al., 2011) and betulabuside B (**47**) (Park et al., 2010) were isolated. From fruits, citric, maleic succinic, malonic, fumaric, and malic acid were isolated (Shin & Kim, 1985).

### 3. NMR data of lupane aglycones

Lupane triterpenes are a class of the most compounds isolated from the leaves and roots of *A. koreanum*, which were determined that this type of compounds are main chemical components of this plant.

Structure of lupanes were elucidated with <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, DEPT (distortionless enhancement by polarization transfer), COSY (<sup>1</sup>H-<sup>1</sup>H shift correlation spectroscopy), TOCSY (total correlation spectroscopy), HMBC (heteronuclear multiple bond correlation), HSQC (heteronuclear single quantum coherence), NOESY (nuclear overhauser enhancement spectroscopy), and ROESY (rotating frame overhauser effect spectroscopy). Proton coupling networks of sugar moieties were indicated with <sup>1</sup>H-NMR, COSY, HMBC and HSQC. Herein, we suggest statistical results of <sup>13</sup>C-NMR data of lupane-type triterpene aglycones and their derivatives in comparison with data of references (Table 1).

Observed the isolated compounds from *A. koreanum*, we found that there are four main classes including lupane triterpenoids, pimarane diterpenoids, *ent*-kaurane diterpenoids, and lignans. Among of them, lupane triterpenes were isolated as numerous of compounds with high yield. These lupanes often contain hydroxyl group at C-3, carboxyl at C-28. In some compounds, hydroxyl, aldehydic, carboxylic groups were at C-11, C-23, and C-30, glycoside was at C-28 and rarely at C-3.

From Table 1, we summarized all <sup>13</sup>C-NMR characteristics of lupane aglycones as follows:

1. When hydroxyl group at C-3, chemical shift of C-3 was about 73.0 ppm and configuration of hydroxyl group at C-3 is  $\alpha$  orientation. When glycosidation is at C-3, chemical shift of C-3 moved to down field with  $\delta_C$  of 81.0 ppm.
2. Free carboxylic group at C-28 were confirmed by chemical shift about 178.0~180.0 ppm. When sugar moiety was at C-28, chemical shift of C-28 is 174.6~176.3 ppm, decreased about 2.5-3.8 ppm.

3. When 23-methyl group was replaced with aldehydic group, chemical shifts of C-23 and C-4 moved to down field from 28.0-28.8 to 209.0-210.0, 37.5-39.5 to 54.9-56.3 ppm, respectively. When 23-methyl group was replaced with carboxylic group, chemical shifts of C-23 and C-4 changed from 28.5 to 178.0, 37.8 to 53.0 respectively, and when 23-methyl group was replaced with CH<sub>2</sub>OH, chemical shift of C-23 had a large change from 28.0 to 71.5 ppm; chemical shift of C-4 had small change about 2.0 ppm.
4. When 30-methyl group was replaced with CH<sub>2</sub>OH, the chemical shifts of C-20 and C-30 downshifted from 151.0 to 156.5, from 19.5 to 64.5 ppm, respectively; chemical shifts of C-19 and C-29 upshifted from 47.5 to 43.0, from 110.0 to 106.0 ppm, respectively.
5. When hydroxyl group was at C-11, chemical shift of C-11 downshifted from 21.1 to 71.0 ppm. Furthermore, configuration of hydroxyl group at this position is  $\alpha$ .

#### 4. Conclusion

This chapter is intended to serve as a reference tool for people in all fields of ethnopharmacology and natural products chemistry. The pharmacological studies on *A. koreanum* indicated the immense potential possibility of this plant in the treatment of conditions such as inflammation, rheumatism, diabetes, cardiovascular, and virus. However, the diverse pharmacological activities of solvent extracts and phytochemicals of *A. koreanum* have only been tested in *in vitro* assay using laboratory animals, and obtained too unclearly and ambiguously for the case of human beings to be conducted on enough. However, these gaps in the studies demand to be bridged in order to exploit medicinal potential of the entire plant of *A. koreanum*. It is still clear that *A. koreanum* is massively and widely consumed, and also continuously studied expecting clinical treatment of various diseases for the future in Korea as well as in the world. From these viewpoints, imperic acid and acanthoic acid, major components of *A. koreanum* are good candidates for further studies in clinical trials, and the development of products derived from *A. koreanum* can be an important part of our biodiversity to respect and sustain for coming generation.

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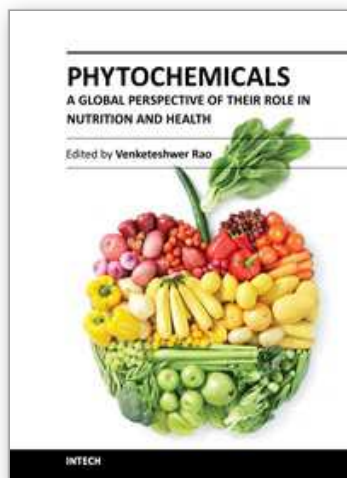
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