Natural Product Sciences
25(4) : 285-292 (2019)
https://doi.org/10.20307/nps.2019.25.4.285

Pharmaceutical Studies on "Dang-Gui" in Korean Journals

Jongmin Ahn[1,2], Mi-Jeong Ahn[3], Young-Won Chin[1], and Jinwoong Kim[1,*]

[1]College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul 08826, Republic of Korea
[2]National Center for Natural Products Research, Research Institute of Pharmaceutical Sciences, School of Pharmacy, The University of Mississippi, University, MS 38677, USA
[3]College of Pharmacy and Research Institute of Pharmaceutical Sciences, Gyeongsang National University, Jinju 52828, Republic of Korea

Abstract – A crude drug "Dang-Gui", belonging to the genus *Angelica,* has been used as a traditional herbal medicine in Asia. Various studies have investigated the chemical components and pharmacological activities of Dang-Gui worldwide. However, domestic research results published in Korean are undervalued in international academia due to language barriers. Therefore, it is necessary to summarize the domestic research findings systematically for greater accessibility. This review focuses on the results published in four Korean pharmaceutical journals between 1970 and 2018, which detail the botanical, phytochemical, and pharmacological properties of three *Angelica* species (*A. gigas*, *A. sinensis*, and *A. acutiloba*) used as "Dang-Gui" in Korea, China, and Japan.
Keywords – Dang-Gui, *Angelica gigas*, *Angelica sinensis*, *Angelica acutiloba*, phytochemical, pharmacological, Korean journal

Introduction

"Dang-Gui" refers to the roots of medicinal plants belonging to the genus *Angelica* (Umbelliferae) that have been widely used as traditional medicine throughout Korea, China, and Japan. Korean, Chinese, and Japanese Pharmacopoeia define Dang-Gui as a different botanical origin: *Angelica gigas* Nakai, *Angelica sinensis* (Oliv.) Diels and *Angelica acutiloba* Kitagawa, respectively.[1-3] For example, in Korean Pharmacopoeia the roots of *A. gigas* are "Dang-Gui", while the roots of *A. acutiloba* are "Il-Dang-Gui", meaning Japanese Dang-Gui.

Multiple pharmaceutical studies on Dang-Gui have been conducted both domestically and worldwide. Between 1970 and 2018, approximately 400, 200, and 3600 international papers have been published about *A. gigas*, *A. acutiloba*, and *A. sinensis*, respectively. Unfortunately, due to language barriers, papers published in Korean journals are often disregarded. For this reason, domestic research results are underestimated in international academia. Therefore, it is necessary to summarize domestic research results systematically for international accessibility. This work summarizes domestic research performed on three *Angelica* species used as Dang-Gui in Korea, China, and Japan. This review is limited to studies published between 1970 and 2018 in four Korean pharmaceutical journals (Korean Journal of Pharmacognosy, Yakhak Hoeji, Natural Product Sciences, and Archives of Pharmacal Research), of which the former two are written in Korean. The number of relevant articles in these journals is 13, 5, 6 and 9, respectively, and their collective findings are summarized herein.

*Author for correspondence
Jinwoong Kim, College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul 08826, Republic of Korea
Tel: +82-2-880-7853; E-mail: jwkim@snu.ac.kr

Inner morphological studies

Comparative histological studies were carried out to clarify the origins of the three *Angelica* species.[4,5] According to these studies, the three species are distinguished by the shape of the cork cortex, resin duct and xylem fiber, frequency and size of secretory cells, and the size of vessels. For example, *A. sinensis* can be recognized by the number of cork cells in the cork layer (4 - 7), which is the greatest among the three species. *A. acutiloba* has the largest resin duct diameter (200 - 300 μm) and the lowest duct frequency. In comparison, *A. gigas* displays the

smallest duct diameter (20 - 60 μm) and the highest frequency among the three species. The diameter and frequency of the resin duct in *A. sinensis* are slightly larger than those of *A. gigas*. *A. acutiloba* also shows the greatest number (25 - 40) of secretory cells surrounding the resin duct, followed by *A. sinensis* and *A. gigas* (5 - 8). The xylem fibers of *A. gigas* are the most well-developed among the three species, while those of *A. acutiloba* and *A. sinensis* are similar to each other. *A. acutiloba* has the smallest vessel diameter (15 - 40 μm), while the vessel diameters of *A. gigas* and *A. sinensis* are similar (20 - 80 μm and 20 - 90 μm, respectively).

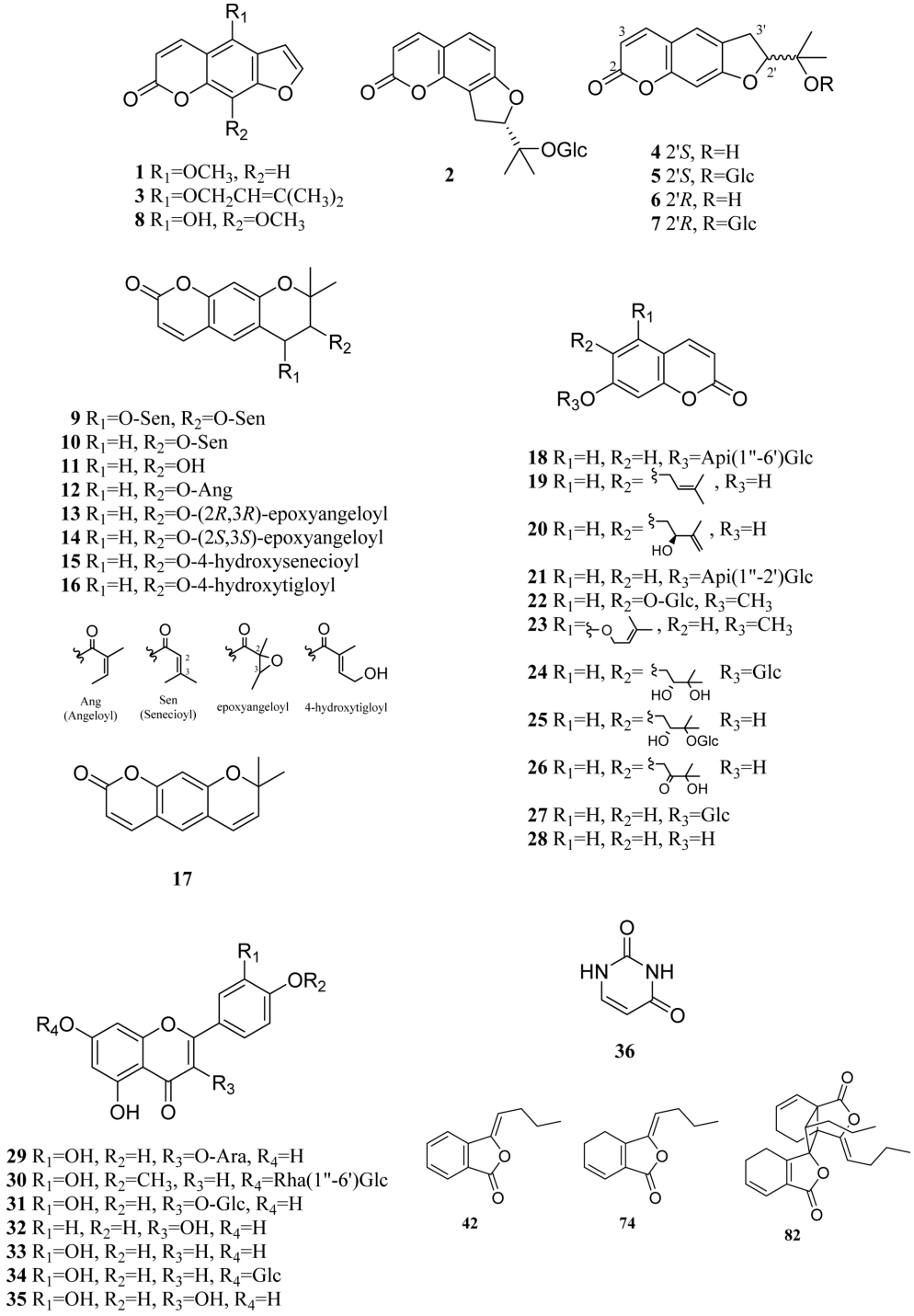

Fig. 1. Compounds from three Angelica species, *Angelica gigas*, *A. sinensis* and *A. acutiloba*.

Phytochemical constituents

Dang-Gui has been shown to contain a variety of constituents including coumarins (**1 - 28**), flavonoids (**29 - 35**), and diverse essential oils (e.g., benzofuranone derivatives) (**42**, **74** and **82**) (Fig. 1). The phytochemical components of Dang-Gui vary depending on the specific plant. Most domestic studies on Dang-Gui ingredients involved *A. gigas* because their roots are the primary source of this medicine in Korea.

The main components of *A. gigas* are decursin (**10**) and decursinol angelate (**12**), which are pyranocoumarins. Angelan is a pharmacologically active pectin polysaccharide isolated from *A. gigas*.[6] The main component of *A. acutiloba* and *A. sinensis* is a benzofuranone, ligustilide (**74**), found in the essential oil fraction (Table 1).[7] Most essential oils of the three *Angelica* species were identified by gas chromatography-mass spectrometry (GC-MS); however, further studies into the pharmacological activity and structure of butylidenephthalide (**42**), *Z*-ligustilide (**74**), and neodiligustilide (**82**) have been performed (Fig. 1).

Pharmacological studies

Although the pharmacological activities of these three *Angelica* species have been reported in Korean and

Table 1. Compounds from three *Angelica* species, *Angelica gigas*, *A. sinensis* and *A. acutiloba* (in Korean paper)

Compounds no.	Compound name	Species (ref.)		
		A. gigas	*A. sinensis*	*A. acutiloba*
Furanocoumarins				
1	Bergapten	roots (8, 9)		
2	Columbianetin-*O*-β-D-glucopyranoside	roots (10)		
3	Isoimperatorin	roots (10), fruits (11)		
4	Marmesin	roots (10)		
5	Marmesinin	roots (10)		
6	Nodakenetin	roots (8, 9, 10)		
7	Nodakenin	roots (8, 9, 10, 12)		
8	Xanthotoxin	roots (10)		
Pyranocoumarins				
9	Decursidin	fruits (11)		
10	Decursin	roots (8, 9, 10, 12, 13)		roots (7)
11	Decursinol	roots (14)		
12	Decursinol angelate	roots (8, 9, 10, 12, 13)		
13	(2"*R*,3"*R*)-Epoxyangeloyldecursinol	roots (10)		
14	(2"*S*,3"*S*)-Epoxyangeloyldecursinol	roots (10)		
15	4"-Hydroxydecursin	roots (10)		
16	4"-Hydroxytigloyldecursinol	roots (10)		
17	Xanthyletin	roots (10)		
Coumarins				
18	Apiosylskimmin	roots (10)		
19	Demethylsuberosine	roots (10)		
20	7-Hydroxy-6-((2*R*)-hydroxy-3-methylbut-3-nyl)coumarin	roots (10)		
21	Isoapiosylskimmin	roots (10)		
22	Magnolioside	roots (10)		
23	7-Methoxy-5-prenyloxycoumarin	roots (10)		
24	(*S*)-Peucedanol-7-*O*-β-D-glucopyranoside	roots (10)		
25	(*S*)-Peucedanol-3'-*O*-β-D-glucopyranoside	roots (10)		
26	Peucedanone	roots (10)		
27	Skimmin	roots (10)		
28	Umbelliferone	roots (10)		

Table 1. continued

Compounds no.	Compound name	Species (ref.)		
		A. gigas	*A. sinensis*	*A. acutiloba*
Flavonoids				
29	Avicularin	leaves (15)		
30	Diosmin	roots (16)		
31	Isoquercetin	leaves (15)		
32	Kaempferol	leaves (15)		
33	Luteolin	leaves (15)		
34	Luteolin-7-*O*-β-D-glucopyranoside	leaves (15)		
35	Quercetin	leaves (15)		
Nucleic acids				
36	Uracil	roots (9)		
Essential oils and Miscellaneous				
37	Aromadendrene			roots (17)
38	1,4-Benzenedicaboxaldehyde			leaves (17)
39	Borneol			leaves (17)
40	Bornyl acetate			roots, leaves (17)
41	Buthylphthalide			roots, leaves (17)
42	Butylidenephthalide		roots (7)	roots (7, 17), leaves (17)
43	α-Bisabolene epoxide			roots, leaves (17)
44	*t*-Cadinol			leaves (17)
45	Camphene	roots (18)		roots, leaves (17)
46	Δ-3-Carene	roots (18)		
47	Carotol			roots (17)
48	β-Caryophyllene			roots, leaves (17)
49	Caryophyllene oxide			roots, leaves (17)
50	α-Cedrene			roots (17)
51	Clovene			leaves (17)
52	Cyclodecane			leaves (17)
53	*p*-Cymene	roots (18)		
54	Dibutylphthalate		roots (7)	roots (7)
55	(11*S*,16*R*)-Dihydroxyoctadeca-9*Z*,17-dien-12,14-diyn-1-yl acetate		roots (19)	
56	4,4',5-Dimethyl-Δ-2-cyclohexanone	roots (18)		
57	2,6-Di-*tert*-butyl-methylphenol	roots (18)		
58	Δ-Elemene	roots (18)		
59	α-Elemene	roots (18)		
60	β-Elemene	roots (18)		roots (17)
61	γ-Elemene	roots (18)		
62	Elemol	roots (18)		
63	α-Eudesmol	roots (18)		
64	β-Eudesmol	roots (18)		
65	(3*R*, 8*S*)-Falcarindiol			roots (17)
66	β-Farnesene	roots (18)		roots, leaves (17)
67	Guaiol	roots (18)		
68	α-Guaiene			leaves (17)
69	β-Guaiene	roots (18)		
70	Δ-Guaiene	roots (18)		

Table 1. continued

Compounds no.	Compound name	Species (ref.)		
		A. gigas	*A. sinensis*	*A. acutiloba*
71	Isopropylidene bicyclo(5,1,0)octane	roots (18)		
72	Khusimone			roots (17)
73	Lavandulyl acetate			leaves (17)
74	*Z*-Ligustilide		roots (7, 19)	roots, leaves (7, 17)
75	Limonene	roots (18)		roots, leaves (17)
76	Linalool			roots, leaves (17)
77	Linoleic acid			roots (7)
78	1-Methyl-4-(1-methylethyl)benzene			roots, leaves (17)
79	α-Muurolene	roots (18)		
80	Myrcene	roots (18)		roots, leaves (17)
81	Neo-allo-ocimene			roots (17)
82	Neodiligustilide		roots (19)	
83	Nerolidol			roots (17)
84	Myristicin	roots (18)		
85	Myristicine	roots (18)		
86	*n*-Nonane	roots (18)		
87	*n*-Undecane	roots (18)		
88	*cis*-Ocimene			roots, leaves (17)
89	Octadecadienoic acid methyl ester		roots (7)	
90	Octanal			roots (17)
91	Pentylbenzene			leaves (17)
92	α-Phellandrene	roots (18)		
93	1-Phenyl-1-pentanone			roots (17)
94	Phthalic anhydride			leaves (17)
95	α-Pinene	roots (18)		leaves (17)
96	β-Pinene	roots (18)		
97	4,5-Pinene oxide	roots (18)		
98	Sabinene			roots (17)
99	α-Terpinene	roots (18)		roots (17)
100	γ-Terpinene	roots (18)		roots, leaves (17)
101	Terpinene-4-ol			roots, leaves (17)
102	Terpinolene	roots (18)		
103	Thymol			roots (17)
104	Thymyl methyl ether			roots (17)
105	Torreyol	roots (18)		
106	4-Vinylguaiacol	roots (18)		
107	Vulgarol B			leaves (17)

international journals, the results in Korean journals are difficult to find outside of Korea. Domestic research has shown that these *Angelica* species have anti-inflammatory, antibacterial, antioxidant, antihyperlipidemic, hepatoprotective, and neuroprotective activities (Table 2).

In addition to studies on pharmacological activity, drug metabolism studies have also been conducted on the components of the three *Angelica* species. Woo et al. used mouse hexobarbital-induced hypnosis to investigate the effects of methanol extracts of *A. gigas* and *A. acutiloba* on drug metabolism and found that the furanocoumarin components of the extracts affected the drug-metabolizing enzymes.[29] Shin et al. showed that decursin (**10**), a major component of *A. gigas*, inhibited the hepatic enzyme system.[30]

To evaluate the efficacy of herbal medicines, Park et al.

Table 2. Bioactivities of the three *Angelica* species, *A. gigas*, *A. sinensis* and *A. acutiloba* (in Korean paper)

Therapeutic target	*In vitro*	*In vivo*	Other assay	Extracts/Active constituents	References
Anticancer	L1210			**65, 74**, **82**, **89**	19
	K562			**74**, **82**	19
	Hela			Essential oil fraction of *A. acutiloba* (roots) **42**, **74**	17
	MCF-7			Essential oil fraction of *A. acutiloba* (roots) **10**, **74**	17 21
	U937, HL60, THP-1, MOLT4, DU145, PC-3, LNCaP			**10**	21, 22
		mouse (ICR)		**10**, **12**	21, 23
Antidiabetic		NOD mouse (Non-Obese Diabetic mouse model)		Angelan	24
Anti-inflammatory		rat (Sprague-Dawley), mouse (ICR)		Water extract of *A. gigas* Water extract of *A. acutiloba*	25
Anti-melanogenic	B16F1			**19**	26
Antimicrobial	*Bacillus subtilis*			Water extract of *A. gigas* Water extract of *A. acutiloba* **10**, **12**	8, 25
	Escherichia coli			Water extract of *A. gigas* Water extract of *A. acutiloba* Essential oil fraction of *A. acutiloba* (roots, leaves)	17, 25
	Helicobacter pylori			**10**, **12**	21
Antimutagenic		mouse (ICR)		Water extract of *A. gigas* Water extract of *A. acutiloba*	25
Antioxidant		rat		**10**, **12**	27
			DPPH radical scavenging test	Essential oil fraction of *A. acutiloba* (roots, leaves) **29**, **31**, **32**, **33**, **34**, **35**, **42**, **74**	17 15
			Reducing power tests	Essential oil fraction of *A. acutiloba* (roots, leaves) **42**, **74**	17
Chemopreventive		mouse (ICR)		Aqua-acupuncture solution of *A. gigas* (roots)	28
Hepatoprotective		mouse (ICR)		Water extract of *A. gigas* Water extract of *A. acutiloba*	25
		rat		Water extract of *A. gigas* (roots) Ethanol extract of *A. gigas* (roots) Water extract of *A. acutiloba* (roots) Ethanol extract of *A. acutiloba* (roots) **10**, **12**	31 27
Anti-hyperlipidemia		rat		Water extract of *A. gigas* (roots) Ethanol extract of *A. gigas* (roots) Water extract of *A. acutiloba* (roots) Ethanol extract of *A. acutiloba* (roots) **10**, **12**	32 21
Immuno-stimulating	primary mouse spleen cells			Crude polysaccharides of *A. gigas (*roots)	33
Neuroprotective	primary cultured rat cortical cells			**2**, **3**, **4**, **5**, 7, **10**, **11**, **13**, **14**	10
		mouse		**10**, **12**	21
Anti-aggregatory		rat (Sprague-Dawley)		**10**, **12**	12, 21
Drug metabolism		mouse		95% Methanol extract of *A. acutiloba* (roots, fruits) **10**, **12**	29 30 20

investigated drug interactions occurring during the administration of *A. gigas* extracts and other herbal medicines. In this study, they measured the concentration of decursinol (**11**) in blood, using decursin (**10**) and its metabolite decursinol (**11**) as indicator substances.[20] This study found that oral administration of ether or methanol extracts of *A. gigas* resulted in higher concentrations of decursinol (**11**) in blood, as compared to treatment with decursin (**10**) alone. Coadministration of decursin (**10**) and Cnidii Rhizoma extracts increased the concentration of decursinol (**11**) in blood, while coadministration of decursin (**10**) and Bupleuri Radix extracts decreased the blood concentration of decursinol (**11**). However, coadministering Cnidii Rhizoma or Bupleuri Radix extracts with decursinol (**11**) increased the level of decursinol (**11**) in blood.

Other studies

As most herbal medicine is generally distributed after cutting and drying, there is a limit to distinguish the origins and producing area only by histological discrimination. To address this limitation, a clearer method for discrimination has been developed. To establish such a method, Cho et al. used non-destructive analytical techniques, including near-infrared spectroscopy, X-ray fluorescence spectrometry, and electronic nose, to compare and analyze *A. gigas* and *A. sinensis*. All three methods showed a discrimination rate of 90% or higher. Additionally, these methods are fast and simple and require no preprocessing.[34]

Kim et al. compared the concentration of coumarins between roots of *A. gigas* cultivated in Korea and China. They found that marmesin (**4**), nodakenin (**7**), decursin (**10**), and decursinol (**11**) were higher on average in Korean than Chinese roots. They successfully distinguished Korean and Chinese roots of *A. gigas* using multivariate analysis [Principal Component Analysis (PCA), Partial Least Squares Discriminant Analysis (PLS-DA)], based on decursin (**10**) and decursinol angelate (**12**).[35]

Decursin (**10**) and decursinol angelate (**12**), which are major components of *A. gigas*, are structural isomers with similar chemical properties, making the two compounds difficult to isolate and purify. To overcome this limitation, the conditions for analytical reverse-phase high-performance liquid chromatography (HPLC) of decursin (**10**) and decursinol angelate (**12**) were explored.[36,37] The peaks were best separated using mobile phases composed of acetonitrile with sodium dodecyl sulfate and sodium dihydrogen phosphate, and acetonitrile with sodium lauryl sulfate and sodium phosphate. The optimum HPLC conditions were identified as a column temperature of 30 - 35 ºC, a flow rate of 1 - 1.2 ml/min, with UV detection at 230 or 280 nm.

An efficient, large-scale extraction process was proposed by comparing and analyzing the extraction efficiency of the components of *A. gigas*.[36] Kang et al. reported that the concentrations of decursin (**10**) and decursinol angelate (**11**) in 100% ethanol extracts were slightly higher than those in 50% ethanol extracts. However, there were greater differences in the extraction efficiency between ethanol extracts and deionized water extraction. As there was not a significant difference between 100% and 50% ethanol extracts, it was predicted that the extraction process using 50% ethanol would be more suitable for safety engineering in large-scale extractions.

In addition, Lee et al. proposed a method for mass-producing decursinol (**11**), a starting material for the synthesis of various derivatives, including decursin (**10**) and decursinol angelate (**12**), by hydrolyzing *A. gigas* extracts.[14] This study established a method for obtaining pure target compounds solely through recrystallization following hydrolysis, without complicated separation processes. They succeeded in producing a large amount of decursinol (**11**) from the root of *A. gigas*, and found that the highest yield of decursinol (**11**) was obtained using NaOH. Additionally, they identified ether as the most effective solvent for hydrolysis.

Conclusions

Dang-Gui has been widely used as traditional medicine in Korea, China, and Japan and its botanical origins in the official compendia differ between the countries. The Korean pharmacopoeia defines the origin of Dang-Gui as *A. gigas*. In Korea, the most studied was carried out on *A. gigas*. Much less is known about the composition of *A. sinensis* than both *A. gigas* and *A. acutiloba*. Furthermore, there are no studies on the pharmacological activity of *A. sinensis* in Korea. Along with studies investigating the phytochemical components of the three *Angelica* species and the pharmacological activities of these components and extracts, this review showed four studies focused on classifying plant origin.

A variety of coumarins have been reported through studies investigating the components of Dang-Gui. Extracts and individual components of the three *Angelica* species were found to have anti-inflammatory, antibacterial, and antioxidant properties. Additionally, anticancer/cytotoxic, antihyperlipidemic, hypoglycemic, hepatoprotective, and neuroprotective activities of these extracts and

individual compounds have been found to be effective in the prevention and treatment of lifestyle diseases such as diabetes, arteriosclerosis, and cancer. However, there are few studies on components other than coumarins, and studies relating to biological activity have focused primarily on decursin (**10**) and decursinol angelate (**12**), the main components of *A. gigas* and its extracts. Therefore, for a better understanding of Dang-Gui and its applications, it is required to expand the studies of various other compounds of this species and perform additional biological activity tests. In addition, continuous research on *A. sinensis* and *A. acutiloba* will improve the availability of Dang-gui for the modern medicinal uses.

Acknowledgements

This work was supported by the Brain Korea 21 Plus program.

References

(1) Anonymous. The Korean Pharmacopoeia 11th Ed.; Ministry of Food and Drug Safety: Republic of Korea, 2014, p 1790.
(2) Anonymous. The Japanese Pharmacopoeia 16th Ed.; The Ministry of Health Labor and Welfare: Japan, 2012, p 1866.
(3) Anonymous. Pharmacopoeia of the People's Republic of China; National Pharmacopoeia Commission of the People's Republic of China; China Medical Science Press: China, 2015, p 133.
(4) Park, J. H.; Lee, Y. J.; Keon, S. J. *Kor. J. Pharmacogn.* **2005**, *36*, 141-144.
(5) Ahn, M. J.; Bae, J. Y.; Park, J. H. *Kor. J. Pharmacogn.* **2011**, *42*, 103-106.
(6) Kim, H. J.; Piao, X. L.; Jang, Y. P. *Nat. Prod. Sci.* **2011**, *17*, 202-205.
(7) Kim, H. M.; Kang, J. S.; Park, S. K.; Lee, K.; Kim. J. Y.; Kim, Y. J.; Hong, J. T.; Kim, Y.; Han, S. B. A*rch. Pharm. Res.* **2008**, *31*, 1489-1496.
(8) Lee, S.; Shin, D. S.; Kim, J. S.; Oh, K. B.; Kang, S. S. *Arch. Pharm. Res.* **2003**, *26*, 449-452.
(9) Lee, S.; Kang, S. S.; Shin, K. H. *Nat. Prod. Sci.* **2002**, *8*, 58-61.
(10) Kang, S. Y.; Kim, Y. C. *Arch. Pharm. Res.* **2007**, *30*, 1368-1373.
(11) Yook, C. S.; Kim, C. W.; Ryu, K. S. *Kor. J. Pharmacog.* **1973**, *4*, 189-190.
(12) Lee, Y. Y.; Lee, S.; Jin, J. L.; Yun-Choi, H. S. *Arch. Pharm. Res.* **2003**, *26*, 723-726.
(13) Ryu, K. S.; Hong, N. D.; Kim, N. J.; Kong, Y. Y. *Kor. J. Pharmacogn*. **1990**, *21*, 64-68.
(14) Lee, J. H.; Choi, Y. S.; Kim, J. S.; Kim, J. H.; Jeong, H. G.; Kim, D. H.; Yun, M. Y.; Kim, J. S.; Cho, S. H.; Shen, G. N.; Kim, E. G.; Jin, W. Y.; Song, G. Y. *Yakhak Hoeji.* **2006**, *50*, 172-176.
(15) Moon, H. I.; Ahn, K. T.; Lee, K. R.; Zee, O. P. *Yakhak Hoeji.* **2000**, *44*, 119-127.
(16) Lee, S.; Kang, S. S.; Shin, K. H. *Nat. Prod. Sci.* **2002**, *8*, 127-128.
(17) Roh, J.; Lim, H.; Shin, S. *Nat. Prod. Sci*. **2012**, *18*, 244-249.
(18) Chi, H. J.; Kim, H. S. *Kor. J. Pharmacogn.* **1988**, *19*, 239-247.
(19) Chen, Q. C.; Lee, J. P.; Jin, W. Y.; Youn U. J.; Kim, H. J.; Lee, I. S.; Zhang, X. F.; Song, K. S.; Seong, Y. H.; Bae, K. H. *Arch. Pharm. Res.* **2007**, *30*, 565-569.
(20) Park, R. J.; Kim, N. J.; Lee, K. T.; Seo, S. H. *Kor. J. Pharmacogn*. **2001**, *32*, 72-78.
(21) Son, C. Y.; Baek, I. H.; Song, G. Y.; Kang J. S.; Kwon, K. I. *Yakhak Hoeji*. **2009**, *53*, 303-313.
(22) Kim, N. S.; Jeong, S. I.; Kim, J. S.; Oh, M. J.; Oh, C. H. *Kor. J. Pharmacogn*. **2016**, *47*, 197-203.
(23) Lee, S.; Lee, Y. S.; Jung, S. H.; Shin, K. H.; Kim, B. K.; Kang, S. S. *Arch. Pharm. Res.* **2003**, *26*, 727-730.
(24) Kim, H. M.; Kang, J. S.; Park, S. K.; Lee, K.; Kim, J. Y.; Kim, Y. J.; Hong, J. T.; Kim, Y.; Han, S. B. *Arch. Pharm. Res*. **2008**, *31*, 1489-1496.
(25) Kim, C. M.; Heo, M. Y.; Kim, H. P.; Sin, K. S.; Pachaly, P. *Arch. Pharm. Res*. **1991**, *14*, 87-92.
(26) Kim, Y. A.; Park, S. H.; Kim, B. Y.; Kim, A. H.; Park, B. J.; Kim, J. J. *Kor. J. Pharmacogn*. **2014**, *45*, 209-213.
(27) Lee, S.; Lee, Y. S.; Jung, S. H.; Shin, K. H.; Kim, B. K.; Kang, S. S. *Nat. Prod. Sci*. **2003**, *9*, 170-173.
(28) Kim, Y. K.; Cho, K. H.; Shon, Y. H.; Choi, H. K.; Kim, S. Y.; Lim, J. K.; Nam, K. S. *Yakhak Hoeji*. **2000**, *44*, 283-292.
(29) Woo, W. S.; Shin, K. H.; Ryu, K. S. *Arch. Pharm. Res.* **1980**, *3*, 79-84.
(30) Shin, K. H.; Han, J. M.; Lee, I. R. *Kor. J. Pharmacogn.* **1996**, *27*, 323-327.
(31) Chung, M. H.; Oh, H. S.; Lim, J. H. *Kor. J. Pharmacogn.* **1998**, *29*, 402-412.
(32) Chung, M. H.; Lim, J. H.; Oh, H. S. *Kor. J. Pharmacogn.* **1998**, *29*, 300-311.
(33) Ahn, K. S.; Sim, W. S.; Kim, H. M.; Han, S. B.; Kim, I. H. *Kor. J. Pharmacogn.* **1996**, *27*, 254-261.
(34) Cho, C. H.; Kim, S. J.; Kim, H. J. *Yakhak Hoeji*. **2002**, *46*, 161-167.
(35) Kim, J. R.; Lee, D. Y.; Sung, S. H.; Kim, J. *Kor. J. Pharmacogn.* **2013**, *44*, 332-335.
(36) Kang, Y. G.; Lee, J. H.; Chae, H. J.; Kim, D. H.; Lee, S.; Park, S. Y. *Kor. J. Pharmacogn.* **2003**, *34*, 201-205.
(37) Lee, J. P.; Chang, S. Y.; Park, S. Y. *Nat. Prod. Sci*. **2004**, *10*, 262-267.

Received September 27, 2019
Revised October 12, 2019
Accepted December 13, 2019