

CHEMISTRY OF GINSENG-SAPONINS : AERIAL PARTS OF *PANAX GINSENG* AND ITS RELATED PLANTS, NEW NATURAL SOURCES OF BIOLOGICALLY ACTIVE DAMMARANE-SAPONINS

Osamu Tanaka

*Dept. of Medicinal Chem. of Natural Products, Institute of Pharmaceutical Sciences,
Hiroshima University, School of Medicine, JAPAN*

Isolation and structure determination of a number of ginseng saponins were already established; ginsenoside-Ro (= chikusetsusaponin V, glycoside of oleanolic acid) and dammarane-saponins, ginsenosides-Rb₁, -Rb₂, -Rb₃, -Rc, -Rd, -Re, -Rf, -Rg₁, -Rg₂, -Rh₁ (6-O-gluco-protopanaxatriol, and 20-O-gluco-ginsenoside-Rf) (see Chart 1). Extensive studies on biological activities of these saponins have also been reported.

Recently, modern procedures for chemical studies on plant glycosides, especially glycosides having an acid-unstable aglycone such as ginseng saponins have been developed; enzymes for mild hydrolysis, application of ¹³C-NMR and mass spectrometry (field desorption mass spectrometry) for identification and structure elucidation, and high performance liquid chromatography for quantitative analysis as well as preparative separation. Using these procedures, our research group have undertaken isolation and structure determination of saponins of ginseng leaves for the purpose to find the other sources of biologically active dammarane-saponins.

From leaves of ginseng (*Panax ginseng*), the following root saponins were isolated; ginsenosides-Rb₁(yield 0.1%), -Rb₂(0.4%), -Rc(0.2%), -Rd(1.5%), -Re(1.5%), and -Rg₁(1.5%). Besides these known saponins, new saponins named ginsenosides-F₁(0.4%), -F₂(0.2%), -F₃(0.2%) (Chart

3), -F_{6a}(minor), and -F_{6bc} (minor) (Chart 2) were isolated. The high contents of ginsenosides-Rd, -Re, and -Rg₁ in the leaves must be notable as the new source of these dammarane-saponins (S.Yahara, O.Tanaka, and T.Komori, Chem. Pharm. Bull., **24**, 2204 (1976), S.Yahara, K.Kaji, and O. Tanaka, *ibid.*, submitted; pharmacological activity of the crude saponin fraction of Korean ginseng leaves: H.Saito, M. Morita, and K.Takagi, Japan J. Pharmacol., **23**, 43 (1973)).

From flower-buds of the same plant which were usually removed before blooming, ginsenosides-Rb₁ (0.2%), -Rb₂(0.25%), -Rc(0.2%) -Rd (0.5%), -Re(surprisingly 4.2% !), -Rg₁(0.3%), and -F₃(0.04%) were isolated and identified (S. Yahara, K.Matsuura, R.Kasai, and O.Tanaka, Chem. Pharm. Bull., **24**, 3212(1976)). This result is significant in view of the utility of the aerial parts of Korean ginseng as the medicinal materials.

Shoji and his co-workers of Showa University reported isolation and structure elucidation of saponins of rhizomes of Japanese wild *Panax*, *Chikusetsu-ninjin* (*P. japonicus* = *P. pseudoginseng* subsp. *japonicus* Hara). In contrast to Korean ginseng and American ginseng, the rhizomes contain a large amount of oleanolic acid saponins, chikusetsusaponins-Ib, -IV, -IVa, and -V (= ginsenoside-Ro of ginseng roots) along with a fairly amount of dammarane-saponins, chikusetsusa-

ponins-Ia and -III (Chart 1).

From the leaves of this plant collected in Hiroshima prefecture, we isolated several new saponins; chikusetsusaponins-L_{3a}, -L_{3bc}, -L₅, -L₈, -L_{9a}, -L_{9bc}, and -L₁₀ (Chart 2 and 3), all of which have 20(S)-protopanaxatriol (Chart 1) or its homologues (oxygenated side chain (Chart 2)) as their sapogenin. It was found that the saponin composition of leaves of this plant highly depends upon the locality. In the leaves collected in Tottori, Kyoto, and Niigata prefectures, saponins of leaves of Hiroshima were not detected but new saponins having a 12-keto-derivative of 20(S)-protopanaxadiol as their sapogenin were characteristically isolated (Chart 2); chikusetsusaponins-LT₅ and -LT₈ from the leaves of Tottori, -LT₅ from the leaves of Kyoto, and -LN₄ from the leaves of Niigata. It is notable that no regional dependence was observed in the saponin-composition of the rhizome of Japanese wild Panax.*

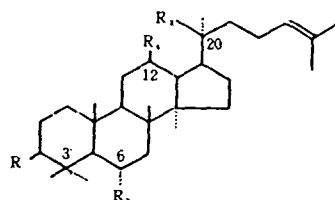
Prof. Hara, University of Tokyo has pointed

out the close taxonomical relationship between Japanese wild Panax and Himalayan Panax (*P. pseudo-ginseng*), both of which have generally long creeping rhizomes unlike Korean and American ginseng (J. Jap. Bot., 45, 198 (1970)). Shoji and his co-workers revealed that rhizomes of this plant collected in Bhutan (*P. pseudo-ginseng* subsp. *himalaicus*) by O. Tanaka contain a large amount of oleanolic acid saponins; saponin A (= chikusetsusaponin-V = ginsenoside-Ro), saponin B (= chikusetsusaponin-IV), and saponin C (= chikusetsusaponin-IVa) (Chart 1) along with the dammarane-saponin of ginseng root, ginsenoside-Rb₁ (Chart 1). With regard to leaf saponins of this plant, we recently isolated ginsenoside-Rb₃ (Chart 1) and two new saponins, designated as pseudo-ginsenosides-F₈ (= monoacetyl ginsenoside-Rb₃) and -F₁₁, the latter of which was demonstrated to be the first example of the dammarane-saponin having the ocotillone type aglycone (Chart 3).**

* Yahara, S., Kasai, R. and Tanaka, O.: Chem. Pharm. Bull., 25, 2041 (1977); S. Yahara and O. Tanaka, *ibid.*, 26, in press (1978).

** Yahara, S. and Tanaka, O.: Phytochemistry, 17, in press (1978).

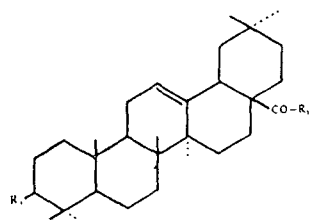
Chart 1



20(S)-protopanaxadiol:
R₁ = R₃ = R₄ = OH, R₂ = H

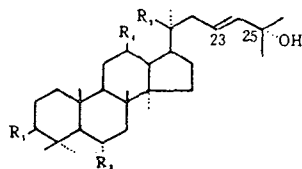
20(S)-protopanaxatriol:
R₁ = R₂ = R₃ = R₄ = OH

	R ₁	R ₂	R ₃	R ₄
Ginsenoside-Rg ₂	-OH	-O-Glc ² - Rha	-OH	-OH
Ginsenoside-Rg ₁	-OH	-O-Glc	-O-Glc	-OH
Ginsenoside-Rf	-OH	-O-Glc ² - Glc	-OH	-OH
Ginsenoside-Re	-OH	-O-Glc ² - Rha	-O-Glc	-OH
Ginsenoside-Rd	-O-Glc ² - Glc	-H	-O-Glc	-OH
20-Gluco-ginsenoside-Rf	-OH	-O-Glc ² - Glc	-O-Glc	-OH
Ginsenoside-Rc	-O-Glc ² - Glc	-H	-O-Glc ⁶ - Ara(pyr)	-OH
Ginsenoside-Rb ₃	-O-Glc ² - Glc	-H	-O-Glc ⁶ - Xyl	-OH
Ginsenoside-Rb ₂	-O-Glc ² - Glc	-H	-O-Glc ⁶ - Ara(fur)	-OH
Ginsenoside-Rb ₁	-O-Glc ⁶ - Glc	-H	-O-Glc ⁶ - Glc	-OH
Chikusetsusaponin III	-O-G ₂ lc ⁶ - Xyl	-H	-OH	-OH
	$\begin{array}{c} \diagup \\ 2 \\ \text{Glc} \end{array}$			
Chikusetsusaponin Ia	-O-Glc ⁶ - Xyl	-H	-OH	-OH

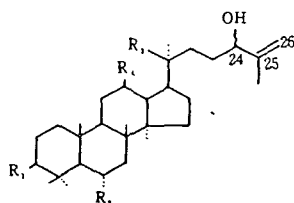


	R ₁	R ₂
Ginsenoside-Ro (Saponin A ₁ , Chikusetsusaponin V)	-O-GlcUA ² — Glc	-O-Glc
Chikusetsusaponin IV (Saponin B)	-O-GlcUA ⁴ — Ara(fur)	-O-Glc
Chikusetsusaponin IVa (Saponin C)	-O-GlcUA	-O-Glc
Chikusetsusaponin Ib	-O-GlcUA ⁴ — Ara(fur) 6 Glc	-OH

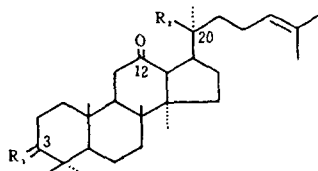
Chart 2



	R ₁	R ₂	R ₃	R ₄
Chikusetsusaponin L _{9a}	-OH	-OH	-OH	-O-Glc
Chikusetsusaponin L _{3a}	-OH	-OH	-O-Glc ⁶ — Ara(pyr) ⁴ — Xyl	-OH
Ginsenoside-F _{6a}	-O-Glc ² — Glc	-H	-O-Glc	-OH

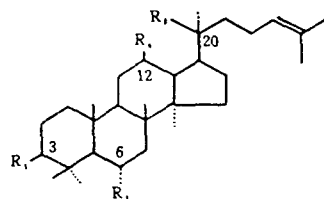


Chikusetsusaponin L _{9bc}	-OH	-OH	-OH	-O-Glc
Chikusetsusaponin L _{3bc}	-OH	-OH	-O-Glc ⁶ — Ara(pyr) ⁴ — Xyl	-OH
Ginsenoside-F _{6bc}	-O-Glc ² — Glc	-H	-O-Glc	-OH

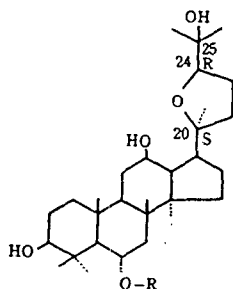


Chikusetsusaponin LT ₈	-O-Glc	-O-Glc
//	H	
LT ₅	-O-Glc	-O-Glc ⁶ — Glc
//	H	
LN ₄	-O-Glc ⁶ — Xyl	-O-Glc ⁶ — Ara(pyr)
//	H	

Chart 3



	R ₁	R ₂	R ₃	R ₄
Ginsenoside-F ₁	-OH	-OH	-Glc	-OH
-F ₂	-O-Glc	-H	-Glc	-OH
-F ₃	-OH	-OH	-O-Glc ⁶ — Ara(pyr)	-OH
Chikusetsusaponin L ₁₀	-OH	-OH	-OH	-O-Glc
L ₈	-OH	-OH	-O-Glc ⁶ — Ara(fur)	-OH
L ₅	-OH	-OH	-O-Glc ⁶ — Ara(pyr) ⁴ — Xyl	-OH
Pseudo-ginsenoside-F ₈	-O-Glc ² — Glc 6 Ac	-H	-O-Glc ⁶ — Xyl	-OH



Pseudo-ginsenoside-F₁₁
R = -O-Glc² — Rha

Glc: β -glucopyranoside, Rha: α -rhamnopyranoside, Xyl: β -xylopyranoside,
GlcUA: β -glucuronide. Ara(pyr): α -arabinopyranoside,
Ara(fur): α -arabinofuranoside.