Lignan Components from *Panax ginseng* C.A. Meyer

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Abstract Two lignanes, Comp.-I, mp 108-10 °C and Comp.-II, mp 50-52 ° were isolated from Korean ginseng extract by repeated column chromatographic purification. Comp.-I was identified as gomisin-N and Comp.-II as gomisin-A by spectrometric analysis, both of which have already been described as the anti-hepatotoxic lignan components of Schizandra chinensis Bail.

Keywords *Panax ginseng* C.A. Meyer, lignans, gomisin A, gomisin N.

Introduction

The new and fantastic concepts, adaptogenic activity of Korean ginseng was firstly phrased by I.I Brekhman[1] in his review article which was appeared in "Annual Review of Pharmacology" to explain the traditional folkloric medical efficacy of Korean ginseng in modern pharmacological view.

This theory triggered the ginseng studies thereafter to be focussed to the chemical and pharmacological studies on the saponin components of Korean ginseng. However, when we look back to the Brekhman's review article, it will be clearly noticed that the adaptogenic activity was described not only for the Korean ginseng, but also for the *Acantopanax sessiliflorum*, *Eleuterococcus senticosus* and *Schizandra chinensis*. Brekhman suggested the ginsenosides (panaxosides), the dammarane triterpene glycosides as the effective components for *Panax ginseng*, and lignane glycosides for the other plants. It will be also noticeable that the three plants, *Panax ginseng*, *Eleutherococcus senticosus* and *Acanthopanax sessiliflorum* belonging to same Araliaceae family contain the same adaptogenic substances belonging to different chemical natures, dammarane triterpen glycosides and lignan glycosides (phenolic glycosides).

It is well known fact that the ginsenosides are specific components to *Panax ginseng* C.A. Meyer[2], while that the phenolic glycosides are not. It will be very reasonable to assume that the same adaptogenic activities from the plants belonging to same taxonomic family may arise from the effective components belonging to same chemical category.

On the other hand, We assumed that the underlining mechanism for the adaptogenic activity of the lignan glycosides may be the antioxidant activity of the lignans. Based on this assumption my previous studies[3-5] for Korean ginseng was targeted to the identification of antioxidant activity and to the isolation of effective components of Korean ginseng.

Fortunately, it was able to identify the strong antioxidant activity and to isolate such phenolic substances as maltol[3], salicylic acid[4], vanilic acid, caffeic acid and ferulic acid as the antioxidant components in my laboratory. Present paper is concerned with the isolation and identification of two lignans, gomisin-N and -A from the extract of Korean red ginseng which have already been described as the adaptogenic[1] and anti-hepatotoxic[6-7] components of *Schizandra chinensis*.

Isolation of lignans

Hexane extract of Korean Red Ginseng was chromatographed on silica-gel column by eluting with solvent-A, (Hexane: EtoAc, 20:1) to obtain five fractions. Fraction-2, which contains highly

nonpolar majour spot on TLC, was chromatographed again on silica-gel column by using solvent-B, (Hexane: EtoAc, 10:1) to obtain Fr.-2B which contains the majour spot. Fr.-2B was chromatographed again on silica-gel column using solvent-D, (Benzene: EtOH, 20:1) to obtain Fr.2-B-b which contains the majour spot in pure state. Comp.-I $C_{23}H_{28}O_6$, mp 108-10° was crystallized as prisms from same solvent.

Fraction-4, which contains majour spot on Rf. 0.3 on TLC using solvent-A, was chromatographed again on silica-gel column using solvent-C (Hexane: EtOAc, 6:1) to obtain Fr.-4-B. Fr.-4-B was rechromatographed on silica-gel column using solvent E(Benz: EtOH, 85:15) to obtain Fr.-4-B-b. Comp. II $C_{23}H_{28}O_7$, mp. 50-52° was crystallized as needles from same solvent upon concentration.

Identification of Compound I

Comp-I, $C_{27}H_{28}O_6$, [M]m/z 400 was shown to be aromatic compound due to its UV-absorption λ_{max} 252 and 280 nm and IR-absorptions on 1500-1600 cm^{-1}. Comp.-I shows 28 protons on PMR-spectra which were assigned as four methoxyl group, one methylene dioxy group, two aromatic singlet protons, two methyl group, and six aliphatic protons of methylene and methines in overlap.

The CMR spectra of Comp.-I shows 23 carbons which were assigned respectively as twelve aromatic carbons, two methine carbons, two methylene carbons, two methyl carbons, one methylene dioxy carbon and four methoxy carbons. Based on the above NMR data, as substituted lignan $(C_6\text{-}C_3)_2$ having four methoxy and one methylene dioxy substitu-

Table 1. ^{1}H-NMR of compound I from *Panax ginseng* and gomisin N

No. of proton	Comp. I ppm (300 MHz)	Gomisin N[10] ppm (100 MHz)
4-H	6.55 (1H, s)	6.55 (1H,s)
6-H_{AB}		2.57 (2H,m)
6-H_A, 9-H_B	2.56 (2H, m)	
7-H, 8-H	1.83 (2H, m)	1.83 (2H, m)
6-H_B	2.03 (1H, dd, J=13.5 & 1)	
9-H_A	2.27 (1H, dd, J=13.5 & 8)	2.27
9-H_B		2.03 (1H, dd, J=13.5 & 1)
11-H	6.48 (1H, s)	6.47 (1H, s)
17, 18-CH_3	0.73 (3H, d, J=7)	0.73 (3H, d, J=7)
	0.97 (3H, d, J=7)	0.97 (3H, d, J=7)
O-CH_2-O-	5.93 (2H, s)	5.93 (2H, s)
	3.55 (3H, s)	3.55 (3H, s)
OCH_3	3.83 (3H, s)	3.82 (3H, s)
	3.93 (6H, s)	3.93 (6H, s)

Table 2. ^{13}C-NMR data of compound I from *Panax ginseng* and gomisin N

No. of Carbon	Comp. I (75 MHz)	Gomisin N (15.04 MHz)[11]
1	151.5	151.7
2	139.9	140.2
3	151.5	151.6
4	110.7	110.7
5	134.0	134.1
6	39.0	39.2
7	33.7	33.6
8	40.7	40.8
9	35.4	35.6
10	137.8	137.8
11	102.9	102.9
12	148.6	148.7
13	134.5	134.6
14	141.0	141.1
15	121.2	121.4
16	123.2	123.4
17	21.5	21.5
18	12.7	12.9
O-CH_2-O-	100.7	100.7
C_2-OCH_3	61.0	61.0
C_1-OCH_3	60.5	60.5
C_{14}-OCH	59.6	59.6
C_3-OCH_3	55.8	55.9

tion on two aromatic-ring could be formulated. It is well known that various type of carbon skeletones has been known in the lignan series.

When we consider that the total number of aromatic substituents are eight in the Comp.-I, the shape of lignan carbon skeleton must be dibenzocyclooctane ring system which may be produced by the participation of two aromatic ring as a part of the cyclooctane ring.

We found by reference studies that the lignans from Schizandra chinesis[8] showed the same carbon skeletones expected for the Comp.-I. By further closs comparison of spectral data of Comp.-I with that of lignans from *Schizandra chinensis*, we could confirm that gomisin-N[9], a antihepatotoxic component of *Schizandra chinensis* and Comp.-I were identical substances. The PMR and CMR data of Comp. I and Gomisin-N[10] are shown on Table 1 and 2.

Table 3. ^{1}H-NMR data of compound II from *Panax ginseng* and gomisin A

No. of proton	Comp. II δ ppm (270 MHz)	gomisin A[12,13] δ ppm (60 MHz) (J = Hz)
6-H_A	2.37 (1H, d, J = 13.5)	2.50 (2H, ABq, J_{AB} = 15.5)
6-H_B	2.69 (1H, d, J = 13.5)	
7-OH	1.87 (1H, s)	1.85 (1H, s)
8-H	1.89 (1H, m)	1.80 (1H, m)
9-H_A	2.34 (1H, d, J = 14.0)	2.44 (2H, $ABX_{octet.}$
9-H_B	2.59 (1H, d, J = 14.0)	J_{AB} = 14, J_{AX} = 2, J_{BX} = 6)
17-CH_3	1.25 (3H, s)	0.80 (3H, d, J = 7)
18-CH_3	0.83 (3H, d, J = 7.2)	1.25 (3H, s)
O | CH_2 | O	5.96 (2H, s)	5.96 (2H, s)
	3.50 (3H, s)	3.50 (3H, s)
-OCH_3	3.80 (3H, s)	3.80 (3H, s)
	3.90 (6H, s)	3.90 (6H, s)
aromatic	6.48 (1H, s)	6.49 (1H, s)
proton	6.62 (1H, s)	6.62 (1H, s)

Identification of Compound II

The spectral data of Comp.-II, $C_{27}H_{28}O_7$, [M^+] *m/z* 416, are very similar to that of Comp.-I except that Comp.-II has one additional oxygen atom than Comp.-I by showing 16 mass unit higher shift on its molecular ion peak. The additional oxygen atom was identified as hydroxyl group based on its IR absorption on 3500 cm^{-1} and also by comparison of PMR-spectra with that of deutrated-PMR spectra of Comp.-II.

Based on the same logical treatment as Comp.-I, Comp.-II was identified as gomisin-A which has already been reported as the antihepatotoxic component of *Schizandra chinensis*[11]. The PMR and

Table 4. ^{13}C-NMR data of compound II from *Panax ginseng* and gomisin A

No. of Carbon	Comp. II (67.5 MHz)	gomisin A[12] (20 MHz)
1	152.1	152.1
2	140.8	140.8
3	152.3	152.3
4	110.4	110.4
5	132.1	132.1
6	40.6	40.6
7	71.7	71.1
8	42.1	42.1
9	33.8	33.8
10	132.5	132.5
11	105.9	105.9
12	147.9	147.9
13	135.0	135.0
14	141.3	141.3
15	121.9	121.9
16	124.2	124.2
17	30.1	15.8
18	15.8	30.1
O- | CH_2 | O-	100.8	100.8
C_2-OCH_3	61.0	61.0
C_1-OCH_3	60.6	60.6
C_{14}-OCH	59.6	59.6
C_3-OCH_3	55.8	55.0

CMR data of both Comp.-II and gomisin-A are tabulated in Table 3 and 4.

In conclusion, we isolated two lignan components Comp.-I and -II from the hexane extract of Korean red ginseng by repeated column chromatographic purifications and identified them as gomisun N and -A which had already been reported as antihepatotoxic components of *Schizandra chinensis*. These facts may sugest that a part of adaptogenic activity of *Panax ginseng* C.A. Meyer may arise from lignan components in ginseng as it does from the other Araliaceae plants.

Literature Cited

1. Brekman, I.I. and Dardynov, I.V.: New substances of Plant Origin Which increase Nonspecific Resistance, *Ann. Rev. Pharmacol.* **9**, 419 (1969).
2. Shibata, S., Tanaka, O., Ando, T., Sado, M., Tsushima, T. and Ohsawa, T.: Chemical Studies on Oriental Plant Drugs, XIV. *Chem. Pharm. Bull.* 595-600, 1966.
3. Han, B.H., Park, M.H., Woo, L.K., Woo, W.S. and Han, Y.N.: Antioxidant components of Korean ginseng, *Korean Biochem. J.*, **12**, 33 (1979).
4. Han, B.H., Park, M.H. and Han, Y.N.: Studies on the antioxidant components of Korean ginseng (III). Indentifation of phenolic acids. *Arch. of Pharm. Resch.*, **4**, 53 (1981).
5. Han, B.H., Park, M.H., Han, Y.N. and Shin, S.C.: Studies on the antioxidant components of Korean ginseng (IV): Antifatigue active components. *Yakhak Hoeji*, **28**, 231 (1984).
6. Maeda, S., Suto, K., Ikeya, Y. and Yoshhioka, I.: The constituents of *Schizandra chinensis* Baill XIII, *Yakugaku Zasshi*, **103**, 743 (1983).
7. Aburada, M.: Pharmacology and Biochemistry of *Schizandra chinensis* Baill, *Gendai Toyo Igaku*, **6**, 58 (1985).
8. Ikeya, Y. and Taguchi, H.: The constituents of *Schizandra chinensis* Baill I, The Structure of Gomisin A, B and C, *Chem. Pharm. Bull.*, **23**, 3296 (1975).
9. Ikeya, Y., Taguchi, H., Yoshioka, I. and Kobayashi, H.: The constituents of *Schizandra chinensis* Baill V, *Chem. Pharm. Bull.*, **27**, 2695 (1979).
10. Ikeya, Y., Taguchi, H., Yoshioka, I. and Kobayashi, H.: The constituents of *Schizandra chinensis* Baill, The structure of two new lignans, *Chem. Pharm. Bull.*, **26**, 3257 (1978).
11. Ikeya, Y., Taguchi, H., Sasaki, H., Nakajima, H. and Yoshioka, I.: The constituents of *Schizandra chinensis* Baill VI, Chem. Pharm. Bull., **28**, 2414 (1980).