The Types of Glycosides from Acanthopanax Species

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Plants belonging to Araliaceae family are much fewer in number compared with other plants of different families. Their distribution is also less wide-spread than others and much limited in their regional representation. Most of plants belonging to this family bear characteristic of being distributed in the northern part of Asia.

Among plants of this family which have been used as rare medicine in Asia since the ancient time, there is *Panax ginseng* as you all well know and remember. Over the past several thousand years, *Panax ginseng* has been known as a panacea because of its Medicinal efficacy in many areas. *Panax ginseng*, being known in oriental societies as having preciously omnipotent efficacy, can be best represented by *Araliaceae.*

Plants which have been widely used as crude drugs for remedial purposes in the Asian region, particularly in Korea, China and Japan, along with *Panax ginseng*, are those belonging to *Acanthopanax* species. These plants are distributed throughout the world in some ten varieties, however, they are heavily concentrated in the Northeastern Asian region. Medicinal plants deriving from *Acanthopanax* species are generally known and called as *Acanthopanacis cortex* (*Radicis*).

Korea is also one of important areas favorable to its distribution. Here, we see some ten varieties growing spontaneously, several of which are indigenous plants confined to Korea in their distribution. They are *Acanthopanax chiisanensis*, *Acanthopanax koreanum*, and so forth.

According to an increasing number of studies, initiated since the 1960's and up to date, on crude drugs of this line, although constituents contained and their pharmaco-biological activities exhibited are of various ranges, the most important efficacies of ethanol extracts of these varieties have been identified to be tonic function, anti-fatigue, anti-rheumatism,anti-diabetic, and going further to include stimulation effect of C^{13}-Leucine incoporation in biosynthesis of liver protein (C.S. Yook, *et al.* Bull. K.H. Pharm. Sc. Vol. 6, 75-77, (1978)). There is no uniformity in their constituents, however.

According to investigations the writer has conducted so far, Lignan glycoside is abundantly distributed in its root cortex, and the stem cortex retains the same pattern as that of the root constituents. However, glycosides obtained from folium of these plants reflect diversification not discernible in roots and stems.

Eleutherococcus senticosus Max. (*Acanthopanax senticosus*) (Nat. Pflanzenfam. III. Abt. 8, p. 50 (1894)).

As for this crude drug, Y.S. Ovodov, *et. al.* (Khim, prir. Soed., **1** (1), 3(1965)) extracted from its root cortex, Eleutheroside A (Daukosterol), Eleutheroside B (Syringin), Eleutheros ide B, (Isoflaxidin-α-galactoside), Eleutheroside C (ethyl-α-D-galactoside), and Eleutheroside D, E ((−)-Syringaresinol diglycoside). I.I. Brekhman, *et. al.* (Lloyidia **32**, 1, 46 (1969)) expla-

ined medicinal efficacy of respective, individual components through the clinical study covering widely their respective biological activities. From folium of this plant the following components are isolated: Eleutheroside I (Mubenin B), Eleutheroside K (Oleanolate), Eleutheroside L (Bioside consist of L-rhamnose and L-arabinose, res.), Eleuthertheroside M (Hedera saponin). When, the writer succeeded in isolating Eleutheroside E from the cortex of this crude drug (Table 1).

Acanthopanax sessiliflorum Seem.

Root constituents of this crude drug are identified by L.A. Elyakova, *et al.* (Izv. Akad. Nauk, USSR, ser. Khim. No. 3, 555(1965)) and C.S. Yook, *et. al.* (Kor. J. Pharmacog., 8 (1), 31 (1977)); its folium constituents by V.Plouvier, et al (Acad. Sc., Paris, ser. D 264(24), 2835 (1967)). Root constituents thus isolated and identified are Acanthoside A, Acanthoside B, Acan-

Table 1. The type of glycosides from *Eleutherococcus senticosus* Max.

Roots: Ovodov, Y.S., *et. al.: Khim. Prir. Soed.*, 1 (1), 3 (1965)
Eleutheroside A: Daukosterol
B: Syringin
B_1: Isoflaxidine-α-D-galactoside
C: Ethyl-α-D-galactoside
D, E: (-)-Syringaresinol diglucoside
Biological activity: Brekhman, I.I., *et. al.: Lloydia*, 32, 1, 46 (1969)
Leaves: Eleutheroside I: Mubenin B
K: Oleanolic acid
L: Bioside consists of L-rhamnose and L-arabinose residue.
M: Hederasaponin
Cortex: Hahn, D.R.: in press (1978)
Eleutheroside E

Table 2. The type of glycosides from *Acanthopanax sessiliflorum* Seem.

Roots; Elyakove, L.A., *et al.*: *Izv. Akad. Nauk USSR, Ser. Khim*, No. 3. 555 (1965)
Biological activity: Zverova, A.V.: *Materials of the 21st Sci., Fissession, Khabarovsk*, p. 122 (1964)

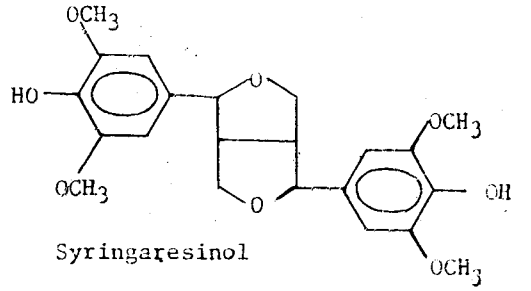
Acanthoside	m.p.	$[\alpha]_D^{20}$	Chemical structure
A	110	−42	lignan 2-(4,5-dimethoxy-3-hydroxy-3-hydroxyphenyl)-6-hydrophenyl-3,7-dioxabicyclo-(3.3.0) octane monoglycoside
B		−36	Syringaresinol-mono-β-D-glucopyranoside
C	119-128	−51.5	diglycoside of Acanthoside A
D	—	−33	Syringaresinol-di-β-D-glucopyranoside

leaves; Plouvier, V.: *C.R. Acad, Sci., Paris, Ser.* D, **264**(24), 2835 (1967)

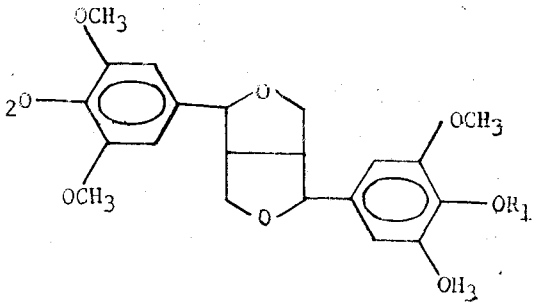
	m.p.	$[\alpha]_D^{20}$	m.wt.	chemical properties
Acanthopanaxoside (heteroside)	220~225°	+370	360	C;59.05%, H;8.03% rhamnose & glucose no OCH_3 no UV bands $IR_{\nu max}^{KBr}$ Cm^{-1}: 1685, 3420

Root Cortex; Yook, C.S., *et. al.: Kor. J. Pharmacog.*, 8(1), 31 (1977) Sesamin
Cortex; Ro, H.S., *et al., J. Pharm. Soc. Kor.*, 21(2), 81 (1977) Liriodendrin from *Acanthopanax sessiliflorum* Seem. *forma chungbunensis*

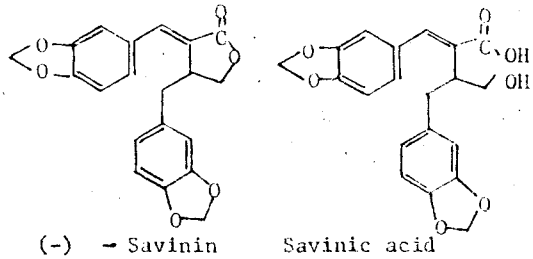
Fig. 1. The Chemical Structure of Glycosides from *Acanthopanax sessiliflorum* Seem. roots.



Syringaresinol



R_1=H, R_2=β-D-glucopyranoside; Acanthoside B
R_1=R_2= β-D-glucopyranoside; Acanthoside D
=Eleutheroside E



(-) - Savinin Savinic acid

m.p.=123° $[\alpha]_D^{20}$ −60° m.p.=146° $[\alpha]_D^{20}$ −90°

thoside C, Acanthoside D. All of these Acanthosides have been further identified to be Lignan glycosides. Furthermore, they are either same as or many being similar to, Radix cortex constituents of *Eleutherococcus senticosus*. Sesamin, lignan substance and several varieties of phytosterol were also isolated from Korean *Acanthopanax sessiliflorum* root cortex. And from its folium, acanthopanaxoside was isolated. Biological activity of Acanthoside A, B, C, and D was intensively investigated by A. V. Zverova (Materials of the 21st Sc. Fissession, Khabaravsk P. 22, (1964)). (Table 2 Fig. 1)

Acanthopanax sessiliflorum forma chungbuensis.

From the cortex of this crude drug, Liliodendrin has been isolated by H.S. Ro, *et. al.* (*J. Pharmaceutical Soc. of Korea*, **21** (2), 81(1970)) concomitant to the discovery of the compound that stimulates the incorporation of C^{14}-Leucine into mouse liver protein.

Eleutherococcus spinosus.

Coumarin from the root of this plant and Flavone from its folium were isolated by N.K. Melekhova (Maslo-Ehiv. Pram. **38** (1), 26(1972)). 40% ethanol extract of this plant is applied to cosmetics because of its estrogenic activity (Table 3).

Table 3. The type of glycosides from *Eleutherococcus spinosus*

Melekhova, N.I.: *Maslo-Zhir. Prom.*, 38 (1), 26 (1972) Russ.	
Roots: Coumarin	
Leaves: Flavones	
	40% EtOH extract: Cosmetics (estrogenic activity)

Acanthopanax gyphiloides.

From its root Saponin of m.p. 215-20°C $[\alpha]_D^{20}$ 22.1±2° (H_2O) was isolated by K. Amanmuradov, *et al.* (*Khim. prir. Soed.*, 2, 143(1965)). (Table 4)

Table 4. The type of glycosides from *Acanthopanax gypsophiloides*

Roots: Amanmuradov, K., *et. al.*: *Khim. Prirodn Soed.*, 2, 143 (1965)
Saponin; m.p.=215~20° $[\alpha]_D^{20}$ 22.1±2° (H_2O)

Acanthopanax sciadophylloides Franch. *et.* Sav.

From its folium, M. Yasue, *et al. Yakugaku Zasshi*, **88** (6), 738 (1968)) isolated Quercetin-3-gluco-7-rhamnoside, Hirsutrin and Kaempferol-7-rhamnoside (Table 5).

Table 5. The type of glycosides from *Acanthopanax sciadophylloides* Franch. *et.* Sav.

Leaves; Yassue, M., *et. al.: Yakugaku Zasshi*, 88 (6), 738 (1968), Japan
Quercetin-3-gluco-7-rhamnoside
Hirsutrin(isoquercetin)
Kaempferol-7-rhamnoside

Acanthopanax chiisanensis Nakai.

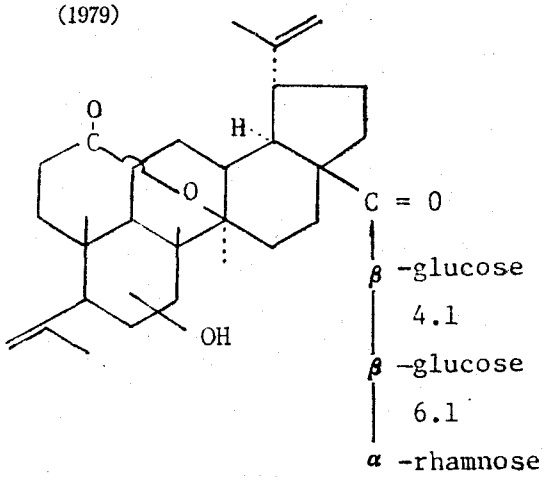
This plant is one of crude drug plants indigenous to Korea widely used for medicinal purposes. Chang isolated sesamin from the root of this plant. (S.H. Chang, *J. Kor. Chem. Soc.*, **14** (3), 277 (1970)). Also, Hahn isolated Eleutheroside E from its root.(D.R. Hahn, In Press (1978)). On the other hand, new glycosides were isolated from its folium, however, this discovery has not been recorded in reference to this date. But it is a kind of A-Seco-triterpenoid trioside and tentatively named chiisanoside. Identification of such chemical structure or the identification of sugar moiety is clarified by comparing the sugar moiety possessed by papirioside *L-vb* isolated from *Tetrapanax papyriferum* (Araliaceae) with C^{13} NMR. That of aglycon part by identifying the chromate oxidation of betulin and through the Beckmann rearrangement process. The writer plans to publish the identification of the chemical structure of this new type glycoside separately on a scientific journal in the immediate future (Table 6).

As quoted above, natural products contained in *Acanthopanax* species (including *Eleutherococcus* species) have been identified covering various varieties. However, what have been revealed to date as representative of such crude drugs and their medicinal efficacy can be safely embodied mainly in Lignan glycoside. The rest of glycosides also possess considerable efficacy, but they are far too short of distribution intensity or biological potency held by lignan glycosides. It has been discovered that the cortex constituents contain lignan glycosides as do the roots. In this context, it is quite rational, though it has been an empirical practice, that not only the roots but also the cortex of crude drugs have been widely used for medicinal purposes in Korea.

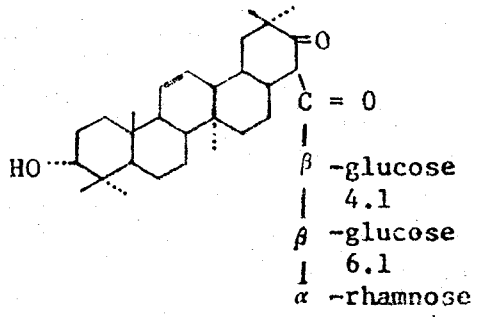
In the folium constituents, its distribution is not so consistent as that of its root counterpart,

Table 6. The type of glycosides from *Acanthopanax chiisanensis* Nakai

Roots: Chang, S.H.: *J. Kor. Chem. Soc.*, 14(3), 277 (1970) Sesamin
Hahn, D.R.: in press. (1978) Eleutheroside E.
Leaves: Hahn, D.R., Tanaka, O., *et al.*: in press (1979)



Kim, C.J.: dessertation (1979) biological activity cf. Papirioside L-V6 from *Tetrapanax papyriferum* (Araliaceae)



differing also in its chemical pattern from that of the root or cortex. Furthermore, since the new type of chiisanoside(tentatively designated is already isolated, if the intensive investigation into these Acanthopanax species plants widely distributed in Korea is continuously pursued, the clearer component pattern could be identified. In order to identify clearly the component pattern, further concentrated efforts should be, and will be, made in the future.