GLYCOSIDES OF ARALIACEAE

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Among medicinal plants, a special place is occupied by representatives of the unique family Araliaceae, which are distributed predominantly in the tropical regions and number about 60 genera, including 800 species. Only in maritime regions do the Araliaceae appear in the temperate zone, especially in the territory of the Soviet Far East, where two species of plants of this family, grouped into six genera, grow. In a number of species, the first place is taken by the genus Aralia, which is represented by small trees — Manchurian aralia (A. manshurica Rupr. et Maxim.) and Japanese aralia (A. elata (Miq.) Seem.), and by herbaceous plants — continental aralia (A. continentalis Kitagawa), udo (A. cordata Thunb.), and Schmidt's aralia (A. schmidtii Pojark). Other genera of the Araliaceae of the Soviet Far East include only one species each. To these belong the herbaceous plant ginseng (Panax ginseng C. A. Meyer), Kalopanax septemlobum (Thunb.) Koidz — a tree about 20 m high — and the bushes Echinopanax elatum Nakai, Acanthopanax sessiliflorum (Rupr. et Maxim.) Seem. and Eleutherococcus senticosus Rupr. et Maxim. The majority of the plants mentioned are widely distributed in the maritime regions of the Far East. In addition, eleutherococcus is found in the woods of southern Sakhalin and kalopanax in southern Sakhalin and the islands of Kunashir and Iturup. Some species of Aralia are known only in southern Sakhalin and some islands of the Kurile archipelago. Only one genus is characteristic for Europe — English ivy (Hedera helix L.) — which, however, in the systematic aspect is not a typical representative of the family Araliaceae.

Among the plants mentioned, a special position is occupied by ginseng — a unique relict plant. Thanks to their high biological activity, ginseng extracts have been used in folk medicine for about 5000 years. Ginseng root is a medicinal agent with a new type of action, increasing the organism's capacity for resistance or enhancing its capacity for work [1]. A biological evaluation of various fractions from ginseng root has shown that the maximum physiological activity is possessed by the glycosides [2], and it can therefore be stated that it is just these that form the active principles of this plant [2, 3]. However, the reserves of ginseng are very limited and attempts to find plants with a similar biological action to that of ginseng among the other Araliaceae are fully justified. In this respect, particular attention has been devoted to eleutherococcus. As a result of the pharmacological investigations performed, it has been concluded that eleutherococcus may act as the best and most promising substitute for ginseng [4]. It has been established that the biological activity of eleutherococcus preparations is due to the glycosides that they contain. Thus, according to I. V. Dardymov [4] the stimulant activity of the so-called "liquid" extract (the combined extractive substances) is 5600 SAU33* per 100 g of roots and 7150 SAU33 per gram of purified glycoside fraction from this plant. Since, according to V. F. Lapchik's estimate [5], the total concentration of glycosides in fractions of the liquid extract of eleutherococcus varies between 0.7 and 0.9%, it can be calculated that the stimulating activity of the combined glycosides from 100 g of roots must average 5800 SAU33; this is very close to the stimulating activity given above for the whole of the extractive substances. Nevertheless, a further chemical investigation has shown that eleutherococcus roots contain only phenolic glycosides [6] sharply differing in structure and properties from the triterpene glycosides of ginseng [3]. Consequently, it is still premature to regard eleutherococcus as a substitute for ginseng. The most promising method of increasing the availability of ginseng preparations may be the complete or partial synthesis of the glycosides that they contain and of their biologically active analogs, all the more since at the present time this task has, in principle, been solved [7].

*Stimulating activity units [4].
Although interest is presented by the influence of eleutherococcus extracts on free-radical processes in radiation damage [8], nevertheless if the pharmacological literature on eleutherococcus is analyzed [4], the impression is created that an extract of this plant affects the majority of processes occurring in the organism (protein-anabolyzing action, action on the carbohydrate metabolism, adaptogenic action, regulation of nervous activity, etc.) and can be used to treat extremely diverse diseases (diabetes, cancer, radiation disease, neurasthenia, atherosclerosis, etc.). Such a variety of biological actions is unwarranted and is probably explained by the weakness of the pharmacological methods used for their determination.

In spite of the large number of investigations devoted to the pharmacology of eleutherococcus [4], the question of the medicinal value of this plant still remains disputed.

There is information in the literature on the biological activity of other plants of the family Araliaceae, as well; in particular, acanthopanax [9], aralia [10], and ivy [11]. But, as in the case of eleutherococcus, none of these plants contains glycosides similar in structure to those of ginseng.

The systematic chemical investigation of the glycosides of Manchurian aralia [12], ginseng [13, 14], kalopanax [15], eleutherococcus [16], and acanthopanax [17] was begun in the sixties; only in the case of the glycosides of ivy had some information been obtained previously [18, 19]. In a structural study of the glycosides of the Araliaceae it was found that the majority of them belong to two classes of natural compounds - triterpene glycosides and phenolic glycosides, and these will be discussed below.

Of other glycosides, we must mention the presence of daucosterol in ginseng [3, 20], eleutherococcus [6], and acanthopanax [21]. Another feature of eleutherococcus is the presence in its roots of small amounts of ethyl α-D-galactopyranoside [6], isolated previously from lupin seeds [22].

**TRITERPENE GLYCOSIDES OF ARALIACEAE**

All the triterpene glycosides isolated up to the present time from plants of the family Araliaceae can be subdivided into two groups: glycosides of tetracyclic triterpenes of the dammarane series and glycosides of pentacyclic triterpenes. The first group includes only the glycosides of ginseng - panaxosides. They have not been found in any other plants of this family. The second group is composed of glycosides of oleanolic acid and of hederagenin; they are absent from ginseng but are present in other species of plants of the family Araliaceae.

**Panaxosides**

In 1962, G. B. Elyakov et al. [3, 13, 23] isolated from ginseng roots seven individual triterpene glycosides, called in order of increasing polarity panaxosides A–G. An analytical investigation of the glycoside fraction showed that the glycosides composing it form two groups: a less polar group comprising panaxosides A, B, and C (A series) [13, 23, 24] and a more polar group comprising panaxosides D, E, F, and G (F series) [25]. The partial separation of the glycoside fraction into these groups was first achieved by gel filtration on Sephadex [26]. Preparative partition and adsorption chromatography on alumina or silica gel enabled the individual glycosides of ginseng to be isolated and characterized [23, 25]. A feature of the panaxosides is the high lability of the glycone: under any conditions of hydrolysis a complex mixture of transformation products of the genin is formed. The main products of acid hydrolysis - panaxadiol [14] and panaxatriol [27] - are artefacts, and the native genins have not hitherto been obtained by direct methods. In order to deduce the structure of the native aglycones, the majority of the substances obtained on acid hydrolysis of the glycosides have been isolated [3, 14, 24, 28–32]. The determination of the structures of these compounds by the methods of nuclear magnetic resonance spectroscopy and mass spectrometry have shown their interrelationship and possible routes of their formation [3, 24–39]. The acid hydrolysis of the panaxosides of the A series under severe conditions [3, 24, 40] forms an equilibrium mixture of six triterpenoids of the dammarane series (A₁–A₆) with a predominance of the least polar compound A₆, the structure of which was established and which was given the name of panaxatriol (I) [27] (see structure on the following page.)

Under conditions of severe acid hydrolysis, the panaxosides of the F series [29, 36–38] form an equilibrium mixture of five triterpenes of the dammarane series (F₁–F₅) differing from compounds A₁–A₆. The predominant component is the most polar one, F₅ - panaxadiol (II) - the structure of which has been established by Japanese workers [33].