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PHYTOCHEMICAL PROFILE AND BIOMEDICAL POTENTIAL OF THE COMPOSITION OF GLEDITSIA TRIACANTHOS L. AND AILANTHUS ALTISSIMA (MILL.)

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Annotation

At present, in modern traditional medicine, the development of safe, multifunctional phytocompositions based on natural raw materials for the prevention and treatment of a number of diseases, including gynecological disorders, is a relevant issue. This review article presents a systematized description of the composition of both plants, as well as the technological and pharmacological advantages of preparing phytocombinations from them and their further application in the form of dietary supplements.

How to Cite

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Introduction. Ailanthus and Gleditsia are plants that are attracting increasing scientific interest, since they possess a rich phytochemical composition and are also invasive woody species. Ailanthus is of particular importance: in traditional medical systems, the bark of Ailanthus, known as “Chunpi,” has been used for various conditions, while a modern systematic review summarizes data on its phytochemistry, pharmacology, pharmacokinetics, quality control, and toxicology [1]. For Gleditsia, in addition to ethnopharmacological indications, experimental studies have accumulated on the composition of fruit/pod extracts and their anti-inflammatory, analgesic, antihyperglycemic, and gastroprotective activities in preclinical models.

Phytochemical Profile of Ailanthus. Representatives of the genus Ailanthus are characterized by a rich content of alkaloids, terpenoids, sterols, flavonoids, and other groups of compounds associated with various types of biological activity [2]. At the same time, the bark of A. altissima occupies a central place in both traditional and modern phytochemical analysis: reviews on the bark systematize information on its multicomponent composition, pharmacological effects, approaches to quality control, and toxicology [1].

Main Part. In a GC–MS study, that is, gas chromatography–mass spectrometry analysis, dozens of biologically active compounds were identified in the leaves and fruits of A. altissima: 35 compounds in the leaves and 41 in the fruits [3]. In the leaves, phytol, approximately 21.15%, hexadecanoic acid, approximately 8.53%, and other compounds were detected in considerable amounts. In the fruits, α-tocopherol, approximately 13.35%, vaccenic acid, approximately 11.42%, and other compounds were identified [3]. The authors emphasize the antioxidant and other effects associated with the detected components and discuss the prospects for using this raw material in the field [3].

Studies of the chemical composition and antibacterial activity of the methanolic leaf extract have described pronounced antioxidant properties of Ailanthus altissima [4]. These data are important for selecting

directions of application, particularly for external dosage forms, where the antimicrobial component is often of key importance.

One of the important advantages of the plant is Ailanthus oil, which is rich in unsaturated fatty acids. A study of oil samples showed the presence of 11 fatty acids, with linoleic acid, approximately 48.6%, and oleic acid, approximately 44.8%, being the main ones, while the proportion of saturated fatty acids, such as palmitic and stearic acids, was below 3% [5]. The authors also describe lipid-soluble components, such as β-sitosterol and γ-tocopherol, and report in vitro DNA-protective activity, as well as a weak antiproliferative effect on certain tumor cell lines, with no cytotoxicity against BALB/c 3T3 cells under experimental conditions [5]. For a phytocomposition, this opens the possibility of forming two-phase systems: a polyphenol-saponin hydrophilic phase and a lipid phase as a carrier and a component supporting the barrier function of the skin and mucous membranes.

Another component characteristic of the Ailanthus plant is the quassinoid “ailanthone,” for which preclinical data on antitumor effects and mechanistic aspects have been reported. For example, in a study on colorectal cancer, effects on the cell cycle, apoptosis, and the PI3K/AKT signaling pathway were described in cellular models [6]. There are also studies on antiproliferative activity in certain cell lines, including breast cancer cell lines [7], as well as data from gastric cancer models, including in vitro/in vivo and PDX studies [8].

Phytochemical Profile of Gleditsia. Gleditsia triacanthos is a plant belonging to the legume family. Analysis of the methanolic extract of G. triacanthos fruits, or pods, showed a pronounced presence of polyphenolic groups and saponins, also referred to as saponosides. The study reported approximate values of total polyphenols at 14.73 ± 2.51 mg GAE/g, flavonoids at 9.65 ± 0.52 mg QE/g, and condensed tannins at 6.95 ± 2.64 mg CE/g [9].

In the same study, an in vivo model of dextran-induced inflammation demonstrated a reduction in the inflammatory response. The degree of inflammation inhibition varied approximately within the range of 6.56–10.76%, depending on the observation time points and experimental conditions [9]. Although these percentages are not considered high by the standards of potent anti-inflammatory agents, they are significant as evidence of an effect in the crude extract.

In a study involving UPLC-ESI/MS/MS profiling of the n-butanol fraction of the methanolic extract of G. triacanthos fruits, phenolic acids, flavonoids, and saponins were identified, and antihyperglycemic and antiulcer, that is, gastroprotective, effects were demonstrated in rats [10]. The authors evaluated both the complete methanolic extract and the n-butanol fraction at doses of 70/140/280 mg/kg, noting a decrease in elevated glucose levels, improvement in a number of lipid parameters, and a reduction in the number and severity of ethanol-induced gastric lesions [10]. For a combination with Ailanthus, this provides an additional property for enhancing metabolic effects alongside the antibacterial effect of Ailanthus.

In a study of the analgesic activity of the methanolic fruit extract and its saponin-containing fraction, both peripheral and central components of the analgesic effect were demonstrated in standard preclinical tests. Moreover, the saponin-containing fraction showed more pronounced protective effects under several conditions compared with the reference drug, Indocin/indomethacin [11]. Saponins in Gleditsia may potentially serve not only as a “chemical marker” but also as a functional driver of activity, which is important for mixture development and for selecting the fraction used in standardization.

There are publications describing the presence of flavonoid compounds in the leaves of G. triacanthos, as well as the results of in vitro antioxidant and cytotoxic activity tests [12].

Advantages of the Combination of Ailanthus and Gleditsia

Taken together, Ailanthus and Gleditsia overlap in their polyphenol-flavonoid component, but differ in their “leading” classes of biologically active compounds and in the most consistently reproducible directions of activity:

A. altissima: a multicomponent profile, including quassinoids [1,2]; confirmed GC–MS profiling of leaves and fruits [3]; antibacterial activity of leaf extracts [4]; a seed lipid platform, namely oil dominated by linoleic and oleic acids [5]; and a number of mechanistic studies on ailanthone [6–8].

G. triacanthos: polyphenols and saponins as the dominant “axis” [9,10]; anti-inflammatory effect in an inflammation model [9]; antihyperglycemic and gastroprotective activity of the extract/fraction combined with chemical profiling [10]; and analgesic activity enhanced in the saponin-containing fraction [11].

Antioxidant–anti-inflammatory interaction: polyphenols and flavonoids of both plants provide a general antioxidant background, against which the anti-inflammatory effects of Gleditsia, demonstrated in vivo, and those of Ailanthus, according to the totality of pharmacological observations, may become more pronounced in the composition when the extraction method is optimally selected [2,9].

Antimicrobial component and anti-inflammatory support: the presence of antibacterial activity in Ailanthus extracts [4], combined with the anti-inflammatory profile of Gleditsia [9], conceptually corresponds to the objectives of external preparations for the skin and mucous membranes, where a simultaneous reduction in microbial load and local inflammation is required.

Cytoprotective, gastroprotective, and metabolic block: the antiulcer and antihyperglycemic effects of Gleditsia fractions [10] may be complemented by the general antioxidant profile of Ailanthus [3,5]. However, oral dosage forms require substantially stricter safety requirements.

Saponins are amphiphilic glycosides with pronounced surface-active properties. In review studies, they are considered natural surfactants and a promising basis for formulations [13]. In addition, it is emphasized that saponins are in demand as natural additives in the food and pharmaceutical industries. However, they may also produce adverse effects, such as cytotoxicity at certain structures or doses, which requires appropriate control [14].

Compositions often make it possible to reduce the proportion of each component when a cumulative effect is achieved through different mechanisms. In the present case, this is particularly important, since there are signals regarding possible adverse effects of Ailanthus in humans, as well as questions concerning the toxicology and bioavailability of individual active components, such as ailanthone [2]. With the approach of “minimally effective proportions” and marker-based standardization, it is theoretically possible to reduce the risk of irritation and adverse reactions without abandoning the beneficial pharmacological effects.

Taking into account the antibacterial activity of Ailanthus leaf extracts [4] and the anti-inflammatory and saponin-related profile of Gleditsia [9,11], the most justified direction is the development of external preparations, such as gels, creams, or lotions. These may include a hydroalcoholic or alcoholic extract of G. triacanthos fruits, or pods, yielding a saponin-polyphenol fraction [9–11], together with a phenolic extract of A. altissima leaves/fruits or a standardized leaf extract with confirmed antibacterial activity [3,4]. Optionally, the lipid phase, represented by A. altissima seed oil, may be used as a carrier of lipophilic components and as a component supporting the barrier function, provided that stability and compatibility testing is mandatory [5].

Despite the interesting data on the antihyperglycemic and gastroprotective activity of Gleditsia fractions [10], the transfer of these results into a product or therapeutic application requires standardization of composition and reproducibility of dosage, toxicological profiling, and consideration of possible adverse effects of saponins [14] and signal risks associated with Ailanthus [2].

Our studies on the development of a phytomixture based on extracts of Ailanthus and Gleditsia plants showed that antioxidant activity was relatively high at a quantitative ratio of 1:1 [17]. This finding is substantiated in Table 1 below.

Table 1. Time-dependent inhibition of reactive oxygen species by aqueous extracts of a mixture of Ailanthus and Gleditsia plants.

Analizing extract	AF, %		
	ailanthus 1: gleditsia 1 (D_2)	ailanthus 1: gleditsia 3 (D_2)	ailanthus 3 : gleditsia 1 (D_2)
1-minute	15,42%	16,49%	17,55%
3-minute	13,43%	16,23%	14,06%

5-minute	6,21%	6,47%	6,47%
10-minute	-3,48%	-1,96%	-4,58%
Average	7,89%	7,44%	6,7%

Discussion. Phytochemical and preclinical data allow Ailanthus altissima and Gleditsia triacanthos to be considered a complementary pair for the development of a standardized phytocomposition. Ailanthus provides a diversity of classes of biologically active compounds, including phenolic constituents, components with antibacterial activity, and a promising seed lipid platform [1–5]. In contrast, Gleditsia contributes a saponin–polyphenol profile associated with anti-inflammatory, analgesic, antihyperglycemic, and gastroprotective potential [9–11].

The most justified applied direction for the initial stage of research is the development of topical dosage forms such as gels, creams, and lotions. In this case, the advantages of the combination are manifested simultaneously in pharmacodynamics (combined antimicrobial and anti-inflammatory effects) and in formulation technology, where saponins act as natural surface-active agents and functional excipients [4,9,13,15].

Conclusion. Summarizing the studies devoted to the analysis of the composition and biological properties of various extracts obtained from Ailanthus and Gleditsia plants, it can be concluded that these plants possess a rich phytochemical composition containing numerous biologically active compounds that are important for human health. Therefore, the development of new biologically active dietary supplements based on Ailanthus and Gleditsia appears to be a promising and effective approach. Furthermore, our own studies confirm the pronounced antioxidant properties of these plant-derived compositions.

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