# BIOLOGICAL ACTIVITY OF IRIDOIDS

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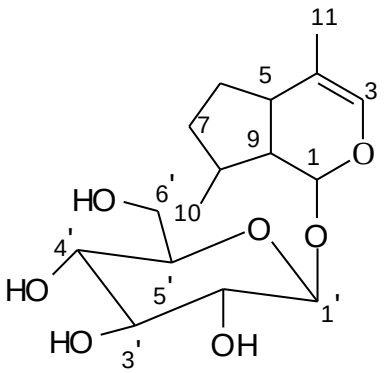
Among the various low molecular weight biologically active substances synthesized by plants, iridoids occupy a prominent place.

Iridoids are widely distributed in the plant world. They are found in all organs of plants of the dicotyledonous class - *Dicotyledones.* Of the 325 families of this class, iridoid glycosides were found only in 33 representatives. The families of *Scrophulariaceae, Rubiaceae, Lamiaceae, Verbenaceae* and *Bignoniaceae* are the richest in iridoid glycosides. However, taking into account the number of genera and species in families, monotypic families *Adoxaceae, Eucommiaceae, Daphniphylaceae*, as well as small families *Globulariaceae, Fouquieraceae* and *Plantaginaceae* should be ranked first in terms of the number of iridoids.

Iridoids are a group of monoterpene compounds of plant origin containing in their structure a cyclopentanepyran skeleton (1) [1].



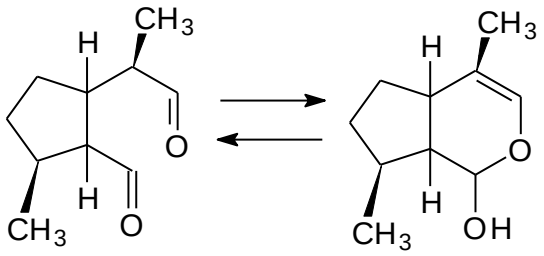

1

Iridoids mainly by chemical structure (1) have two cyclic nuclei: one of them is a-pyran, and the second is cyclopentane. In position 1, as a rule, b-glucose is attached, between the C-3-C-4 atoms there is a double bond that forms a typical enol ether. The double bond can also often be present on the cyclopentane ring.

Iridoids were first isolated in the middle of the 19th century, but only in 1958 O. Halpern and others proposed the basic structure of iridoids in their study. Intensive study of iridoid glycosides began in the second half of the 20th century.

Iridoid glycosides are glycosides, the aglycone part of which has an iridoid nature. The name "iridoidal glycosides" was proposed in 1963 by Briggs and is based

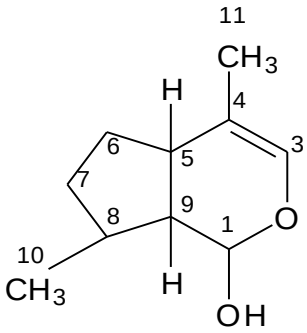
on the structural and possible biogenetic relationship of the aglycone part of these glycosides with the iridodial (2) substance isolated for the first time from the ants *Iridomyrmex detectus*.



2

Isolation and structural studies of iridoid glycosides were hampered by their sensitivity to acids and the instability of aglycones. However, intensive studies of plant iridoids began after 1946 with the classical works of P. Carrera and N. Schmidt on aucubin.

In 1982, Weinges proposed to accept as the basis for the chemical name of iridoid glycosides the heterocyclic system (3), which he called iridan, retaining in it the skeletal numbering adopted for the hemiacetal form of iridodial (2), and for all iridoid glycosides.



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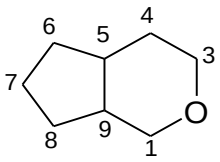

3

Iridoid glycosides are currently considered as promising for the search for new drugs of the class of natural compounds [2].

A pharmacological study of iridoids isolated from various plants confirms that these compounds have a fairly wide spectrum of action. Their presence of a number of valuable biological properties - antitumor, antimicrobial and other activities make their further study very promising from a practical point of view.

It was found that in most cases the carrier of biological activity is the aglycone part of the molecule, and as a rule, the aglycone is superior in its activity to the glycoside.

Tests of a number of iridoid glycosides have shown that their antimicrobial activity is observed only in the presence of b-glucosidase. This unequivocally points

to aglycones as the active principle. It was assumed that the antimicrobial activity of aglycones is due to their reaction in the aldehyde form with the enzymes of microorganisms. Aucubin aglycone exhibits the highest antimicrobial activity.

Protoplumericin is considered as an iridoid source for the production of plumericin, which has anti-leukemic activity. The same activity has penstemide.

In Chinese medicine, for the treatment of certain types of tumors, the aerial part of diffuse hediotis - *Hedyiotis diffusa Willd.* is used. (family *Rubiaceae*), containing in addition to other biologically active compounds and asperuloside. Plumericin - which also has antimicrobial activity, is used for various skin diseases.

The drug stachiridine is a mixture of iridoid glycosides: harpagide, acetylharpagide, harpagoside and ayugol, exhibits pronounced choleretic activity and is recommended for the treatment of diseases of the liver and biliary tract. Pharmacological studies of the amount of iridoids of the drug "Irichol" (harpagid and acetylharpagid), isolated from the plant Ajuga turkestanica, showed that it has a hepatoprotective and choleretic effect.

Japanese scientists have patented a number of choleretic drugs based on iridoid glycosides.

Valopatriates are used as a sedative for autonomic disorders. A mixture of iridoid glycosides - odontoside and aucubin, has a pronounced property to increase the body's endurance to combined stress and increase physical performance.

Aucubin has a stimulating effect on the excretion of uric acid from the kidneys, and is also used in the case of dermatomycosis, asthma and peptic ulcer of the digestive tract.

The amount of iridoids of the viburnum bark has a pronounced hemostatic effect.

I. Suzuki established the diuretic property of *Catalpa* fruits, which is due to the presence of iridoid compounds in them: catalposide and catalpol.

Secoiridoid is a gentiopicroside isolated from various plant species of the genus *Gentiana L.*, which has antipyretic, analgesic and choleretic effects. In addition, anti-inflammatory action was revealed for gentiopicroside.

Many iridoids are characterized by laxative activity. It was found that for the maximum manifestation of this activity, the presence of a carbomethoxyl group at the C-4 of the aglycone part of the molecule is necessary. The introduction of a hydroxyl group at position C-6 leads to a decrease in activity.

A number of iridoid glycosides exhibit pronounced antifeedant activity, for example, ipolamid, in relation to some types of caterpillars, catalpol iridoids - in relation to insects leading a nocturnal lifestyle, and the toxicity of iridoid glycosides for arthropods is also known.

Experiments have shown that iridoid glycosides are not toxic. Their administration to mice at doses of 1000-3000 mg/kg did not cause any significant

changes in the behavior of animals and their death. In experiments on cats, it was found that the compounds do not have a noticeable effect on blood pressure and respiration. The main effect of iridoids in the body is realized at the metabolic level. They improve the indicators of carbohydrate and lipid metabolism in the liver, show a slight antioxidant effect. As a result, the process of bile secretion increases, the synthesis of bile acids increases, and the cholesterol-excreting function of the liver improves. This is especially clear when the drugs are administered to rats with CCl4-induced hepatitis (introduced as a 50% oil solution, 0.5 ml/100 g for four days, subcutaneously). Thus, in particular, under the influence of one of the most active compounds of this series, harpagide acetate, administered at a dose of 50 mg/kg (per os), after 3 days, normalization of bile secretion and the content of glycogen, lactic and pyruvic acids, as well as phospholipids and triglycerides. In the blood serum, by this time, the activity of alanine aspartate aminotransferases decreased to the level of the intact control (in the control, these parameters normalized only on the 14th day).

Under the action of harpagide acetate, the normalization of the detoxifying function of the liver and the complete restoration of the bile secretion process with the restoration of its chemical composition also occurred 1.5-2 times faster. The hepatoprotective effect of harpagid acetate was more pronounced than the corresponding effect of the known drug Liv-52.

In a series of experiments, it was found for the first time that harpagid and 8-O-acetylharpagid have the ability to enhance the process of milk secretion in lactating animals.

These agents proved to be quite effective in stimulating erythropoiesis. This was found not only in normal animals, but also in animals with hemotoxic phenylhydrazine anemia. In the latter case, iridoids accelerated red blood regeneration by 1.23 times [3].

The biological activity of aucubin was studied in terms of preventing stress reactions and the effect on bile secretory activity. The administration of aucubin to rats, in which the stress reaction was induced by immobilization in the supine position for 16 hours, showed that iridoid prevents an increase in the relative mass of the adrenal glands by 24%, which corresponds to the level of intact ones, and prevents a drop in the content of ascorbic acid and cholesterol in the adrenal glands. The weight of the thymus in the control decreased by 40.2%, but this was not observed in the experimental group. Aukubin prevented the appearance of ulcers in the gastric mucosa. The entire complex of data obtained reliably confirms that aucubin increases the adaptive capacity of the body. Significantly increases endurance to stress, removing the stress reaction, which allows it to be classified as an adaptogenic agent. Along with this, the study of bile secretory activity revealed the presence of choleretic properties inherent in aucubin. On average, under the action of aucubin, the intensity of secretion

increased by 12-15%, and the total amount of bile for 4 hours of the experiment - by 12.4%.

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