A brief review on biological and chemical activities of flavonoids in plants

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Abstract. Flavonoids are a group of plant pigments, the combination of which determines one or another color of flowers and fruits. In plants, flavonoid dyes play the role of light filters that protect tissues from negative influences. Flavonoids are widely distributed secondary metabolites with different metabolic functions in plants. Flavonoids - a group of polyphenolic compounds C6-C3-C6 -series that are synthesized exclusively in higher plants. This review considers four main functions of flavonoids in the plant body. These compounds take an active part in redox processes, in plant reproduction they play the role of bright attractants for insects and animals. An important function of flavonoids is to protect plants from external adverse abiotic and biotic factors. They are signal molecules in auxin metabolism, as well as at various stages of the plant symbiosis with mycorrhizal fungi and nitrogen-fixing bacteria.

1. Introduction

The term "flavonoid" was proposed in 1949 by the English scientist Geissman more than a century after the isolation of the first flavonoid quercetin (Quercus) not only for flavones - yellow substances, but also for other compounds of a flavonoid nature that have a different color - white or colorless (flavanones), orange (aurons, chalcones), red, raspberry, blue (anthocyanins). Flavonoids are the most numerous group of water-soluble natural phenolic compounds, heterocyclic oxygen-containing compounds predominantly yellow, orange, red. They belong to the C6-C3-C6 series of compounds - their molecules have two benzene nuclei connected to each other by a three-carbon fragment [1, 2, 3]. Most flavonoids can be thought of as derivatives of a flavone or a flavan.

Flavonoids are natural heteroaromatic compounds that are products of the secondary metabolism of plant tissues [4, 5]. It is obvious that this class of biologically active substances, numbering up to 10,000 registered representatives, is distinguished by great structural diversity and is of high value as a subject of study.

The interest of scientists of various specialties in the study of flavonoids is caused by the variety of biological and pharmacological effects that these compounds exhibit in humans and animals. The biological effect of flavonoids is explained by the regulation of redox processes, the stabilization of cell membranes, and the modulation of the activity of enzymes and receptors. To date, the spectrum of action of these compounds in the human body has been determined: capillary-strengthening, antispasmodic, anti-stress, anti-inflammatory, antifungal, antibacterial, antiviral, antiulcer, antitoxic, antiallergic, antiatherosclerotic, antiarrhythmic, antihypertensive, immunomodulatory, anticarcinogenic, nephroprotective, estrogen-like, hepatoprotective [6, 7, 8]. The established properties of flavonoids open up wide opportunities for their use as medicines that do not have serious side effects, unlike synthetic analogues.

Along with this, the issue of the functions of flavonoids in plants, the direct site of their biosynthesis, is less covered in modern literature, which, in our opinion, is a gap in the general biological understanding of their role. In this regard, we analyzed the available information on the physiological role of flavonoids in the plant body. Flavonoids are active

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metabolites of the plant cell. The important biological role of these compounds is evidenced by the nature of their distribution in the plant. Most flavonoids are found in actively functioning organs: leaves, flowers, fruits (color, aroma), seedlings, as well as in integumentary tissues that perform protective functions. Different organs and tissues differ not only in quantity, but also in the qualitative composition of flavonoids [9, 10, 11].
Relatively recently, it was found that flavonoids also affect the signaling processes occurring in living systems due to specific interaction with proteins that perform regulatory functions. Numerous data have been accumulated on the effect of these compounds with other protein and non-protein structures, which can lead to a change in the functional state of cells and the whole organism as a whole [12, 13, 14]. Despite the fact that now the redox properties of phenolic compounds are not given so much importance, their comprehensive study still remains an important task.
In addition, numerous studies confirm that flavonoids act as effective phytoalexins, exhibiting a broad spectrum of antibacterial and antifungal activity. A correlation has been established between their content in plants and plant resistance to fungal diseases and some pests [15, 16]. The appearance of these compounds in plants in response to the action of parasitic fungi of cultivated plants and the inhibition of the growth of fungal mycelium is considered as a protective reaction. Flavonoids with antimicrobial activity are found in large quantities in the seed coat.
In this review paper, biological and chemical features of the flavonoids, as well as flavonoids in medicinal plants will be highlighted and discussed.

2. Biology of flavonoids

The biological role of flavonoids lies in their participation in redox processes occurring in plants. They perform protective functions, protecting plants from various adverse environmental influences. Flavonoids play an important role in plant metabolism and are very widely distributed in higher plants. Many flavonoids are pigments that give various colors to plant tissues [17, 18]. So, anthocyanins determine the red, blue, purple color of flowers, and flavones, flavonols, aurones, chalcones - yellow and orange [19].
Flavonoids take part in photosynthesis, formation of lignin and suberin, as protective agents in plant pathogenesis. Flavonoids diversity is explained by the fact that most of them are present in plants in the form of compounds with sugars - glycosides. Sugar residues can be represented by monosaccharides - glucose, galactose, xylose, etc., as well as various di-, tri- and tetrasaccharides [20, 21]. Molecules of hydroxycinnamic and hydroxybenzoic acids are often attached to sugar residues. Catechins and leucoanthocyanins are colorless. They are the ancestors of condensed tannins.
The natural functions of flavonoids have been little studied. It was assumed that due to the ability to absorb ultraviolet radiation (330-350 nm) and part of visible light (520-560 nm), they protect plant tissues from excess radiation. The color of flower petals helps insects find the right plants and thus promote pollination. Animals are not able to synthesize compounds of the flavonoid group, and the flavones present in the wings of some butterflies enter their body with food.

2.1 Important Sources of Plant Flavonoids

Flavonoids are widely distributed in the plant world. Higher plants are especially rich in flavonoids. There are flavonoids in various organs, but more often in the aboveground: flowers, leaves, fruits [22, 23]. Young flowers, unripe fruits are the richest in them. They are localized in the cell sap in a dissolved form [24]. The content of flavonoids in plants varies: an average of 0.5-5%, sometimes reaches 20% (in the flowers of Japanese Sophora).
In many fruits and berries, bioflavonoids are more or less evenly distributed in the skin and pulp. Therefore, plum, cherry, blueberry have an even color. In contrast, the fruits of some other plants contain flavonoids mainly in the skin and, to a lesser extent, in the pulp. And in apples, for example, they are present only in the skin.
Good sources of flavonoids are citrus peel, other fruits and berries, onions, green tea, red wines, sea buckthorn and dark chocolate (70% cocoa and above). Cheap and effective bioconcentrates of flavonoids are obtained from wine and juice production wastes (grape pomace) [25, 26].
Let us consider in more detail the representatives of the legume family.
Astragalus falcatus L. Astragalus falcatus L. is a perennial herbaceous plant of the legume family - Fabaceae (Leguminosae) 45-100 cm high. The stems are erect, finely furrowed, covered with pressed black and white hairs. Leaves 10-16 cm long, with short petioles and a white fluffy axis. Leaflets 9-18-paired, oblong, 10-20 cm long, leaflets at the apex, rounded with a short apex, glabrous above, covered with small hairs below Flowers drooping, whitish, with a slight purple tint, collected in oblong loose multi-flowered racemes 10- 12 cm. The calyx is bell-shaped, 5 mm

long. The corolla is whitish with a slight purple tint. The fruits are sessile, up to 22 mm long and 4 mm wide, linear-oblong, sickle-curved, keeled, pointed into a straight awl-shaped spout (Fig. 1). Blossoms in June-July, fruits ripen in late July-August. In the year of sowing, it forms only one large rosette of leaves and does not reach the fruiting phase. In culture in clean crops it lasts up to 10 years.

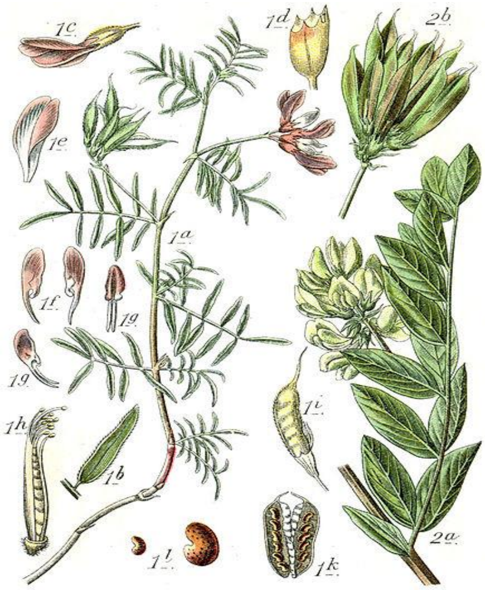

Fig. 1. *Astragalus falcatus L.* - perennial herbaceous plant of the legume family - Fabaceae (Leguminosae)

Ononis arvensis L. Ononis arvensis L. is a perennial herbaceous plant of the legume family - Fabaceae (Leguminosae). The root is powerful, taproot, woody, whitish in fracture, up to 200 cm long, slightly branched, passing at the top into a short multi-headed rhizome. Stems numerous, straight, rarely ascending, pubescent with simple and glandular hairs, woody at the base, usually purple-reddish, with or without spines, up to 80 cm in height. The leaves are alternate, petiolate, the lower and middle ones are trifoliate, the upper ones are simple. Leaflets are oval or oblong-elliptical, sharp-toothed, glandular-pubescent on both sides. Flowers numerous, bisexual, irregular papilionaceous; corolla pinkish-white, pale pink or almost white, longer than calyx. The flowers are located 2 in the axils of the leaves, forming rather dense spike-shaped inflorescences at the ends of the stems and side branches. The fruit is a broadly ovoid, glandular-pubescent, two- or four-seeded bean about 7 mm. length. Seeds with small tuberculate surface, light brown. The whole plant has a peculiar smell (Fig. 2). It blooms in June-August, the fruits ripen from August to frost.

Fig. 2. *Ononis arvensis L*. is a perennial herbaceous plant of the legume family - Fabaceae (Leguminosae)

Sophora japonica L. Sophora japonica L. is a deciduous tree of the legume family - Fabaceae (Leguminosae), reaching a height of 25 m, with a wide crown. The bark of old trunks is dark gray, with deep cracks, young branches and shoots are greenish-gray, short-pubescent. Leaves pinnate, 11-25 cm long, with 11-15 pairs of leaflets; leaflets ovate or oval-lanceolate, pointed, dark green above, gray-white below, due to the presence of many hairs, the petiole of the compound leaf is strongly thickened at the base. The flowers are irregular, 1-1.5 cm long, fragrant, in large loose terminal panicles, reaching a length of 20-30 cm. Corolla moth type, yellowish-white. The fruits are juicy beans, fleshy, naked, indehiscent, 6-10 cm long and 1 cm wide, flattened-cylindrical, bead-shaped with deep constrictions between the seeds, filled with yellowish-green sticky juice, not falling for the winter. Each bean contains 2-6 oval, smooth, dark brown seeds, similar to beans, but smaller. Seeds usually do not ripen. Unripe beans are green, fully mature - reddish. Known weeping cultural form S.japonica, which is convenient to collect buds and fruits. From other trees of the legume family, Japanese Sophora is well distinguished by its unswollen beans and the absence of thorns (Fig. 3). Blooms in late summer, in July-August; fruits ripen in September-October and stay on the tree all winter.

Fig. 3. *Sophora japonica L* - an attractive medium to tall tree with a rounded canopy

3. Chemistry of flavonoids

Chemical properties are due to the peculiarity of the structure of flavonoids: the presence of aromatic, pyran or pyrone rings, functional groups.

a) Glycosides undergo enzymatic and acidic hydrolysis to aglycones and sugars. O-glycosides are hydrolyzed more or less readily by the action of dilute mineral acids and enzymes. Sglycosides are hardly split only under severe conditions under the action of strong acids (concentrated hydrochloric or acetic acids) or their mixtures (Kiliani mixture) with prolonged heating.
b) Thanks to rings A and B, flavonoids are capable of:
   1) form complex compounds with metal salts (iron, aluminum, zirconium). With iron salts - depending on the number of hydroxyl groups from green and blue to brown; with aluminum salts - yellow in color, with yellow-green fluorescence;
   2) enter into an azo coupling reaction with diazonium salts to form azo dyes.
c) Flavonoids containing the pyrone cycle (flavones and flavonols) are capable of:
   1) be reduced in an acidic environment by atomic (free) hydrogen, obtained as a result of the reaction of the acid with metallic magnesium or zinc, to anthocyanidins (Shinoda test, or cyanidin test);
   2) dissolve in alkalis with the formation of water-soluble phenolates.
d) Flavonoids containing the pyran cycle (catechins, leucoanthocyanidins) can be easily oxidized to flavones and flavonol derivatives.
e) Flavonoids, when fused under harsh conditions with alkali, decompose into their constituent parts, which is used to establish their structure.

Physical and chemical properties are used in the analysis of raw materials for authenticity and good quality.

Flavonoids are secondary metabolites of higher plants, however, compared with other secondary metabolites, they are involved in many processes of plant growth and development, they are chemical messengers of cell signaling [27].

Flavonoids play an important role in plant reproduction in the development and accumulation of pollen, and their content also determines the color of flowers, fruits, seeds of plants. But the most prominent role of flavanoids is their function of protection against various adverse factors for plants, such as temperature fluctuations, the influence of ultraviolet rays, the attack of viruses, bacteria, and so on.

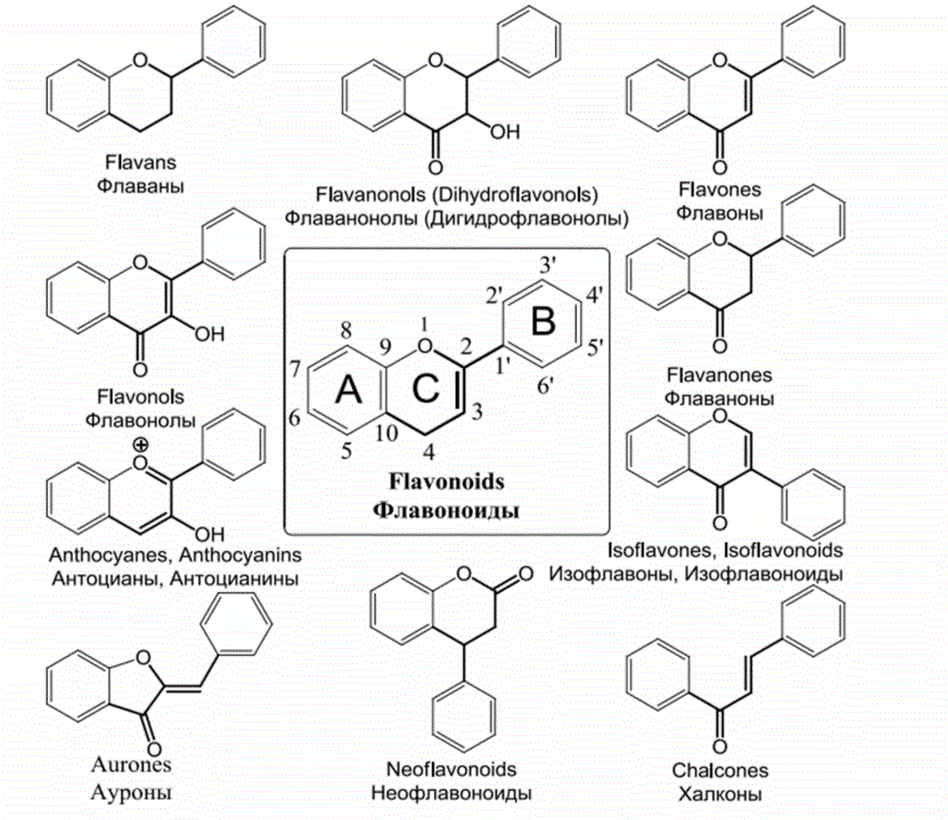

Fig. 4. Chemical structure of flavonoids

Flavonoids, similar to other representatives of phenolic compounds, contain aromatic rings with a hydroxyl group in their structure, based on the 15 carbon skeleton of the flavan C6 (Ring A) -C3 (Ring C) -C6 (ring B), where two benzene rings (A, B) are connected by an oxygen-containing cyclic group (C). In nature, there is a huge variety of structural forms of flavanoids, which can be classified due to the difference in the three carbon atoms that connect the rings. In accordance with this, flavonoids are divided into the following groups: catechins, leicoanthocyanidins, anthocyanins, flavanones, flavanones, flavanonols, flavones, flavonols, isoflavones, chalcones, dihydrochalcones, aurones [28, 29] (see Fig. 4). Despite the similarity of the structure, individual groups of flavonoids differ significantly from each other in biological activity, which is due to the replacement of hydrogen in various positions of the nuclei A and B by groups -OH, -OCH3, -CH3 and the presence of asymmetric carbon atoms.

4. Flavonoid medicinal plants

Flavonoids are widely distributed in the plant world. Especially rich in flavonoids are higher plants that are of interest to the Rosaceae family (various types of hawthorn, chokeberry), legumes (*Japanese Sophora*, field harrow, licorice), buckwheat (various types of highlanders - peppery, kidney, bird: buckwheat), aster (sandy immortelle, marsh cudweed, tansy), *Lamiaceae* (motherwort), etc. More often flavonoids are found in tropical and alpine plants [3]. Flavonoids have also been found in lower plants: algae (duckweed), spores (mosses, ferns), horsetails (horsetail), as well as some insects (marble-white butterfly). There are flavonoids in various organs, but more often in the aerial parts: flowers, leaves, fruits; there are significantly fewer of them in stems and underground organs (licorice, Baikal skullcap, field harrow), young flowers, immature fruits are the richest in them. They are localized in the cell sap in a dissolved form. The content of flavonoids in plants is different: on average 0.5-5%, sometimes 20% disappears (in the flowers of *Japanese Sophora*) [30]. In plants, flavonoids are found in the form of glycosides and in free form. They are broken down into sugars and aglycones under the action of enzymes. D-glucose, D-galactose, D-xylose, L-rhamnose and L-arabinose, D-glucurolic acid are found as sugars. All flavonoid glycosides fall into three groups: O-glycosides, C-glycosides and complex compounds [21].

Fruit of the plant *Ammi visnagae L.* (pick-tooth). General view of the *Ammi visnagae L*. plant is shown in Fig. 5. It grows as a wild plant in Azerbaijan. Cultivated in Ukraine, North Caucasus, Moldova. The raw material contains furanochromones, the representative of which is Kellin; pyranocoumarins, flavonoids, essential and fatty oils. The fruits of ammi tooth have an antispasmodic effect. It is used for chronic coronary insufficiency, cardiosclerosis, bronchial asthma, spasms of the stomach and intestines, spasms of the ureters and renal colic. Ammi dental preparations are moderately effective and are used prophylactically to prevent pain attacks.

Fig. 5. Fruit of the plant *Ammi visnagae L.* (pick-tooth)

Aronia fruit (*Fructus Aroniae melanocarpae*). General view of the aronia fruit *(Fructus Aroniae melanocarpae)* plant is shown in Fig. 6. It is widely cultivated as a garden and ornamental shrub. The raw materials are fruits and juice containing glycosides, flavonoids hesperidin, rutin, quercetin, etc., catechins, tannins, ascorbic acid, vitamins B1, B2, E, PP, organic acids, carotenoids, sugars and microelements. Fruit picking is carried out in September - the first half of October. The fruits are stored in a cool place at the receiving points for no more than three days from the date of collection, and at a temperature not higher than 5 ° C - up to 2 months.

Fig. 6. Aronia fruit (Fructus Aroniae melanocarpae)

Dry or fresh fruits and chokeberry juice are prescribed for the prevention of P-vitamin deficiency, the treatment of stage I and II hypertension and other diseases accompanied by high blood pressure. Fruits and juice are contraindicated in patients with increased blood clotting, with peptic ulcer of the stomach and duodenum, hypersecretion of gastric juice.

Astragalus Woolly Flowering Grass (*Herba Astragali dasyanthi*). General view of the Astragalus Woolly Flowering Grass (*Herba Astragali dasyanthi*) plant is shown in Fig. 7. It is a steppe plant of Ukraine, Moldavia, Ciscaucasia and central Russia.

The raw material contains starch, mucous and coloring substances, glycyrrhizin, organic acids, polysaccharides, triterpene saponins, flavonoids, mineral salts and trace elements. The grass is harvested in the phase of mass flowering, before the formation of fruits, cutting it with sickles or knives. It is impossible to pluck the grass, as this damage the buds of renewal and the plant dies. Annual harvesting on the same massifs is not allowed. Dry in rooms with good ventilation or in dryers at a temperature of 50-55 ° C. The herb astragalus woolly has a hypotensive, cardiotonic and sedative effect. It has a positive inotropic and negative chronotropic effect on cardiac activity, dilates the coronary vessels and improves blood circulation in the kidneys, which determines its diuretic properties.

Applied in the initial forms of hypertension, chronic circulatory failure stage I and II, with acute glomerulonephritis in the early stages of the disease. Astragalus is effective in case of insufficiency of the cardiovascular system, accompanied by minor edema, symptoms of irritability and increased excitability.

Fig. 7. Astragalus Woolly Flowering Grass (*Herba Astragali dasyanthi*)

Sand immortelle flowers (*Flores helichrysi arenarii*). General view of the sand immortelle flowers (*Flores helichrysi arenarii*) plant is shown in Fig. 8. It is distributed in the steppe regions of the European part of Russia, in the North Caucasus, Central Asia and South Siberia. It grows on sandy soils on open sunny slopes.

The raw material contains flavonoids, tannins, essential oil, vitamin K, sterols, fatty acids, mineral salts and trace elements. When harvesting in the forest zone, inexperienced pickers can collect cat's paw inflorescences instead of immortelle - Antennaria dioica - a plant that is often found in the same growing conditions. Inflorescences of cat's paws are easily distinguished by pink or white baskets.

Immortelle flowers are harvested at the beginning of flowering, before the opening of the side baskets. A later date is unacceptable, as the baskets open, the flowers fall off and only the receptacle with the wrapper remains. The collection is carried out in dry weather, when the dew comes down. Inflorescences with peduncles up to 1 cm are cut, loosely folded into a container and delivered to the place of drying as quickly as possible. Storage in a container longer than 3-4 hours leads to deterioration of raw materials.

On the same array, the collection of inflorescences can be carried out up to 3-4 times as the plants bloom. Re-collection can usually be done after 5-7 days. You can not pluck inflorescences with stems and pull out plants with roots. Repeated preparations can be carried out in 1-2 years; at the same time, 1-2 flowering stems should be left per 1 m2 of thickets to ensure seed renewal.

The collected raw materials are dried in a cool room. When dried in warm rooms or in attics, immortelle baskets quickly disintegrate, resulting in non-standard raw materials. Dryers can be dried at a temperature not exceeding 40°C.

Immortelle flowers enhance the secretion of bile, change its chemical composition: reduce the viscosity and relative density of bile, increase the content of cholates; reduce the level of bilirubin and cholesterol in the blood, improve the metabolic function of the liver; have a pronounced antispasmodic effect.
Used for cholecystitis, incl. chronic calculous cholecystitis (contribute to the washing out of sand and small stones), cholecystoangiocholitis, cholelithiasis and hepatitis.

Fig. 8. Astragalus Woolly Flowering Grass (*Herba Astragali dasyanthi*)

Hawthorn flowers (*Flores Crataegi*). General view of the Hawthorn flowers (*Flores Crataegi*) plant is shown in Fig. 9. The State Pharmacopoeia provides for the use of 14 species of hawthorn, including b. smoothed, Dahurian, Korolkov, etc. The raw material contains flavonoids hyperoside, quercetin and hyperin; triterpene glycosides, organic acids.

Fig. 9. Hawthorn flowers (*Flores Crataegi*)

Flowers are harvested at the beginning of flowering, when some of them have not yet opened. Flowers collected at the end of flowering darken when dried. The fruits are harvested at the stage of full maturity - from the end of September until frost. Impurities are removed from raw materials. The fruits are cleaned from the stalks and sepals.
It is impossible to collect wet raw materials (until the dew has dried up and after rain): when dried, such raw materials darken. Raw materials are collected in baskets and laid out for drying no later than 1-2 hours after collection. Hawthorn

blooms quickly, sometimes in 3-4 days, especially in dry, hot and windy weather. Collection of flowers damaged by insects is not allowed. The harvesting of fruits does not lead to the depletion of thickets, so annual harvesting from the same bushes is possible.

The flowers are dried in dryers at the temperature of their raw material heating up to 40ºC; in attics, under sheds or in rooms with good ventilation, spreading out in a thin layer on paper or fabric. Due to the hygroscopicity of the raw materials, the premises where hawthorn flowers are dried must be closed at night. The fruits are dried in warm rooms or in dryers on grates at a raw material heating temperature of up to 70°C.

Flowers and fruits of hawthorn have a very valuable and unique effect. They mainly have a cardiotonic effect with a simultaneous antispasmodic effect, selectively expanding the coronary and cerebral vessels, which allows the targeted use of plant preparations to improve the oxygen supply to the myocardium and brain neurons.

Applied with functional disorders of cardiac activity, especially against the background of hypertension. Recommended extemporaneous forms - infusion of flowers 1:40; fruit decoction 1.5:20.

5. Conclusion

The study of biological activity, structural and functional dependencies, as well as the physicochemical properties of plant phenol compounds makes it possible not only to deepen fundamental knowledge about their chemistry and physiological functions, but also to expand the scope of their application both as medicines and food and technological additives. Summing up this review, it should be emphasized that many aspects of the redox reactions of flavonoids occurring in living organisms still need to be carefully studied. Most of the important enzymes and genes involved in flavonoid pathways have been identified. However, several aspects of flavonoid biology are still unknown. For instance, it is still unclear how and what a number of transcription factors that regulate this branching pathway perform. The immense range of plants that evolved throughout evolution has produced a matching diversity of flavonoid structures, many of which have yet to be found. The identification of novel structures and possibly new metabolic pathways will be made possible by further study on numerous plant species. The food, chemical, and floriculture industries will all benefit from future study as well.

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