*Biological acitivity of flavonoids*

For the first time, the ability to increase the capillary strength was discovered in 1936 by Saint-Gyorgyi, who established that preparations of lemon juice and red pepper containing the flavone derivatives have a curative effect in the treatment of some diseases. That’s why these compounds are named as P-vitamin.

Flavonoids have broad spectrum of biological activity. They have been shown to exert vitamin P acitivity, antimicrobial, sedative, hypotensive, antispasmodic and oth. acitivities. They protect ascorbic acid against the oxidation.

It has long been known, that antocyanins and flavanes have antibiotic action, quercetin, quercitrin, rutin, hesperidin and naringenin exert effective action against rabies virus, typhus and parathyphoid, ectromelia virus, but anthocyanins – cutaneous condition in children. The positive results were obtained in use of flavonoids as an antitumor.

Flavonoids exert antitoxic effect. For example, galascorbin and other phenolic compounds are effective compounds in Botkin’s disease – toxic infection of liver, medicinal idiosyncrasy and intoxication, experimental muscular dystrophy and myocarditis. Phenolic compounds have detoxifying action on the liver function. In addition to this the phenolic compounds have an ability to from different complexes. Phenolic compounds form complex compounds with metal ions, transition metals (copper, iron, cobalt, manganese, zinc and etc.). That’s why they are used as an antidotes to heavy metal poisoning. Flavonoids have an influence on the endocrine system.

Vitamin P with glucocorticoides increase the accumulation of glycogen in muscles. The most effective action of poliphenolic compounds is during the rheumatism and other inflammatory diseases. The most effective effect of polyphenolic compounds in rheumatism and other inflammatory diseases. Rutin and quercetin have a photosensitizing property.

Antocyans have a special place among flavonoids. It was established that the leaves of blueberries reduce the sugar in the blood. Flavanes of plant origin exert P-vitamin activity, which hav an ability to reduce the permeability of capilliaries in organism of human and animals and they are named as bioflavonoids. More than 600 biflavonoids are found in plants. In addition, d-catechin, l-epicatechin, quercetin, 7-rhamnoglucoside – hesperitin and other forms of flavonoids exert P-vitamin activity.

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Flavonoid compounds are found in all organs of higher plants. The qualitative and quantitative composition of flavonoids in plants depend on the location, light, high altitude, humidity and other factos of environment. Physiological role of flavonoids in plants is various and has been completely studied.

Flavonoids have a protective function in plants, protecting against harmful effect of UV-rays. They are involved in transpiration, enzymatic oxidation - reduction processes of plants and other biological reactions.

Biological activity of flavonoid compounds is due to the presence of active phenolic hydroxyl and carbonyl groups in molecule, and the ability to biochemical conversions.

Flavonoids have a broad range of therapeutic effects: capillary-enhancing, cholagogic, diuretic, hepatoprotector, sedative, anabolic, radioprotective, antioxidant, anti-inflammatory, batericid, cardiotonic, hemostatic, antiulcer and etc.

The spectrum of pharmacological action of flavonoids is very broad, that’s why only the main and most proven aspects will be considered.

1**.** Capillary-enhancing of flavonoids i.e. vitamin P activity (рermicabilitis **– permeability). Capillary-enhancing action, i.e. P-vitamin activity is inherent in different flavonoids, these properties are expressed in catechins of tea leaf and apples (epicatechin, epigallocatechin); flavonone (eriodyctiol, hesperitin, naringinin) citrus, ashberry and rosehip; flavonols (quercetin, kaempferol, quercetin glycoside - rutin, quercitin), onion, sorrel, flowers and leaves of buckwheat, fruits of ashberry and dogrose; leucoanthocyanidins and anthocyanins of many colored fruits and berries.** Quercetin and rutin, obtained synthetically, are also used in practice. Vitamin P is found with vitamin C practically in all plants. They potentiate the capillary-enhancing action of each other, they are necessary in biochemical “bundle”, but not interchangeable. In P-hypovitaminosis (especially in winter and spring), the permeability of capillaries for proteins and erythrocytes increases, their durability increases, the predisposition to point (petechiae) and micro-hemorrhages increases. The mechanism of action of vitamin P (as a redox system) is explained by several effects: a) takes part in the oxidation of proline - an important connecting substance in the synthesis and stabilization of collagen - in hydroxyproline and inhibition of hyaluronidase; b) stabilizes ascorbic acid due to delayed oxidation of vitamin C and irreversible opening of the lactone ring; c) enhances the secretion of corticosteroids and adrenaline and the action on the vssel walls and, as a result, exert a strengthening effect. High doses of long-term use of vitamin P does not cause hypervitaminosis. Its action is associated with ascorbic acid, therefore it is recommended to prescribe simultaneously. Flavonoids are probably assimilated after hydrolysis of glycosides in a weakly acidic medium of intestine. In the body, they almost completely degraded. The difference in the properties of flavonoid glycosides from the sugars contained in them was not confirmed.

2. Cardiotropic actiom. The following three activities are referred to this action: cardiotonic, coronary vasodilating and antiarrhythmic. These actions accompany each other, each of them is expressed quite moderately. At the same time their combination is useful and effective for mild forms of cardiac disorders (weaking of contractions, extrasystols, pain syndrome and etc.), vegetovascular dystonia and neurotic disorders, hypertension and etc. The effect of flavonoids with more severe cardiac abnormalities is insufficient, and they can help only in more active therapy.

Cardiotropic effect is more pronounced in flavonoids of hawthorn flowers and fruits. These properties have been well studied. Plant produces more than 15 flavonois (in aglycone and glycosidic forms), in which hyperoside, quercetin, vitexin and its rhamnoside have been more interested. Pharmacological analysis of cardiotonic analysis of individual components shows that hyperoside is more active, but the sum of flaovnoids and the fraction of triterpene glycosides have a strong enough effect. They differ from cardiac glycosides by the mechanism of action, In addition, the preparation of hawthorn decrease the toxic effect of glycosides and negative action on permeability.

Mechanism of cardiotonic acitivity of hyperoside and other substances, isolated from hawthorn has not been comprehensively studied. Mechanism of cardiotonic activity of hyperoside is associated with primary positive effect of flavonoids on miocardial energetic metabolism (the increases of glucose utilization, efficiency of oxygen usage), enrichment of heart with potasium ion. Other plants containing hypersoide but with different composition have less cardiotonic effect. The preparations of motherwort, mullein, astragalus, hypericum, ginger, linden flowers have this acitivity.

3. Anti-spasmodic and hypotensive activity. Anti-spasmodic and hypotensive activities are specific for flavonoids of most plants and due to their combinations with other active substances (essential oils, chromons, coumarins and etc.). **Anti-spasmodic acitivity of flavonoids is represented to coronary, less brain vessels, intestine, bronchi, bile passages and uterus.**  They have most likely myotropic nature. This action is short-term (about 20-30 min intravenous administration) and its strength is comparable to papaverine. Flavonoids have anti-spasmodic activity on smooth muscles, caused by different endo- and exogenous factors. Hyperin is the most active.

Medicinal plants containing hyperoside, vitexin, hyalosides, skutellarenin, baikalein and other flavonoids are prescribed in the early stage of hypertensive disease (in the free state) and more complex forms (in conjunction with modern antihypertensive drugs). The character and compatibility of flavonoids determine their hypotensive activity. Характер и совместимость флавоноидов определяют их гипотензивную активность This effect is often found in motherwort, low-cudweed, baikal skullcap, geranium, astragalus, rowanberry and other plants. The mechanism of action is associated with an antispasmodic effect on blood vessels. Some plants have a sedative activity, which enables to associate it with the stabilization of blood pressure and reduction stress on vasomotor center. Plant species are more active and have found their application in the treatment of hypertensive diseases, hypertensive type of neurocirculatory dystonia and symptomatic arterial hypertension.

4. Diuretic activity. The diuretic action of many plants is unequivocally or significantly attributed to the presence of flavonoids of different groups in fairly high concentration. These plants include common horsetail, knotgrass, dyer’s madder, dyer’s broom, blue cornflower, heather, elderberry, madowsweet, rest-harrow, rupturewort, leaves and buds of birch, asparagus, parsley, corn silk, sorrel and etc. According to the degree of diuretic activity flavonoids concede to synthetic saluretics, but it does not cause complications which are typical to saluretics, and accompanied by increased elimination of both water and nitrogen waste (lespedeza), other stone-forming substances.

The use of flavonoid-containing plants does not lead to the development of urine diathesis, to a diabetic effect (moreover, flavonoids have a mild hypoglycemic effect), changes in acid-base balance, and potassium deficiency. The diuretic activity of flavonoids is related to the dilation of renal vessels and increasing of filtration of primary urine (euphyllinum). There is no reliable data on the change in sodium reabsorption in the nephron channels, and ion excretion has only secondary character. In addition, there is no information on the effect of flavonoids on the secretion of renin. Despite limited use, diuretics of plant origin are well received by the body and therefore are used for edema of various origins, chronic heart failure, hypertensive illnesses and kidney diseases.

Medicinal plants containing flavonoids have a weak diuretic effect, so medicinal plants with a strong diuretic effect should be added to these species.

5. Cholagogic and hepatoprotective action.  **Cholagogic anf hepatoprotective action can be related to the most important and widely used activities of flavonoid-containing plants. Most plants especially sandy everlasting, common licorice, holy thistle, tansy, common wormwood, mountain ash, corn silk and oth. exert these activities. Cholagogic action is due to the enhancing of production and secretion of bile by hepatocytes. Pharmaceutical companies produce many pharmaceuticals based on dry and pure extracts and individual flavonoids (for example, silibinin) containing the sum of flavonoids. Accompanying substances – coumarins and essential oils are same, but exert a weaker effect.** The excretion of both solid components and the liquid component of bile is enhanced. As a result its flow in biliary capillaries and ducts becomes more intensive, drainage is enahnced and flow of bile into gall bladder. The conditions for maintaining infection and crystallization of bile acids with sand fallout in biliary ducts are worsened. Accompanying substances - essential oils reflexively irritate the mucous membrane of the duodenum, which causes its release. These processes contribute to the anti-spasmodic effect of flavonoids and essential oils. It is considered that increasing the secretion of bile is the main and most valuable phenomenon. Choleretic action increases in the number of flavonols- flavones- chalcones- flavonones.

Along with choleretic action flavonoids enhance the antitoxic function of the liver. It is due to the direct inclusion of some flavonoids which are able to form redox- pairs in the oxidation – reduction reactions. It is also related to hepatotoxic agents, which rate of detoxification increases as its excretion with bile.

6. Hemostatic action. Hemostatic action of flavonoids has long been established and it is widely used in medicine for the treatment of uterine, hemorrhoidal, intestinal and other non-major bleeding. **This effect is presented in the whole organism and associated with the joint action of individual accompanying substances of different flavonoids. The connection of haemostatic action of flaovnoids with vitamin K is less convincing. Because the amount of vitamin K in flaovnoid-containing plants is less that therapeutic dosage. Similarly, to connect the hemostatic effect with platelet aggregation and the increase in the factor of blood coagulability in the liver does not allow us to reach a final conclusion. It would be useful to relate this effect to the capillary-strengthening activity of flavonoids.** Part of flavonoid-containing plants which are used in the treatment of uterical bleeding, uterotonic effect. Part of flaovnoid-containing plants used in uterine bleedings, also exert uterotonic effect. Preparations of water piper and red-shanks, dead-nettle, lady’s-purse, sophora and some other plants have a hemostatic action.

7. Studying the mechanism of anti-radiation action, N.M. Emanuel and his co-workers in 1954-1957 created the doctrine of the role of chain reactions of self-oxidation in fats and lipids and put forward a hypothesis about the role of free radical processes in the development of radiation damage, carcinogenesis and the aging process. In 1983, this provision was recognized as a discovery. On the basis of the conducted studies it was recommended the use of food antioxidants for inhibition of free radical reactions in malignant growth, irradiation and aging. It was also proved that the introduction of plant polyphenols, including flavonoids, which increase the antioxidant activity of animal tissues, increases their resistance to radiation.

The deficiency of antioxidants in the body stimulates the accumulation of free radicals and brings aging closer, while the normalization of the level of antioxidants in the systems contributes to the prolongation of life. From the perspective of this theory, chemical protection against aging is possible by prolonged introduction of antioxidants into the body - inhibitors of free-radical processes. In experiments on animals, a significant increase in life expectancy was obtained due to the continuous addition of these substances to their food. Antioxidants are very important for the normal metabolism of a living cell. It is known that the cell membranes include easily oxidized lipids. When the lipids of the cell membranes are re-oxidized, toxic products are formed, the metabolism in the cell is disrupted, and its work is inhibited up to cell death.

Normalization of exogenous antioxidants leads to the disappearance of such processes as mitosis, malignant degeneration, atherosclerosis, etc. Most flavonoids: rutin, quercetin, citrine, delphinidin, catechin and others are useful in radiation injuries.

Polyphenols and ascorbic acid complement and potentiate the influence of each other on capillaries. Therefore, they are often contained together in medicinal preparations. It should also be noted that this combination is a natural model and in many berries, as well as in plant organs (lemon, black currant, dog rose, etc.), ascorbic acid and flavonoids always are found in combination. It should be noted not only medicinal products of vegetable origin, as well as fruits and vegetables rich in vitamins (C, R, etc.) are used as angioprotector.

8. All flavonoid-containing plants have anti-inflammatory action, which is associated with antioxidant, capillary-enhancing effect.

9. Hypoazotmic action. This action is specific for flavonoids of round-headed bush clover (lespenephryl), shrubby bushclover (lespeflan) and astragal (flaronine).

10. Antiulcerous action. The glycosides of common licorice – flavanone and chalcone (liquiritone, flacarbin), the glycosides of bastard hemp – flavanole (datiskan) are as classic example of antiulcerous action of flavonoids.

11. Anticancer activity. Some phenolic compounds have an anticancer activity. Anticancer activity is specific for quercetin, catechin, leucoallergonidin, leucoanthocyanidin, leucodelphinidin and oth. These substances have a direct impact on the tumor, increase the sensitivity of neoplastic tissue to irradiation injury and potentiate the action of alkylating agents. Mechanism action of flavonoids is associated with its ability to reduce the activity of cytoplasmic and mitochondrial ATP.

12. Antiviral action. Antiviral action of the preparations of Amur cork tree (flakoside), bush-clover (chelepin) and oth. is used in medical practice. The viral effect of widespread flavonoid - cinnaroside in the plant world is proven, however, its medications have not been created.

13**.** Other types of activities of flavonoids are various. **Some of them are specific for plants, some – individual plants with specific flavonoids and related substances, in which it is not difficult to determine the role of any compounds.** The group of plants (motherwort, calendula, woundwort, bupleurum, bush clover, rhododendron and oth.) does not have a strong activity, clear analgesic activity which is explained by the presence of flavonoids of quercetin group such as hyperin, avicularin. Mechanism action is unknown, probably, it interacts with opioid receptors. Because the usage does not cause dependency. In some studies the ability of flavonoids to inhibit phospholipase, cyclooxygenase and lipoxygenase and inhibit the arachidonic acid, synthesis of prostaglandins, leukotrienes. If these results are accurately proved, then the mechanism of anti-inflammatory, analgesic acitvities will find the solutions. A combined action of these substances (anti-inflammatory, cytoprotective) is due to their wound- healing, epithelizing effects on the regenerative gastric mucosa, intestines, skin. In this case flavonoids act with other active substances of plant (terpenoids, coumarins). The preparations of hypericum, wartwort, sophora, the leaves of walnut, pot marigold, white dead nettle, common licorice and other flavonoid-containing plants are used for the stimulation of healing of ulcers and skin damage.

laxis of blood vessels sclerosis.

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| MPM name | **Source** | Constituents | Action, use |
| ***Fructus Crataegi, Flores Crataegi*** | *Crataegus sanguinea*Pal, *C. monogyna* Jacq. Lindm, *C. laevigata*(Poiret) D.C. (*C. oxyacantha*), *C. pentagyna* Waldst. et Kit. ex Willd, *Rosaceae* | Fruits: procyanidins(hyperoside) epicathechins, leucoanthocyanidin oligomers; pectins; ascorbicacid.  Flowers : vitexin and its glycosides, biosides, di- and oligoglycosides of leucoanthocyanidins, epicathechins, (+)-cathechin, dihydrocathechin dimers;   triterpenoid acids (ursulic, oleanic, crataegic, acanthic acid) occur in both MPM. | cardiotonic, hypotensive, sedative andspasmolytic;  increase coronary and myocardial circulation; treat abnormalities of the cardiac rhythm in the adult |
| ***Herba Equiseti*** | *Equisetum arvense* L.,(horsetail), *Equisetaceae* | flavonoids (isoquercitroside; derivatives of apigenin, luteolin, kaemferol, quercitin); minerals (silicon SiO2); sterols; phenolic acids | diuretic, to enhance urinary and digestive elimination functions |
| ***Folia Ginkgo*** | *Ginkgo biloba* L.,*Ginkgoaceae* | flavone glycosides; flavan-3-ols, proanthocyanidins, and biflavonoids;terpenes–diterpenes (ginkgolides A, B, C, J) and sesquiterpenes (bilobalide) | spasmolytic, vasodilatating; vasoregulating agent for "cerebral insufficiency" |
| ***Herba Hyperici*** | *Hypericum perforatum* L.,*Hypericaceae* | flavonoids (hyperin, rutin, quercitrin, isoquercitrin; biflavonoids); naphthodianthrones (hypericin, pseudohypericin, protohypericin and protopseudohypericin);  essential oil; phenolics: caffeic acids, chlorogenic acid,  prenylated derivatives of phloroglucinol; condensed tannins | wound-healing; antiseptic, antimicrobial, anti-inflammatory, antihaemorrhage, astrigent action;antidepressant(mild and moderate depression) |
| ***Flores Tiliae*** | *Tilia cordata* Miller,*Tilia platyphyllos* Scop.,*Tiliaceae* | flavones: acacetin-7-glucoside (tilianin), flavanones: rutinoside of hesperitin, flavonoles: derivatives of kaemferol (tiliroside), quercitin and herbacetin; volatile oil (pharnesol, 2-phenylethanol, monoterpenoids); mucilage;. tannins, leucoanthocyanidins | sweated, emmolient, anti-inflammatory, diuretic remedy; increases blood coagulation |
| ***Herba Leonuri*** | *Leonurus cardiaca*L., *L.quinquelobatus*Gilib., *Lamiaceae* | flavonoids: quinqueloside, rutin, quercitin, cosmosiin, isoquercitin, hyperoside;  iridoids of aucubin type (harpagide, ajugol, ajugoside);  diterpenes (marubin), terpenoids; tannins; volatile oil | sedative and hypotensive in cardiac and vessel neurosis, initial stage of hypertony, casdiosclerosis |
| ***Flores Sambuci nigrae*** | *Sambucus nigra* L.(elder), *Caprifoliaceae* | flavonoids (isoquercitroside; rutin, derivatives of quercitin, kaemferol, astragalin; anthocyanidins; cyanoglycoside sambunigrine); phenolic acids; amines; tannins; mucilages | sweated (colds and catarrhal conditions, chronic bronchitis), mild expectorant; anti-inflammatory (gynecology); diuretic |
| ***Fructus etAlabastrae Sophorae japonicae*** | *Sophora japonica,Fabaceae* | rutin (up to 20%), quercitin, kaemferol-3-sophoroside, quercitin-3-rutinoside, genistein-4-sophorobioside | sourse of rutin and quercitin (vitamin P), used for internal haemorrhages, poor peripheral circulation. The tincture of fruits is antibacterial |
| ***Fructus Aroniae melanocarpae  recentes*** | *Aronia melanocarpa*(Michx.) Elliot*,*(black chokeberry), *Rosaceae* | flavonoids – rutin, quercitin, hesperidin, cathechins; cyanidins and its glycosides; phenolic acids; lipids;pectins; ascorbic acid (110mg%), nicotinic acid, folic acid, riboflavin, tocoferol, carotenoids; iodine (5-6 mcg/100g) | vitaminic remedy; prophylaxis of vitamin P insufficience; hypotensive |
| ***Flores Helichrysi arenarii*** | Helichrysum arenarium *(L.) Moench.,*  *Asteraceae* | flavanone naringenin and its glycosides – salipurposide, isosalipurposide, helichrysin; flavones apigenin and its 5-glycoside; flavonoles – kaemferol derivatives; derivatives of phtalic anhydryte; tannins; sterols; mucilages; carotenoids | cholagogue, stimulating gastric and pancreatic secrection |
| ***Herba Gnaphalii uliginosi*** | *Gnaphalium uliginosum*L*., Asteraceae* | flavonoles quercetin, kaemferol, flavones – gnaphalosides A,B, scutellarin 7-O-glucoside, 6-methoxyluteolin; tannins; resins; carotenoids | vasodilatating, hypotensive; antibacterial; oil extract acts as wound-healing agent |
| ***Radices Scutellariae baicalensis*** | *Scutellaria baicalensis*Georgi*, Lamiaceae* | flavones and their glycosides- baicalin (baicalein-7-O-glucurenide), scutellarin (scutellarin7-O-glucurenide), vogonin; oroxylin | sedative; hypotensive; tincture is used in hypertension of 1stand 2nd stages |
| ***Radices Ononidis*** | *Ononis arvensis*L*, Fabaceae* | isoflavonoids- formonetin, ononin, onogenin, ononegenin-7-glucoside, onospin; volatile oil; tannins; triterpenoid saponins | decoction is diuretic and antihaemorrhage in haemorrhoid; tincture is anabolic |
| ***Herba Polygoni persicariae*** | *Polygonum persicaria*L*.,*(redshank, lady’s thumb),*Polygonaceae* | Flavonoids ( hyperoside, isoquercitin, avicularin, persicarin, tetramethylquercitin); vitamin K; tannin, phlobaphens, free gallic acid; phyloquinones; pectins | antihaemorrhage action in haemorrhoidal vaginal bleedings |
| ***Herba Polygoni avicularis*** | *Polygonum aviculare*L. (knot-grass, goose-grass)*, Polygonaceae* | flavonoids avicularin (=quercitin-3-arabinoside), quercitin, hyperoside, cathechins;   phenolic acids, water soluble silicates, tannins (about 4%), lignan aviculin | astringent; diuretic, lytolytic;  in pulmonary complaints;  haemostatic in gynecology |
| ***Herba Polygoni hydropiperis*** | *Polygonum hydropiper*L.,*Polygonaceae* | flavonoids: rutin, quercitin, hyperoside, kaemferol, isorhamnetin, rhamnetin, rhamnosin; persicarines; tannins, free gallic and ellagic acids; vitamins K, C; essential oil,  bicyclic sesquiterpenoid, polygodial | anti-inflammatory, astringent, diuretic, lytolytic; in the treatment of  excessive menstrual bleeding and haemorrhoids |
| ***Herba Tanaceti*** | *Tanacetum vulgare*L. (tansy), *Asteraceae* | flavonoids : derivatives of apigenin, luteolin; alkaloids, tannins; organic acids; a bitter substance tanacetin; volatile oil containing thujone, borneol, pinenes, isothujone | antihelmintic; aromatic bitter, cholagogue; hypertensive |
| ***Folia Theae*** | *Thea sinensis L*. (syn. *Camellia sinensis (L.) Kuntze*) (tea), *Theaceae* | cathechin, its derivatives (vitamin P), flavonoids and tannins; alkaloids caffeine and  theophylline; vitamins C, PP, B1, B2 | CNS stimulant; antidotal, antitoxic; vitamin P activity;  astringent, cardiotonic |
| ***Flores Centaureae cyani*** | *Centaurea cyanus*(Bachelor’s buttons, bluebonnet), *Asteraceae* | anthocyanes - cyanin (cyanidin-3,5-diglycoside), derivatives of pelargonidin; flavones – apigenin diglucoside, luteolin; flavonoles – quercetin-glucoside, quercetin-7-rutinoside, rutin; saponins; coumarin cichorin; pectins | mild diuretic in liver and gallbladder complaints; antibacterial, anti-inflammatory |