Finding in nature, cell cultures, use and pharmacological action of betalains and their derivatives

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SUMMARY

The review is devoted to information on natural sources of alkaloids-pigments of the betalain class, biotechnology of cell cultures for the production of these substances, application and pharmacological action of betalains and their derivatives. Information on plants containing betalains, general characteristics of these pigments of various structures, data on their use on the basis of their pharmacological action, shows that they are promising for the creation of new drugs.

Key words: betalains, pigments, alkaloids, application, pharmacological action.

RESUME

Data on some natural sources of alkaloids-pigments of betalaines class and their derivatives, pharmacological action and application are provided.

Keywords: betalains, pigments, alkaloids, application, pharmacological action.

The aim of this study is to analyze information about the finding of betalains in nature, the technology of cell culture producers of this group of compounds, the use and pharmacological action of betalains and their derivatives, which are promising for the creation of drugs.

Betalaines and their derivatives are the most common group of colored alkaloids. These dihydroindole compounds, both in free form and in the form of glycosides, are found in many plant species of the order Clove (Caryophyllales), accumulating in leaves, stems, roots,fruits, inflorescences, flowers, petioles, fruits and seeds [1, 2].

Betalaines are vacuolar pigments consisting of the nitrogenous structure of the core, betalamic acid [4 (2oxoethylidene) 1,2,3,4tetrahydropyridine2,6dicarboxylic acid], which condenses with imino compounds (cyclo13,4 dihydroxyphenylalanine and its glucosyl derivatives) or amino acids and their derivatives with the formation, respectively, of betacyanins (red-violet) and betaxanthins (yellow-orange) [3].

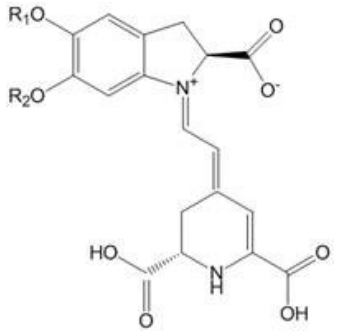
Due to glycosylation (with glucose, apiose, rhamnose, xylose) and acylation, betalains exhibit tremendous structural diversity. An important property of betacyanins is their low stability, depending on pH, the presence of oxygen, exposure to light, etc. [2, 4-6].

The most significant sources of betalains are plants of the family. Amaranthaceae (genera Beta, Amaranthus, Alternanthera, Chenopodium, Celosia, Gomphrena) and Cactaceae (Opuntia ficus-indica, Hylocereus undatus).

To date, more than 250 betalains and their glycosides have been identified [2] from plants of 20 families: Aizovye (Aizoaceae) - ten-chained bay (Zaleya decandra L.) [7]; carpobrotus edible (Carpobrotus edulis (L.) NEBr.) And saber-shaped (Carpobrotus acinaciformis L.) [8, 9]; glottiphyllum long (Glottiphyllum longum (Haw.) NEBr.) [10]; crystal mesembriantemum (Mesembryanthemum crystallinum L.) [10].

Amaranth (Amaranthaceae) - common beet (Beta vulgaris L.) [11], amaranth tricolor (Amaranthum tricolor L.), crimson (A. cruentus L.), Powell (A. powellii S. Wats.), Prickly (Amaranthus spinosus L.) [12, 13], glaucous (Amaranthus lividus L.) [14]; comb celosia (Celosia cristata L.); irezin Herbst (Iresine herbstii Hook.); gomphrena spherical (Gomphrena globose L.); alternantera brazilian (Alternanthera brasiliana Colla), the thinnest (A. tenella Colla.) [15, 16], sedentary (A. sessilis (L.)

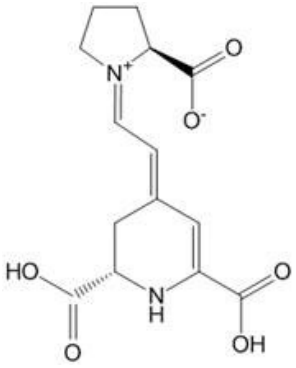
R.Br. ex DC) [17, 18].



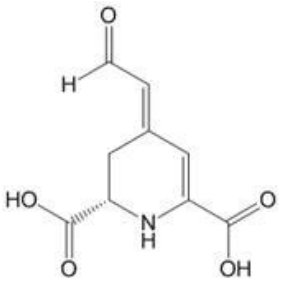
Betacyanin

R1 = carbohydrate residue from mono or disaccharide (H)

R2 = H (carbohydrate residue)



Betaxanthin



Betalamic acid

Basell (Basellaceae) - red basella or Indian spinach (Basella rubra L) [19] white basella or malabar spinach (Basella alba L). [twenty]; ulyuko tuberous (Ullucus tuberosus Loz.) [22].

Gizekiev (Gisekiaceae) - African Gisekia (Gisekia africana (Lour.) And farnaceous Gisekia pharnaceoides L.) [23].

Halophytic (Halophytaceae) - Halophytum ameghinoi (Speg.) Speg) [24]. Hectorial (Hectorellaceae) - hectorella soddy (Hectorella caespitosa Hook) [25]. Didier -Didiereaceae, Didierea madagascar (Didierea madagascariensis Baill.) [26]. Cactus (Cactaceae), fig prickly pear (Opuntia ficus-indica [L.] Mill.), Mighty prickly pear (O. robusta Wendl.) [27], pitahaya hilocereus (Hylocereus polyrhizus (Weber) Britton & Rose) [28], peresky prickly (Pereskia aculeata Miller) [29], representatives of the genera Mammillaria (Mammillaria candidaScheidweiler, M. Roseo-alba (Boedecker), M. donatii (Berge), M. coronata (Scheidweiler), M. karwinskiana(Martius), M. gummifera (Engelmann), M. infernillensis (Craig), M. centricirrha (Lemaire), M. krameri(Muehlenpfordt) and M. magnimamma (Haworth) [30 31] as well Cereus, Epifillum, Gimnocalicium, Lobivia, Parodia, Rebutia [32, 33].

Lakonosovye (Phytolaccaceae) - American Lakonos (Phytolacca americana L.) and berry lakonos (Phytolacca acinosa Roxb.) [34].

Lofiocarp (Lophiocarpaceae) - creeping corbichonia (Corbichonia decumbens (Forssk.) Exell.), Lofiocarpus many-spiked (Lophiocarpus polystachyus Turcz.) [35]

Haze (Chenopodioideae) - quinoa (Chenopodium quinoa Will) [36], Julis or Mary Formoskaya (Chenopodium formosanum Koidz.) [37]; Sveda saline (Suaeda salsa (L.) Pall.) [38].

Montievs (Montiaceae) - amazing parakeelia (Parakeelya mirabilis Chinnock & JG West) [39], claytonia lanceolate (Claytonia lanceolate Pall. ex Pursh) and Virginian (Claytonia virginica L.) [40]. Niktaginovye (Nyctaginaceae) - Mirabilis jalapa L.) [41] Bougainvillea nude(Bougainvillea glabra Choisy.) [42], direct burhavia (Boerhavia erecta L.) [15].

Petiverievs (Petiveriaceae) - low rivina (Rivina humilis L.) [43].

Purslane - Portulacacea (large-flowered purslane Portulaca grandiflora) [44, 45], as well as some representatives of the genera Ceraria, Portulacaria and Talinella [46].

Tallin (Talinaceae) - triangular talinum or Ceylon spinach (Talinum triangulare (Jacq.) Willd.) [47].

The families of Achatocarp are also mentioned as plant sources of betalains.(Achatocarpaceae), Anacampsuria (Anacampserotaceae),Sarcobate (Sarcobataceae)and Stegnospermaceae (Stegnospermataceae) [32, 49, 50].

Betalains are produced by some higher fungi of the family. Amanite, or Fly agaric(Amanitaceae) - red fly agaric (Amanita muscaria), Caesar's fly agaric (Amanita caesarea), fam.Hygrophoric (Hygrophoraceae) - hydrocybe (Hygrocybe appalachianensis, H. citrina, H. citrinovirens, H. Coccinea); hygrophors (Hygrophorus aureus, H. hypotheftus, H. Speciosus, etc.) [50] and bacteria Gluconacetobacter diazotrophicus [51].

Betalaines as brightly colored pigments are used in the food and textile industries as chemical biosensors, markers - fluorophores for proteins, markers for genetic transformation [2], sensitizers in solar cells [52].

Betanin (betanidin5Oβglucoside) is the most abundant betacyanin in the plant kingdom. It is used as a natural red dye (E162) in the food industry, cosmetics, and pharmacy [53]; the yellow pigment betaxanthin is also widely used [54].

In recent years, a number of advantages of using betalains as therapeutic agents have been identified, which are due to antioxidant, anti-inflammatory, antitumor, hypotensive, hypolipidemic, antidiabetic and anti-obesity effects [55, 56].

The estimated potential of the annual world production of betalains is 96.8 Gt, of which 99.99% are beets, and the remaining 79.1 tons are amaranth, pitaya, prickly pear, etc. [3].

Due to the importance of betalains as natural pigments and their high biological activity, the biotechnology of cell cultures containing these substances is of interest. Such production does not depend on natural factors, it is economically profitable, because more pigments are synthesized in raw materials during the optimization of growth and light regulators [12, 13, 17, 57].

In brightly colored callus culture of celosi Celosia cristata L. identified betacyanins and betaxanthins, incl. malonyl derivative, 6 ›Omalonylamarantine (celoscristatin). Its stereoisomer 4 ›Omalonylamarantine (acylmigrated celoscristatin) as well as its 15 R diastereomer have also been found in the callus as a result of migration of the malonyl group to celoscristatin / isocelоscristatin, respectively. Amarantin is found in callus as the main betacyanin, followed by helocristatin, betanin, phyllocactin and other minor betacyanins. The effect of various carbon sources on the growth rate of Celosia callus, as well as on the profiles of betalains in callus cultures, was studied. Revealed a high content of dopamine in callus culture and compared with the content in inflorescencesC. cristata. Dopamine-based betalain(Miraxanthin V) was found to be the main betaxanthin in callus, however at a concentration level much lower than that of the identified betacyanins. Studied callus cultureC. cristata can accumulate betalains in amounts approachingproduced by most of the known high-yielding plant species [58]. It should be noted that the betacyanins betanidin and decarboxybetanidine, as well as the betaxanthins dopaxanthin and miraxanthin V, are the only natural betalains that contain the catechol substructure. These four pigments were obtained in cell cultures obtained from hypocotyls of celosia silvery (Celosia argentea). Two stable and differentially stained cell lines,yellow and red, were maintained on Murashige and Skoog medium supplemented with plant growth regulators 6benzylaminopurine (6.66 μM) and 2.4 dichlorophenoxyacetic acid (6.79 μM). The obtained suspension cultures showed increased production of dihydroxylated betalains in cells and were secreted into the medium with a maximum reached after 8 days of cultivation. In addition, precursor molecules of betalamic acid and dopamine were also obtained, the joint presence of which will allow cell culturesC. argentea becomea stable source of valuable phytochemicals [59].

The production of betalains by callus cultures of quinoa (Chenopodium quinoaWilld), which developed from multi-colored plant varieties. Stable callus lines produced pigments when grown on Murashige and Skoog medium supplemented with plant growth regulators 6benzylaminopurine (8.88 μM) and 2.4 dichlorophenoxyacetic acid (6.79 μM) with a decrease in the nitrogen source to 5.91 mM, while phyllocactin was identified and vulgaxanthin [60].

Betalains possess antioxidant and gene-regulatory properties, which may be due to the activity associated with the erythroid nuclear factor (Nrf2), activating a dependent signaling pathway in cells (Nrf2). Betanine can induce phase II enzymes and antioxidant defense mechanisms. In addition, betanin may prevent oxidation of low density lipoproteins (LDL) and DNA damage [61]. These properties allow betalains to become an alternative to supplement therapy for oxidative stress, inflammation, dyslipidemia, cancer, etc. [62].

The dihydroindole alkaloid betanidine and its derivatives, first obtained from beets (Beta

vulgarus L.) exhibit a number of important pharmacological properties, incl. antioxidant, antihypertensive, anti-inflammatory, antitumor and antiglycemic effects [55, 63–69]. Betacyanine pigment amaranthine from leaves of amaranth tricolor has a pronounced antioxidant activity (Amaranthus tricolor L.) [70], pigments from cactus fruits Hylocereus and Opuntia [71-74].

The extract obtained from Beta vulgaris L., significantly reduced the proliferation and viability of cancer cells, in particular cell lines of breast adenocarcinoma (MCF7), human hepatocellular carcinoma (HepG2), pancreatic cancer (PaCa) and prostate (PC 3), which allows betalains to be considered therapeutic anticancer compounds [75–78]. Betalains isolated from berriesRivina humilis L. (Petiveriaceae), in vitro have a cytotoxicaction on HepG2 cells [79].

Betacyanin from the fruits of the fig prickly pear Opuntia ficus-indica induces apoptosis in the cellthe line of human chronic myeloid leukemia K562 [80]. The yellow pigment indicaxanthin, isolated from the fruits of prickly pear and fig, has a prooxidant effect, modulates arachidonate metabolism and prostaglandin synthesis through the production of lipid peroxide in LPS (lipopolysaccharide) stimulated macrophages of the RAW264.7 line [81], is a promising neuromodulatory agent [82], has an anti-inflammatory effect with carrageenan-induced pleurisy in rats [83].

Cladode and mesocarp extracts Opuntia ficus-indica f. inermis. containing betaxanthin and betacyanin, have antioxidant and thermal protective properties that prevent the death of lymphocytes caused by hyperthermia [84].

Yellow Pigments - Miraxanthines Found in Plants Portulaca oleracea (Portulacaceae), Mirabilis jalapa (Nyctaginaceae), representatives of the family. Caryophyllales showed in silico the potential anticancer effect due to the ability of miraxanthines to inhibit lactate dehydrogenase [85]. Alsoin silico, their property of a neuroglobin activator was revealed, which canbe used in the treatment of strokes [86]. Miraxanthin V and indigoxanthin are potential agonists of erythropoietin, which can be used to treat anemia in chronic kidney disease [87] and hepcidin antagonistsin silico, which will allow you to use themin the treatment of iron deficiency anemia [88].

Thus, betalains are natural dyes that are in demand in the food, pharmaceutical and perfumery and cosmetic industries, are non-toxic, possess a number of important pharmacological properties (antioxidant, anti-inflammatory, anti-cancer, antihypertensive, hypolipidemic, anti-diabetic, thermoprotective), which makes the search for new sources of this groups of substances and the development of technologies for their production as a promising alternative to synthetic drugs in the treatment of many diseases.

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