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Review Article

Apocarotenoids: A Brief Review

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ABSTRACT

Carotenoids are broad group of natural pigments, extending from red to orange, to yellow colours. Produced by plants and certain microorganisms (e.g.: fungi, bacteria and microalgae), carotenoids have significant physiological function (e.g.: light harvesting). Apocarotenoids are organic compounds, which is cleavage products of C40 isoprenoid pigments, named carotenoids, catalyzed by enzyme carotenoid oxygenase, produced absolutely by plants and microorganisms. Apocarotenoids show vital roles in several biological activities (e.g., plant hormones). Various carotenoids and apocarotenoids have great economic significance in feed, cosmetics, food supplements, pharmaceutical industries and also possess high commercial values

Key Words: Carotenoids, Apocarotenoids, Carotenoid oxygenase

INTRODUCTION

Carotenoids are broad group of isoprenoid pigments, which comprises more than 600 different compounds. Carotenoids are existing in all clades of life; but, their production is limited to photosynthetic organisms and certain nonphotosynthetic fungi and bacteria. In plants, carotenoids are crucial constituents of the photosynthetic apparatus where they deed as photoprotective pigments and involve in the light harvesting process. And also, plant carotenoids deliberate their bright orange, reddish, or yellow colors to several fruits and flowers. Animals are unable to produce carotenoids de novo and be dependent on nutritional sources to get their needs of these pigments that play as vitamin A precursor and antioxidants. [1]

The development of apocarotenoids is started by oxidative cleavage reactions that can be catalyzed by enzymes, generally CCDs, or take place via exposure of carotenoids to ROS. β-Cyclocitral is an example for a carotenoid cleavage product that can be produced following both scenarios. The formation of this β-carotene–derived volatile in photosynthetic tissues is initiated by a singlet oxygen $^1O_2$ attack, which takes place in the photosystem II, particularly in the presence of high light stress, while in citrus fruits, it is catalyzed by a CCD (CCD4b) that cleaves β-carotene, β-cryptoxanthin, and zeaxanthin. Although some CCDs display a quite relaxed substrate and site (double bond) specificity , cleavage reactions catalyzed by these enzymes generally take place at definite double bond(s) in defined carotenoid/apocarotenoid substrate(s). It should be also stated here that some bacterial and fungal members of the CCD family split biphenylic, stilbene substrates instead of carotenoids.[2]

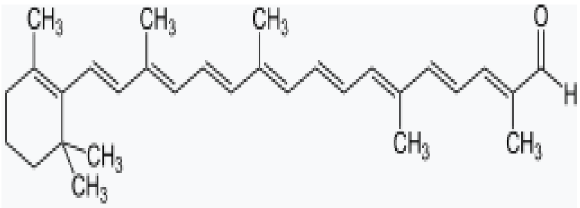
The electron-rich polyene system of carotenoids makes them liable to oxidation cleavage that cleave the carotenoid backbone. This cleavage reaction is catalyzed by carotenoid cleavage dioxygenases (CCDs), which construct a ubiquitous family of non-heme iron enzymes, and give the products called apocarotenoids. Apocarotenoids can similarly obtain through non-enzymatic cleavage by reactive oxygen species (ROS). In these two processes, apocarotenoids fulfill, with or without further enzymatic modifications, various important biological functions. The group of plant apocarotenoids includes important phytohormones, such as abscisic acid and strigolactones, and signaling molecules, such as β-cyclocitral, 3',4'-Didehydro-2'-apo-b-caroten-2'-al, Apo-2-lycopenal, Apo-6'-lycopenal(6'-Apo-y-caroten-6'-al), Azafrinaldehyde (5,6-Dihydroxy-5,6-dihydro-10'-apo-β-caroten-10'-al), Bixin (6'-Methyl hydrogen 9'-cis-6,6'-diapocarotene-6,6'-dioate), Citranaxanthin (5',6'-Dihydro-5'-apo-β-caroten-6'-one or 5',6'-dihydro-5'-apo-18'-nor-β-caroten-6'-one or 6'-methyl-6'-apo-β-caroten-6'-one), Crocetin (8,8'-Diapo-8,8'-carotenedioic acid), Crocetinsemialdehyde (8'-Oxo-8,8'-diapo-8-carotenoic acid), Crocin (Digentiobiosyl 8,8'-diapo-8,8'-carotenedioate), Hopkinsiaxanthin(3-Hydroxy-7,8-didehydro-7',8'-dihydro-7'-apo-b-carotene-4,8'-dione or 3-hydroxy-8'-methyl-7,8-didehydro-8'-apo-b-carotene-4,8'-dione), Methyl apo-6'-lycopenoate (Methyl 6'-apo-y-caroten-6'-oate), Paracentrone (3,5-Dihydroxy-6,7-didehydro-5,6,7', 8'-tetrahydro-7'-apo-b-caroten-8'-one or 3,5-dihydroxy-8'-methyl-6,7-didehydro-5,6-dihydro-8'-apo-b-caroten-8'-one), Sintaxanthin (7',8'-Dihydro-7'-apo-b-caroten-8'-one or 8'-methyl-8'-apo-b-caroten-8'-one). [3]

APOCAROTENAL OR TRAN-β-APO-8'-CAROTENAL

Apocarotenal, or *trans*-β-apo-8'-carotenal is a carotenoid seen in spinach and citrus fruits. Aapocarotenal plays a part as a precursor of vitamin A,but it has 50% less pro-vitamin A activity when compare with β-carotene. The empirical chemical formula for apocarotenal is $C_{30}H_{40}O$.

Apocarotenal posses an orange to orange-red colour and is used in foods, pharmaceuticals and cosmetic products. Depending on the product forms, apocarotenal is used in fat based food (margarine, sauces, salad dressing), beverages, dairy products and sweets. Its E number is E160e and it is approved for usage as a food additive in the US, EU, and Australia and New Zealand.

Epidemiological data have revealed that people with high β-carotene ingestion and high plasma levels of β-carotene have a considerably reduced danger of lung cancer. Though, studies of supplementation with bulky doses of β-carotene in smokers have revealed an surge in cancer risk, possibly as excessive β-carotene results in breakdown products that reduce plasma vitamin A and aggravate the lung cell proliferation prompted by smoke. The chief β-carotene breakdown product assumed of this behavior is *trans-beta*-apo-8'-carotenal (common apocarotenal), which has been found in one study to be mutagenic and genotoxic in cell cultures which do not react to β-carotene itself. [4]

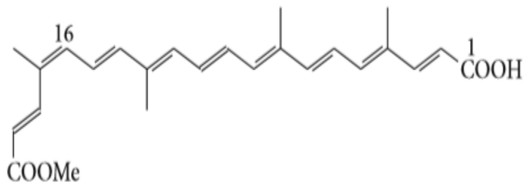


BIXIN

Bixin is an apocarotenoid seen in annatto, a natural food coloring obtained from the seeds of the achiote tree (*Bixa orellana*). Annatto seeds contain about 5% pigments, which consist of 70-80% bixin.

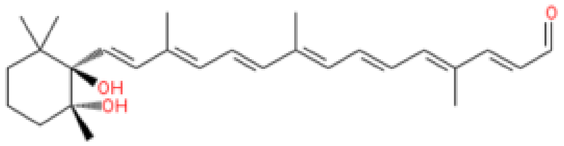
Bixin is chemically unstable when isolated and converts via isomerization into *trans*-bixin (β-bixin), the double-bond isomer.

Bixin is soluble in fats and alcohols but insoluble in water. Upon exposure to alkali, the methyl ester is hydrolyzed to produce the dicarboxylic acid norbixin, a water-soluble derivative. [5]



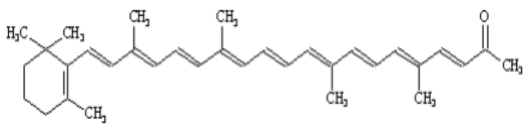
Bixin (Z-bixin or *cis*-bixin)

AZAFRINALDEHYDE[6]



CITRANAXANTHIN

Citranaxanthin is a carotenoid pigment used as a food additive under the E number E161i as a food coloring agent. There are natural sources of citranaxanthin, but it is generally prepared synthetically. It is used as an animal feed additive to impart a yellow color to chicken fat and egg yolks.[4] Citraxanthin is deep violet crystals; sensitive to oxygen and light and should therefore be kept in a light-resistant container under inert gas . Chemical names of Citranaxanthin is 6'-methyl-6'-apo- ß-carotene-6'-one, 5',6'-dehydro-5'-apo-18'-nor- ß-caroten-6'one , and the chemical formula is $C_{33}H_{44}O$. [7]

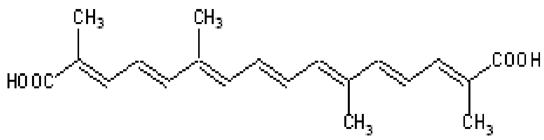


CROCETIN

Crocetin is a natural apocarotenoid dicarboxylic acid that is seen in the crocus flower and *Gardenia jasminoides* (fruits). It gives brick red crystals having melting point of 285 °C. [6]

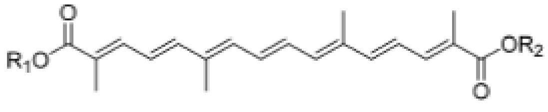
The chemical structure of crocetin forms the central core of crocin, the compound responsible for the color of saffron. Crocin and crocetin may provide neuroprotection in rats by reducing the production of various neurotoxic molecules, based on an in-vitro cell study. [7] A 2009 study including 14 individuals showed that oral administration of crocetin may reduces the effects of physical fatigue in healthy men [8] A 2010 pilot study considered the effect of crocetin on sleep. The clinical trial included a double-blind, placebo-controlled, crossover trial of 21 healthy adult men with a slight sleep complaint. It concluded that crocetin may ($p=0.025$) give to improving the quality of sleep [9] In high concentrations, it has protective effects against retinal damage *in vitro* and *in vivo.* [8]

The sodium salt of crocetin, transcrocetinate sodium (INN, also known as trans sodium crocetinate or TSC) is an experimental drug that increases the movement of oxygen from red blood cells into hypoxic (oxygen-starved) tissues. [9] Transcrocetinate sodium belongs to a group of substances known as bipolar trans carotenoid salts, which constitute a subclass of oxygen diffusion-enhancing compounds. Transcrocetinate sodium was one of the first such compounds discovered. [10]



CROCIN DIGENTIOBIOSYL

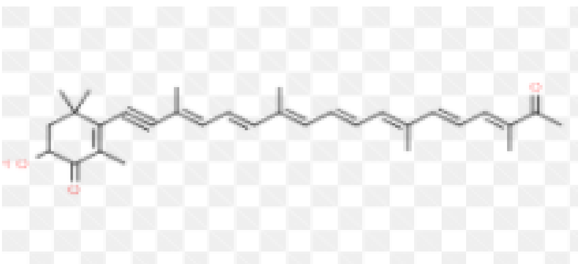
Crocetin and crocin (digentiobiosyl ester of crocetin) are the chief bioactive ingredients of saffron which is used as a costly spice, food colorant and traditional herbal medicine. These specific carotenoids have extended much research attention for their widespread pharmacological activities. [11] Following oral administration, crocetin is quickly absorbed into the blood circulation and broadly distributed into the extra-vascular tissues of the body, whereas the water-soluble compound crocin is scarcely absorbed through the gastrointestinal tract. [12] Crocetin and crocin have been shown to be effective in the inhibition and/or treatment of several diseases such as, myocardial ischemia, atherosclerosis, hemorrhagic shock, cerebral injury and cancer. [13] The compounds employ their biological and pharmacological effects mainly through their strong antioxidant activity. Though, there seems to be substantial difference in the efficacy of both phytochemicals when used in diverse diseases. [14]



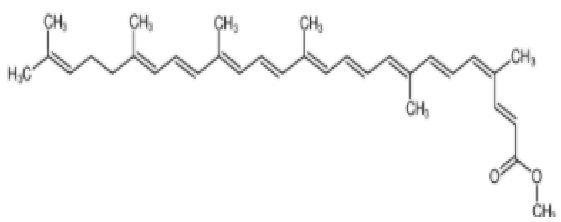
crocetin: $R_1 = R_2 = H$
crocin: $R_1 = R_2$ = gentiobiosyl

HOPKINSIAXANTHIN

Hopkinsiaxanthin, the principal pigment of the nudibranch, Hopkimia rosacea, is an acetylenic apo-carotenoid (C81H88Oa). The pigments obtained from Hopkinsia were seen to be similar to those of its food organism. In a specific study of the carotenoids of the beautiful, pink-colored nudibranch Hopkinsia rosacea MacFarland, Strain (1949) detected that the main pigment was exclusive and formerly undescribed. He called the pigment "hopkinsiaxanthin", stated a few of its properties, but did not depict it. As a additional study on the carotenoids of nudibranchs, the pigments of Hopkinsia were observed more carefully in an attempt to clarify the structure of hopkinsiaxanthin using some of the innovative techniques now employed in carotenoid chemistry. The pigments from the food of Hopkinsia were also observed as alternative probable source of hopkinsiaxanthin. [(15)]

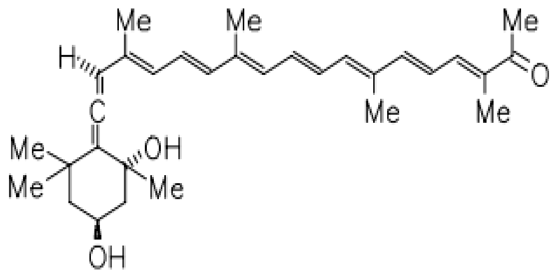


METHYL APO-6'-LYCOPENOLATE [(16)]



PARACENTRONE

The chemical formula for Paracentrone is $C_{31}H_{42}O_3$. , The stereocontrolled total production of a C_{31}-allenic *apo*-carotenoid, paracentrone, was accomplished by the convergent $C_{20} + C_{11} = C_{31}$ strategy. The key components of the synthesis were the Pd-catalyzed cross-coupling to stereoselectively construct the conjugated polyene backbone skeleton and the designed geometrical isomerization at the central double bond of the conjugated polyene chain. In addition, the terminal oxygenated cyclohexane ring possessing the allenic moiety was synthesized by the highly diastereoselective Sharpless epoxidation under the reaction conditions. [(17)]



CONCLUSION

Apocarotenoids are organic compounds, which is cleavage products of C40 isoprenoid pigments, named carotenoids, catalyzed by enzyme carotenoid oxygenase, produced absolutely by plants and microorganisms. apocarotenoids fulfill, with or without further enzymatic modifications, various important biological functions

This review has fulfilled significant information about structure, vital information regarding individual apocarotenoid and various properties of Apocarotenoids. It may be concluded that Apocarotenoid l is a resourceful and vital compound possessing medicinal importance and is a promising lead compound for the cosmetics, food supplements, pharmaceutical industries and also possess high commercial values.

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