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EUROCAROTEN

EUROPEAN NETWORK TO ADVANCE CAROTENOID RESEARCH AND APPLICATIONS IN AGRO-FOOD AND HEALTH

CAROTENOIDS: ANCIENT AND WIDESPREAD VERSATILE COMPOUNDS FOR AGRO-FOOD AND HEALTH

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Carotenoids: ubiquitous compounds in Nature

Carotenoids are special compounds of great relevance in agro-food and health, a subject recently covered in a dedicated book[1]. Although they are traditionally considered as pigments providing yellow, orange or red hues, they were not “invented” to provide colour, as colour vision appeared much more later than them. They are biosynthesized by all cyanobacteria, photosynthetic bacteria, algae and plants as well as by some fungi and non-photosynthetic bacteria. Recently, it has been found that some arthropods can also biosynthesize them *de novo*[2], although virtually all animals incorporate them through the diet[3].

To date over 700 carotenoids have been described in different types of animals (sponges, jellyfish, fish, molusks, insects, reptiles, mammals, birds, and so on), diverse plant structures (roots, photosynthetic tissues, petals, anthers, stigmas, fruits, seeds, etc.), macroscopic algae and fungi and a wide variety of microbes adapted to different conditions. In fact, carotenoids are found in organisms adapted to environments as disparate as the bottom of the oceans, glaciers, thermal ponds or hypersaline waters[4,5].

Taking all these facts into consideration it might be hypothesized that both the structure and the actions of carotenoids have evolved during Evolution on Earth.

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Chemistry and properties of carotenoids

Carotenoids are isoprenoids formed from blocks of five carbon atoms. A typical carotenoid has 40 carbon atoms although they can have also more (like decaprenexanthin) or fewer (like crocetin). They can be cyclic (like β-carotene) or acyclic (like lycopene) and contain oxygen atoms (xanthophylls) or just carbon and hydrogen atoms (carotenes). The oxygen atoms can be present in different functional groups like hydroxy (like zeaxanthin), carbonyl (like canthaxanthin), carboxylic (like crocetin) or epoxide (like violaxanthin) groups.

Chemical structures of diverse carotenoids are represented in **Figure 1**. As it can be observed, the most distinctive chemical feature of these compounds as a group is the presence of a polyene chain of conjugated double bonds (c.d.b).

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Carotenoids are ubiquitous in Nature and can be found in many different organisms and environments. Some examples are termophilic bacteria, algae, plant structures (like leaves, roots, flowers, fruits), sponges, fish and birds, among many others.

Association with other molecules

Xanthophylls can be either free or esterified. Thus, in some sources like peppers, citrus, potatoes and many others they are typically esterified with fatty acids, which increases their lipophilicity. Other carotenoids like crocetin (in saffron stigma or gardenia fruits) are associated with sugars, which makes them more hydrophylic. On the other hand, carotenoids can also form complexes with proteins (carotenoproteins), which can be found typically in invertebrates. This association with proteinds leads to increased stability and changes in their colours[5,6].

Stereochemistry

On the other hand, there can exist different spacial isomers of carotenoids. Thus, there can be different geometrical isomers (cis/trans, or more correctly Z/E) of a given carotenoid (**Figure 2**), which differ greatly in shape. Besides, some carotenoids have chiral centers, so that there can exist different optical isomers of them. One example of chiral carotenoid is zeaxanthin (**Figure 3**). It is important to note that although a defined carotenoid isomer can adopt many different shapes in space, it is expected that it exists in a specific preferred conformation of low energy[6].

Properties

With very few exceptions, carotenoids are extremely hydrophobic and therefore they are usually found in hydrophobic areas. However, as a result of the association with sugar moieties or proteins they can have access to an aqueous milieu. As already mentioned, the most characteristic chemical feature of carotenoids is the system of conjugated double bonds, which is much responsible for their shapes, light absorption properties and reactivity, among others. As it can be observed in **Figure 1**, phytoene and phytofluene have much fewer c.d.b. than typical representatives of the different kinds of carotenoids, hence some of their properties differ considerably relative to most carotenoids. As an example, they are colourless[7].

As it can be observed in **Figure 2**, (all-E)-isomers of carotenoids have a rod-like shape, whilst the Z isomers have an angular shape. The system of c.d.b. accounts for their colours, which are typically yellowish, orangeish or reddish, as they usually absorb blue and violet light (400-500 nm). At least 7 c.d.b. are needed for a carotenoid to exhibit colour. However, the colour of carotenoid is also dependent of other factors, like concentration, aggregation of molecules or interaction with other molecules like proteins, which can extend the palette of carotenoid colours to green, blue or purple[5,6,8]

CAROTENOIDS: ANCIENT AND WIDESPREAD VERSATILE COMPOUNDS **FOR AGRO-FOOD AND HEALTH**

The chromophore of c.d.b., apart from being responsible for the absorption of light by carotenoids is key in relation to their photochemical properties, which are essential in photosynthesis for the efficient energy transfer with chlorophylls and singlet oxygen. Furthermore, the polyene chain is rich in electrons and is important in relation to the antioxidant or pro-oxidant activities of carotenoids.

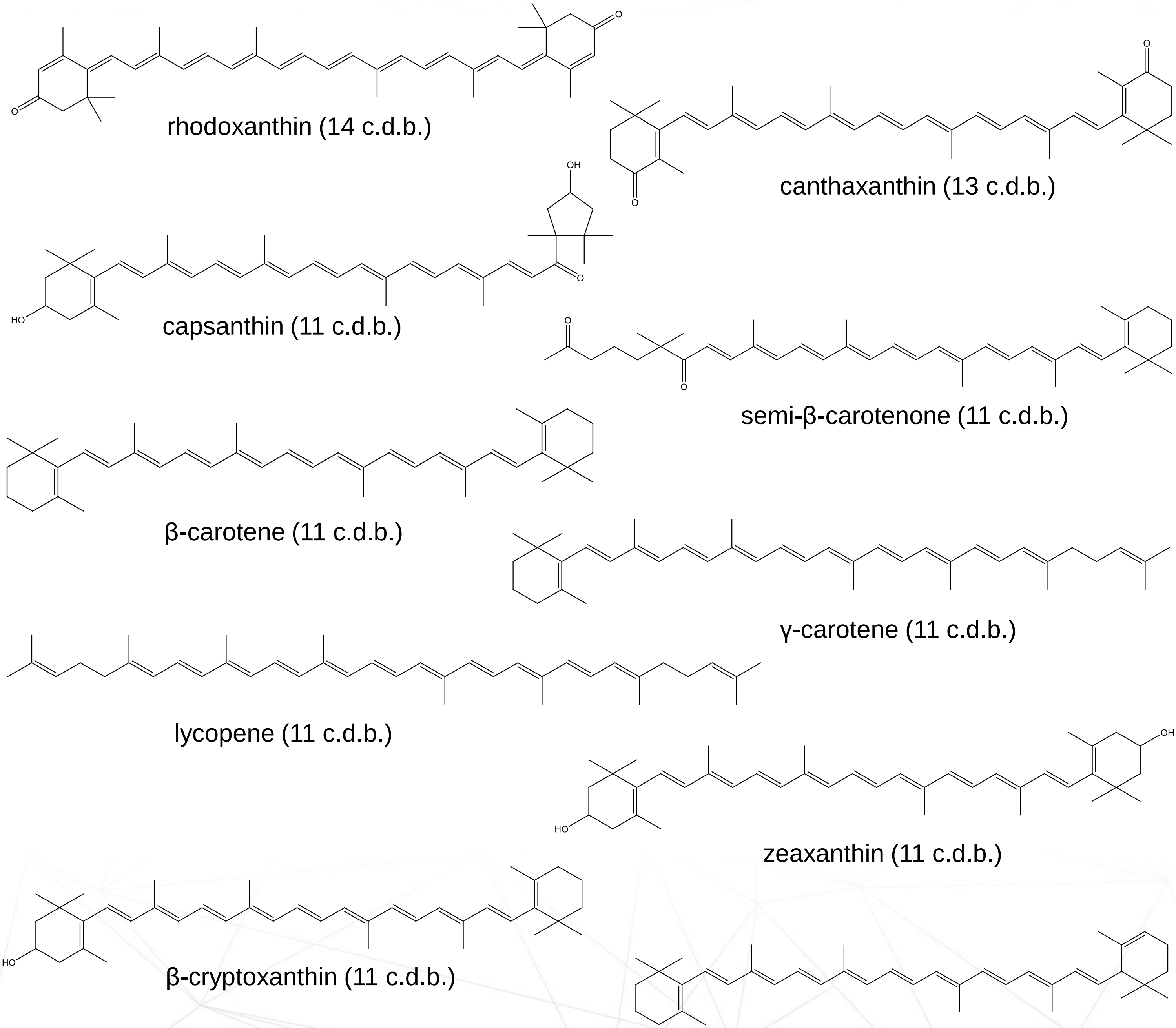

Figure 1. Chemical structures of some carotenoids.

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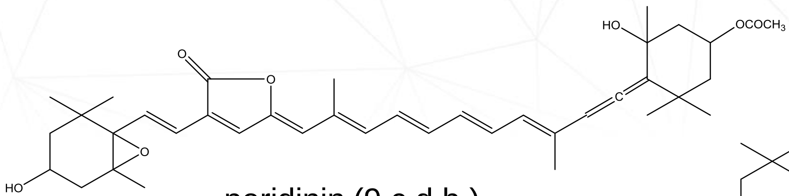
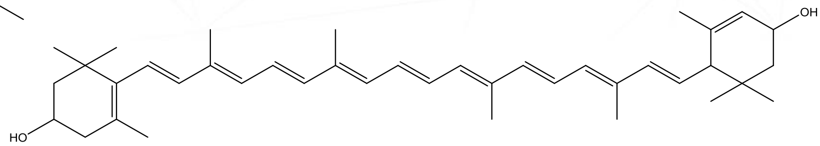
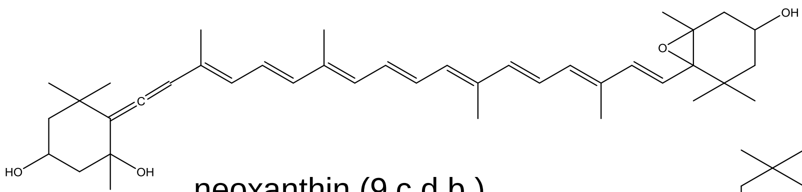


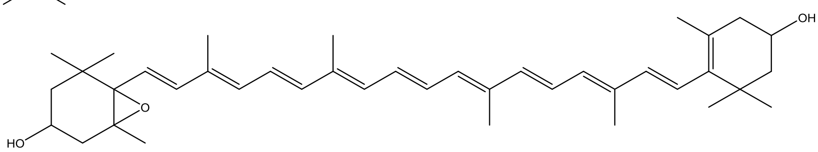
peridinin (9 c.d.b.)



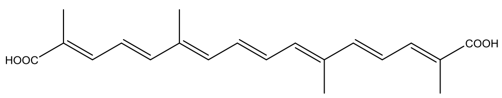
lutein (10 c.d.b.)



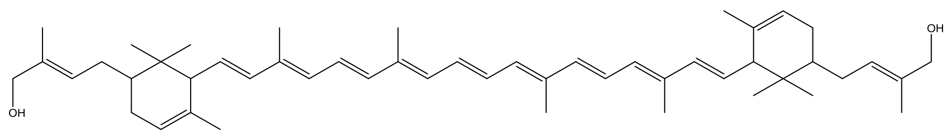
neoxanthin (9 c.d.b.)



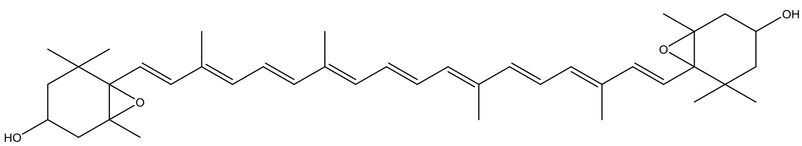
antheraxanthin (10 c.d.b.)



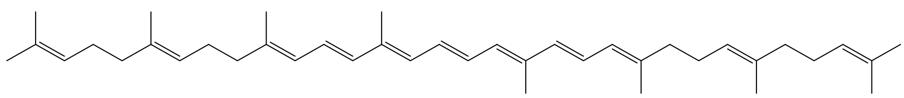
crocetin (9 c.d.b.)



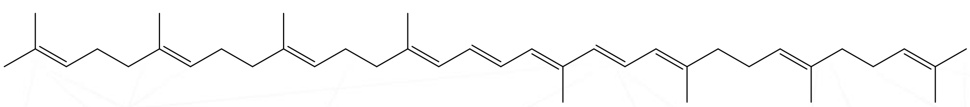
decaprenoxanthin (9 c.d.b.)



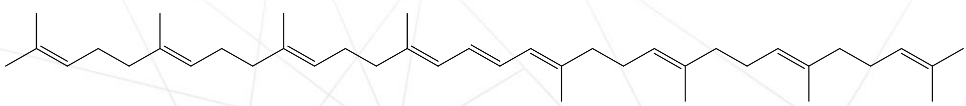
violaxanthin (9 c.d.b.)



ζ-carotene (7 c.d.b.)

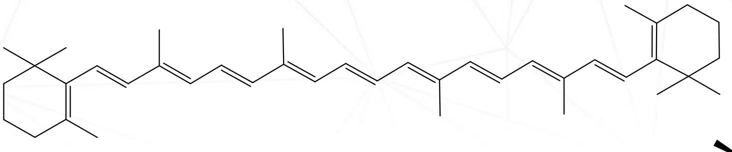


phytofluene (5 c.d.b.)

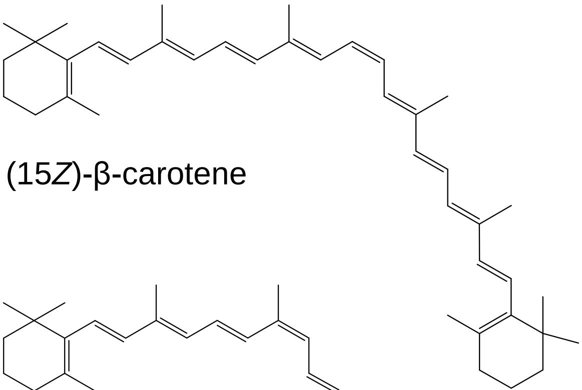


phytoene (3 c.d.b.)

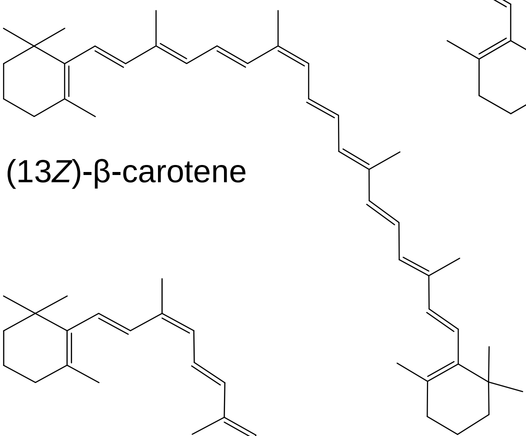
Figure 1. Chemical structures of some carotenoids .



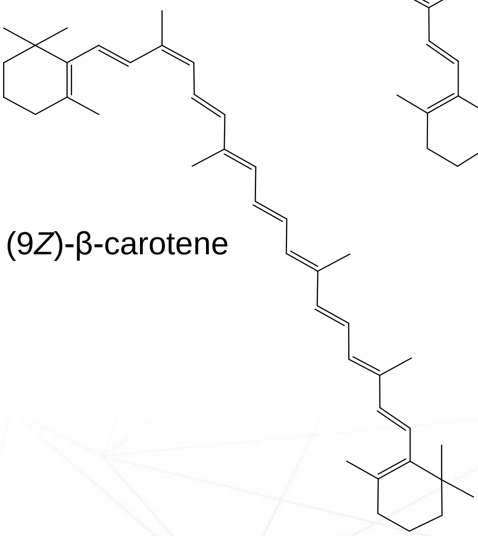
(all-*E*)-β-carotene



(15*Z*)-β-carotene

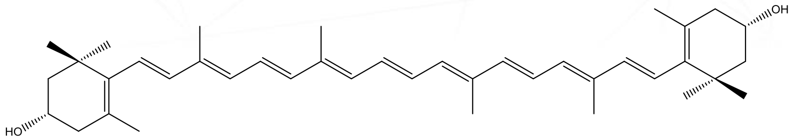


(13*Z*)-β-carotene

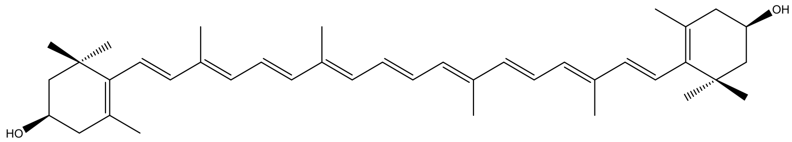


(9*Z*)-β-carotene

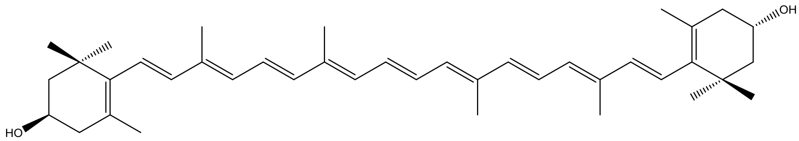
Figure 2. Chemical structure of some geometrical isomers of β-carotene.



(3*R*-3'*R*)-zeaxanthin



meso-zeaxanthin ((3*R*-3'*S*)-zeaxanthin)



(3*S*-3'*S*)-zeaxanthin

Figure 3. Chemical structures of optical isomers of zeaxanthin.

Functions

As commented before, carotenoids appeared very early in the history of life on Earth. Thus, they are present in one of the first inhabitants of our planet, the cyanobacteria, which are the oldest known oxygenic photosynthetic organisms and regarded as the origin of chloroplasts. They were not invented to provide colour as vision in colour appeared at a much later stage. Indeed, it is thought that among their first functions would be the harvesting of light, photoprotection and the modulation of membranes structures and properties[9]. Apart from this, since they are present in different structures of organisms adapted to the most disparate environments and more than 700 have been described so far, it appears interesting to hypothesize that both their structures and functions have evolved during the history of life in our planet. It is important to note that carotenoids can be converted chemically or enzymatically in other compounds which expands the range of actions somehow attributable to carotenoids.

CAROTENOIDS: ANCIENT AND WIDESPREAD VERSATILE COMPOUNDS **FOR AGRO-FOOD AND HEALTH**

Functions of intact carotenoids

The functions of carotenoids have been the subject of a comprehensive book[10]. According to Britton[11] carotenoids are important in Nature due to their roles in a series of processes like:

- Light harvesting: having an absoprtion spectra markedly different to that of chlorophylls, carotenoids contribute to the harvesting of light. This is subsequently transferred to chlorophylls for its use in photosynthesis[11].
- Photoprotection: the combination of light and oxygen favours the formation of singlet oxygen ($^1O_2$), which is a extremely reactive and damaging species that can be easily formed in the photosynthetic apparatus. However, the carotenoids present in such apparatus are very efficient at preventing its formation or quench it if already formed[11]. Besides, carotenoids can also protect from photooxidation by means of the so called xanthophyll cycle, by which violaxanthin (**Figure 1**) is enzymatically converted into zeaxanthin (**Figure 1**) under high light[12]. In this sense, according to Britton[11] life may not have developed in our planet without carotenoids as these are essential for the survival of photosynthetic organisms.
- Protection towards oxidizing species: The characteristic system of c.d.b. of carotenoids render them very prone to oxidation[11]. The antioxidant activity of carotenoids in model systems is beyond doubt, although demonstrated it in complex biological systems is very challenging. However, under certain conditions they can behave like pro-oxidants[11].
- Vision: in humans, the macula lutea of the retina contains high levels of lutein and zeaxanthin. Similarly, in some birds there are carotenoid-containing oil droplets in cells of the retina. Carotenoids here are thought to protect from oxidation and to improve vision[11].
- Communication between living beings by means of colour: In plants, the colours of flowers and fruits afforded by carotenoids contrast with the green of the photosynthetic tissues and attract pollinators and seed dispersers, which is essential for the survival and propagation of the species[11]. In animals, colours can be used for species recognition, warning, mimicry, crypsis, sexual signalling, social status signalling, parent-offspring signalling. In relation to in animals provide information about nutritional state, parasite load, immune defence, antioxidant activity, fecundity, genetic quality and photoprotection[13].
- Modulation of the properties of membranes: Carotenoids are components of membranes, where they are thought to protect against oxidation and have an effect in their structures and properties. In bacteria, carotenoids are thought to have a role similar to that of cholesterol in mammals in relation to reinforcing and maintaining the structure, properties and dynamics of membranes[11]. According to Britton[11], the importance of carotenoids in membranes may be even greater as many essential processes in cells are related to membrane components like elements of signal transduction systems.
- Fertility and reproduction: Carotenoids are often found in high levels in eggs and reproductive tissues of animals[11]. Examples are the high levels of carotenoids in egg yolk and the eggs of some fish. In fish, carotenoids have been associated to the reproductive success as well as the health status and rate of survival of the young. Hence it is hypothesized that they may have a role in fertility and reproduction[11].

Functions of carotenoid derivatives

Carotenoids derivatives can be formed enzymatically or chemically and can also have a role in important biological actions. This was the subject of a dedicated book chapter by Britton[14].

Typical examples of biologically active carotenoid metabolites are retinoids exhibiting vitamin A activity, like retinol, retinal or retinoic acid. There are also widespread carotenoid-derived norisoprenoids compounds with great aromatic potency, like β-damascenone (with an estimated detection threshold of 2 ng/L), safranal , β-ionol, theaspirane, megastigmente, or β-ionone, among others, that contribute to the aroma of the structures of many plants and derived products (rose, tomato, watermelon, quince, passion fruit, raspberry, grape, wine, tea, tobacco and so on). Similarly to colour, these aroma compounds attract animals for pollination and seed dispersal[14]. Some of these compounds could also act like pheromones, i.e. sexual attractants, for insects[15].

The carotenoids (9Z)-violaxanthin and (9’Z)-neoxanthin are also precursors of the plan hormone abscisic acid, which has been traditionally linked to processes related to senescence, the abscission of leaves and the induction of dormancy in both seeds and buds. This phytohormone is also thought to be involved in the closure of stomata, the response to abiotic stress (for instance to drought, temperature, light), and the induction of the defence against pathogens, among many others[14,15].

Other examples of carotenoid derivatives with biological actions are trisporic acid (that intervenes in the regulation of sexual reproduction in some fungi) and the grasshopper ketone, which repels predators of some grasshoppers[14].

Recently, there is much interest in strigolactones, a “new” kind of phytohormones involved in important actions (like the establishment of arbuscular mycorrhizae or the inhibition of shoot branching, among many other) which have been shown to derive from carotenoids 16. Furthermore, there is increasingly more interest in the study of the actions of apocarotenoids derived from dietary carotenoids in humans, which may have health-promoting actions, for instance in relation to carcinogenesis or the protection against oxidative stress[17–19].

Carotenoids in nutrition and health

The interest of carotenoids (beyond the role as vitamin A precursors of some of them) in nutrition and health grows incessantly as studies of different nature indicate that they (or their derivatives) may have a role in the reduction of the risk of developing different types of cancer or other diseases (for instance of the eye, the cardiovascular system, the skin or the bones). Detailed information in this respect can be found in scientific texts of different type[20–23].

Although it is frequent to attribute the health-promoting actions of carotenoids to their antioxidant activity, the undisputable demonstration of such activity in vivo is extremely challenging. Besides, it is important to bear in mind that such beneficial actions could stem from other mechanisms. Thus, there are studies indicating that some may be due to their pro-oxidant activity, the modulation of routes of intracellular signalling or membrane properties and even to their role in the immune system. Ample information about this can be found in books, reviews and original research articles[20,24–28]. However, the undisputable demonstration of the role of carotenoids in health-promoting actions is extremely complicate for reasons like the complexity of the human body, the wide variety of compounds ingested together with carotenoids in the diet, the limitations of intervention studies or those of other types of studies used to evaluate their biological actions. In any case, their chemical structure, their constant presence in the diet of humans, the consistent presence of some of them in tissues and biological fluids (plasma, colostrum, milk) and epidemiological studies relating carotenoid-rich diets with a reduced risk of of developing certain diseases suggest that, beyond the role of some of them as vitamin A precursors, carotenoids are important compounds in nutrition and health.

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