

CHAPTER 1

TITLE: Structures, nomenclature and general chemistry of carotenoids and their esters

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ABSTRACT

Carotenoids are widespread isoprenoids that intervene in actions ranging from the collection of light and photoprotection to the regulation of gene expression or the communication within or between species, just to mention only some examples. They are therefore much more than natural pigments as they are versatile compounds that elicit increasing interest in different disciplines like plant science, agriculture, food science and technology, nutrition or health, among others. Although carotenoids in humans are found almost exclusively free, in foods they can be associated to other molecules, like sugars, proteins or fatty acids. Such associations can result in important changes in their properties. Indeed, it is very common that food xanthophylls are in the form of esters, above all in many fruits. This can modify markedly properties like solubility and susceptibility to oxidation, which in turn can have an impact in aspects relevant to explain their levels in foods and humans, like their biosynthesis, deposition, stability and bioavailability, among others. The study of the esterification of carotenoids is undoubtedly gaining popularity. In this chapter, structural aspects related to isoprenoids, carotenoids, fatty acids and, finally, carotenoid esters are dealt with, with references to some physico-chemical properties and their importance at different levels.

1.1. INTRODUCTION

Carotenoids are widespread isoprenoids in Nature that intervene in many actions ranging from the collection of light and photoprotection to the regulation of gene expression or the communication within or between species, just to mention only some examples ¹. Interestingly, they can be chemically or enzymatically converted into other derivatives that can act as compounds with vitamin activity, phytohormones or aromas, among others ².

Carotenoids are therefore much more than natural pigments providing mainly yellow, orange or red colours. Indeed, they are very versatile compounds that elicit increasing interest in different disciplines like plant science, agriculture, food science and technology, nutrition or health, among others. In relation to these three latter disciplines, although their roles in as natural pigments and precursors of retinoids with vitamin A activity have been long known, the renewed interest in these compounds is mainly due to a large body of evidence accumulated in the last 30 years indicating that they may be health-promoting compounds and be important in the context of functional foods ³. Thus, they are thought to contribute to reduce the risk of developing certain types of cancers as well as cardiovascular, eye, skin or bone diseases, or even be beneficial for the cognitive function ⁴⁻⁸. Interestingly, carotenoids can provide cosmetic benefits ⁹, which can be used in the context of public health as a strategy to promote the consumption of fruits and vegetables ¹⁰. Although, the beneficial health-promoting effects of carotenoids are often attributed to their possible role as antioxidants, it is important to note that there can be other underlying mechanisms, like prooxidant or anti-inflammatory actions or the modulation of membrane properties, among others ^{4,11-17}. Interestingly, carotenoids and/or their derivatives can play important roles in cell signalling pathways, for instance by interacting with transcription factors like nuclear

factor erythroid 2-related factor 2 (Nrf2) ^{18,19} or nuclear factor-κB (NF-κB) ^{20,21}. Although carotenoids in human fluids and tissues are found almost exclusively free (albeit sometimes esters have been reported in plasma and skin ^{22,23} at level markedly lower compared to the unesterified carotenoids, and recently in colostrum but not in mature human milk ²⁴), in foods they can be associated to other molecules, like sugars, proteins or fatty acids. Such associations can result in important changes in their properties. Indeed, it is very common that food xanthophylls are in the form of esters, above all in many fruits. Although the esterification does not have an impact on the carotenoid chromophore and therefore on its colour, it can modify markedly its solubility and susceptibility to oxidation, which in turn can have an impact in aspects relevant to explain their levels in foods and humans, like their biosynthesis, deposition, stability and bioavailability, among others ²⁵. The study of the esterification of carotenoids is undoubtedly gaining popularity and has been greatly facilitated by important advances in analytical techniques that make possible the separation and identification of a great variety of carotenoid esters ²⁶.

In this chapter, structural aspects related to fatty acids, isoprenoids, carotenoids, and, finally, carotenoid associations with other molecules, with emphasis on carotenoid acyl esters are dealt with. References to some physico-chemical properties and their importance at different levels .

1.2. FATTY ACIDS

Fatty acids (FAs) are ancient and ubiquitous molecules present in all living matter. Both free and as part of complex lipids, they play a number of key roles in metabolism, as critical structural components of phospholipids and other complex lipids in cellular

membranes, as gene regulator and as parts of triacylglycerols, major metabolic fuel (storage and transport of energy).

1.2.1 Occurrence in Nature

The quantitative proportion and qualitative composition of fatty acids in various organisms are characteristic for every species and genus, and depend also on the environment. In bacteria more than 300 fatty acids and related compounds have been found. The fatty acid profiles are unique from one species to another and both the qualitative differences (usually at genus level) and quantitative differences (commonly at species level), can be used for identification purposes ²⁷. Large microbial libraries are available, as the Sherlock System library which has over 1,500 bacterial species, along with 200 species of yeast and identifies them by the analysis of fatty acid methyl esters (FAMES) ²⁸. FAs have also been used for chemotaxonomic perspectives in cyanobacteria ²⁹ and microalgae ³⁰. Microalgae are the primary producers of long chain polyunsaturated fatty acids that are eventually accumulated through the various trophic levels. The FAs derived from microalgae are gaining importance because of their potential application in food ³¹ and biofuel industries ³².

In the Plant Kingdom, an amazing variety of FA structures are found particularly in angiosperm seed oils. An electronic data base of seed oil fatty acid composition (SOFA) (<http://sofa.mri.bund.de/>) at the Max Rubner-Institute has been made available for researchers for different purposes, from biochemical systematics and plant phylogeny chemotaxonomy to the search for genes useful for tailor-made industrial fats ³³.

In animal's tissues, the FAs profile reflects the tissue biosynthesis and the fatty acid composition of ingested lipids especially for monogastrics (pigs, poultry and rabbits) since ruminants can hydrogenate fatty acids in the rumen ³⁴. Some FAs have also important metabolic roles as biosynthetic precursors of oxylipins, including the

eicosanoids (prostaglandins, leukotrienes, thromboxanes and lipoxins) and docosanoids (protectins, resolvins and maresins), while in plants, also hormones like the jasmonates are derived from α -linolenic fatty acids acid.

1.2.2. Chemical structure

Fatty acids (FAs) are defined by the International Union of Pure and Applied Chemistry (IUPAC) as “aliphatic monocarboxylic acids derived from or contained in esterified form in animal or vegetable fat, oil or wax which may be saturated or unsaturated. By extension, the term is sometimes used to embrace all acyclic aliphatic carboxylic acids”³⁵. The structures of some FAs is shown in Table 1.1.

[Table 1.1 near here]

The classification of fatty acids in classes and subclasses according to the LIPID MAP is shown in Table 1.2.³⁶ More information is available at the LIPID MAPS-Nature Lipidomics Gateway that is a free, comprehensive online resource providing tutorials and instructional material, experimental data for lipids and genes along with protocols and standards, databases of lipid structures and lipid-associated genes or proteins, and a variety of lipidomics tools. The database is accessible through any web browser (<http://www.lipidmaps.org/>).

[Table 1.2 near here]

According to this classification the fatty acyls (FA) are a diverse group of molecules synthesized by chain elongation of an acetyl-CoA primer with malonyl-CoA (or

methylmalonyl-CoA) groups that may contain a cyclic functionality and/or are substituted with heteroatoms. Thirteen subclasses are considered indicating the large variants of structures that can be found in nature. The first subclass includes the most common straight-chain saturated fatty acids containing a terminal carboxylic acid. Although several hundred of forms have been identified in nature the number occurring frequently in the common lipids is much fewer (from 10 in plants to about 20 in animal tissues). Most common fatty acids are straight chain, and have an even number of carbon atoms (from 12 to 22) because the biosynthetic pathway common to all organisms involves chemically linking two-carbon units together, though FA with shorter, longer and odd-numbered chain also exist in nature ³⁷. They can be classified in three categories: saturated FAs (SFA) (that lacks unsaturated linkages between carbon atoms) and unsaturated, which can be further divided in monounsaturated FAs (MUFA) and polyunsaturated FAs (PUFA) depending on the number of unsaturated bonds (one or more respectively). In PUFA double bonds are usually separated by a single methylene group what is known as methylene-interrupted pattern ³⁸. However, although much less frequently, there are also present "conjugated structures" where double bonds are not separated by a methylene group. These structures are now gaining much interest because some "conjugated fatty acids" have shown special nutritional properties, most of them derived from the unconjugated structure of linoleic acid (C18:2 n-6). According to their chain length the FAO/OMS Expert consultation ³⁹ recommends a further division in four sub-classes in the SFA group: short-chain (3-7), medium-chain (8-13), long-chain (14-20) and very long chain (> 21). Similarly unsaturated fatty acids are also further classified into three sub-groups: Short-chain (≤ 19) Long-chain (20-24), Very-long-chain (≥ 25) or more carbon atoms.

1.2.2.1 Isomerism in unsaturated fatty acids

Unsaturated fatty acids show isomerism, which can be either positional or geometrical. The positional isomers occur when the double(s) bond (s) are located at different position in the carbon chain. Geometrical (*cis/trans*) stereoisomerism occurs when substituents are arranged differently in space due to restricted rotation of a double bond in the molecule. If the two ligands attached to separate atoms connected by the double bond lie on the same side of a plane are said to be located *cis* to each other. If they are on opposite sides, their relative position is described as *trans*. For alkenes the terms *cis* and *trans* may be ambiguous and have therefore largely been replaced by the *E/Z* convention, which is based on the application of sequence rules ³⁵ (Figure 1.1).

[Figure 1.1 near here]

In Nature the geometry of the double bonds in eukaryotes is exclusively *cis* and usually positioned in the 3rd, 6th or 9th carbon from the terminal methyl group. The significance of the ubiquitous *cis* structural feature of the unsaturated lipid double bond is based on its contribution to the organization of phospholipids in one of the most important units of living organisms: the cell membrane ⁴⁰. Membrane homeostasis is obtained by a precise balance between saturated and *cis* unsaturated structures as the key feature of the homeoviscous adaptation ⁴¹. Because of its essentiality in living organisms, the *cis* geometry is strictly controlled by the regiospecific and stereoselective enzymatic activity of desaturases during MUFA and PUFA biosynthesis ^{42,43}

Fatty acids with double bonds of *trans* (or *E*) configuration are found occasionally in natural lipids from ruminants animal's tissues, where they are formed naturally by biohydrogenation in the rumen, or are formed during industrial processing

(hydrogenation) and so enter the food chain, but they tend to be minor components. Their suitability for human nutrition has been widely discussed and related with increases in all-cause mortality ⁴⁴. Both industrial and ruminant TFA consumption have been positively associated with an increased risk of CVD ⁴⁵. For this reason the elimination of industrial TFA in foods has been proposed and limits of content have been legislated in some countries ⁴⁶.

1.2.3. Nomenclature

FAs terminology can be confusing due to the different nomenclature systems in use. Whatever the system used, it must clearly identify the structure and indicate the different aspect comment above: carbon chain, number of unsaturation, stereo isomeric configuration and the position of the first double bond in relation to the carboxylic or methyl end and the presence of other substituents like branched chains, ring systems and oxygen groups.

Trivial names give no clues on the structure but they are frequently used. They are derived from a common source of the compound or the source from which it was first isolated ie. myristic acid was first identified in seed oils from the Myristicaceae family and oleic acid is the major constituent of olive oil (*oleum*). Similar names may correspond to very different structures i.e. arquidonic and araquidic, both have 20 carbons but have different structures one is a PUFA (4 double bonds) and the other is a SFA. Similarly isomeric forms have different names ie. oleic (C18 *cis*) and elaidic (C18:1 *trans*).

Systematic nomenclature is more technically clear and descriptive. It is derived from official chemical nomenclature established by the International Union of Practical and Applied Chemistry ⁴⁷. Fatty acids are numbered with the carbon atom of the carboxyl

group as C-1. Shorthand notation, like trivial names, save space and contribute to rapid understanding. Fatty acids are named by their number of carbon atoms, and their number of double bonds after a colon, e.g., 18:0 stands for stearic acid and 18:1 for oleic acid. For unsaturated fatty acids two different abbreviation are used to make clear where the double bonds are located in molecules:

cis/trans-Δx: The double bond is located on the xth carbon-carbon bond, counting from the carboxyl terminus. The *cis* or *trans* (*Z/E*) notation indicates whether the molecule is arranged in a *cis* or *trans* conformation. This is the systematic recommended notation⁴⁷.

n-x: The “n minus” system is also referred to as the omega system, but omega –notation is discouraged although widely used. *n* is the number of carbon atoms in the chain and *x* is the (lower) locant of the double bond closest to the methyl end of the molecule. This system defines easily the different metabolic series, such as n-9, n-6 and n-3, etc. The “n minus” system is applicable only to *cis* unsaturated fatty acids and to those *cis* polyunsaturated fatty acids whose double bonds are arranged in a methylene interrupted manner.

Different denominations of common fatty acids and information about some of their sources are shown in Tables 1.3, 1.4 and 1.5.

[Tables 1.3, 1.4 and 1.5 near here]

1.2.4. Physical properties

The physical properties of the different fatty acids, such as their solubility, the melting point and the susceptibility to oxidation will depend on the number of carbon

atoms of the molecule and the number of double bonds. They also determine the physical properties of the molecules they take part as components.

1.2.4.1 Solubility

FA are amphipathic molecules containing a hydrophobic (the aliphatic moiety) and hydrophilic (carboxyl group) part. Short chain fatty acids ($C < 4$) are freely soluble in water in their protonated and ionized form and have a pKa of about 4.5, but longer carbon chain FAs are poorly soluble in water. As the aliphatic chain length of the fatty acid increases the protonated fatty acids become much less soluble so for FAs over 12 carbons the aqueous solubility is quite low. On the other hand at high pH a negatively charged carboxylate group (COO^-) is formed. This property gives ionized FAs their detergent properties. Thus, the actual water solubility, particularly of longer-chain acids, is often very difficult to determine since it is markedly influenced by pH and temperature, and also because fatty acids have a tendency to associate, leading to the formation of monolayers or micelles ⁴⁸.

1.2.4.2 Melting points

A major factor that affects the melting point of FAs is the geometric shape of the molecules. SFAs are more linear than unsaturated FAs with *cis* double bonds (Table 1.1), allowing them to pack together closely and thus have the potential for more attractive molecular interactions. Thus, SFAs have higher melting points than unsaturated FAs with the same carbon number. However 'even' acids show higher melting points than that of the 'odd' acid immediately below and above it ⁴⁹. In the case of unsaturated fatty acids, the presence of double bonds produces a large decrease in the melting point. So, the oils due to a high proportion of unsaturated fatty acids have low

melting temperature. Animals that live at low temperature (i.e. fish) have a large proportion of long chain unsaturated fatty to prevent their fats from solidifying. Table 1.6 shows the melting points of some fatty acids ⁵⁰. Although unsaturation has a pronounced lowering effect on melting points, in isomeric pairs, the trans form of the acid show higher melting temperatures ⁵¹.

1.2.4.3 Susceptibility to oxidation

The susceptibility of fatty acids to oxidation is dependent on their degree of unsaturation. Saturated fatty acids are very stable but as the number of double bonds increases, the susceptibility to oxidation increases. The oxidation rates of oleic (*cis* 18:1), linoleic (*cis* 18:2), and linolenic (*cis* 18:3) have been reported to be 1:27:77 ⁵². The carbon-hydrogen bond strength in double bonds is reduced in comparison to the aliphatic chain of stearic acid (99 kcal/mol vs 80 kcal/mol in oleic and 69 kcal/mol in linoleic). This reduction of bond strength allows hydrogen to be more easily abstracted from the fatty acid leading to the formation of a free radical, the first step in the lipid oxidation cascade ⁵³.

However there is evidence indicating that kinetics of fatty acid oxidation depends upon the milieu in which they react with oxidants: aqueous environments such as those at the cell membrane/plasma and cytosol/cell membrane interfaces yield different oxidation profiles than the organic ones. In fact some experiments in cell cultures point out that some fatty acid might indirectly act as anti- rather than prooxidant in vascular endothelial cells, hence diminishing inflammation and, in turn, the risk of atherosclerosis and cardiovascular disease ⁵⁴. Enzyme catalyzed oxidation is the initial step in the production of eicosanoids and jasmonates (biologically active metabolites in animals and plants respectively) ⁵⁵.

1.2.5. Overview of biosynthesis

The biosynthesis of fatty acid occurs in all living organisms in the cytosol and requires NADPH and acetyl-CoA. The standard way for cells is through the fatty acid synthesis cycle. This cycle includes eight enzymes (acyl-CoA synthase, acyl-CoA carboxylase, acyltransferase, ketoacyl synthase, ketoacyl reductase, hydroxyacyl dehydratase, enoyl reductase, and thioesterase) and is initiated with acetic acid, CoA, and ATP to make acetyl-CoA using acyl-CoA synthase as catalyst. Acetyl-CoA is converted to malonyl-CoA by a biotin-dependent acetyl-CoA carboxylase. This step is the committed step of fatty acid biosynthesis. Malonyl-CoA and NADPH are used by the multienzyme fatty acid synthase to yield palmitate. This mechanism leads to a wide variety of lipids that contain the fatty acyl chain, including fatty acids, phospholipids and glycerolipids. In animals, it occurs primarily in liver, adipose tissue, central nervous system, and lactating mammary gland (Phan et al. 2014).

The enzymes of fatty acid biosynthesis are divided into two groups, while in animals and fungi these fatty acid synthase (FAS) reactions are carried out by a single multifunctional protein (FAS I) that consists of a single gene that produces a multifunctional protein⁵⁶ in plants, bacteria and lower eukaryotes consist of two genes (FASII) and their polypeptide products coalesce to form a multifunctional complex⁵⁷. While FAS I produces only palmitate, FASII is capable of producing a large diversity of fatty acids with different chain lengths. Unsaturated fatty acids, iso- and anteiso-branched-chain fatty acids, and hydroxy fatty acids.

Fatty acids can further be elongated into very long chain fatty acids by individual membrane-bound enzymes, named elongases located in the endoplasmic reticulum. The synthesis of very long chain fatty acids is a ubiquitous system found in different organisms and cell types⁵⁸. Fatty acid desaturase, an enzyme in the endoplasmic

reticulum, introduces double bonds between carbons 9 and 10 in palmitate and in stearate, producing palmitoleic acid (16:1:Δ9) and oleic acid (18:1:Δ9), respectively. Mammals lack the Δ12- and Δ15-desaturase enzymes necessary for desaturation of an 18-carbon fatty acid at the omega-3 (or Δ15) or omega-6 (or Δ12) positions. Thus, Linoleic acid (LA; 18:2:Δ9,12) and α-linolenic acid (ALA; 18:2:Δ9,Δ12, Δ15) are essential fatty acids (EFA) that must be supplied by the diet because cannot be synthesized in the body. By comparison, plants and algae contain the enzymes Δ12- and Δ15-desaturase and as a result, LA and ALA are two of the most prevalent fatty acids found in plant tissues and oils (Lee et al. 2016). EFAs are metabolized to their respective long-chain metabolites: dihomo-gamma-linolenic acid (DGLA), and arachidonic acid (AA) from LA; and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) from ALA. Some of these long-chain metabolites form precursors to respective prostaglandins (PGs), thromboxanes (TXs), and leukotrienes (LTs), lipoxins (LXs) and resolvins ⁵⁹.

1.2.6. Overview of actions

Among lipids, FA are of crucial relevance in the structure and physiology of the body because free or as part of complex lipids have a range biological activities from storage to energy transport, as essential components of all membranes, or as gene regulators ⁶⁰.

1.2.6.1. Sources of energy

As part of triglycerides, they are the primary source of energy (9 kcal /g or 37.62 kJoules/g) and in infants, provide more than 50% of the daily energy requirements. All fatty acids can be oxidized by most aerobic tissues but not the brain, but the exact

energy yield depends on the structure of the fatty, providing an alternative to glucose. Fatty acid oxidation becomes important in times of limited glucose availability.

1.2.6.2. Modulation of membrane properties

As components of cell membranes phospholipids influences the physical nature of the membrane (called “fluidity”) which in turn influences the function of membrane proteins and the movement of proteins within the membrane. Polyunsaturated fatty acids confer distinctive properties to the membranes in particular decrease their rigidity while saturated and monoenoic acids ensures that there is a correct balance between rigidity and flexibility. Indeed, saturated and 2-hydroxy fatty acids in sphingolipids appear to give additional rigidity and hydrogen-bonding stability to the sub-domains of membranes termed 'rafts'. The fatty acid compositions of phospholipids, may be influenced by diet, metabolism, hormonal milieu, state of cell activation, and genetics, among other factors ⁶¹.

1.2.6.3. Regulation of gene expression

Fatty acids released from membrane lipids or taken up into cells can have specific metabolic, functional, or signaling roles such as diacylglycerols, ceramides, lysophospholipids, and endocannabinoids, and there is evidence that the fatty acid composition of those signaling molecules, influences their biological activity ⁶².

Some fatty acids are of essential character and are precursors of powerful locally acting metabolites, i.e. the eicosanoids and docosanoids (of 20 and 22 carbon atoms, respectively), such as leukotrienes, prostaglandins, thromboxanes, prostacyclins, protectins and resolvins ^{62,63}.

Some of them are able to regulate the expression or activity of transcription factors, so they play a role in controlling gene expression and protein production by cells. These effects enable fatty acids to regulate metabolic processes such as fatty acid synthesis and oxidation and lipoprotein assembly and clearance, insulin sensitivity, and inflammation ⁶⁴.

1.3 ISOPRENOIDS

Isoprenoids, which have also been termed terpenes or terpenoids, are considered the biggest family of natural compounds in living organisms. They are ancient and widespread compounds. Thus, they have been identified in sediments dating back ca. 2.5 billion years and over 23000 members of the family have been identified in the most diverse organisms ^{65,66} They are built by consecutive condensations of building blocks of 5 atoms of carbon, namely isopentenyl diphosphate (IPP) and its isomer, dimethylallyl diphosphate (DMAPP) (Scheme 1.1).

[Scheme 1.1. near here]

These isoprene building units are biosynthesized via two distinct metabolic routes, namely the mevalonate (in eukaryotes, archaeobacteria, and the cytosol of higher plants) and the non-mevalonate pathways (eubacteria, green algae and plastids of higher plants).

Being a very large group of compounds, they can be classified into different groups depending on the number of such isoprene units (Table 1.7, Scheme 1.2) ^{66–68}.

Being ancient and widespread natural compounds it is not surprising that they are involved in key processes. Thus they can act like regulators of gene expression, modulators of membrane properties, vitamins, antimicrobial agents, hormones, pheromones, electron transporters, pigments, aroma, flavour compounds, etc. ^{65,68}.

1.4 CAROTENOIDS

1.4.1. Occurrence in Nature

Carotenoids are biosynthesized by all photosynthetic organisms and by some non-photosynthetic bacteria and fungi ⁶⁹. In general, animals cannot synthesize them *de novo*, although they can modify them. As an example, humans and other mammals can express at least two carotenoid cleavage oxygenases (usually termed as β,β -carotene 15,15'-monooxygenase and β,β -carotene 9',10'-dioxygenase) that cleave carotenoids into oxidized derivatives like retinoids and apocarotenoids, respectively ^{70,71}. However, recently it was demonstrated that some arthropods like aphids and adelgids among others, can biosynthesize them thanks to the presence in their genomes of carotenogenic genes laterally transfer from fungi, as a result of which they could be regarded as "natural transgenic organisms" ²⁵.

Carotenoids are widespread in Nature. Thus, it is estimated that they are present in ca. 700 organisms belonging to the three domains of life, more specifically in ca. 10 organisms within Archaea, ca. 170 of Bacteria and ca. 500 of Eukaryotes ⁷². Thus, their occurrence is well-described in different plant structures (photosynthetic tissues, petals, anthers, stigmas, fruits, seeds, roots), land and water animals (sponges, jellyfish, fish, mollusks, arthropods, reptiles, mammals, birds, and so on), macroscopic algae and fungi and a myriad of microorganisms including cyanobacteria, one of the first inhabitants of our planet ³. Indeed, it is noteworthy that carotenoids are present in organisms adapted

to the most disparate environmental conditions, from the bottom of the oceans to glaciers, thermal ponds, hypersaline waters or in even very dry, oxidizing or radiative conditions^{73–77}

1.4.2. Chemical structure

The main structural feature of carotenoids is their system of conjugated double bonds (c.d.b.), that is usually termed “polyene chain”. The colourless carotenoids phytoene and phytofluene are rarities within the carotenoid family as their systems of conjugated double bonds are much shorter (Scheme 1.3). Thus, phytoene has 3 c.d.b. and phytofluene 5 c.d.b.. Such clear differences with respect to other carotenoids are expected to have an impact in the properties and actions of these carotenoids that are eliciting much interest at different levels, including the promotion of health and cosmetics^{9,78}.

[Scheme 1.3. near here]

Although there are exceptions, a typical carotenoid is a tetraterpenoid containing eight isoprenoid building blocks, hence it usually has 40 atoms of carbon. Depending on the presence or absence of rings in their molecules, they can be classified into two main groups: cyclic or acyclic carotenoids, respectively. The different basic end groups described in carotenoids are shown in **Scheme 1.4** and further information is given in **Table 1.8**.

[Scheme 1.4. near here]

[Table 1.8. near here]

The numbering of the atoms of carbon goes from the ends to the center of the molecule, from 1 to 15 in one side of the molecule and from 1' to 15' in the other. The methyl groups are counted from 16 to 20 and from 16' to 20', respectively (Scheme 1.5)

⁷⁹.

[Scheme 1.5. near here]

Similarly, carotenoids can be classified into two groups considering the presence or absence of oxygen in their molecules. Hydrocarbon carotenoids, that is, those containing exclusively carbon and hydrogen atoms in their molecules are termed carotenes. Those also containing oxygen are termed xanthophylls. Among the most common oxygenated functions in food carotenoids are hydroxyl (present in β -cryptoxanthin, lutein, zeaxanthin), epoxide (violaxanthin, neoxanthin), furanoid (auroxanthin) or carbonyl (canthaxanthin, capsanthin) groups. Other oxygenated groups that can be naturally found in carotenoids are carboxylic, acetate, lactone or sulphate groups ^{79,80}.

Apart from these two general classifications of carotenoids as cyclic or acyclic or carotenes and xanthophylls, other subgroups of carotenoids can be distinguished on the basis of their structure. Thus, there are bacterial carotenoids that have one or two additional isoprenoid units and contain 45 or 50 atoms of carbon. One typical example is decaprenoxanthin (Scheme 1.3). There are also two distinct subgroups of carotenoids that contain fewer than 40 atoms of carbon, like peridinin (Scheme 1.3), are carotenoids that lack one to three atoms of carbon in the central hydrocarbons backbone.

On the other hand, apocarotenoids lack fragments at one or both ends of the molecules, like the saffron carotenoid crocetin which contains 20 atoms of carbon (Scheme 1.3). On the other hand, there are carotenoids in which a bond between adjacent carbons (except the carbons 1 and 6 in rings) has been broken, like semi- β -

carotenone (Scheme 1.3). These are termed secocarotenoids. Lastly, there are carotenoids in which the system of conjugated double bonds is shifted, such that there is a simple bond between carbons 15 and 15' rather than the usual double bond. Carotenoids with this structural feature, like rhodoxanthin (Scheme 1.3), are termed retrocarotenoids.⁸⁰

Apart from these natural carotenoids, more than 150 obtained chemically that contain heteroatoms have been obtained (Scheme 1.6)⁸¹.

1.4.2.1. *Stereochemistry*

There can exist different spatial isomers of carotenoids. Featuring many double bonds in their molecules, carotenoids can exist as all-*trans* (all-*E*) or *cis* (*Z*) isomers, which can differ markedly in shape. Furthermore, many carotenoids have chiral centers in their molecules, so that there can exist different optical isomers of them. In relation to the stereochemistry of carotenoids, it is important to note that, although a specific carotenoid isomer can adopt many different shapes in space, it will be expected to exist in a specific preferred conformation of low energy⁷⁹.

1.4.2.1.1. Geometrical isomers

Geometrical isomerism refers to the relative position of substituents around a planar carbon-carbon double bond. Carotenoid geometrical isomers are often designated using the *cis/trans* designations, although the *E/Z* designation is considered to be more precise. This is based on the application of sequence rules (Figure 1.1)⁸². Different geometrical isomers of a carotenoid can differ greatly in size and shape as it can be readily observed in Scheme 1.8.

In general, the (all-*E*)-isomers of carotenoids are the most stable and the major ones. Most theoretical *Z* isomers are not detected as there are important steric hindrances in them, although some are commonly found in Nature and can be readily formed in carotenoid extracts ^{79,83}. Some typical examples of *Z* isomers of carotenoids that occur naturally in certain sources are (15*Z*)-phytoene (usually the major isomer in carotenogenic organisms) ⁸⁴, (9*Z*)-bixin in the seeds of *Bixa orellana* ⁸⁰ or the highly sterically hindered (7*Z*,9*Z*,7'*Z*,9'*Z*)- lycopene (polycopene), a major carotenoid in tangerine tomatoes ⁸⁵ (Scheme 1.9).

[Scheme 1.9. near here]

In any case, the presence of *Z* isomers of carotenoids in any source should always be interpreted with the understanding that they may be formed as a result of diverse industrial or culinary treatments or during carotenoid handling in the laboratory ^{86–88}.

1.4.2.1.2. Optical isomers

A molecule that contains carbon atoms to which four different substituents are attached (that is, asymmetric carbon atoms, which constitute chiral or stereogenic center) can exist in different configurations. A classical example of carotenoid with chiral centers is zeaxanthin, that can exist as different isomers, namely (3*R*-3'*R*)-zeaxanthin, (3*S*-3'*S*)-zeaxanthin and (3*R*-3'*S*)-zeaxanthin (*meso*-zeaxanthin) (Scheme 1.10). The discernment of the different optical isomers of zeaxanthin is particularly important as two of them, specifically (3*R*-3'*R*)-zeaxanthin and (3*R*-3'*S*)-zeaxanthin (*meso*-zeaxanthin) are found in the macula lutea of the human retina ⁸⁹.

[Scheme 1.10. near here]

1.4.2.2. *Associations of carotenoid molecules: carotenoid aggregates*

Carotenoids, like other molecules, can form aggregates as a result of weak and reversible bonding by H-bridges, van der Waals interactions, dipole forces and hydrophobic effects of hydrophobic molecules, their polar groups and the surrounding solvent. Obviously, the aggregates have different physico-chemical properties as compared with the individual molecules ^{90,91}.

Carotenoids are known to form two different kinds of aggregates when they are in hydrated polar solvents. In one of them (the so-called H-aggregates), the carotenoid molecules are stacked such that their unsaturated backbones are rather parallel to each other and closely packed. These self-assemblies are characterized by a pronounced blue shift (hypsochromic shift) of their absorption maxima as compared to the single molecule. Contrastingly, in the so-called J-aggregates, the backbones of conjugated double bonds are organized in a more head-to-tail fashion producing in loose association of the carotenoid molecules. These aggregates are characterized by exhibiting a red shift (bathochromic) of their absorption maxima in comparison to the single carotenoid molecules. It is thought that both types of aggregates can form assemblies resembling ladders, brickworks or staircases (Figure 1.2) and that the formation of carotenoid J- or H-aggregates in hydrated solvents like hydroalcoholic mixtures depend on factors like the pH, the initial concentration of the carotenoid and the ratio ethanol:water ⁹¹.

1.4.2.3 *Structure of diverse carotenoid breakdown derivatives*

The electron-rich polyene backbone of carotenoids make them very susceptible to oxidative either enzymatic or non-enzymatic breakdown. As a result of such transformations many different compounds that retain some characteristic carotenoid structural features are formed. Like carotenoids, these compounds can be involved in important biological actions and have important applications. Thus, within this miscellaneous group there are compounds with vitamin A activity, hormones or aroma/flavour compounds ². The derivatives resulting from the breakdown of carotenoids can be either symmetric or asymmetric and can undergo further cleavage ⁶⁷.

Carotenoids can be oxidatively cleaved by means of non-enzymatic non-specific reactions, for instance via singlet oxygen, lipoxygenase cooxidation or photooxidation ⁹².

On the other hand, carotenoid cleavage oxygenases (CCOs) are a family of non-heme iron enzymes that intervene in the the oxidative breakdown of carbon–carbon double bonds in different locations of the polyene backbones producing derivatives containing carbonyl functions (aldehyde or ketone groups) in the cleaving ends. Some of these enzymes, which can be found in plants, algae, fungi, bacteria and mammals and other animals act specifically on apocarotenoids and have been usually named apocarotenoid cleavage oxygenases (ACOs) ⁹³.

1.2.2.4.1. Compounds with vitamin A activity: retinoids

Retinoids are diterpenes formed by four isoprene units joined in a head-to-tail manner. Hence, they have 20 atoms of carbon. Some of them exhibit vitamin A activity. In mammals, the cleavage of carotenoids into retinoids is catalyzed by a cytoplasmatic non-heme iron oxygenase enzyme usually referred to as β,β -carotene 15,15'-monooxygenase 1. This carotenoid cleavage oxygenase (hereafter CCO1) can cleave

centrally β -carotene to produce two molecules of all-trans-retinal. This can be oxidized irreversibly into retinoic acid by retinal dehydrogenase or reduced reversibly into retinol by a retinal reductase (Scheme 1.11). Apart from β -carotene, β,β -carotene 15,15'-monooxygenase 1 can also cleave other carotenoids as long as they have at least one unsubstituted β -ring, a condition met by other common dietary carotenes (α -carotene) and xanthophylls (like β -cryptoxanthin and some β -apo-carotenals). ^{70,71 70,94,95}.

[Scheme 1.11 near here]

1.4.2.4.2. Mammalian apocarotenoids

Besides β,β -carotene 15,15'-monooxygenase 1, mammalian genomes can also encode at least another non-heme iron oxygenase enzyme that catalyze the cleavage of carotenoids. This is usually named β,β -carotene 9',10'-dioxygenase and can cleave β -carotene, other provitamin A and non-provitamin A carotenoids (like lycopene, zeaxanthin or lutein among oth others) at both the 9,10 and 9',10' double bonds as it exhibits a wider substrate specificity. As a result both non-volatile apocarotenoid and volatile compounds cleavage products are formed (Scheme 1.12) ^{70,71}.

[Scheme 1.12 near here]

Apocarotenoids derived from the cleavage of dietary carotenoids in humans, are eliciting increasig interest as they may have health-promoting actions through their interaction with cell signalling pathways, for instance in relation to carcinogenesis or the protection against oxidative stress ^{18,96,97}.

1.4.2.4.3. Odorant compounds

Carotenoids can be cleaved at different asymmetrical locations giving a series of carbonylic odorant compounds with 9 to 13 atoms of carbon (Scheme 1.13).

[Scheme 1.13 near here]

These oxidized breakdown derivatives of carotenoids are called norisoprenoids and can be formed both in reactions catalyzed or not by enzymes and either by direct degradation of carotenoids or via glycosylated intermediates ^{67,98}.

Some important derived aroma compounds is safranal a potent aroma compound mainly responsible of the scent of the saffron spice can be originated via the enzymatic cleavage of zeaxanthin or by thermal treatments ^{99,100}. Other norisoprenoids that are potent fragrance compounds are β -ionone, β -damascenone and β -cyclocitral (Scheme 1.14), among many others, such that carotenoids are considered to be very important for the production of the typical aromas of not only flowers like violets or roses ⁶⁷ but also products as widely consumed as tomatoes, grapes, raspberries, wines, tea, watermelon ^{2,98,101–104}.

[Scheme 1.14 near here]

1.4.2.4.4. Sapid compounds

The glycosylated monoterpene picrocrocin (Scheme 1.15) is the main contributor to the sour taste of saffron spice and the precursor of safranal ^{99,100}.

[Scheme 1.15 near here]

1.2.2.4.3. Fungal hormone

Trisporic acid (Scheme 1.16) is a carotenoid breakdown derivative that is formed from β -carotene via retinol. It acts like a regulator of fungal sexual reproduction in some moulds, which is often accompanied by an elevated biosynthesis of β -carotene. This is harnessed for the commercial production at industrial scale of this carotene from *B. trispora* ².

[Scheme 1.16 near here]

1.4.2.4.7 Insect repellents

1.4.2.4.7.1 Grasshopper ketone

The grasshopper ketone (Scheme 1.17) was first noticed in the frothy exudate of the grasshopper *Romalea microptera* when it was disturbed ¹⁰⁵.

[Scheme 1.17 near here]

1.4.2.4.7.2 β -ionone

The scented compound β -ionone (Scheme 1.14) has been recently shown to have a repellent effect against certain insects in plants ¹⁰⁶.

1.4.2.4.8 Phytohormones

1.4.2.4.8.1 Abscissic acid (ABA)

Abscissic acid (Scheme 1.18) is a phytohormone derived from the cleavage of the (9Z)-isomers of the epoxycarotenoids neoxanthin and violaxanthin. ABA intervenes in a broad diversity of actions including senescence and abscission of leaves, dormancy of buds and seeds, stomatal closure, seedling development and the tolerance to diverse kinds of stress, among others ^{2,107,108}.

[Scheme 1.18 near here]

1.4.2.4.8.2 *Strigolactones*

In the last year, there has been expanding interest in the study of the production and actions of strigolactones, a “new” kind of carotenoid-derived plant hormones that favour the establishment of arbuscular mycorrhizae, the parasitism of roots by other plants and the adaptation of plant architecture to the availability of nutrients, among others ^{109–111}. The structures of some members of the family, carlactone and strigol, are shown in Scheme 1.19.

[Scheme 1.19 near here]

1.4.3. Nomenclature

Carotenoids usually have trivial names, usually deriving from the sources they were first described or where they are particularly abundant. Thus β -carotene owes its name to the scientific name of carrot (*Daucus carota*) ¹¹².

Apart from these traditional designations, there is also a common semi-systematic nomenclature that has the advantage of providing information about the structure of the carotenoid. In this case, the two halves of the carotenoid are considered and the compound is named as a derivative of the corresponding carotene. For this purpose, references to the end groups are made by means of Greek letters (Scheme 1.4). Besides, numbers and suffixes are used to denote the presence of substituents at certain locations, quiral centers, etc ⁸³. The official rules for carotenoid nomenclature were approved by the International Union of Pure and Applied Chemistry (IUPAC) in 1974 ¹¹³. Some examples of semi-systematic nomenclature of common food carotenoids shown in Table 1.9.

[Table 1.9 near here]

1.4.4. General properties and relation to some actions

The main structural feature of carotenoids is their long system of conjugated double bonds (c.d.b.). This polyene backbone is generally the key contributor to their general properties (colour, reactivity, photochemical properties, shape, etc.), which in turn are ultimately key to understand the diverse actions and applications of these versatile compounds ⁷⁹. The acyclic carotenes phytoene and phytofluene, which are the precursors of the rest of carotenoids, are rarities in the sense that they have much fewer c.d.b. (3 and 5, respectively, Fig 2) as compared to most carotenoids, as a result of which they are colourless and are expected to have other distinctive properties and actions ⁹.

1.4.4.1. *Size and shape*

The high number of conjugated double bonds characteristic of carotenoids render endow their molecules with much rigidity, such that carotenoid molecules in their (all-*E*)-configuration typically exhibit a rod-like shape. The corresponding *Z* isomers have an angular shape ⁷⁹ (Scheme 1.8). These differences in shape can have important consequences. For instance, *Z*-isomers are thought to be less susceptible to aggregation in biological milieus, which in turn can have an impact in their solubility and bioavailability. On the other hand, it seems reasonable to think that the ability of different geometrical isomers to fit in cellular structures or interact with enzymes and other proteins can be markedly different ¹¹⁴.

1.4.4.2. *Solubility*

With very few exceptions, carotenoids are hydrophobic compounds. Therefore, the extraction of carotenoids requires solvents like acetone, hexane, diethyl ether, chloroform, etc.¹¹⁵. Thus, in biological systems they are usually found in lipidic milieus like membranes, mixed micelles (structures where lipid-soluble digested dietary components are incorporated for their uptake by enterocytes), lipid droplets or lipoproteins^{79,116–118}. Carotenoids with carboxylic groups like bixin (Scheme 1.4) can form water-soluble sodium or potassium salts^{119,120}.

1.4.4.3. *UV/Vis light absorption and colour*

1.4.4.3.1 UV/Vis light absorption

Coloured carotenoids absorb maximally in the range 400-500 nm, depending on the number and arrangement of the c.d.b. that conform their chromophore. Their absorption spectra differs greatly from those of chlorophylls and since both kind of pigments form part of the photosynthetic apparatus, carotenoids contribute to the harvesting of light for this key process in Nature¹²¹. The relationship between the chemical structure of carotenoids and the features of their spectra has been long well-known and is dealt with in great detail in classical texts¹²².

The UV/VIS spectra of a typical carotenoid usually contain three absorption maxima whose wavelengths depend on the number and arrangement of c.d.b. and the solvent used to obtain the spectra^{122,123}. Regardless of the solvent used, the values of λ_{\max} increase as the number of conjugated double bonds do. When the chromophore extends into a ring (an example would be the β ring), the λ_{\max} appear at shorter wavelengths as compared to an acyclic carotenoid with the same number of conjugated double bonds, which is due to that the ring is not coplanar with the linear polyene chain.

This can be observed when comparing the λ_{\max} in petroleum ether of the cyclic carotenes γ -carotene (1 c.d.b. in ring) and β -carotene (2 c.d.b. in ring) (462 and 449 nm, respectively) with that of the acyclic carotene lycopene (470 nm) (Table 1.10).

[Table 1.10. near here]

Carbonylic groups conjugated with the polyene chain do increase the length of the chromophore and therefore they have a clear impact in the location of λ_{\max} . The presence of one conjugated ketonic or aldehydic group in a ring or in the polyene chain causes a bathochromic shift of ca. 10 nm and 30 nm, respectively^{123,124}.

[Figure 1.3. near here]

On the other hand, the general shape of the spectrum as well as the sharpness of the absorción bands (commonly known as fine structure and calculated as %III/II, Figure 1.3) depend on the degree of planarity of the chromophore. In acyclic carotenoids, like ζ -carotene, the chromophore can adopt an almost planar conformation as a result of which their UV/VIS spectra have sharp absorption bands, although the sharpness decreases from 9 c.d.b. onwards. Contrastingly, in carotenoids exhibiting c.d.b. in rings the chromophore is not coplanar due to steric hindrances between the methyl group in C5 and the hydrogen atom in C8, as a result of which the c.d.b. in the rings and the linear polyene chain are not in the same plane. Thus, in the spectrum of carotenoids like β -carotene, the bands are not as sharp and the first one is a shoulder. When there are carbonylic groups conjugated with the chromophore, the loss of fine structure is even higher. Indeed the spectra of such carotenoids usually present an unique maximum, sometimes with inflexions at one or two sides. Thus the fine structure decreases in the order ζ -carotene > β -carotene > canthaxanthin (Figure 1.4)^{112,122}

[Figure 1.4. near here]

The absorption spectra of *Z* isomers differ considerably from that of the all-*E* isomer. Specifically, λ_{\max} appears at shorter wavelengths (for instance, there is a 2-6 hypsochromic shift in the case of mono-*Z* isomers, longer for di-*Z* isomers). Additionally, there is loss of fine structure. Furthermore a new band, the so-called *cis*-band appear at a wavelength ca. 142 nm lower relative to that of the thir absorption maxima in the visible region in hexane ^{122,123,125}. The height of this new band relative to that of the main absoprtion band (Figure 1.5) is usually considered for the tentative indentification of *Z* isomers ¹²⁶.

[Figure 1.5. near here]

1.4.4.3.2 Colour

Absorbing mostly blue and violet light, carotenoids typically exhibit yellowish, orangeish or reddish colours ^{122,127,128}.

At least 7 c.d.b. are needed for a carotenoid to exhibit colour, although this attribute also depends on other factors. One of them would be obviously the concentration, but there are others like the aggregation of carotenoid molecules or the association with other molecules like proteins (Britton, 1995; Meléndez-Martínez, 2016; Meléndez-Martínez et al., 2007a). Thus a carotenoid-containing solution can vary from transparent, to light yellow, yellow, orange, red and even beyond upon concentration, a phenomenom that can be commonly observed when working in the isolation and concentration of carotenoids. As already discussed in an earlier section, the aggregation of carotenoid

molecules can be accompanied by red (bathochromic) or blue (hypsochromic) shifts, with the consequent colour modifications ⁹¹.

Natural pigments in general and carotenoids in particular have a great ecological importance as they are key for the communication between and within species. Thus, the colour of flowers or fruits are essential for pollination and seed dispersal, and therefore for their propagation ^{1,129}. In animals, colour can convey key information of great value for species recognition, warning, mimicry, crypsis, sexual signalling and other processes. More specifically, it is assumed that the colour afforded by carotenoids in animals can inform about parasite load, nutritional and immunological states, fecundity, genetic quality and photoprotection ^{130–132}.

As far as foods are concerned, colour is one of the attributes more related to the acceptability by consumers. The effect of certain structural differences among some common food carotenoids in their colours in terms of the parameters of the CIELAB uniform space ¹³³ have been studied in detail ¹³⁴. The results revealed that the carotenoids clustered in the a^*b^* plane as a function of their number of c.d.b. As far as hue was concerned, the decrease in conjugation of the molecules was accompanied by increases in its values and the aperture of the end ring lead to clear decreases.

1.4.4.4. *Reactivity*

The long polyene chain of carotenoids is rich in electrons, hence it is important to explain the antioxidant or pro-oxidant activities of carotenoids ⁷⁹. The relationship of chemical structure of carotenoids with their *in vitro* antioxidant and prooxidant properties of carotenoids has been the subject of many original papers over the last 20 years ^{135–138} in which different experimental conditions (oxidants, concentrations of carotenoids, solvents, etc.) have been used. There is also a wealth of

revisions on the subject, from which it can be concluded that, normally, carotenoids can act like antioxidants, but also like pro-oxidants under certain conditions ^{139–143}.

In any case, it is well established that carotenoids act in plants protecting them from photooxidation phenomena, through different mechanisms, like the prevention of the formation of singlet oxygen or its quenching. Due to these and other essential functions of carotenoids in photosynthesis, it can be argued that life may not have developed in our planet without them ^{144,145}. On the other hand, carotenoids can protect humans from photooxidation in the skin ¹⁴⁶ and probably in the eye ¹⁴⁷.

1.5. ASSOCIATION OF CAROTENOIDS WITH OTHER MOLECULES: CAROTENOID GLUCOSIDES, CAROTENOPROTEINS AND CAROTENOID ACYL ESTERS

Carotenoids can be either free or associated to other molecules, which undoubtedly can have an impact in some of their properties. Typical molecules carotenoid can be associated with are sugars, proteins and, more frequently in common foods, fatty acids.

1.5.1. Association of carotenoids with other molecules

1.5.1.1 Sugars

Some carotenoids can also be associated to sugar moieties like glucose or gentobiose forming thus glucosides. As an example, crocetin is found glycosilated in saffron (*Crocus sativus*) stigmas and gardenia (*Gardenia jasminoides*) fruits ^{148,149}. The compounds resulting from the association of crocetin and sugar moieties are termed

crocins (Scheme 1.20), which are indeed glycosidic esters of crocetin, and can exist as (all-*E*)- or *Z*-isomers¹⁰⁰.

1.5.1.2 Proteins

On the other hand, it has been long known that some carotenoids can form complex with diverse proteins (carotenoproteins) in several animals. The study of carotenoproteins has been particularly prolific in invertebrate animals like crustaceans, where many carotenoproteins containing frequently astaxanthin and canthaxanthin have been described in ovaries, eggs, exoskeleton and hemolymph¹⁵⁰.

The flesh of salmonid fish can exhibit pink hues as a result of the accumulation of carotenoid pigments like astaxanthin and canthaxanthin, acquired from their diets. After absorption, these carotenoids reach the muscle where they can bind the actomyosin complex by means of non-specific hydrophobic bonds¹¹⁶. Carotenoids are also associated to proteins in the mature feathers of many birds¹⁵¹

Carotenoproteins have also been described in microbes. A notorious example is the water-soluble modular cyanobacterial orange carotenoid protein (OCP), which intervenes in the photoprotection of these microorganisms¹⁵².

Apart from microbes and animals, carotenoproteins have also been reported in carrots^{153 154}.

1.5.1.3. Fatty acids

1.5.1.3.1 Types and occurrence of carotenoid esters

In general, either the term “Carotenoid ester” or “Xanthophyll ester” is used for referring to carotenoid acyl esters, although other less frequent ester forms can also be included under this terminology. Carotenoids can be found in *Nature* either as free or

conjugated with other molecules to produce sulphate esters, glycosides, glycoside esters, glycosyl esters and acyl esters, among others ^{80,155,156}.

Carotenoid sulphate derivatives are mostly restricted to bacteria (e.g. caloxanthin 3-sulphate from the bacterium *Erythrobacter longus* ¹⁵⁷ and animals (e.g. bastaxanthin D from the sponge *Ianthella basta*, and ophioxanthin from the starfish *Ophioderma longicauda*). In contrast, carotenoid glycosides (e.g. decaprenoxanthin diglucoside from *Arthrobacter* sp. ¹⁵⁸, and astaxanthin glucoside from *Agrobacterium aurantiacum* ¹⁵⁹), glycoside esters of carotenoids (e.g. thermocryptoxanthins and thermozeaxanthins from the thermophilic eubacterium *Thermus thermophilus*) ^{77,160}, glycosyl esters of carotenoic acids (e.g. crocin from stigmas of *Crocus sativus*) ¹⁰⁰ and acyl esters (e.g. zeaxanthin dipalmitate from *Physalis* fruits, also known as physalien) ^{161,162} are more widely distributed in bacteria, algae, animal and plant. Structures for some of the above mentioned carotenoids are shown in Scheme 1.20.

[Scheme 1.20 near here]

Undoubtedly, carotenoid acyl esters (xanthophyll esters) involving medium- and long-chain fatty acids are the most ubiquitous carotenoid derived forms distributed among living organisms. Consequently, xanthophyll esters are frequently found in food from plant and animal origin. Interestingly, peridinin, one of the most abundant carotenoids in nature has an acetyl group in its molecule at position 3' (Scheme 1.3) ⁸⁰. Some recent papers ^{26,163,164}, as well as Chapter 7 in this volume, compiled and critically reviewed the occurrence of xanthophyll esters in food.

[Scheme 1.21 near here]

Acylation reaction (Scheme 1.21) must necessarily be performed over a hydroxyl group, thus only hydroxy-xanthophylls may derive into xanthophyll esters. Scheme 1.4 contains the structures of various hydroxy xanthophylls, some of them very commonly found esterified with fatty acids as part of the carotenoid profile in food.

In general, hydroxy-xanthophylls have one or two hydroxyl groups which can be esterified with a range of fatty acids. Hydroxyl groups are normally located at carbon 3 of the end-groups (β , ϵ , κ , etc) (e.g. zeaxanthin, lutein, capsanthin, violaxanthin and astaxanthin), although other positions such as carbon 4 are also possible (e.g. isozeaxanthin (Scheme 1.3).

Thus, for a particular xanthophyll, the diversity of derived xanthophyll esters will depend on the number of hydroxyl groups in the carotenoid molecule and the number of fatty acids involved (usually from 4 to 6). Therefore, a monohydroxy-xanthophyll (such as β -cryptoxanthin and β -critraurin) will render only monoesters (e.g. β -cryptoxanthin laurate and β -critraurin myristate), whereas a dihydroxy-xanthophyll (such as zeaxanthin and lutein) derived into monoesters or diesters when one or two hydroxy groups are acylated, respectively (Scheme 1.22). Hydroxyl groups in the central chain of the carotenoids structure can also be esterified, as in the case of vaucheriaxanthin 3-acetate 19'-octanoate from the alga *Nannochloropsis salina*⁸⁰.

[Scheme 1.22 near here]

Consequently, the number of possible acylated forms is greater for dihydroxy-xanthophylls.

1.5.1.3.1. Nomenclature

Depending on the nature of the acyl groups, diesters can be grouped into two classes, namely homodiesters when both acyl moieties are identical (e.g. zeaxanthin dipalmitate) and heterodiesters when the acyl moieties are different (e.g. zeaxanthin myristate-palmitate). This nomination system was first used by Mellado-Ortega and Hornero-Méndez¹⁶⁵, and widely adopted thereafter^{26,164,166}, although other similar systems have also been used, i.e. homogeneous diesters for homodiesters, and heterogeneous or mixed diesters for heterodiesters^{163,167}. Additionally, for the case of a dihydroxy-xanthophyll with an asymmetrical structure (e.g. lutein), the two hydroxyl groups are not equivalent and subsequently two different regioisomers will be possible for each monoester and heterodiesters. For instance, lutein 3-*O*-palmitate and lutein 3'-*O*-palmitate are the two possible regioisomers for lutein palmitate (monoester), having the acyl moieties in the hydroxyl group located at the position 3 of the β -ring or at the position 3' of the ϵ -ring, respectively. Analogously, two regioisomers are possible for lutein myristate-palmitate, namely lutein 3'-*O*-myristate-3-*O*-palmitate and lutein 3'-*O*-palmitate-3-*O*-myristate. Figure 1.6 exemplifies the great diversity of different esterified forms that can be derived for a single xanthophyll (zeaxanthin for symmetrical structure and lutein for unsymmetrical structure) and three common saturated fatty acids (palmitic, myristic and stearic acids). Taking all this together, it is easy to understand the great analytical complexity of the natural extracts containing xanthophyll esters. In fact, the presence of carotenoid esters has been often overlooked in many studies, mainly due to the extensive use of saponification as a routine step in carotenoid analysis. Fortunately, the continuous improvement in the performance of modern analytical techniques, in particular HPLC with UV-visible and mass spectrometry detectors, has facilitated recent developments in the analysis, identification and

characterisation of the xanthophyll esters in natural sources ^{26,166,168,169} (for detailed information see Parts II and III in this volume).

[Figure 1.6 near here]

1.5.2. Impact of the association with other molecules in the properties of carotenoids

1.5.2.1 Size and shape

Obviously, the association of carotenoids with other molecules have an impact in the size and shape of the carotenoid and consequently in their interactions with structures.

1.5.2.2. Solubility

The association with sugars can lead to their solubilization in water, like is the case of saffron crocins ^{3,100}. Carotenoproteins are water-soluble ^{151,170,171}.

The esterification of xanthophylls render them more lipophilic and can have an impact on their biosynthesis and accumulation as this increased lipophilicity could favor their sequestration by chromoplast structures ¹⁷².. Free carotenoids (i.e. non-esterified) are located in the chloroplasts of green plant cells, together with chlorophylls, and in the chromoplasts of other plant tissues such as fruits, tubers and flower petals. However, it is in the chromoplasts where the carotenoids, free and esterified with fatty acids, are massively synthesized and accumulated. The esterification of xanthophylls takes place during the ripening of most fruits and the senescence of leaves, coinciding with the transformation of the chloroplasts into chromoplasts ^{173,174}. High amounts of

xanthophyll esters are found in chromoplastic tissues which is a direct evidence indicating the important role of esterification in the carotenoid accumulation capacity of plant cells ^{175–178}. Through the esterification mechanism, fruits and flowers enhance their external colour in order to increase attraction of animals as pollinators and seed dispersion vectors ^{179,180}. At present, there is great interest in deciphering the biochemistry and genetic of the xanthophyll esterification process, including the identification and characterization of the responsible gen(es) and enzyme(s) (XAT: xanthophyll acyl transferase) ^{26,165,177181182–185} (see Part II for more information).

From a nutritional point of view, it should be taken into consideration that an important proportion of the carotenoids present in our diet are in esterified form (see Chapter 7). The increased solubilisation and extractability of xanthophyll esters during food digestion in presence of dietary fat has been shown to enhance carotenoid bioavailability ¹⁸⁶, however this aspect has been ignored in most studies. Moreover, xanthophyll esters have also shown to be more stable than free carotenoids ^{186–195}

1.5.2.3. UV/Vis light absorption and colour

The association of carotenoids with proteins can extend the palette of carotenoid colours to grey, black, brown, green, blue or purple. Interestingly, thermal treatments like those used to cook some of these animals cause the dissociation of the carotenoproteins and the appearance of the typical carotenoid hues ^{150,151}.

Carotenoids in the mature feathers of many birds are thought to be strongly bound to keratin, which are structural inert and insoluble proteins. Interestingly, these associations can have a strong impact on the colour provided by the same carotenoid both in different bird species and in different feathers of the same species. In other words, the same carotenoid can appear yellow, orange or red in feathers of different

species or different feathers of the same species. Besides, as a result of these associations with keratin, the extraction of carotenoids from feathers is particularly difficult ¹⁵¹.

1.5.2.4. Reactivity

Carotenoproteins are regarded to stabilize carotenoids ^{151,170,171}. On the other hand, it is thought that the esterification of carotenoids with fatty acids can modify the immediate environment and lead to modifications of their reactivity towards oxidizing agents, such modifications being dependent to the type of fatty acid bound to the xanthophyll ¹⁸⁶. In general, it is thought that the esterification with fatty acids increase the stability of carotenoids ²⁵. The higher stability of esterified xanthophylls seems to be related to the increase in the liposolubility compared to free xanthophylls, providing a better integration into membrane structures, therefore reducing the susceptibility to adverse conditions in their environments ¹⁷³.

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Adapted from ¹²².

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
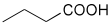
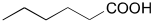

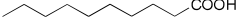






Table 1.7. Classification of isoprenoid compounds according to the number of isoprene units. Adapted from ⁶⁷

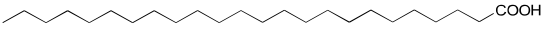
Table 1.8. Carotenoid end-groups designations. Adapted from ¹¹³

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Table 1.10. Effect of the number and arrangements of conjugated double bonds in the absorption maxima of carotenoids. Adapted from ¹²³

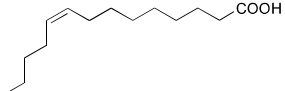
Table 1.1. Trivial names and chemical structures of common saturated and unsaturated fatty acids

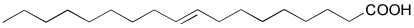
Fatty acid		Structure
Saturated		
Acetic	C2:0	
Butiric	C4:0	
Caproic	C6:0	
Caprilic	C8:0	
Capric	C10:0	
Lauric	C12:0	
Myristic	C14:0	
Palmitic	C16:0	
Stearic	C18:0	
Arachidic	C20:0	
Behenic	C22:0	

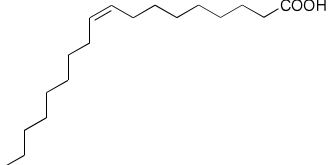
Lignoceric	C24:0	
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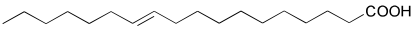
**Mono-
unsaturated**

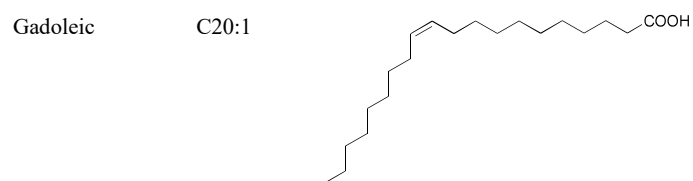
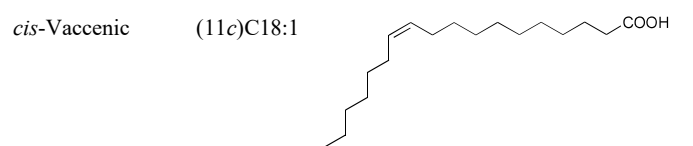
Caproleic	C10:1	
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Myristoleic	C14:1	
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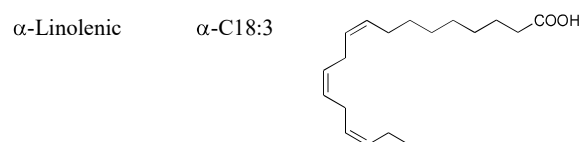
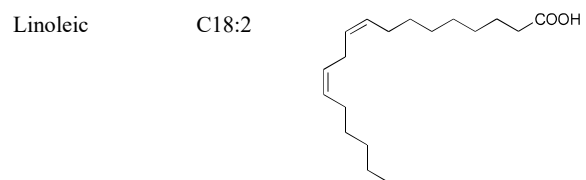
Elaidic	(9 <i>t</i>)C18:1	
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Oleic	(9 <i>c</i>)C18:1	
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<i>trans</i> -Vaccenic	(11 <i>t</i>)C18:1	
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Poly-unsaturated



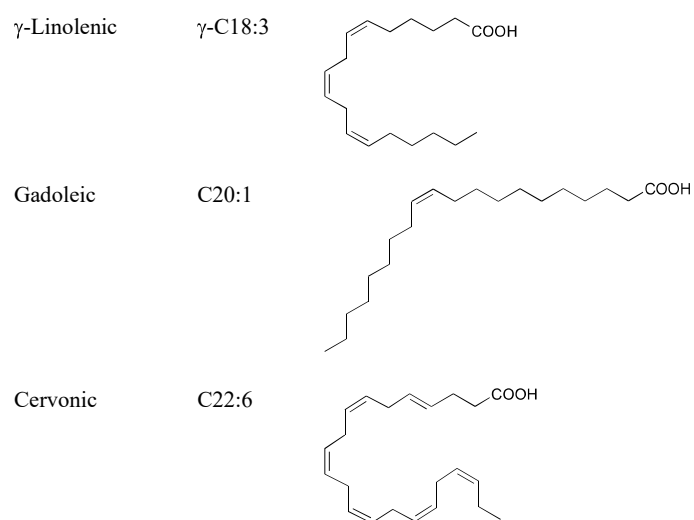


Table 1.2. Fatty Acid Classification according to LIPID MAPS classification system including the LIPID MAPS ID's [LM_ID], which reflects their position in the classification hierarchy (<http://www.lipidmaps.org/>).

FAs and Conjugates [FA01]	Docosanoids [FA04]
Straight chain FAs [FA0101]	Neuroprostanes [FA0401]
Branched FAs [FA0102]	Neurofurans [FA0402]
Unsaturated FAs [FA0103]	Docosa-1,2-dioxolanes [FA0406]
Hydroperoxy FAs [FA0104]	Resolvin Ds [FA0403]
Hydroxy FAs [FA0105]	Protectins [FA0404]
Oxo FAs [FA0106]	Maresins [FA0405]
Epoxy FAs [FA0107]	Other Docosanoids [FA0400]
Methoxy FAs [FA0108]	Fatty alcohols [FA05]
Halogenated FAs [FA0109]	Fatty aldehydes [FA06]
Amino FAs [FA0110]	Fatty esters [FA07]
Cyano FAs [FA0111]	Wax monoesters [FA0701]

<p>Nitro FAs [FA0112]</p> <p>Thia FAs [FA0113]</p> <p>Carbocyclic FAs [FA0114]</p> <p>Heterocyclic FAs [FA0115]</p> <p>Mycolic acids [FA0116]</p> <p>Dicarboxylic acids [FA0117]</p>	<p>Wax diesters [FA0702]</p> <p>Cyano esters [FA0703]</p> <p>Lactones [FA0704]</p> <p>Fatty acyl CoAs [FA0705]</p> <p>Fatty acyl ACPs [FA0706]</p> <p>Fatty acyl carnitines [FA0707]</p> <p>Fatty acyl adenylates [FA0708]</p>
<p>Octadecanoids [FA02]</p> <p>12-oxophytodienoic acid metabolites [FA0201]</p> <p>Jasmonic acids [FA0202]</p> <p>Phytosteranes [FA0203]</p> <p>Phytofurans [FA0204]</p> <p>Octadeca-1,2-dioxolanes [FA0205]</p> <p>Other Octadecanoids [FA0200]</p>	<p>Fatty amides [FA08]</p> <p>Primary amides [FA0801]</p> <p>N-acyl amines [FA0802]</p> <p>Fatty acyl homoserine lactones [FA0803]</p> <p>N-acyl ethanolamines (endocannabinoids) [FA0804]</p> <p>Fatty nitriles [FA09]</p>

Eicosanoids [FA03] Prostaglandins [FA0301] Leukotrienes [FA0302] Thromboxanes [FA0303] Lipoxins [FA0304] Hydroxy/hydroperoxyeicosatrienoic acids [FA0305] Hydroxy/hydroperoxyeicosatetraenoic acids [FA0306] Hydroxy/hydroperoxyeicosapentaenoic acids [FA0307] Epoxyeicosatrienoic acids [FA0308] Hepoxilins [FA0309] Levuglandins [FA0310] Isoprostanes [FA0311] Isofurans [FA0313] Eicosa-1,2-dioxolanes [FA0315] Resolvin Es [FA0314]	Fatty ethers [FA10] Hydrocarbons [FA11] Oxygenated hydrocarbons [FA12] Fatty acyl glycosides [FA13] Fatty acyl glycosides of mono- and disaccharides [FA1301] Sophorolipids [FA1302] Rhamnolipids [FA1303] Other Fatty acyl glycosides [FA1300] Other Fatty Acyls [FA00]
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Clavulones [FA0312]	
Other Eicosanoids [FA0300]	

Table 1.3. Different designations and sources of common saturated fatty acids in foods

Chain length	Abbreviation	Sytematic name ^a	Trivial name ^b	Sources
Short	4:0	Butano-	Butyr-	Dairy fat
	6:0	Hexaeno-	Capro-	Dairy fat
Medium	8:0	Octano-	Capryl-	Dairy fat, coconut, palm kernel oils
	10:0	Decano-	Capr- ^c	Widespread as a minor component. Major component in dairy fat coconut, palm kernel oil
	12:0	Dodecano-	Laur-	Widely distributed, a major component of coconut, palm kernel oils
Long	14:0	Tetradecano-	Myrist-	Widespread, occasionally found as a major component (e.g.. Nut meg)
	16:0	Hexadecano-	Palmit-	Most common saturated fatty acid in in animals, plants and microorganism. Major in Palm oil
	18:0	Octadecano-	Stear-	Major fatty acid in animals and some fungi, minor in plants (but predominant in some like cocoa butter)

	20:0	Icosano- ^d	Arachid-	Widespread as minor component, occasionally a major component (e.g. ground nut)
Very Long	22:0	Docosano-	Behen-	Fairly widespread as minor component in seed oils and plant waxes
	24:0	Tetracosano-	Lignocer-	Fairly widespread as minor component in seed oils and plant waxes
	26:0	Hexacosano-	Cerot-	Widespread in plant and insect waxes (Beeswax and carnauba wax). Also in some bacterial lipids
	28:0	Octacosano-	Montan-	Major component of plant waxes Montan wax, and insect Chinese wax.

^a Ending in '-ic', '-ate', '-yl', for acid, salt or ester, acyl radical, respectively.

^b Ending in '-ic', '-ate', '-oyl' for acid, salt or ester, or acyl radical, respectively.

^c Not recommended because of confusion with caproic (hexanoic) and caprylic (octanoic) acids. Decanoic is preferred.

^d Formerly 'eicosa' (Changed by IUPAC Commission on Nomenclature of Organic Chemistry, 1975)

Table 1.4. Different designations and sources of some monounsaturated fatty acids found in nature

Shorthand	Chemical Structure $\text{H}_3\text{C}-(\text{R})-\text{CO}_2\text{H}$	Systematic name ^a	Delta notation	Trivial name ^a	Typical Sources
14:1n-5	$-\text{[CH}_2\text{]}_3\text{CH=CH[CH}_2\text{]}_7-$	(9Z)-tetra-dec-9-eno-	14:1-Δ ⁹ c	Myristole-	Seed oil from plants of the family Myristicaceae
16:1n-7	$-\text{[CH}_2\text{]}_5\text{CH=CH[CH}_2\text{]}_7-$	(9Z)-hexa-dec-9-eno-	16:1 Δ ⁹ c	Palmitole-	Widespread: marine oils, macadamia oil, most animal and vegetable oils.
16:1n-9	$-\text{[CH}_2\text{]}_7\text{CH=CH[CH}_2\text{]}_5-$	(7Z)-hexa-dec-7-eno-	16:1 Δ ⁷ c	Hypoge-	Human milk, higher plants, algae and bacteria
16:1n-11	$-\text{[CH}_2\text{]}_9\text{CH=CH[CH}_2\text{]}_3-$	(5Z)-hexa-dec-5-eno-	16:1 Δ ⁵ c	-	Some higher plants, bacilli, sponges
18:1n-7	$-\text{[CH}_2\text{]}_5\text{CH=CH[CH}_2\text{]}_9-$	(11Z)-Octadec-11-eno	18:1Δ ¹¹ c	Cis-vaccen-	<i>E. Coli</i> and other bacteria
*	$-\text{[CH}_2\text{]}_5\text{CH=CH[CH}_2\text{]}_9-$	(11E)-octa-dec-11-eno-	18:1Δ ¹¹ t	Vaccen-	Ruminants and in dairy products
18:1n-9	$-\text{[CH}_2\text{]}_7\text{CH=CH[CH}_2\text{]}_7-$	(9Z)-octa-dec-9-eno-	18:1Δ ⁹ c	Ole-	All fats and oils, especially olive oil, canola oil and high-oleic sunflower and safflower oil

*	-[CH ₂] ₇ CH=CH[CH ₂] ₇ -	(9E)-octa-dec-9-eno-	18:1Δ ⁹ t	Elaid-	Ruminant fat, hydrogenated vegetable oils
20:1 n-9	-[CH ₂] ₇ CH=CH[CH ₂] ₉ -	(11Z)-eicos-11-eno-	20:1-Δ ¹¹ c	Gondo-	Seed oil of rape, fish oil
20:1 n-11	-[CH ₂] ₉ CH=CH[CH ₂] ₇ -	(9Z)-eicos-9-eno-	20:1-Δ ⁹ c	Gadole-	Marine oil
22:1n-9	-[CH ₂] ₇ CH=CH[CH ₂] ₁₁ -	(13Z)-docos-13-eno-	22:1-Δ ¹³ c	Eruc-	Seed oil of Cruciferae (rape, mustard)
24:1n-9	-[CH ₂] ₇ CH=CH[CH ₂] ₁₃ -	(15Z)-tetracos-15-eno-	24:1Δ ¹⁵ c	Nervon-	Marine oils, major fatty acid in brain sphingolipids

^a Ending in '-ic', '-ate', '-yl', for acid, salt or ester, acyl radical, respectively.

^b Ending in '-ic', '-ate', '-oyl' for acid, salt or ester, or acyl radical, respectively.

- Trans fatty acids do not have shorthand n-x notation

Table 1.5. Different designations and sources of some polyunsaturated fatty acids found in nature

Shorthand	Chemical Structure $\text{H}_3\text{C}-(\text{R})-\text{CO}_2\text{H}$	Systematic name ^a / Delta Notation	Trivial name ^b	Typical Sources
18:2n-6	- [CH ₂] ₃ (CH ₂ CH=CH) ₂ [CH ₂] ₇ -	(9Z,12Z)-octadeca-9,12-dieno- 18:2Δ ⁹ c,12c	Linole- (LA)	Most vegetable oils
18:3n-6	-[CH ₂] ₃ (CH ₂ CH=CH) ₃ [CH ₂] ₄ -	(6Z,9Z,12Z)-octadeca-6,9,12-trieno- 18:3Δ ⁶ c,9c,12c	γ -Linolen- (GLA)	Evening primrose oil, starflower oil, and human milk
20:3n-6	-[CH ₂] ₃ (CH ₂ CH=CH) ₃ [CH ₂] ₆ -	(8Z,11Z,14Z)-icosa-8,11,14-trieno- 20:3Δ ⁸ c,11c,14c	Dihomo-γ-linolen- (DGLA)	Very minor component in animal tissues
20:4n-6	-[CH ₂] ₃ (CH ₂ CH=CH) ₄ [CH ₂] ₃ -	(5Z,8Z,11Z,14Z)-icosa-5,8,11,14-tetraeno- 20:4Δ ⁵ c,8c,11c,14c	Arachidon- (AA)	Animals' phospholipids. Major component in marine algae and some animals as mosses
22:4n-6	-[CH ₂] ₃ (CH ₂ CH=CH) ₄ [CH ₂] ₅ -	(7Z,10Z,13Z,16Z)-Docosa-7,10,13,16-tetraeno- 22:4Δ ⁷ c,10c,13c,16c	Adren-	Minor component in animal tissues

22:5n-6	-[CH ₂] ₃ (CH ₂ CH=CH) ₄ [CH ₂] ₇ -	(4Z,7Z,10Z,13Z,16Z)-Docosa-4,7,10,13,16-pentaeno- 22:4Δ7c,10c,13c,16c	Osbond (DPA)	Minor component in animal tissues
18:3n-3	-(CH ₂ CH=CH) ₃ [CH ₂] ₇ -	(9Z,12Z,-15Z)-octadeca-9,12,15-trieno- 18:3Δ9c,12c,15c	α-Linolen- (ALA)	Flaxseed oil, perilla oil, canola oil, soybean oil
18:4n-3	-(CH ₂ CH=CH) ₄ [CH ₂] ₄ -	(6Z,9Z,12Z,15Z)-octadeca-6,9,12,15-tetraeno- 18:4Δ6c,9c,12c,15c	Stearidon- (SA)	Oils from Primulaceae and Boraginacea families
20:5n-3	-(CH ₂ CH=CH) ₅ [CH ₂] ₃ -	(5Z,8Z,11Z,14Z,17Z)-icosa-5,8,11,14,17-pentaeno- 20:5Δ5c,8c,11c,14c,17c	Eicosapentaeno- ^c (EPA) Timnodon-	Fish, especially oily fish (salmon, herring, anchovy, smelt and mackerel) and marine algae
22:5n-3	-(CH ₂ CH=CH) ₅ [CH ₂] ₅ -	(7Z,10Z,13Z,16Z,19Z)-docosa-7,10,13,16,19-pentaeno- 22:5Δ7c,10c,13c,16c,19c	Docosapentaeno- (DPA) Clupanodon-	Animals' phospholipids Fish, especially oily fish (salmon, herring, anchovy, smelt and mackerel)
22:6n-3	-(CH ₂ CH=CH) ₆ [CH ₂] ₂ -	(4Z,7Z,10Z,13Z,16Z,19Z)-docosa-4,7,10,13,16,19-hexaeno-	Docosahexaeno- (DHA)	Animals' phospholipids Fish, especially oily fish (salmon,

		22:6Δ4c,7c,10c,13c,16c,19c	Cervonic-	herring, anchovy, smelt and mackerel)
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^a Ending in '-ic', '-ate', '-yl', for acid, salt or ester, acyl radical, respectively.

^b Ending in '-ic', '-ate', '-oyl' for acid, salt or ester, or acyl radical, respectively.

^c Formerly 'eicosa' (Changed by IUPAC Commission on Nomenclature of Organic Chemistry, 1975)

Table 1.6. Melting points of different fatty acids ⁵⁰

Fatty Acid structure	Melting points °C
Palmitic (16:0)	62.20
Margaric (17:0)	60.85
Steric (18:0)	69.29
Nonadecanoic (19:0)	67.76
Lignoceric (24:0)	83.82
Oleic (18:1Δ9c)	12.82
Elaidic (18:1Δ9t)	43.35
Linoleic (18:2Δ9,12c)	-7.51
Linolenic (18:3 Δ9c,12c,15c)	-11.58
Araquidonic (20:4Δ5c,8c,11c,14c)	-49.5

Table 1.7. Classification of isoprenoid compounds according to the number of isoprene units. Adapted from ⁶⁷

No. of units	No. of C atoms	Group	Example
1	5	Hemiterpenoids	Isoprene
2	10	Monoterpenoids	<i>p</i> -menthadienol
3	15	Sesquiterpenoids	α -bisabolol
4	20	Diterpenoids	Trisporic acid
5	25	Sesterterpenoids	Pentaprenol
6	30	Triterpenoids	Ambrein
8	40	Tetraterpenoids	Neoxanthin
> 8	> 40	Polyterpenoids	Rubber

Table 1.8. Carotenoid end-groups designations. Adapted from ¹¹³

Prefix	Type	Formula
ψ	Acyclic	C_9H_{15}
β, ϵ	Cyclohexene	C_9H_{15}
γ	Methylenecyclohexane	C_9H_{15}
κ	Cyclopentane	C_9H_{17}
ϕ, χ	Aryl	C_9H_{11}

Table 1.9. Trivial and semi-systematic names of diverse carotenoids (Figure 2). Adapted from ¹²³

Trivial name	Semi-systematic names
Antheraxanthin	5,6-epoxy-5,6-dihydro- β,β -carotene-3,3'-diol
Astaxanthin	3,3'-dihydroxy- β,β -carotene-4,4'-dione
Auroxanthin	5,8,5',8'-diepoxy-5,8,5',8'-tetrahydro- β,β -carotene-3,3'-diol
Canthaxanthin	β,β -carotene-4,4'-dione
Capsanthin	3,3'-dihydroxy- β,κ -caroten-6'-one
Capsorubin	3,3'-dihydroxy- κ,κ -carotene-6,6'-dione
α -Carotene	β,ϵ -carotene
β -Carotene	β,β -carotene
ζ -Carotene	7,8,7',8'-tetrahydro- ψ,ψ -carotene
Crocetin	8,8'-diapocarotene-8,8'-dioic acid
β -Cryptoxanthin	β,β -caroten-3-ol
Lutein	β,ϵ -carotene-3,3'-diol
Lycopene	ψ,ψ -carotene

Neoxanthin	5',6'-epoxy-6,7-didehydro-5,6,5',6'-tetrahydro- β,β -carotene-3,5,3'-triol
Phytoene	7,8,11,12,7',8',11'12'-octahydro- ψ,ψ -carotene
Phytofluene	7,8,11,12,7',8'-hexahydro- ψ,ψ -carotene
Violaxanthin	5,6,5',6'-diepoxy-5,6,5',6'-tetrahydro- β,β -carotene-3,3'-diol
Zeaxanthin	β,β -carotene-3,3'-diol

Table 1.10. Effect of the number and arrangements of conjugated double bonds in the absorption maxima of carotenoids. Adapted from ¹²³

Carotenoid	Number of c.d.b. (c.d.b. in rings)	λ_{max} in petroleum ether (nm)
Phytoene	3	276, 286, 297
Phytofluene	5	331, 348, 367
ξ-Carotene	7	378, 400, 425
Neurosporene	9	414, 439, 467
Lycopene	11	444, 470, 502
γ-Carotene	11 (1)	437, 462, 494
β-Carotene	11 (2)	425, 449, 476

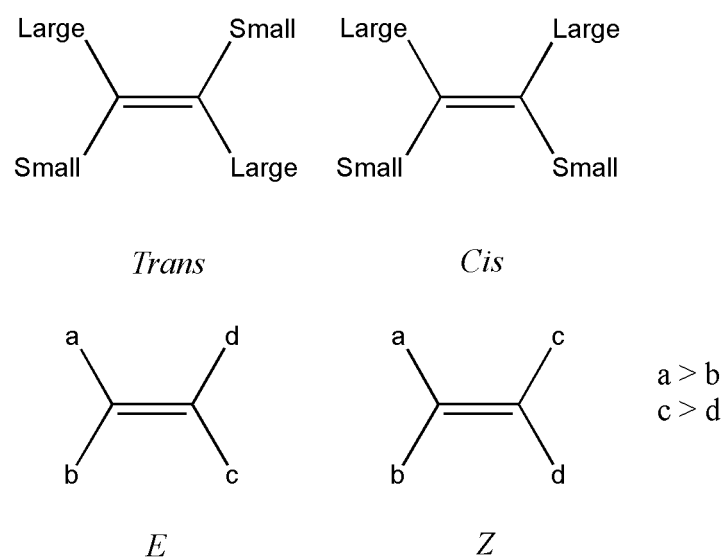
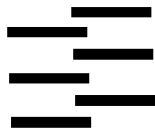


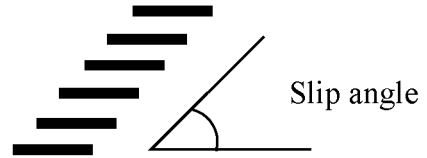
Figure 1.01



Ladder



Brick work



Staircase

Figure 1.02

Figure 1.03

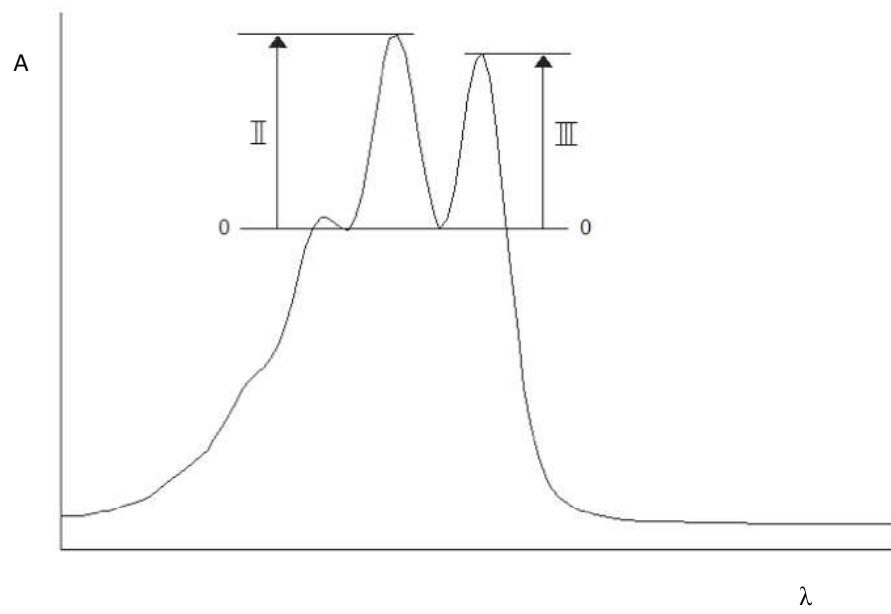


Figure 1.04

A

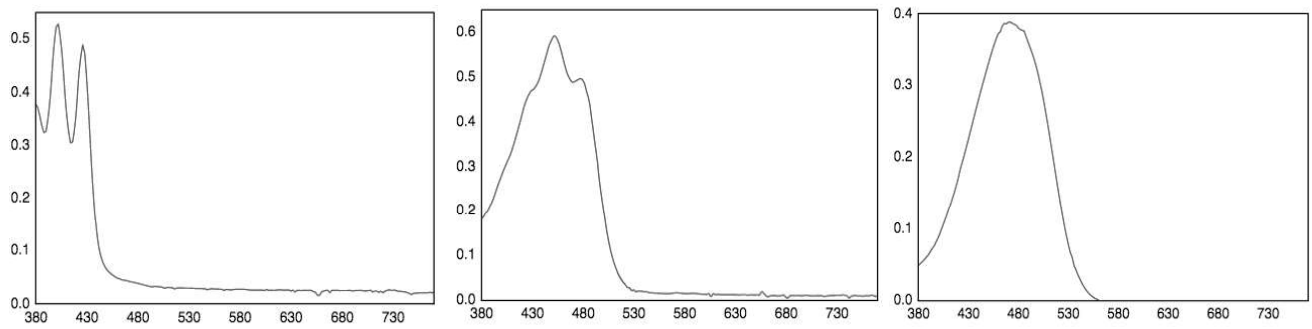
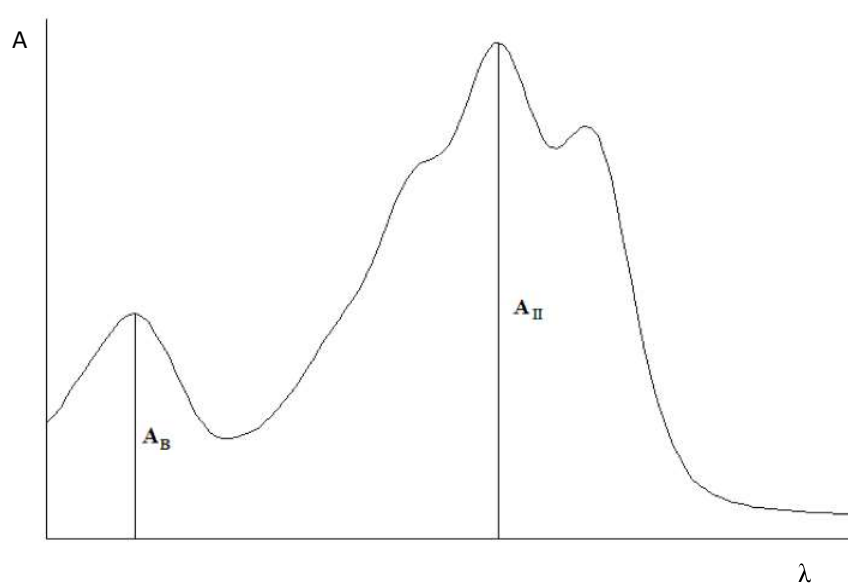


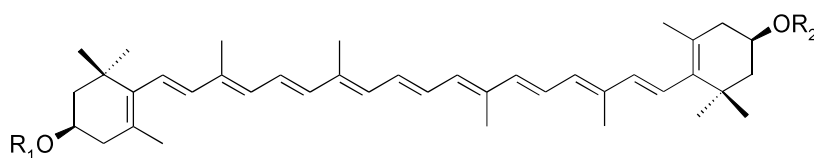
Fig 1.05 cis spectra



Representation of the intensity of the *cis* band of the spectrum relative to that of the main absorption band. $\%A_B/A_{II} = A_B/A_{II} \times 100$.

Figure 1.06

Symmetric carotenoid



Zeaxanthin

Monoesters

Zeaxanthin myristate ($R_1 = \text{myristoyl}$, $R_2 = \text{H}$)

Zeaxanthin palmitate ($R_1 = \text{palmitoyl}$, $R_2 = \text{H}$)

Zeaxanthin stearate ($R_1 = \text{stearoyl}$, $R_2 = \text{H}$)

Homodiesters

Zeaxanthin dimyristate ($R_1 = R_2 = \text{myristoyl}$)

Zeaxanthin dipalmitate ($R_1 = R_2 = \text{palmitoyl}$)

Zeaxanthin distearate ($R_1 = R_2 = \text{stearoyl}$)

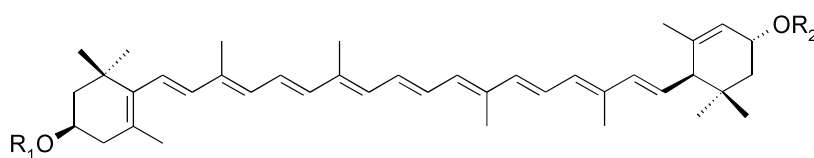
Heterodiesters

Zeaxanthin myristate-palmitate ($R_1 = \text{myristoyl}$, $R_2 = \text{palmitoyl}$)

Zeaxanthin myristate-stearate ($R_1 = \text{myristoyl}$, $R_2 = \text{stearoyl}$)

Zeaxanthin palmitate-stearate ($R_1 = \text{palmitoyl}$, $R_2 = \text{stearoyl}$)

Unsymmetric carotenoid



Lutein

Monoesters

Lutein 3-*O*-myristate ($R_1 = \text{myristoyl}$, $R_2 = \text{H}$)

Lutein 3'-*O*-myristate ($R_1 = \text{H}$, $R_2 = \text{myristoyl}$)

Lutein 3-*O*-palmitate ($R_1 = \text{palmitoyl}$, $R_2 = \text{H}$)

Lutein 3'-*O*-palmitate ($R_1 = \text{H}$, $R_2 = \text{palmitoyl}$)

Lutein 3-*O*-stearate ($R_1 = \text{stearoyl}$, $R_2 = \text{H}$)

Lutein 3'-*O*-stearate ($R_1 = \text{H}$, $R_2 = \text{stearoyl}$)

Homodiesters

Lutein dimyristate ($R_1 = R_2 = \text{myristoyl}$)

Lutein dipalmitate ($R_1 = R_2 = \text{palmitoyl}$)

Lutein distearate ($R_1 = R_2 = \text{stearoyl}$)

Heterodiesters

Lutein 3'-*O*-myristate -3-*O*-palmitate ($R_1 = \text{palmitoyl}$, $R_2 = \text{myristoyl}$)

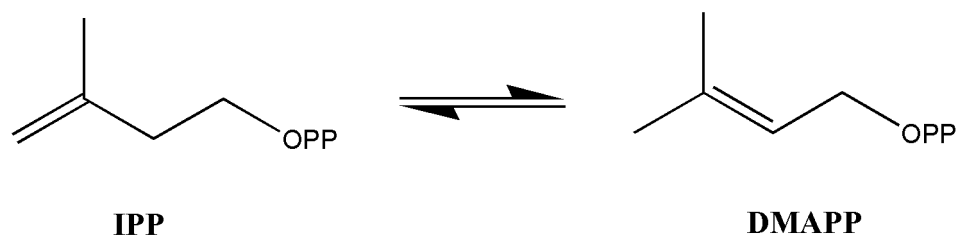
Lutein 3'-*O*-palmitate-3-*O*-myristate ($R_1 = \text{myristoyl}$, $R_2 = \text{palmitoyl}$)

Lutein 3'-*O*-myristate-3-*O*-stearate ($R_1 = \text{stearoyl}$, $R_2 = \text{myristoyl}$)

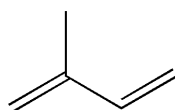
Lutein 3'-*O*-stearate -3-*O*-myristate ($R_1 = \text{myristoyl}$, $R_2 = \text{stearoyl}$)

Lutein 3'-*O*-palmitate-3-*O*-stearate ($R_1 = \text{stearoyl}$, $R_2 = \text{palmitoyl}$)

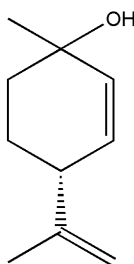
Lutein 3'-*O*-stearate -3-*O*-palmitate ($R_1 = \text{palmitoyl}$, $R_2 = \text{stearoyl}$)



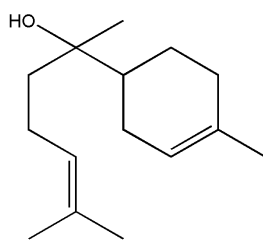
Scheme 1.1. Chemical structures of isopentenyl diphosphate (IPP) and dimethylallyl diphosphate (DMAPP).



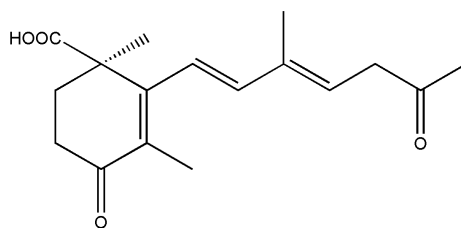
Isoprene



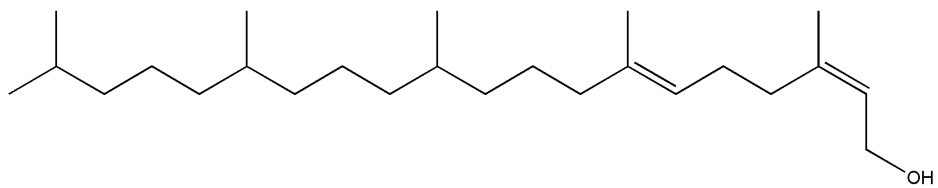
p-Menthadienol



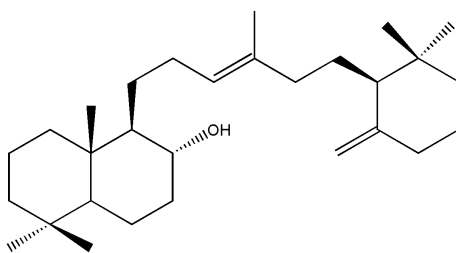
α -Bisabolol



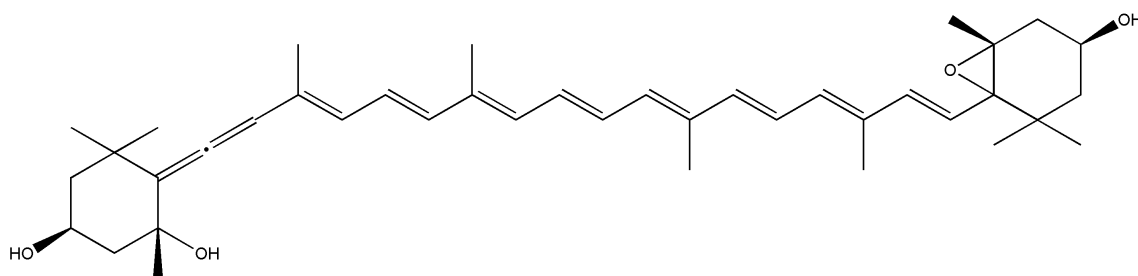
Trisporic acid



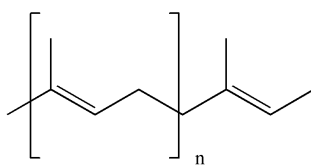
Pentaprenol



Ambrein



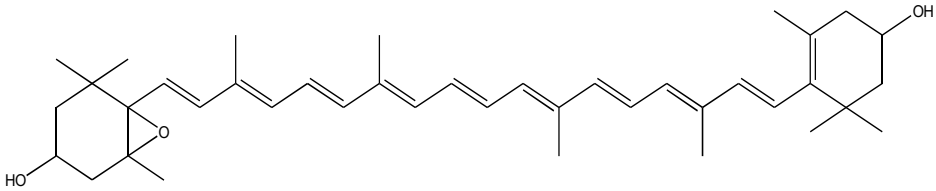
Neoxanthin



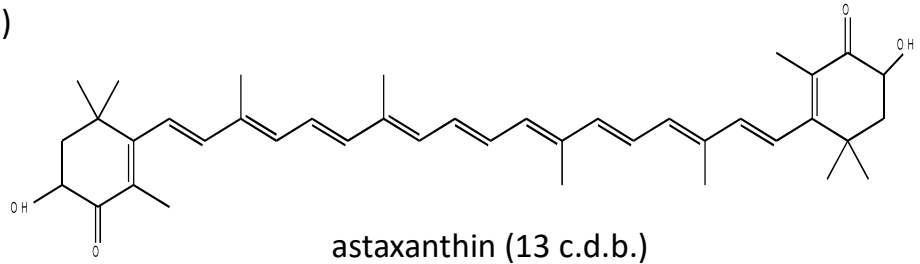
$n = 500 - 5000$

Rubber

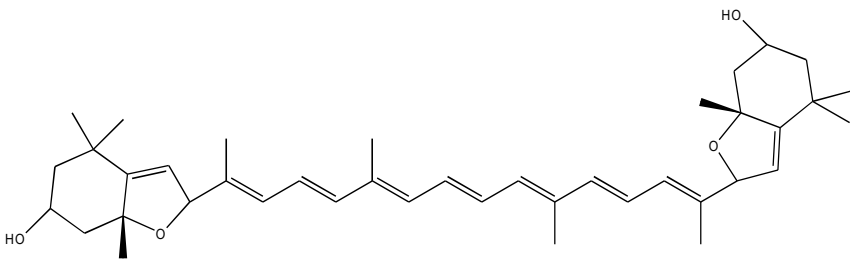
Scheme 1.2. Chemical structures of diverse isoprenoid compounds.



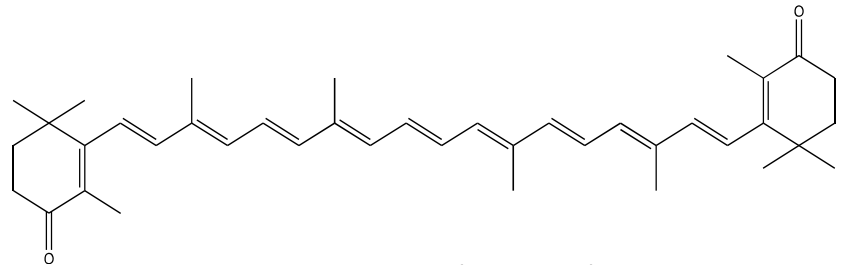
antheraxanthin (10 c.d.b.)



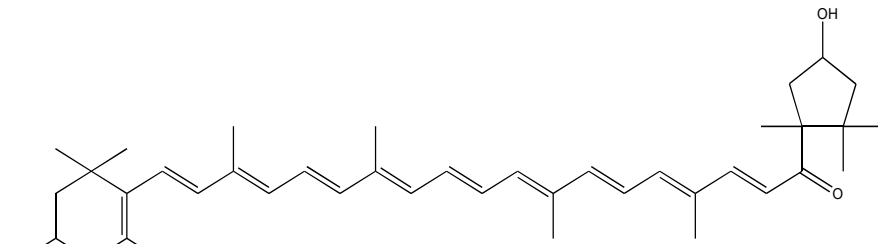
astaxanthin (13 c.d.b.)



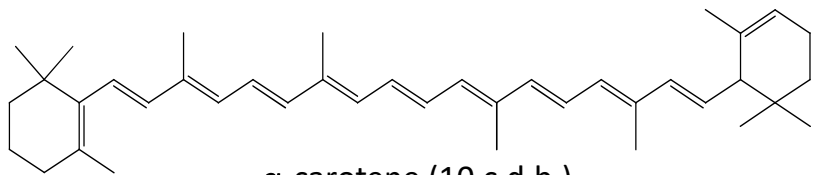
auroxanthin (7 c.d.b.)



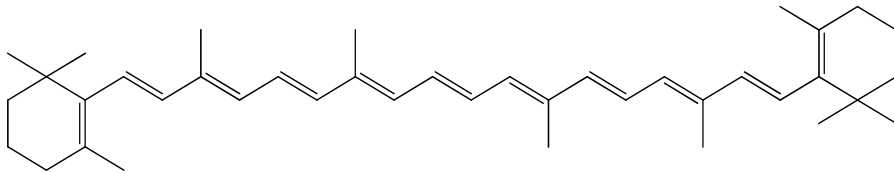
canthaxanthin (13 c.d.b.)



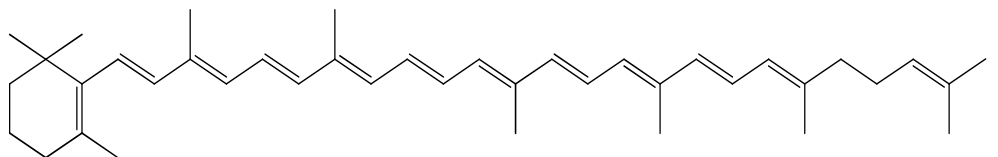
capsanthin (11 c.d.b.)



α -carotene (10 c.d.b.)

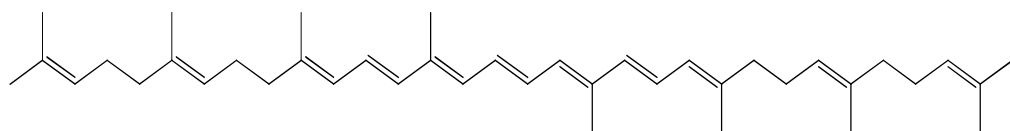


β -carotene (11 c.d.b.)

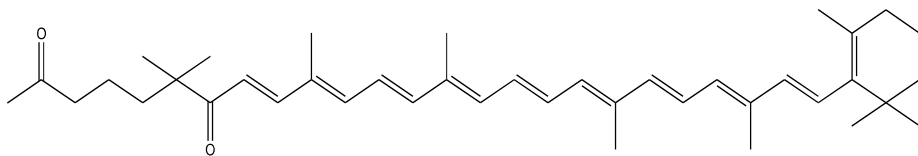


γ -carotene (11 c.d.b.)

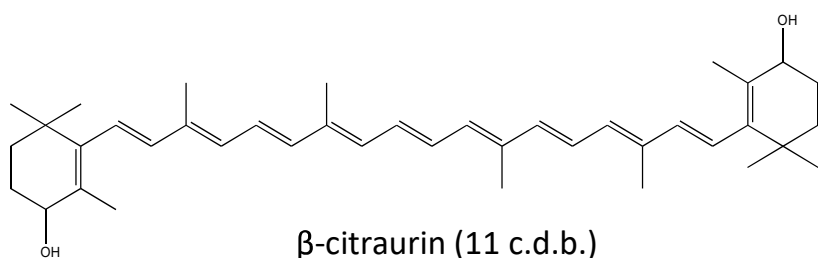
Figure 2. Chemical structures of diverse carotenoids .



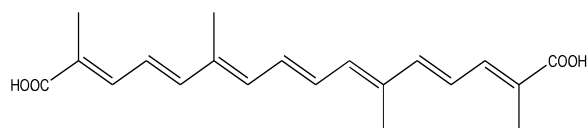
ζ-carotene (7 c.d.b.)



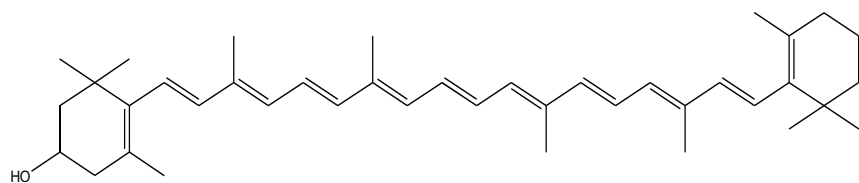
semi-β-carotenone (11 c.d.b.)



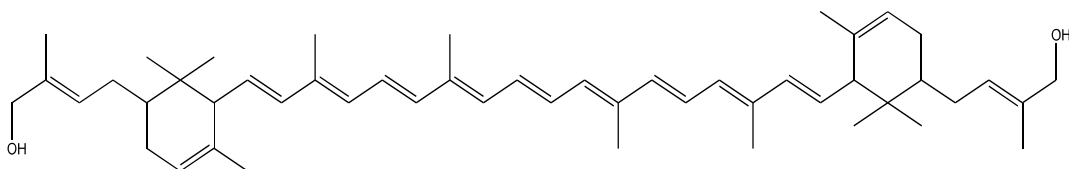
β-citraurin (11 c.d.b.)



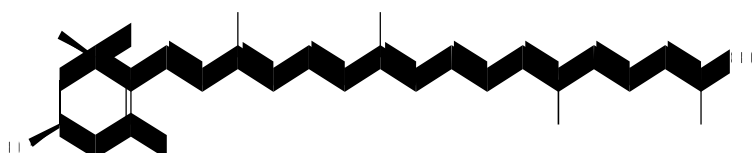
crocetin (9 c.d.b.)



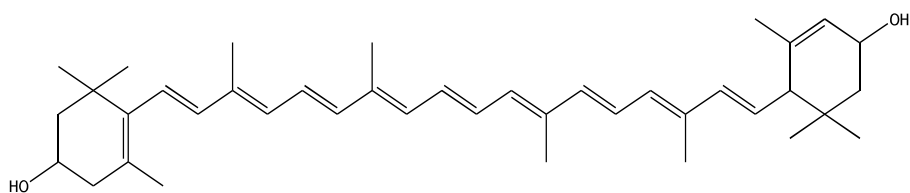
β-cryptoxanthin (11 c.d.b.)



decaprenoxanthin (9 c.d.b.)

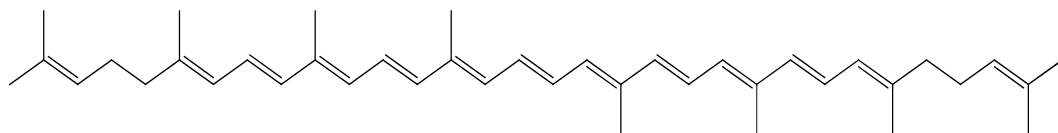


isozeaxanthin (9 c.d.b.)

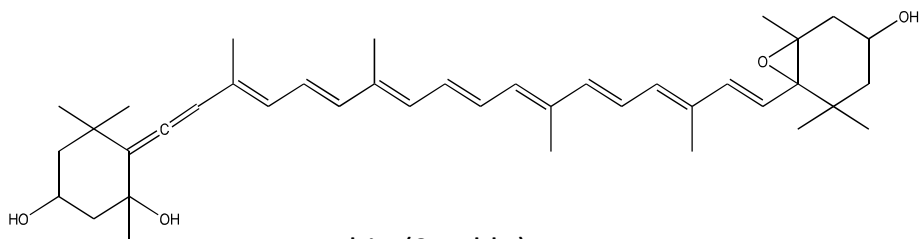


lutein (10 c.d.b.)

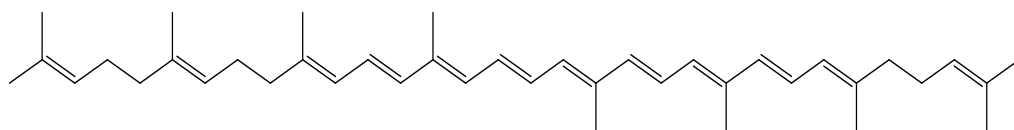
Figure 2. Chemical structures of diverse carotenoids .



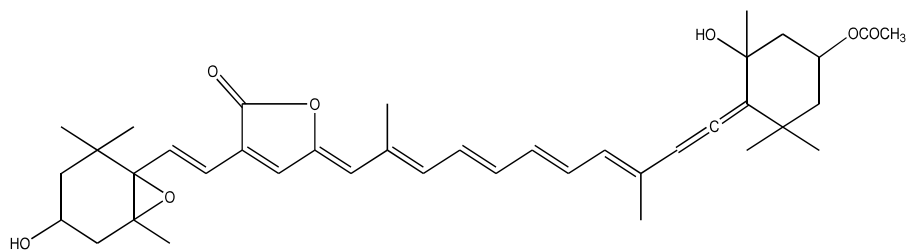
lycopene (11 c.d.b.)



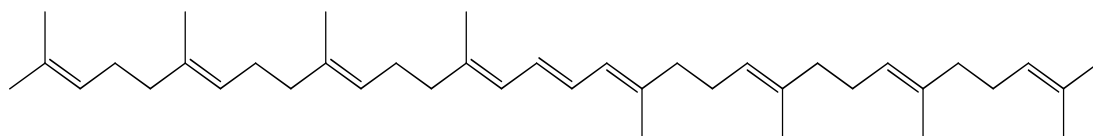
neoxanthin (9 c.d.b.)



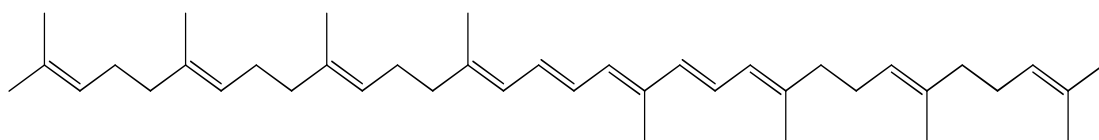
neurosporene (9 c.d.b.)



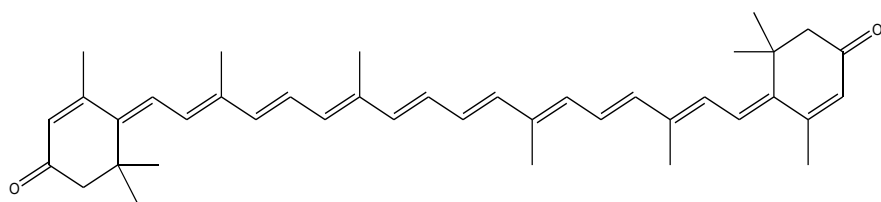
peridinin (9 c.d.b.)



phytoene (3 c.d.b.)

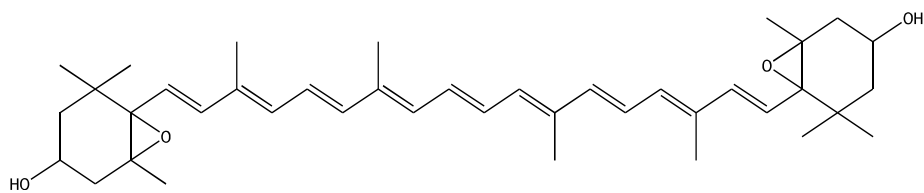


phytofluene (5 c.d.b.)

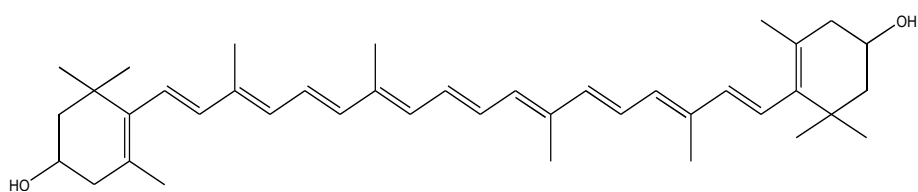


rhodoxanthin (14 c.d.b.)

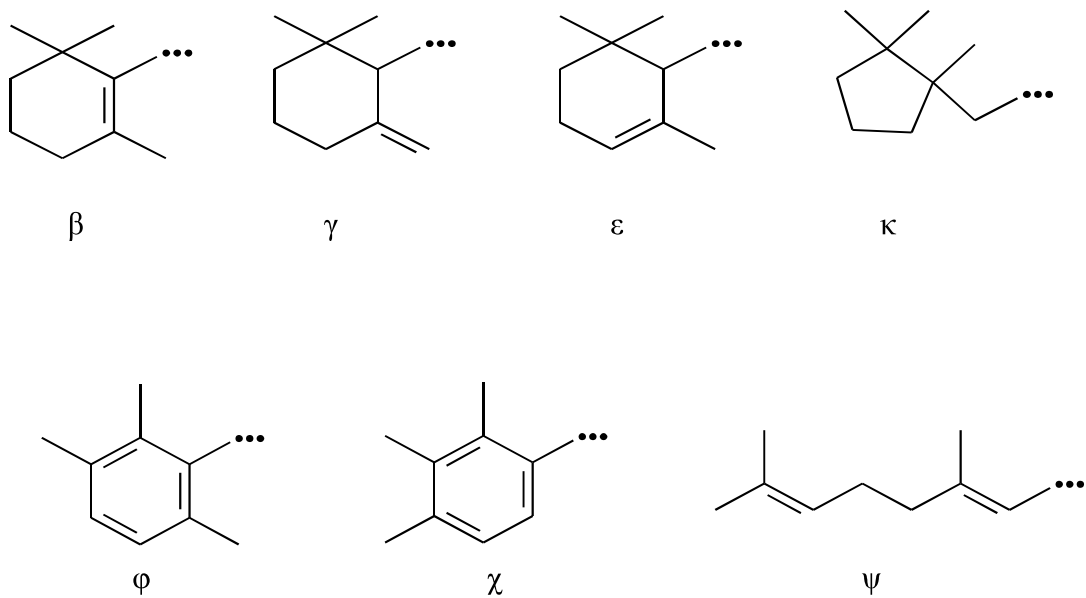
Figure 2. Chemical structures of diverse carotenoids .



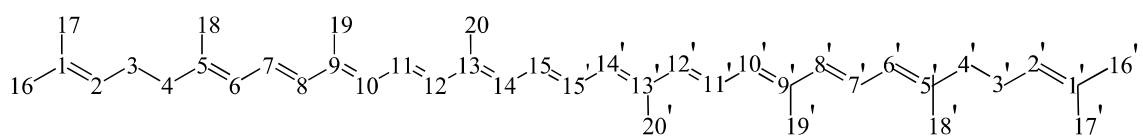
violaxanthin (9 c.d.b.)



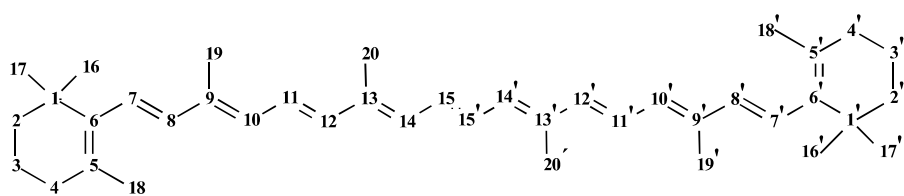
zeaxanthin (11 c.d.b.)



Scheme 1.4. End groups present in carotenoid molecules

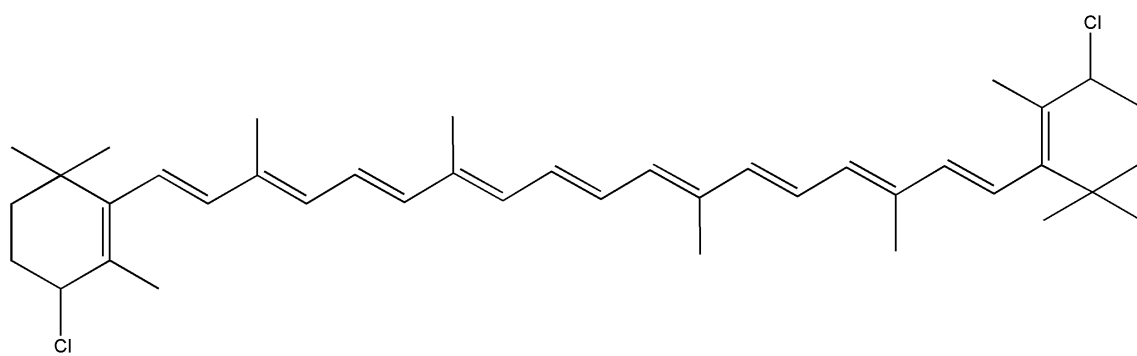


lycopene

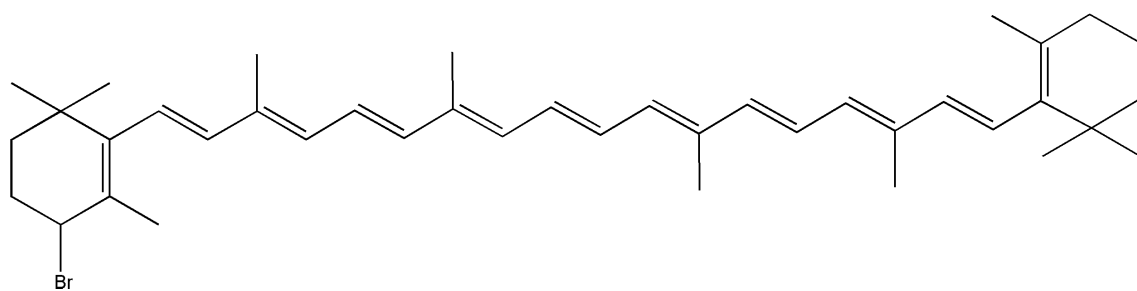


β -carotene

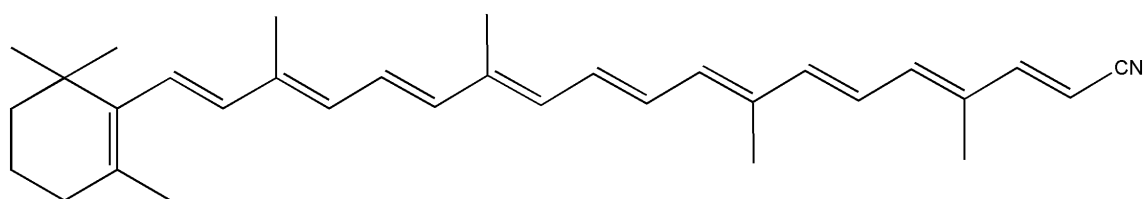
Scheme 1.5. Numbering of carbon atoms in an acyclic (lycopene) and a cyclic (β -carotene) carotenoid



4,4'-Dichloro-β,β-carotene

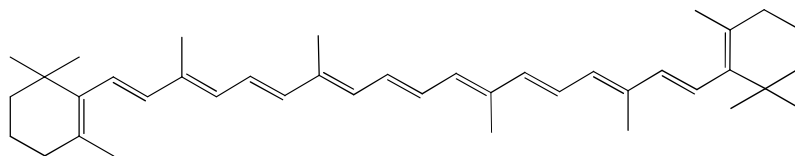


4-Bromo-β,β-carotene

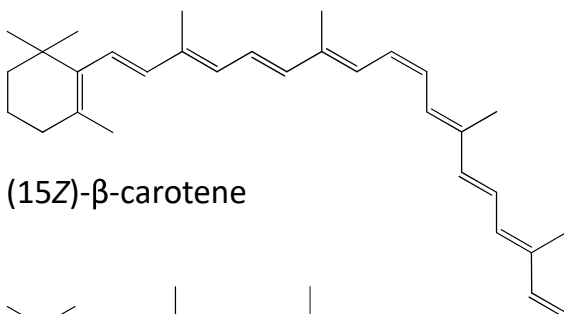


6'-Apo-β-carotene-6'-nitrile

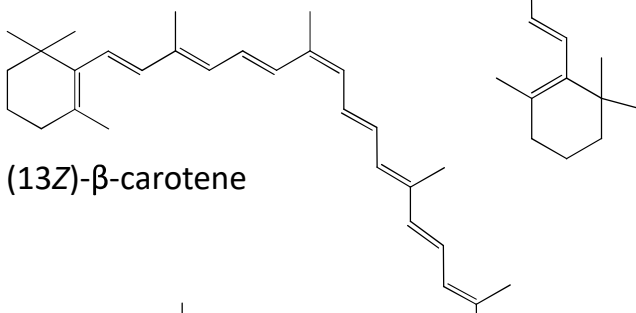
Figure 5. Chemical structures of some heterocarotenoids.



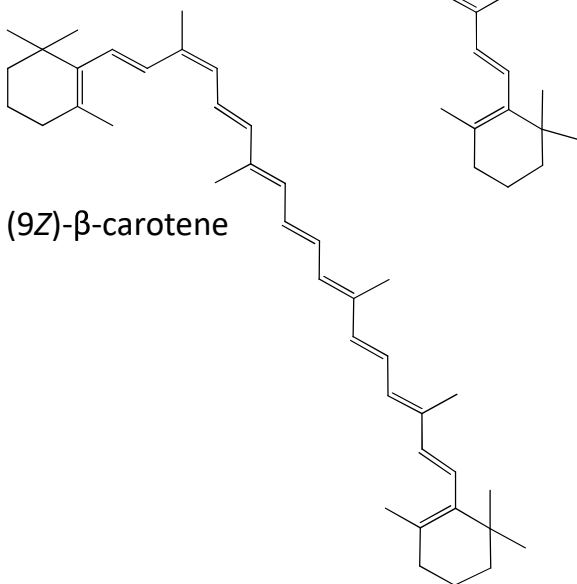
(all-*E*)-β-carotene



(15*Z*)-β-carotene

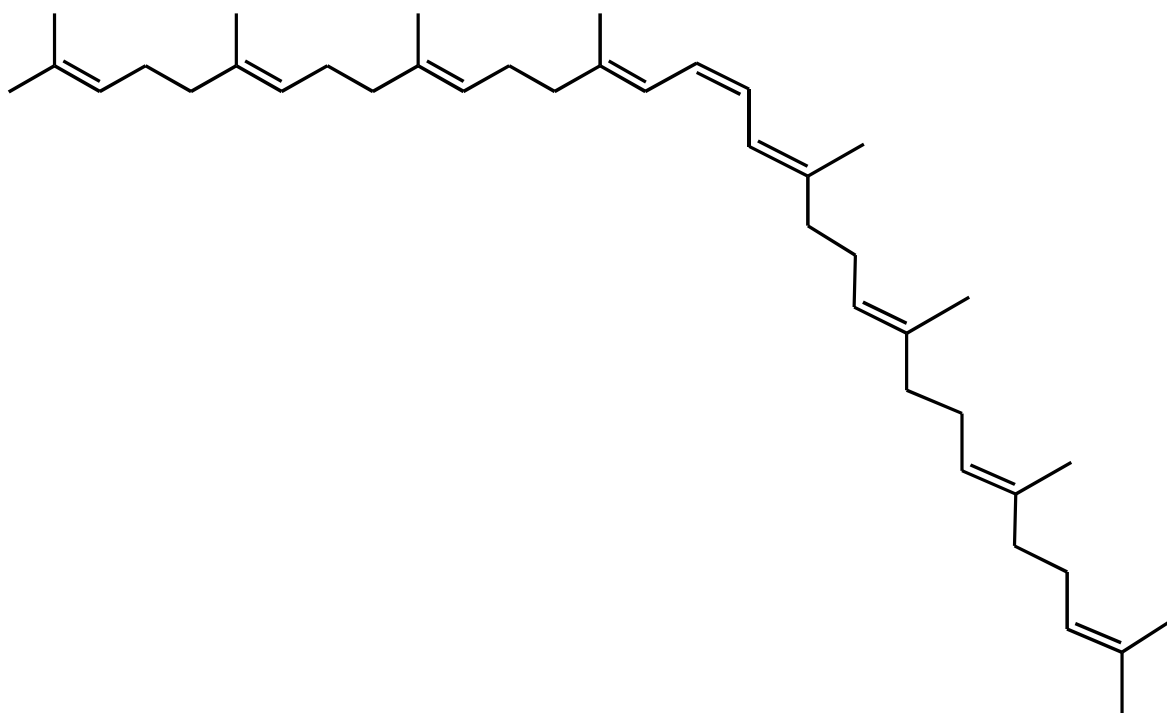


(13*Z*)-β-carotene

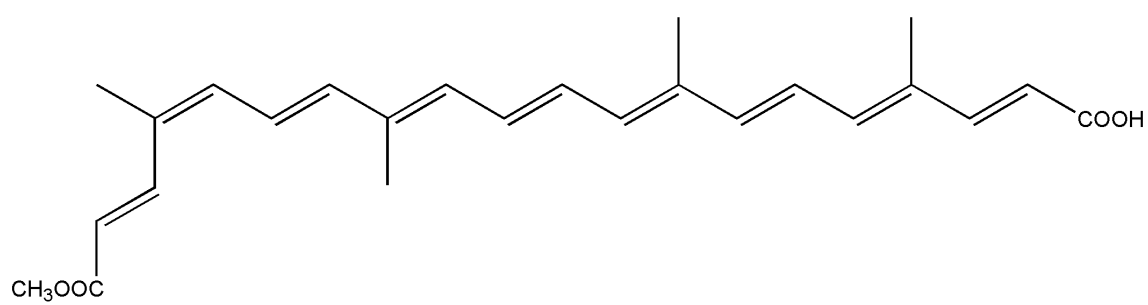


(9*Z*)-β-carotene

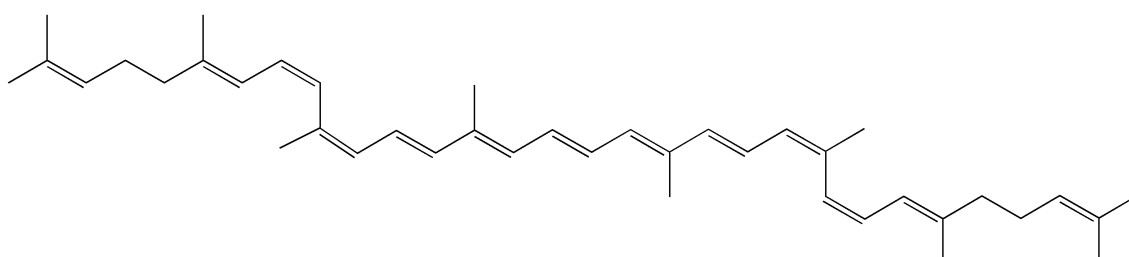
Scheme 1.08. Chemical structure of some geometrical isomers of β-carotene



(15Z)-phytoene



(9Z)-Bixin



Prolycopene

Scheme 1.9. Chemical structure of (15Z)-phytoene, (9Z)-bixin and (7Z,9Z,7'Z,9'Z)-lycopene (prolycopene).

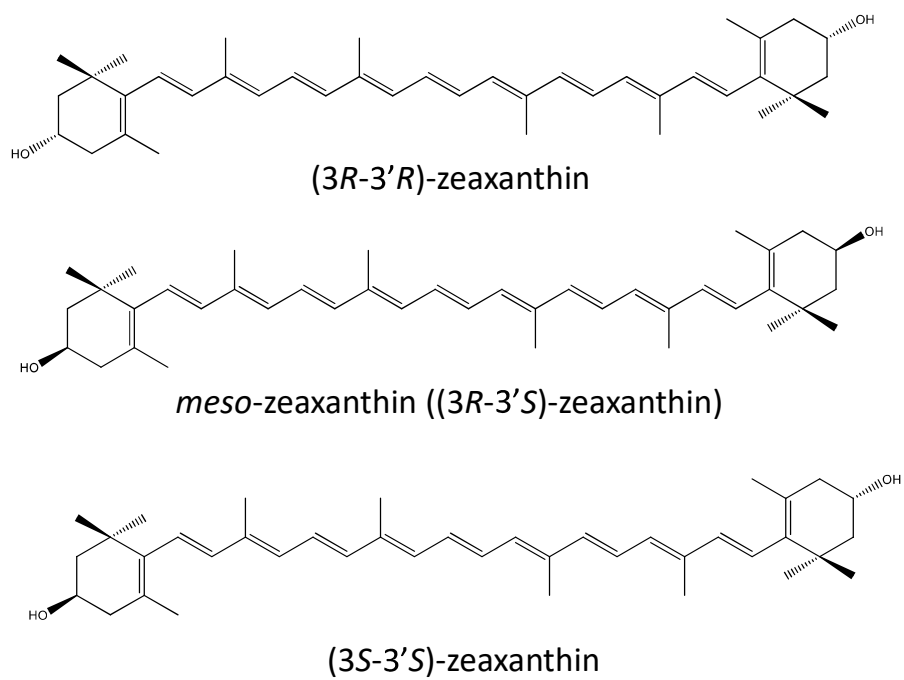
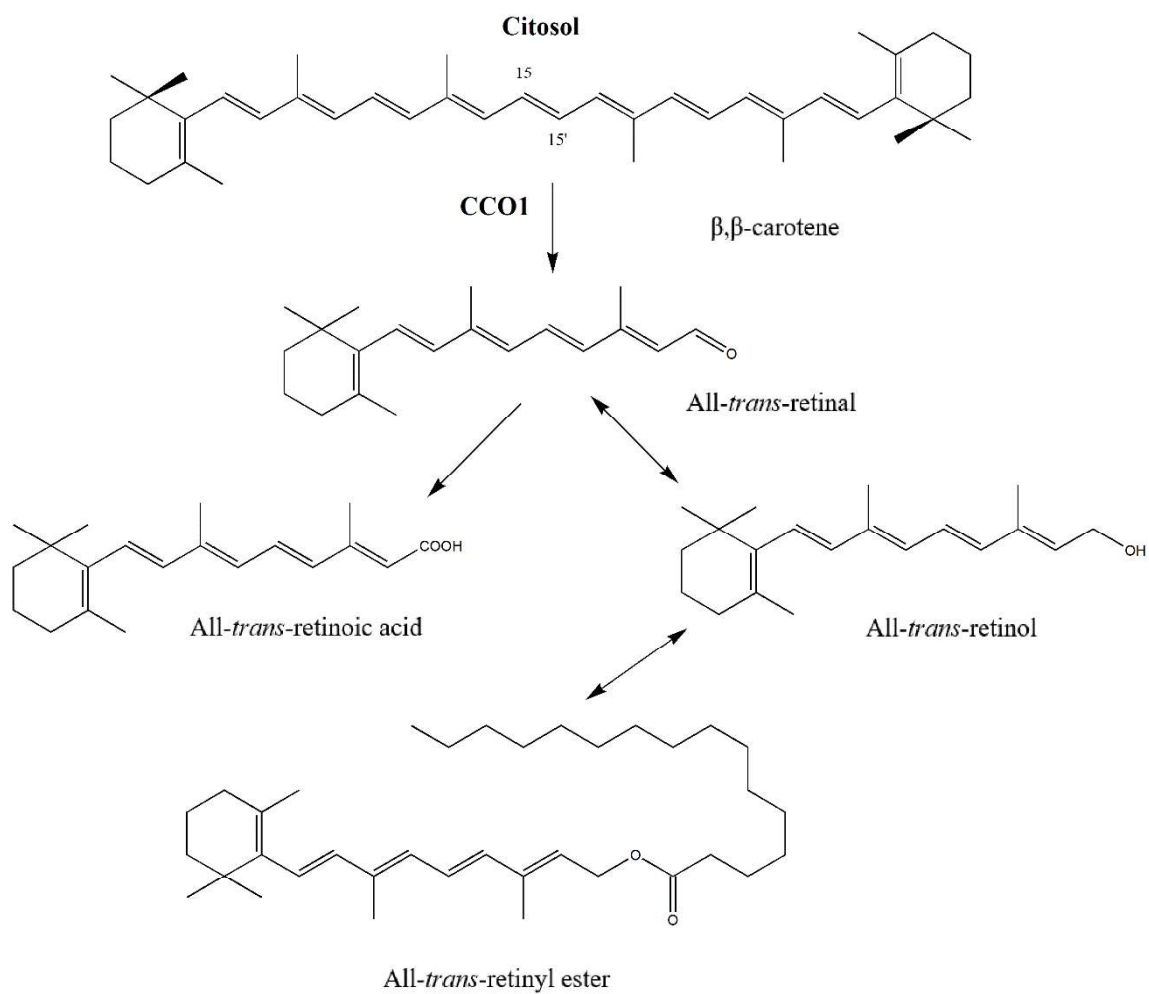
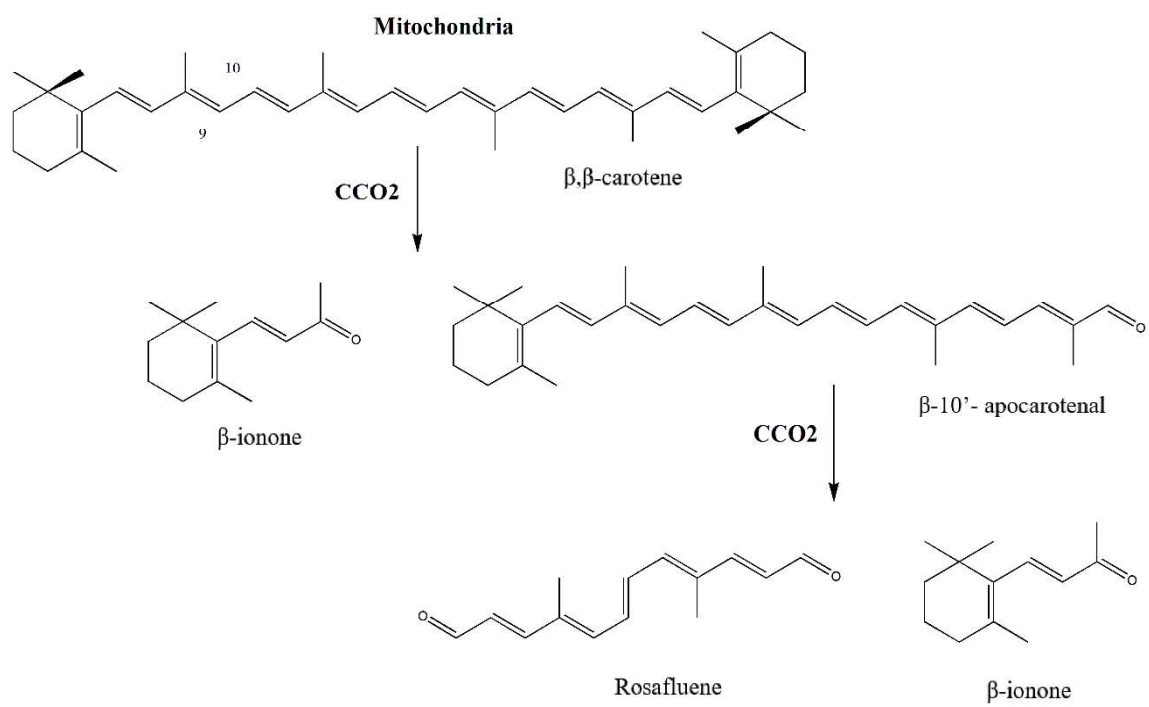


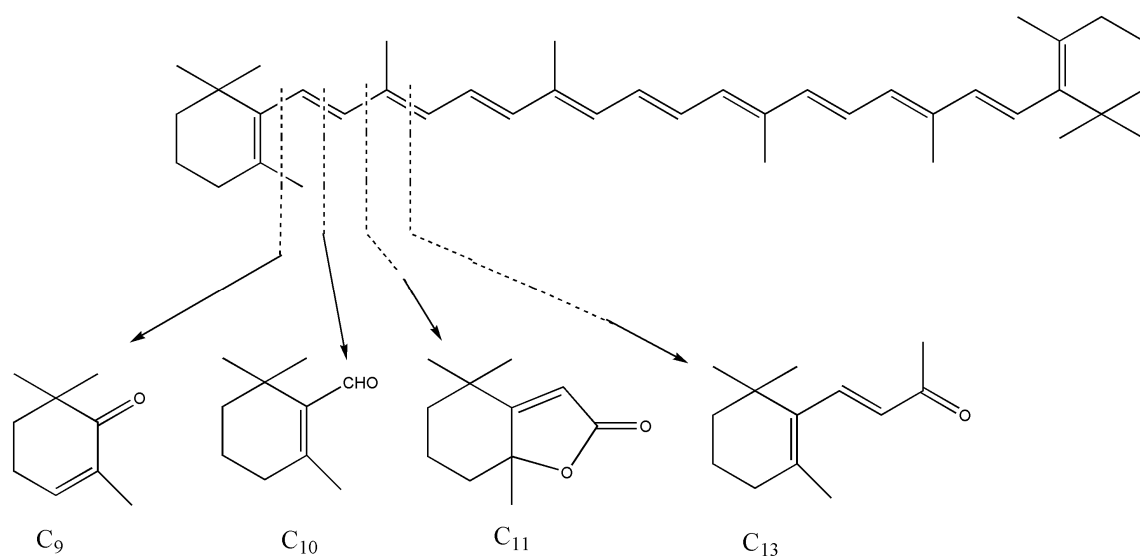
Figure 1.10. Chemical structures of optical isomers of zeaxanthin



Scheme 1.11. Cleavage of β -carotene by β,β -carotene 15,15'-monooxygenase 1 (CCO1).

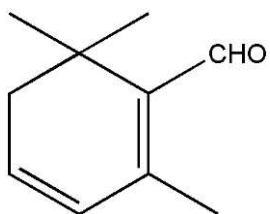


Scheme 1.12. Cleavage of β -carotene by β , β -carotene 9',10'-dioxygenase (CCO2).

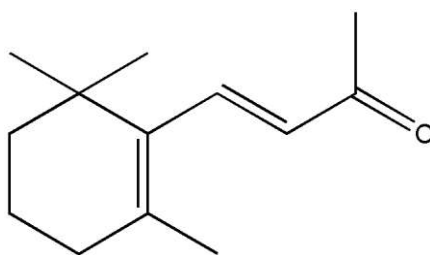


Scheme 1.13. Schematic representation of the cleavage of β -carotene into different norisoprenoids (adapted from²).

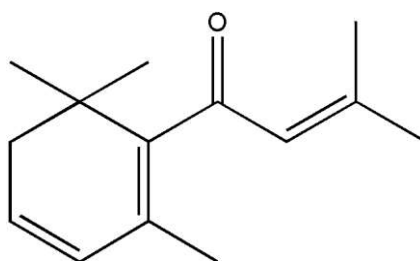
Scheme 1.14. Chemical structures of some carotenoid-derived aroma compounds.



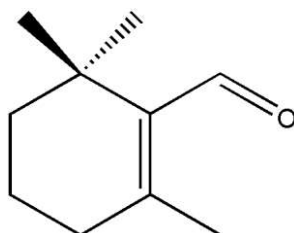
Safranal



β -Ionone

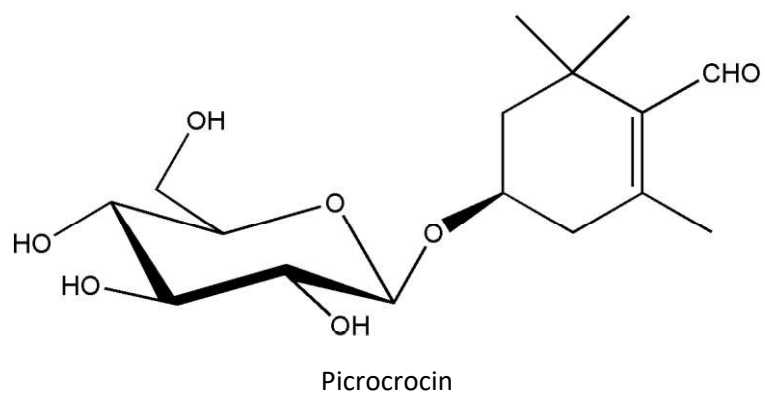


β -Damascenone

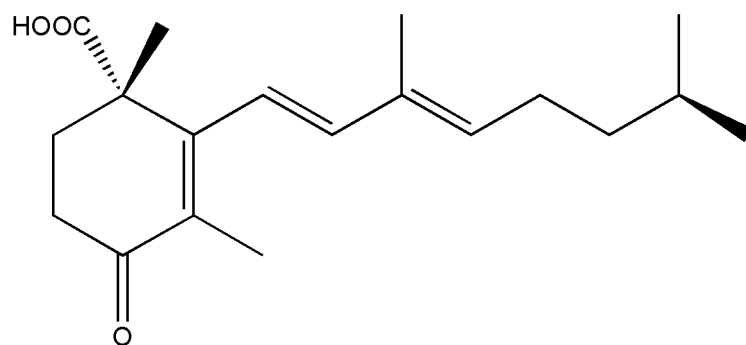


β -Cyclocitral

Scheme 1.15

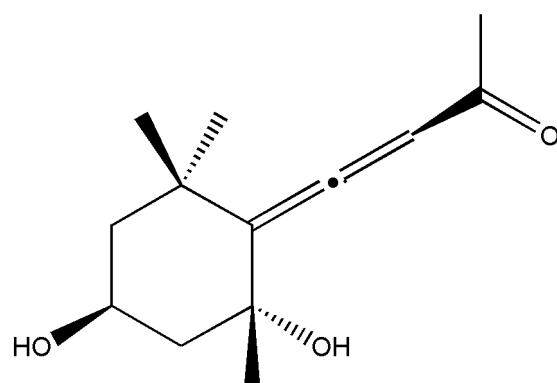


Scheme 1.16. Chemical structures of trisporic acid



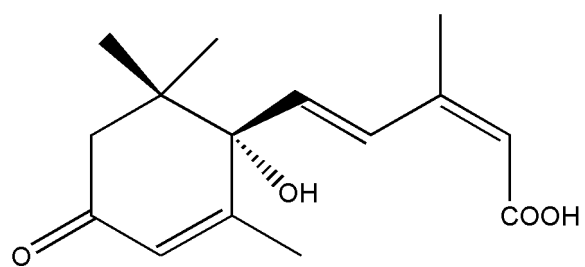
Trisporic acid

Scheme 1.17. Grasshopper ketone

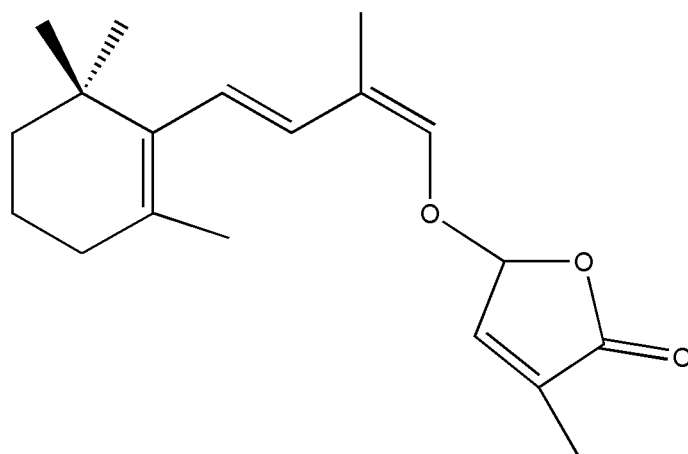


Grasshopper ketone

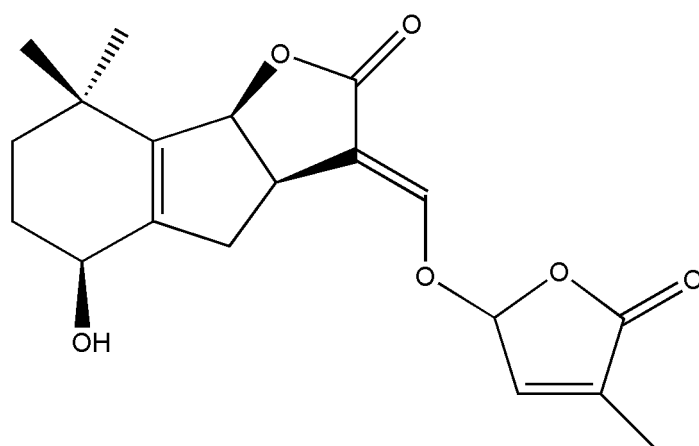
Scheme 1.18. Chemical structure ABA



Absciscic acid



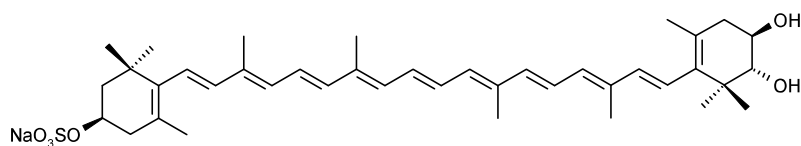
Carlactone



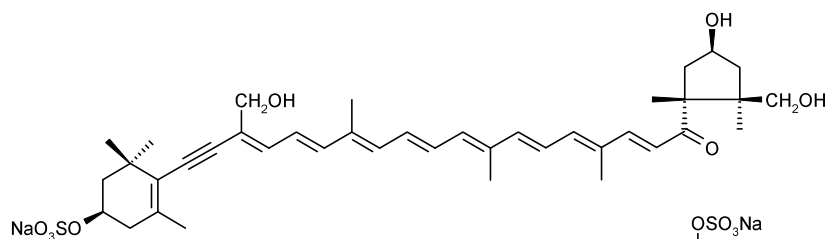
Strigol

Scheme 1.19. Chemical structures of strigolactones

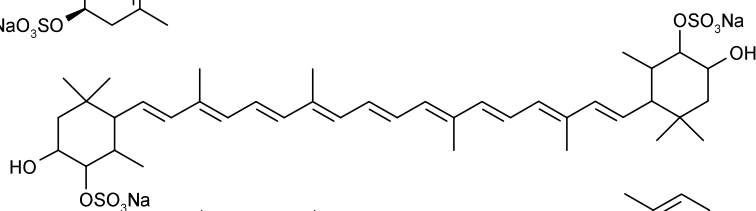
Scheme 1.20



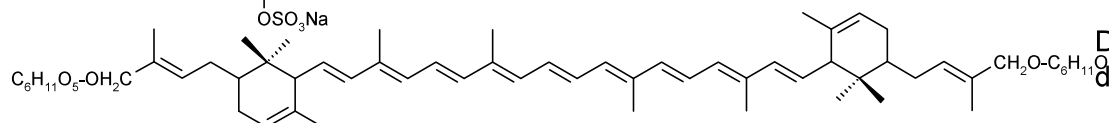
Caloxanthin 3-sulphate



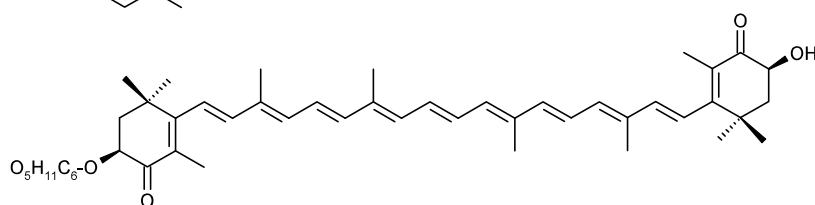
Bastaxanthin D



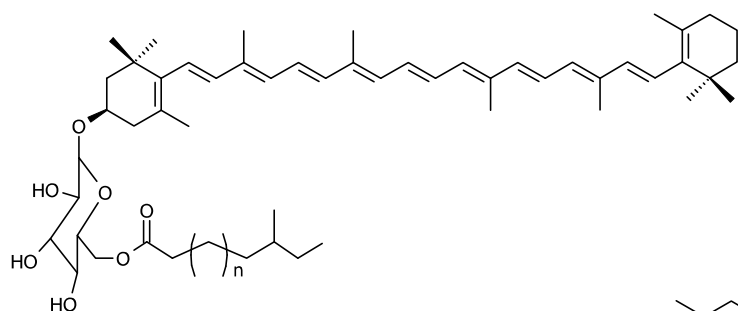
Ophioxanthin



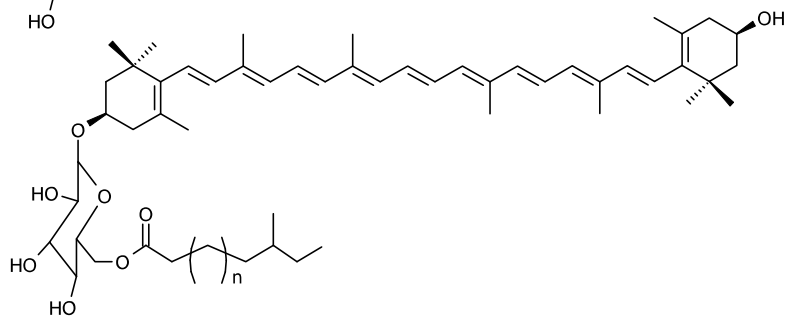
Decaprenoxanthin diglucoside



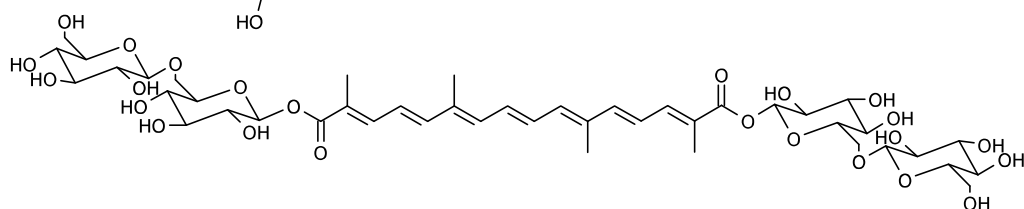
Astaxanthin glucoside



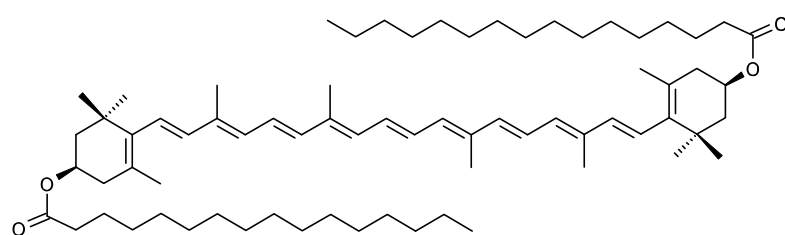
Thermocryptoxanthins



Thermozeaxanthins

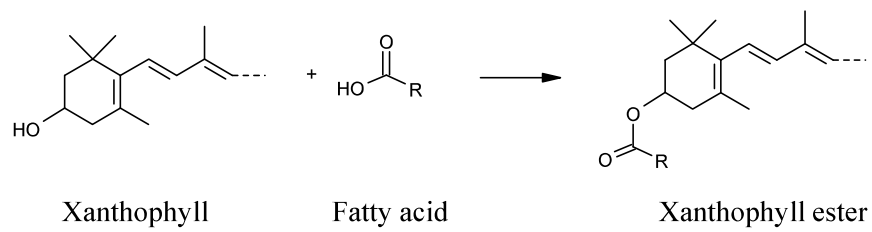


Crocin

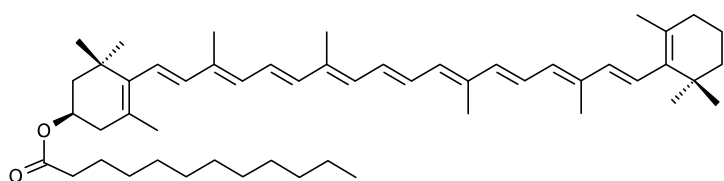


Zeaxanthin dipalmitate

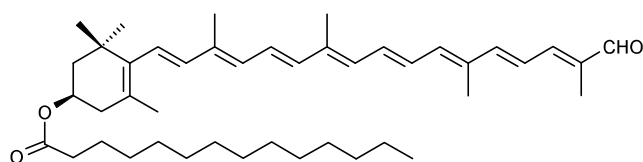
Scheme 1.21



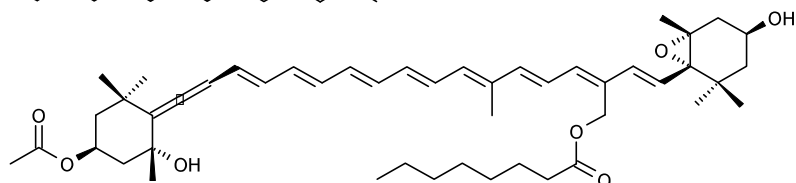
Scheme 1.22



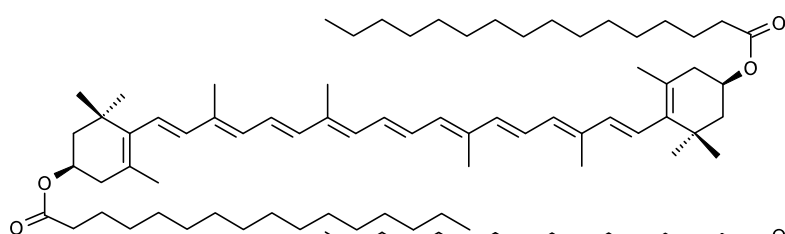
β -Cryptoxanthin laurate



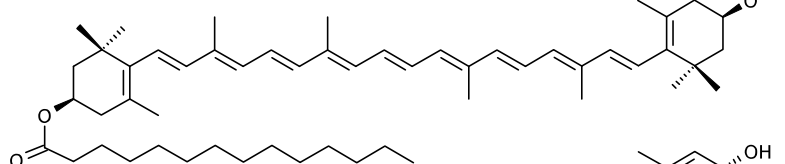
β -Citraurin myristate



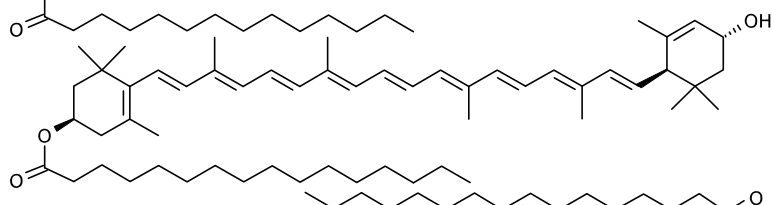
Vaucherixanthin
3-acetate-19'-octanoate



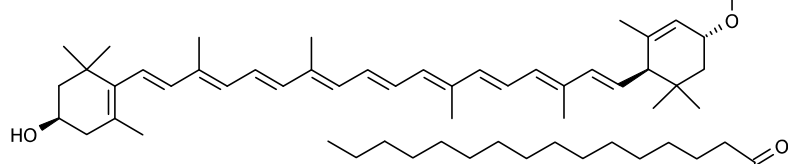
Zeaxanthin dipalmitate



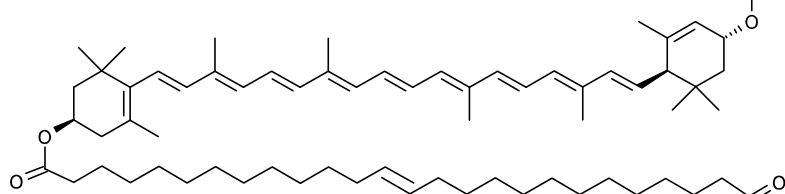
Zeaxanthin myristate-palmitate



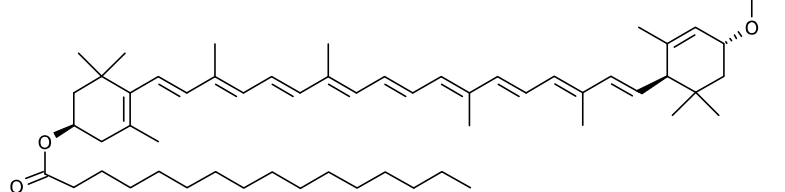
Lutein 3-*O*-palmitate



Lutein 3'-*O*-palmitate



Lutein 3'-*O*-palmitate-3-*O*-myristate



Lutein 3'-*O*-myristate-3-*O*-palmitate