



Carotenoid Structures, an Illustration of a New Kind of Symmetry in Chemistry

Dumitru Petru I. Iga*

* University of Bucharest, former C. I. Parhon, Bucharest, Rumania

* University of Oradea, B-dul Armata Romana, Oradea, Nagyvárad, Rumania, pdiga49@yahoo.com

Abstract *Meso* compounds usually possess a dimeric structure. Their molecule is formed of two enantiomeric halves. According to Kelvin-Prelog theory they are heterochiral. A subgroup of important isomers of *meso* compounds, much more numerous and diverse than the latter ones, have a chiral molecule formed of two identical chiral halves, i.e., they suggest an internal twinning path of formation. Of this reason, we have called them *chitwin*. According to Kelvin-Prelog concepts they are homochiral. The third subgroup of isomers of *meso* compounds are also chiral and they are characterized by a molecular skeleton identical to *meso* ones, still their chiral centers are irregularly distributed in their molecule, i.e. *irrechi* isomers. The fourth subgroup of isomers of the above mentioned ones are also chiral but their molecular skeleton is quite different of *meso* ones, in fact they are remote of idea of symmetry. We have called them *CROM* isomers. An exceptional illustration of our new systematization was found within carotenoids, and it is presented in this paper.

Keywords carotenoids, *meso*, *chitwin*, *irrechi*, *CROM*

Introduction

A vast and ever increasing group of natural and synthetic compounds is on the way to take its place of honour in chemistry and biochemistry, i.e. compounds with dimeric structure. Dimers are produced by chemical or physical linkages of precursors called monomers. If monomers are identical (with the same basic skeleton) homodimers are obtained, and if they are different the products are heterodimers [1]. The molecule of the latter is formed of two different halves [2-6]. According to a structural criterion, four remarkable subgroups can be distinguished inside the vast group of dimeric compounds:

(A) Symmetric compounds, including two major sections: (A1) *meso* ones, whose molecule is characterized by a mirror plane of symmetry; (A2) compounds possessing a center of symmetry, or an alternating axis of symmetry [7]. *Meso* compounds are non-rotatory and their molecule is formed of two enantiomeric chiral halves [8-12]. According to Kelvin and Prelog theory [13-16] *meso* compounds are internally heterochiral. The manner, by which E. Fischer expanded the subgroup of homodimeric compounds, belongs equally to physical sciences and to philosophical ones, since some heterodimers are treated as homodimers. This discovery, in fact a chemical paradox, concern especially polyols with linear chain and an odd number of C atoms, beginning with heterodimers as xylitol [2] and adonitol (ribitol) [3]. (They can be considered as products of reductive dimerization of glycol aldehyde and glyceraldehyde). He found out that both pentitols are devoid of optical activity, hence they have symmetrical molecules. In fact, the equalization between *meso* homodimers and some

meso heterodimers is made by their mirror plane of symmetry. In case of *meso* homodimers (not necessarily produced by dimerization) the symmetry plane is drawn between atoms and in this way every equivocal situation is avoided. *Meso* compounds with heterodimeric structure, contrary to homodimers, have a molecule characterized by a nonuniform composition. Of this reason their mirror plane of symmetry has to be drawn through an atom (or a group of atoms), the entity which is cut is imaginarily eliminated, and implicitly the envisaged structure is evaluated as a homodimeric one. (The mirror symmetry plane is a physical instrument and as every instrument has its own force). This coexistence of nonuniform composition and a mirror plane of symmetry is a privilege of *meso* heterodimeric compounds. *Meso* compounds having a mirror plane of symmetry [17-19] have a molecule formed either of two identical or of two different halves. Subsequently, other carbohydrates [20,21] as well as compounds of other families were added to this type: amino acids and their derivatives [22-25], phenols [26,27], lignans [28-32], terpenoids [33], etc. *Meso* compounds devoid of a mirror plane of symmetry have to be submitted to Cahn-Ingold-Prelog analysis [34-35]. Finally one must find out that the compound contains two sets of enantiomeric chiral centers. And the answer to a question raised by Metzler [36] – compare two chromatids coiled with opposite handedness with the existence of snail shells or flowers with both right and left handedness within the same species [37-38] is this one: every pair i. e., two chromatids coiled with opposite handedness, or two flowers or two snail shells with both right and left handedness forms *symmetric* systems. And the same are gloves, shoes, augers, screws, of opposed handedness, all in pairs. *Meso* compounds have been used as a structural reference in this paper.

- (B) Chiral compounds formed of two identical halves, linked in the same manner as in *meso* isomers, constitute another subgroup. In describing the phenomenon of crystals formation by the aggregation of smaller ones (rudimentary or embryonic), to form grown, mature crystals, Jaeger [39] used the term *twin* (or *twining*), especially when two such components are united. We adopted this term and adapted it for chemical and biochemical purposes. In fact, we have patterned it as *chitwin* (*chi* from chiral plus *twi*n). Hence we have called the constituents of this group *chitwin* compounds, and therefrom their definition: chiral molecules formed of two identical chiral halves are *chitwin*. In fact a chiral molecule can be twinned outwardly, i.e. a simple multiplication, or internally, and in this case a *chitwin* molecule might be produced. Moreover, in order to describe the symmetry of crystalline systems, Jaeger [39] used the term *twining*-plane. This could disclose a new type of symmetry at molecular level, and even at macrocosmic one. As mirror plane of symmetry involves two enantiomeric halves, the *twining*-plane (we have called it *chitwin* plane) associates two chiral identical halves. This concept is supported by many hundreds of natural and artificial compounds, about an order of magnitude bigger than the number of *meso* compounds. And their multitude is increasing every day. This concept applies especially in chemistry and biology but also in practical life. Many decades after Jaeger's book, they were called C_2 symmetrical [19,40-44]. *Chitwin* molecules possess a distinctive structure, being formed of two sets of identical chiral carbons and two sets of identical chemical functions. They are internally homochiral and they are C_2 symmetrical since they are *chitwin*. The principle used by E. Fischer to expand the subgroup of homodimeric compounds, also works for *chitwin* ones although in a more limited manner. E.g. D- and L-arabinitol (and D- and L-lyxitol), the isomers of xylitol, are simply chiral. Their 3-keto- and 3-deoxy-derivatives instead, although they fail to fulfill the definition of *chitwin* compounds – to possess two identical sets of chiral centers and of chemical functions, they are *chitwin* [23]. Many derivatives of L-arabinitol have been synthesized as *chitwin* compounds [45-47].
- (C) The third subgroup is formed of compounds with asymmetric form, possessing only an identity operation. Chiral compounds isomer with *meso* ones [48-53] and possessing a molecular skeleton similar to the latter have been called by us *irrechi* (from irregular distributed chiral centers).
- (D) The members of the fourth subgroup are isomer with the preceding ones but no structural regularities can be distinguished in their molecules. Of this reason we have called them *CROM* (from chiral remote of *meso*) [54-70].

All the above mentioned dimers can be found especially among the secondary metabolites of plants and this aspect can be scored as an argument for the relative oldness of phenomenon. All four subgroups are characterized by



structural and metabolic relationships with other compounds. At the same time, the vast, ever increasing group of dimers include numerous synthetic compounds, especially of *chitwin* type.

Besides dimers of which the two halves are linked by strong covalent bonds, a different type of dimers has been evidenced whose monomeric units are linked by weak physical bonds – hydrogen bonds, van der Waals, etc., – and their linkage is reversible [71,72]. A strong and convincing argument in favor of this phenomenon, is the behavior of some amphiphilic chiral molecule, e. g., cholesterol, in an environment formed of membrane constituents, in well defined molar ratios. Some independent research groups have undoubtedly established that cholesterol, when mixed with lipids such as phospholipids [73], dipalmitoylphosphatidylcholine [74], phosphatidylcholine or phosphatidylethanolamine [75], forms dimers, i. e., *chitwin* structures linked by physical forces. Moreover, attaching of a series of residues to hydroxyl group [76] or a fluorescent group on the lateral chain of cholesterol [77,78] did not affect this behavior. On the other hand the association by ionic bonds of polymers mediated by Ca^{2+} or Na^+ has been evidenced [79]. It is widely accepted that a large number of proteins that are responsible for biochemical and cellular functions exist as dimers or need to be activated by dimerization before mediating certain signaling pathways [80]. Simultaneously targeting both monomeric moieties of the dimeric proteins has shown potential in the development of various therapeutic agents. At the same time, non-protein dimeric molecules, which are generated biogenetically from coupling of two identical chiral monomeric molecules, might be able to act on both moieties of a dimeric protein. The small dimeric molecules have attracted in recent years great attention for their peculiar structures and biological activities, especially since in dimeric state they are more potent than their monomeric precursors, concerning some important biological activities [81]. Testosterone was dimerized *via* an aliphatic as well as *via* an aromatic residue, the result being two *chitwin* compounds. Then the affinity of testosterone and its dimers against tRNA were measured and the following order was found: testosterone dimer-aromatic > testosterone dimer-aliphatic > testosterone [82].

As is evident from this paper, we could find compounds presenting all four types of isomers – *meso*, *chitwin*, *irrechi* and *CROM*, but this rule also has remarkable exceptions.

There are two major natural pathways in the production of dimeric compounds: (i) The association of identical or similar chemical entities, by strong chemical bonds (covalent, ionic) or by weak ones (hydrogen, van der Waals, etc) is a well known phenomenon in chemistry and biochemistry. The immense majority of dimeric compounds reaches this state by a dimerization reaction of chiral or achiral monomeric units, possibly followed by some trimming physical-chemical transformations [83-85]. Dimerization process is made in such a manner to block the process at this stage. (ii) On the other hand, some compounds with dimeric structure, characterized by an equal force of representativeness, are produced by indirect biochemical pathways, dimerization reactions being omitted.

The concepts of Kelvin and Prelog [13-16] concerning homo- and heterochirality are usually applied between molecules [86]. The aim of our paper is to disclose the gain of applying these concepts *inside* molecules which are feasible to this process [87]. Both *meso* and *chitwin* molecules allow us to establish interesting and important relationships between them as well as inside them.

A general consideration of natural compounds shows us a consistent illustration of dimeric ones within secondary metabolites of plants, by the following families: (1) carbohydrates; (2) amino acids, their derivatives and chiral hydroxyacids; (3) carotenoids (polyprenyl or isoprenoid compounds) and perhydro isoprenoid hydrocarbons; (4) lignans and neolignans; (5) cyclobutane derivatives; (6) phenolic compounds; (7) alkaloids; (8) terpenoides; (9) lipids; (10) coenzymes based on nucleosides or on cysteine and cysteamine, in oxidized state; (11) homodimeric proteins; (12) palindromes [88,89].

In this paper the potential of illustration of carotenoids concerning the four types of isomers – *meso*, *chitwin* (C_2 *symmetrical*), *irrechi*, *CROM*, within carotenoids, will be presented.

1. Carotenoids (polyprenyl or isoprenoid compounds)

Carotenoids (polyprenyl or isoprenoid compounds) are characterized by structural regularities determined by their biosynthesis from prenyl pyrophosphate (isopentenyl diphosphate). It is almost certainly that few other classes of natural compounds offer such a significant number of *chitwin* molecules as carotenoids, both in free state or



glycosylated. Chain length of carotenoids can serve as a classification criterion, C_{40} type having the most numerous biological implications. C_{50} are also well exemplified in natural materials. At the same time, their metabolism discloses a complex relationship with other chiral or *chitwin* compounds as well as with achiral ones.

From their beginnings, carotenes and carotenoids were associated with colour phenomenon, and subsequently with vision process. Their isolation and structure elucidation [51,90-91] were associated with the knowledge of their metabolism and physiological role. Beside its scientific value, the memorable work of Kuhn and Winterstein [92] has also an instructive appraisal. They proved that a chemical system formed exclusively of carbon and hydrogen could present colours of different nuances.

Carotenoids are probably amongst the most widespread natural pigments. Moreover, they have a large variety of biochemical and physiological functions in plants and animals, connected especially with their interaction with light. An essential trait in the hydrocarbonate skeleton of carotenoids is a system of conjugated double bonds mediating their interaction with a wide range of electromagnetic radiation. Chemical functional groups of carotenoids confer them the capacity to interact with other types of compounds so as to increase their lipophilic character (fatty acids esters) or to transform them in amphiphilic derivatives (glycosides). Keto groups could serve for reaction with amines to produce Schiff bases.

As expected, carotenoids possessing two asymmetric carbons present only two types of optical isomers, *meso* and *chitwin*.

The most spectacular and best illustration of our chemical systematization of chiral homodimers is made by carotenoids and their derivatives, especially glycosides.

All C_{40} carotenoids of Figs. 1.1A-1.1D are isomers i.e. they possess the same molecular formula, $C_{40}H_{56}O_2$. *Meso*-carotenoids include: *meso*-zeaxanthin, 2,2'-dihydroxy- β,β -carotene, tunaxanthin D, tunaxanthin E. (Fig. 1.1A).

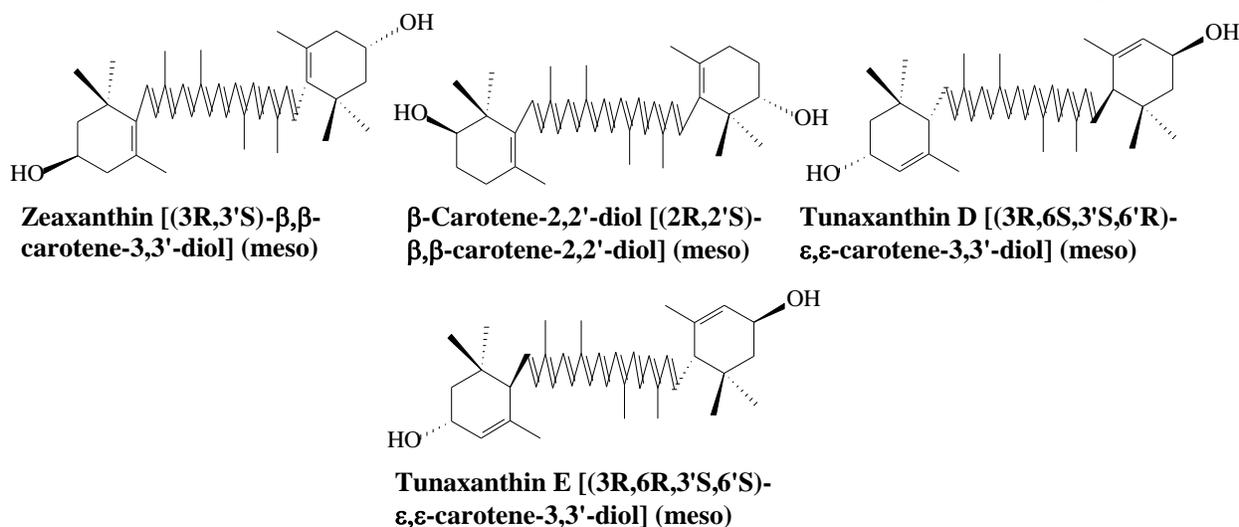


Figure 1.1A: C_{40} *meso*-Carotenoids isomers of β,β - and ϵ,ϵ -carotenes.

NOTE. In designating figures, the four types of isomers – *meso*, *chitwin*, *irrechi*, *CROM* are indicated by the letters A, B, C, D, respectively. Hence, when a figure contains e.g. letter A in its name, it contains exclusively *chitwin* compounds, etc.

Chitwin isomers are: 2,2'-dihydroxy- β,β -carotene, two zeaxanthins, isozeaxanthin, lactucaxanthin, tunaxanthin A, tunaxanthin C, tunaxanthin J, β -carotene-diepoxyde, cucumariaxanthin A (Fig. 1.1B). *Irrechi* isomers are: 2,3-dihydroxy- β -carotene, lutein, 6'-epilutein, 3'-epilutein, 3',6'-diepilutein, tunaxanthin B, tunaxanthin I, tunaxanthin G, tunaxanthin H, 2-hydroxy- β -carotene-5,6-epoxyde, cryptoxanthin-5,6-epoxyde, cryptoxanthin-5',6'-epoxyde, 2-hydroxy- α -carotene-5,6-epoxyde, cryptoflavin, luteochrome, 4'-hydroxy-5',6'-dihydroechinenone (Fig. 1.1C). Fig. 1.1D contains *CROM* isomers: sproxanthin, plectaniaxanthin, 2,3-dihydroxy- γ -carotene, cryptocapsin. Similarly, all C_{40} carotenoids of Figs. 1.2A-1.2D are isomers i.e. they possess the same molecular formula, $C_{40}H_{52}O_4$. In this case also, all four types of isomers – *meso*, *chitwin*, *irrechi*, *CROM* are present. It seems extremely probably that

such an exceptional structural variety as in the previous two cases, must be correlated with a remarkable genetic development. Carotenoids with molecular formula $C_{40}H_{54}O_2$ possess only three types of isomers: *chitwin*, *irrechi*, *CROM* (Figs. 1.3B-1.3D). And the same situation is with C_{40} carotenoids having the molecular formula, $C_{40}H_{56}O_4$ (Figs. 1.4B-1.4D). Hence, the latter series is without *meso* isomers. Instead, C_{40} carotenoids having the molecular formula, $C_{40}H_{52}O_2$ (Fig. 1.5A-1.5C) is devoid of *CROM* isomers, while carotenoids hydrocarbon series is devoid of *meso* isomers (Figs 1.6B-1.6D).

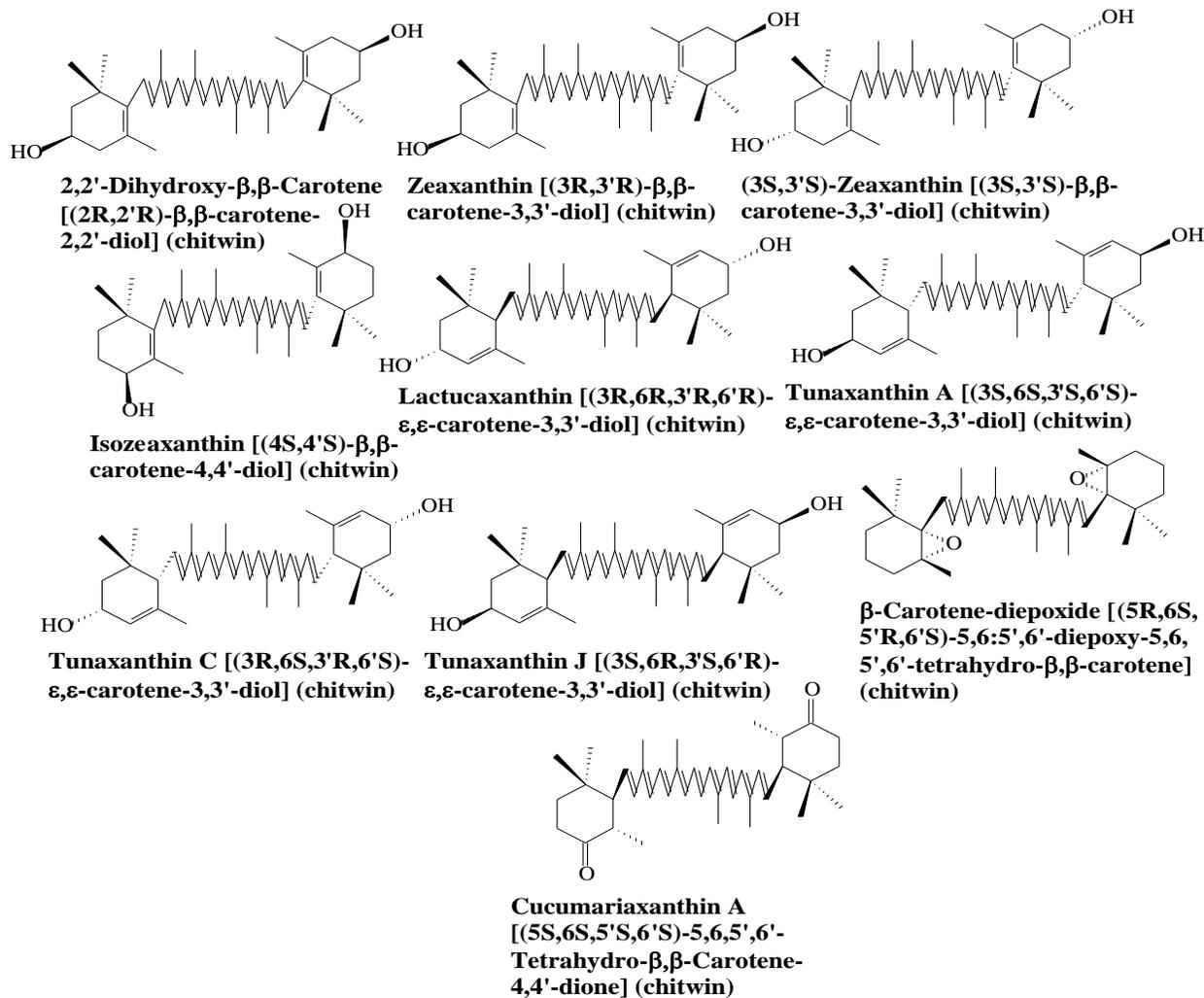
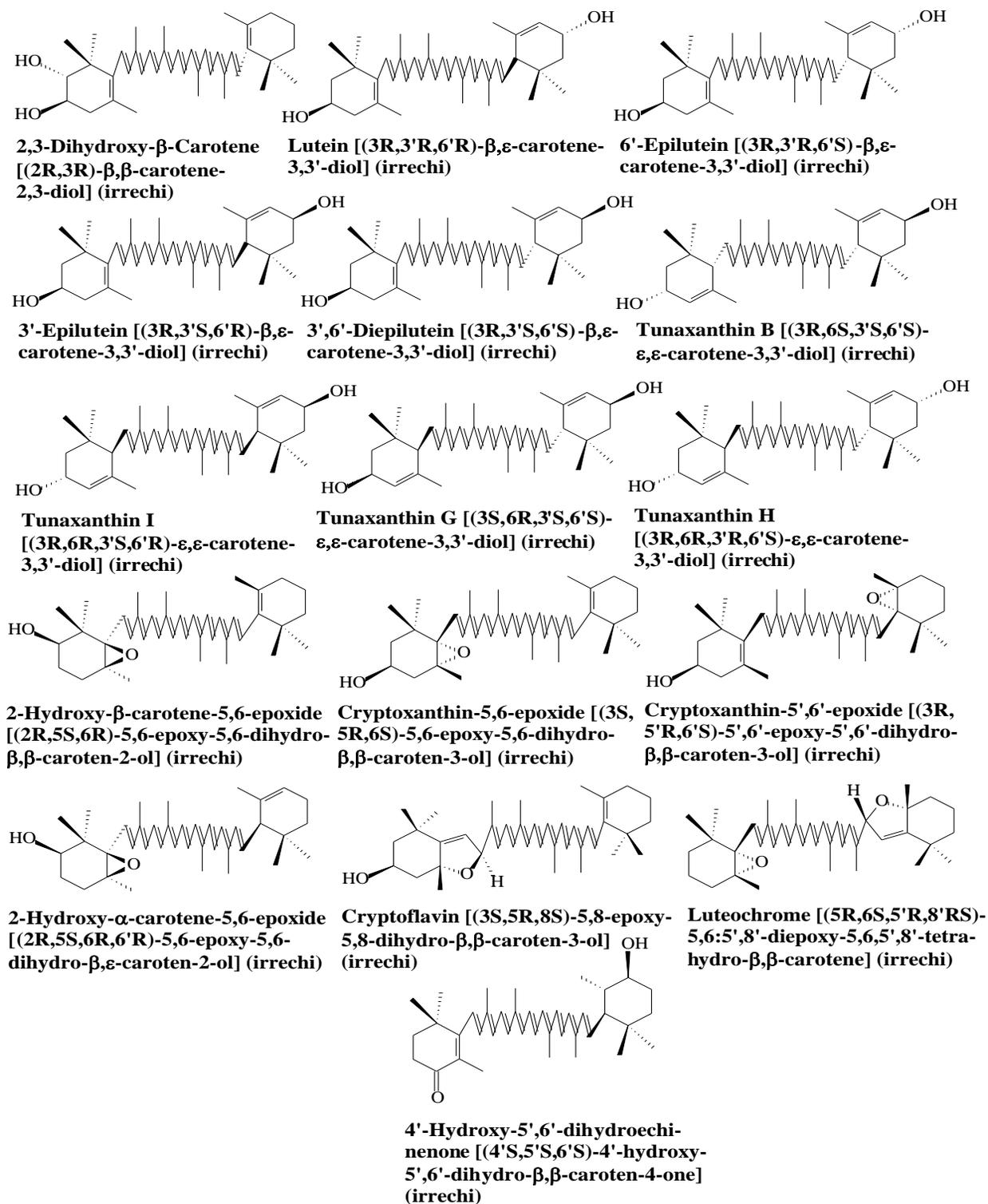
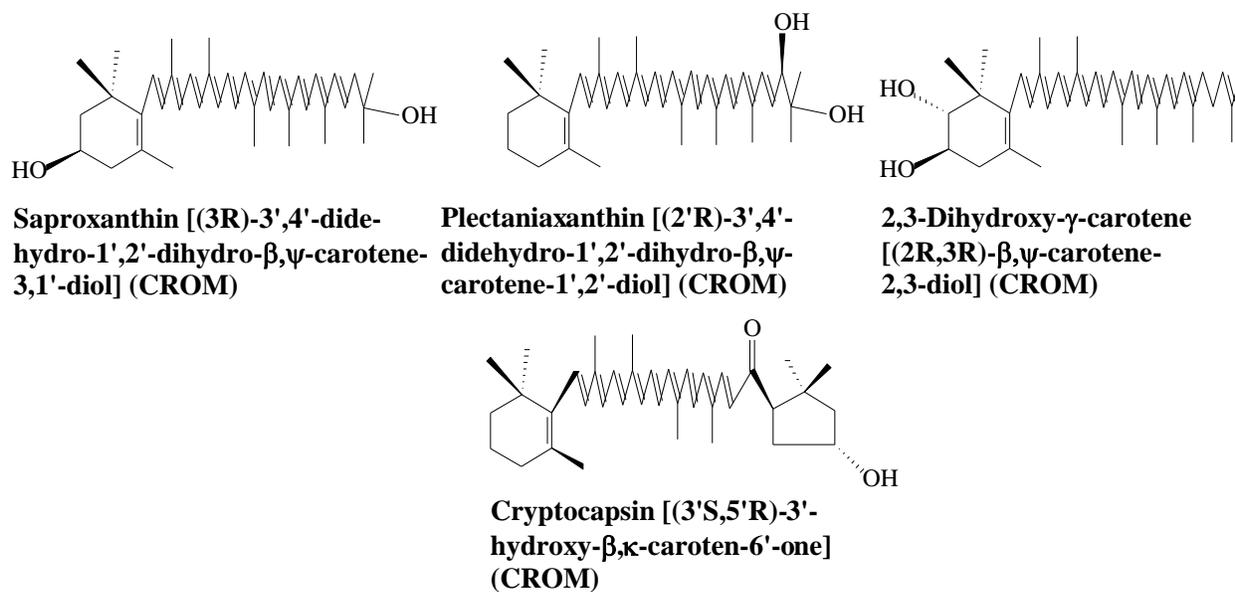
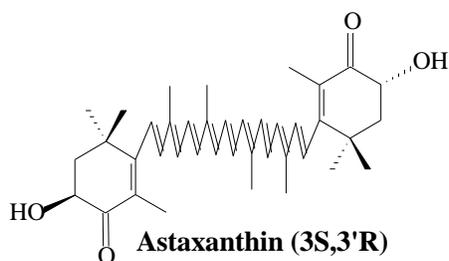
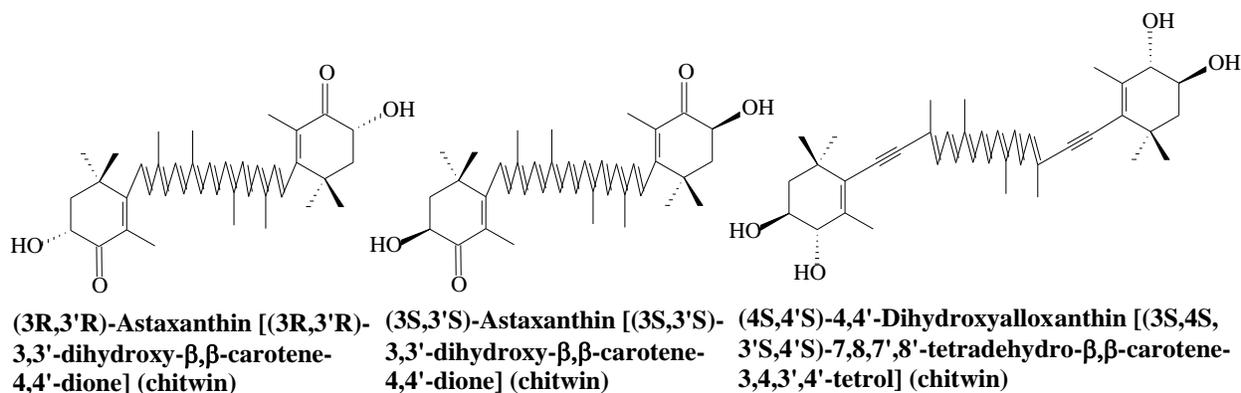


Figure 1.1B: C_{40} *chitwin*-Carotenoids of β,β - and ϵ,ϵ -carotenes.

Carotenoids with molecular formula $C_{40}H_{54}O_4$ possess only two types of isomers: *irrechi* and *CROM* (Figs. 1.7C and 1.7D) and carotenoids with molecular formula $C_{40}H_{58}O_4$ possess also two types of isomers: *chitwin* and *irrechi* (Figs. 1.8B and 1.8C). And the same position is met with C_{50} series ($C_{50}H_{72}O_2$), it has *chitwin* and *CROM* (Figs. 1.9B and 1.9D). There are also series ($C_{40}H_{50}O_4$) (Fig. 1.10C) and $C_{38}H_{48}O_4$ (Fig. 1.11B) containing *irrechi* and *chitwin* carotenoids, respectively. At the same time there are numerous carotenoids presenting themselves as unique isomer [51]. Zeaxanthin [(3R,3'R)- β,β -carotene-3,3'-diol] was discovered by Karrer, Salomon and Wehrli [93] and called in this way since it was found in maize (*Zea mays*). The same group led by Karrer elucidated its chemical constitution in the next three years [90].



Figure 1.1C: C_{40} irrechicarotenoids of β , β - and ϵ , ϵ - and β , ϵ -carotenes

Figure 1.1D: C_{40} CROM-Carotenoids of β,ψ - and β,κ -carotenes.Figure 1.2A: C_{40} meso-Carotenoid of β,β -caroteneFigure 1.2B: C_{40} chitwin-Carotenoids of β,β -carotenes

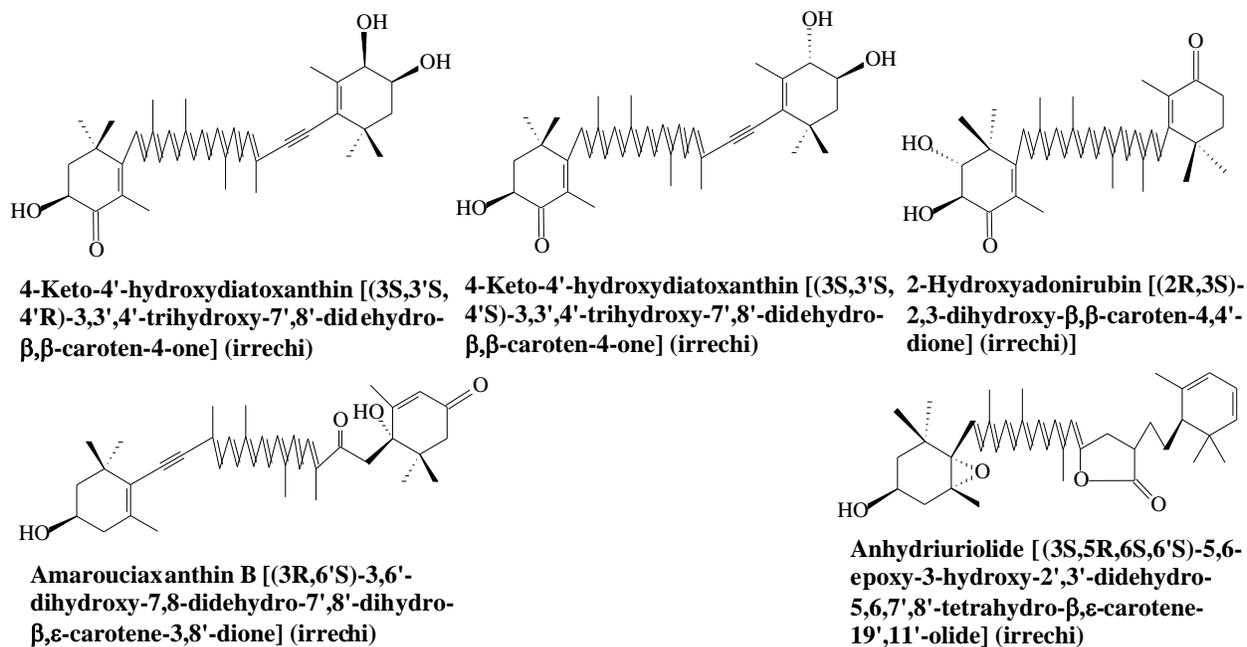


Figure 1.2C: C_{40} irrechii-Carotenoids of β,β - and β,ϵ -carotenes

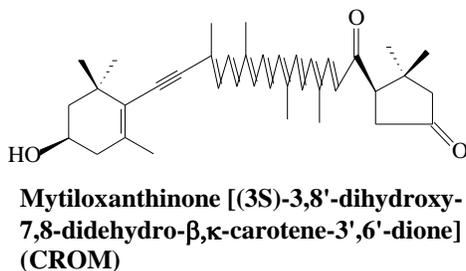


Figure 1.2D: C_{40} CROM-Carotenoid of β,κ -carotene.

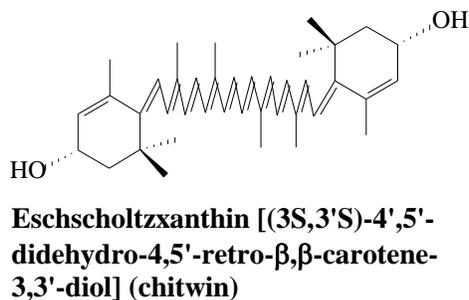


Figure 1.3B: C_{40} chitwin-Carotenoid of retro-β,β-carotene

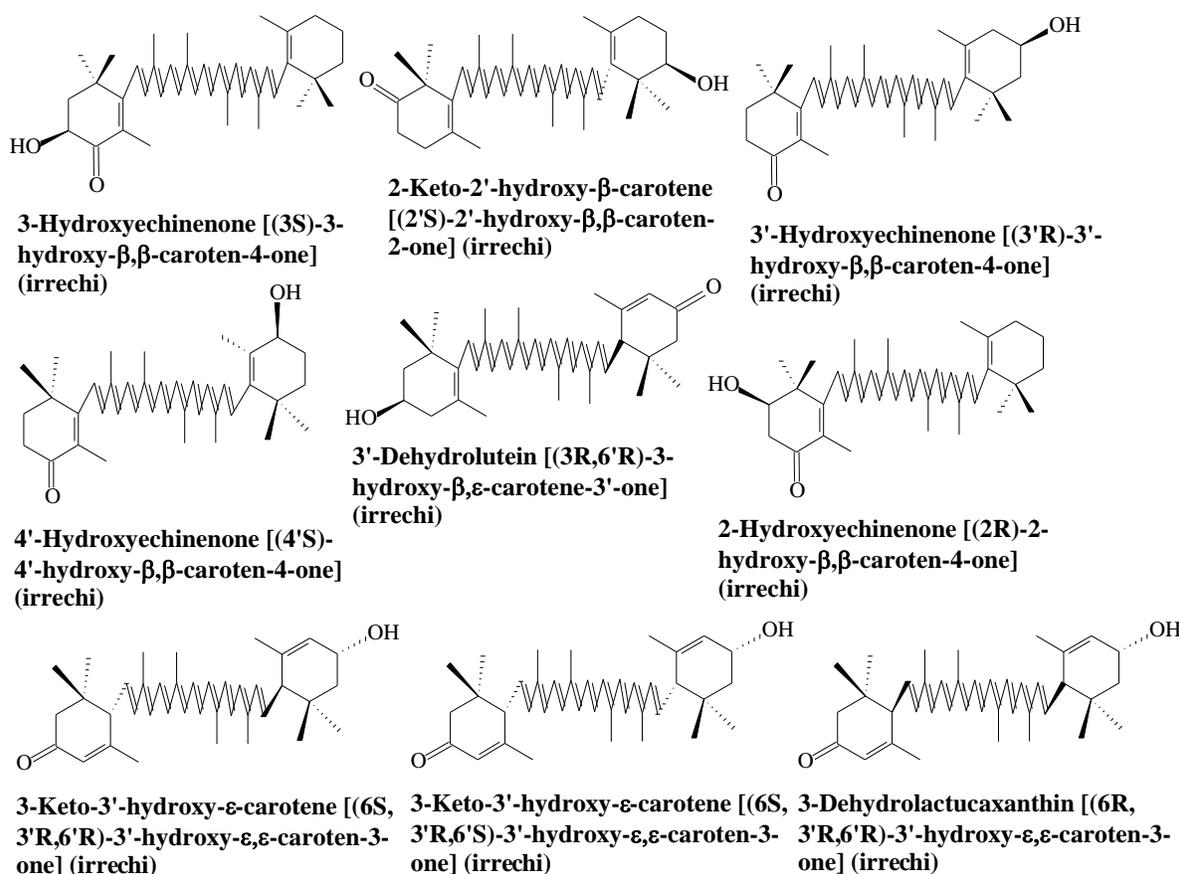


Figure 1.3C: C_{40} irrechi-Carotenoids of β,β -, β,ϵ - and ϵ,ϵ -carotenes

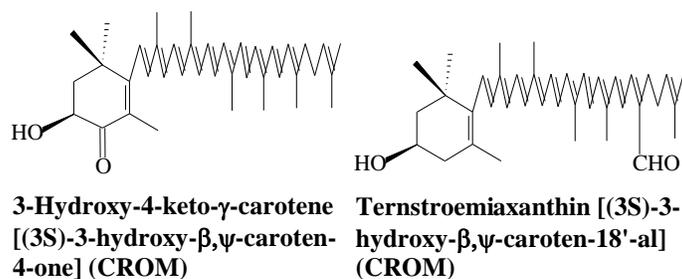


Figure 1.3D: C_{40} CROM-Carotenoids of β,Ψ -carotenes

Zeaxanthin is widely distributed in plants in the free state as well as esterified with fatty acids (physalien), especially palmitic. Some plants contain zeaxanthin as the main pigment, so that its isolation in appreciable amounts is relatively easy to achieve [94]. Zeaxanthin is biosynthesized from geranyl-geranyl-pyrophosphate via phytoene, ζ -carotene, lycopene, β -carotene [95,96]. (3S,3'S)-Zeaxanthin [(3S,3'S)- β,β -carotene-3,3'-diol] was isolated as a minor carotenoid from some shrimps and from turtle and fish. The retina is unique in the human body in containing three xanthophyll carotenoids: 3R,3'R-zeaxanthin, *meso*-zeaxanthin [(3R,3'S)- β,β -carotene-3,3'-diol] and lutein [(3R,3'R,6'R)- β,ϵ -carotene-3,3'-diol].



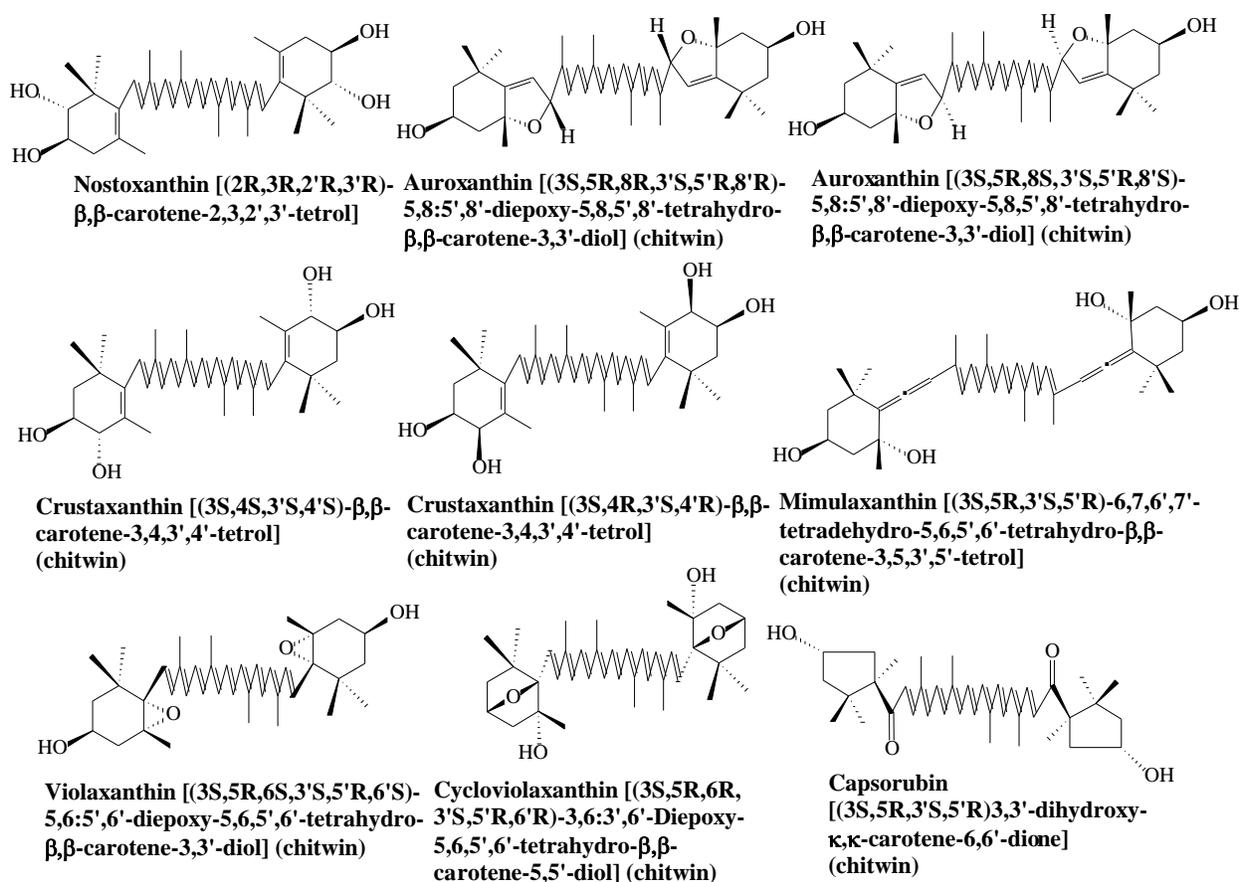
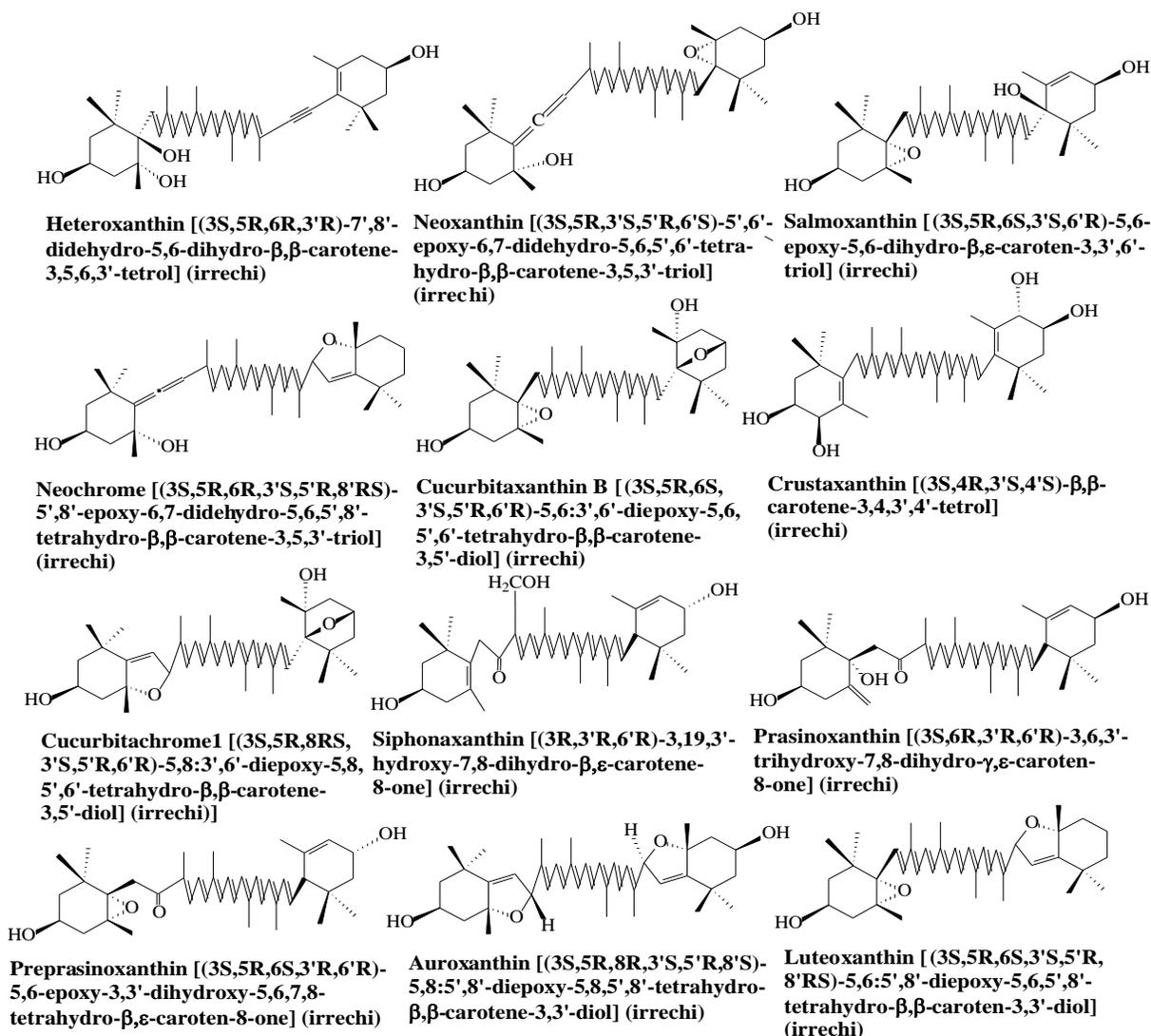
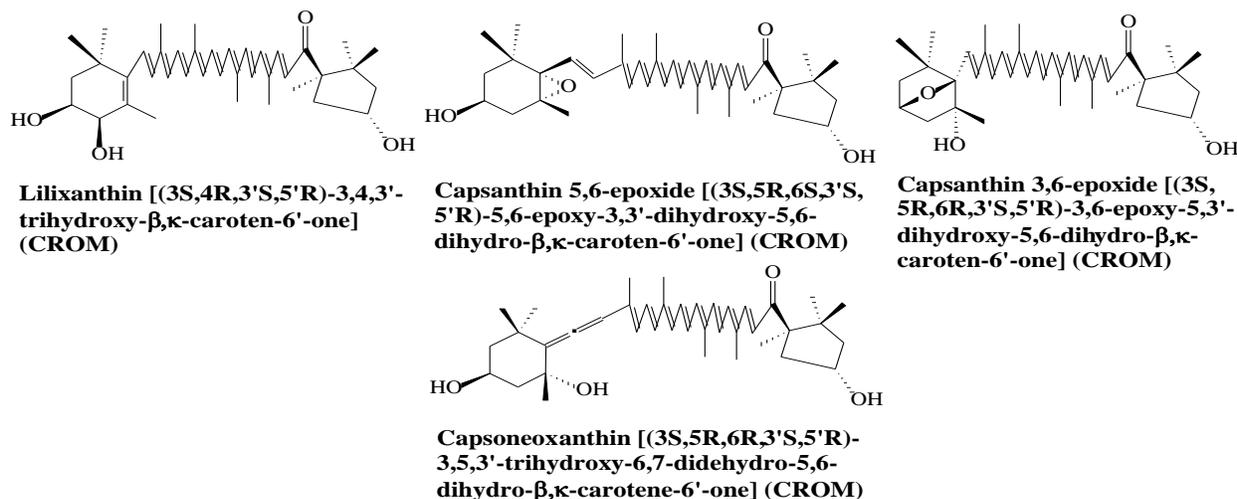
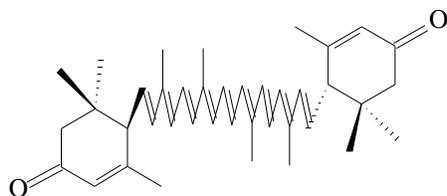


Figure 1.4B: C_{40} chitwin-Carotenoids of β,β - and κ,κ -carotenes

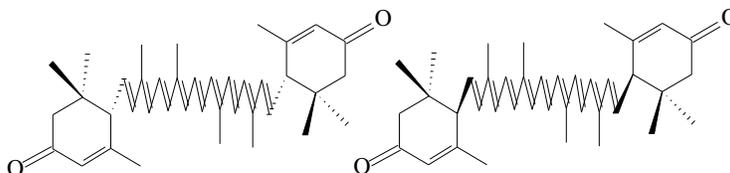
Humans consume 1 to 3 mg lutein per d and the lutein:zeaxanthin ratio in the diet is about 5:1. Although xanthophyll pigments occur widely in vegetables and fruits, *meso*-zeaxanthin is found in only a few foods such as the shrimp carapace and fish skin. In spite of variable abundance of the different xanthophylls in the diet, zeaxanthin and *meso*-zeaxanthin occur in approximately equal amounts in the eye [97]. Lutein and zeaxanthin are found highly concentrated in the macula of the retina. They are thought to protect the macula through their role as blue-light filters and because of their antioxidant and singlet oxygen quenching properties [98]. Configuration of C-3' of lutein was established as R on the basis of PMR analysis of (+)-3-methoxy- α -ionone, chemically derived from lutein, and by chemical correlation with synthetic 3-methoxy- α -ionones of established stereochemistry. Another argument was brought by isomerization of lutein to zeaxanthin by avoiding racemization. The configuration of zeaxanthin was known at that time. Isomerization of carotenes in the presence of NaOEt was discovered by Karrer and Jucker and applied to transform β,ϵ -carotene to β,β -carotene and lutein (β,ϵ -carotene-3,3'-diol) to zeaxanthin (β,β -carotene-3,3'-diol). Other authors [99] reported the isomerization of ϵ,ψ -carotene to β,ψ -carotene by the same procedure. The use of other isomerization agents (KOH, KOMe) improved the yields and minimized racemization. The following reasoning due to Buchecker was adopted in the interpretation of the results. (3R,3'S,6'R)-Lutein would give (3R,3'R)-zeaxanthin (identical to natural zeaxanthin). On the other hand, isomerization of (3R,3'R,6'R)-lutein would provide (3R,3'S)-zeaxanthin (*meso* compound). The experiment led to *meso* zeaxanthin. And when (3R,3'R)-zeaxanthin was submitted to the isomerization process, it displayed a proportion of racemization of about one fifth. Hence natural lutein is (3R,3'R,6'R) [100-102]. Lutein was also found in the crab *Paralithodes brevipes* [103].

Figure 1.4C: C_{40} irrechii-Carotenoids of β,β -, β,ϵ - and γ,ϵ -carotenesFigure 1.4D: C_{40} CROM-Carotenoids of β,κ -carotenes



(6R,6'S)-3,3'-Diketo-ε-carotene
[(6R,6'S)-ε,ε-Carotene-3,3'-dione] (meso)

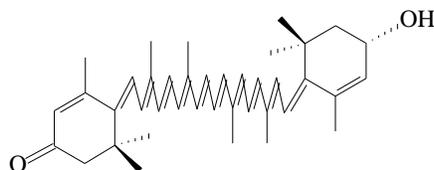
Figure 1.5A: C_{40} meso-Carotenoid of ε,ε-carotene.



3,3'-Diketo-ε-carotene [(6S,6'S)-ε,ε-Carotene-3,3'-dione] (chitwin)

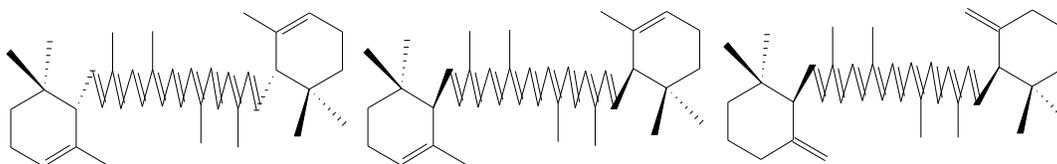
3,3'-Diketo-ε-carotene [(6R,6'R)-ε,ε-Carotene-3,3'-dione] (chitwin)

Figure 1.5B: C_{40} chitwin-Carotenoid of ε,ε-carotene



Eschscholtzxanthone [(3'S)-3'-hydroxy-4',5'-didehydro-4,5'-retro-β,β-carotene-3-one] (irrechi)

Figure 1.5C: C_{40} irrechi-Carotenoid of retro β,β-carotene

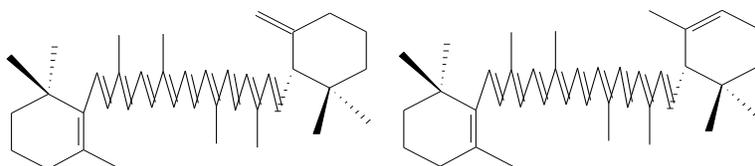


[S,S]-ε-Carotene [(6S,6'S)-ε,ε-carotene] (chitwin)

ε-Carotene [(6R,6'R)-ε,ε-carotene] (chitwin)

γ,γ-Carotene [(6R,6'R)-γ,γ-carotene] (chitwin)

Figure 1.6B: C_{40} chitwin ε,ε- and γ,γ-carotene.

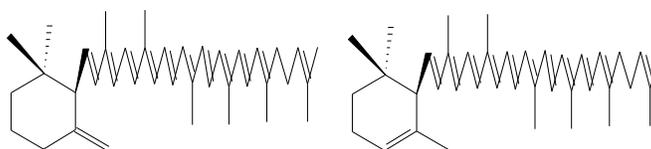


β,γ-Carotene [(6'-S)-β,γ-carotene] (irrechi)

α-Carotene [(6'-R)-β,ε-carotene] (irrechi)

Figure 1.6C: C_{40} irrechi β,γ- and β,ε-carotenes.

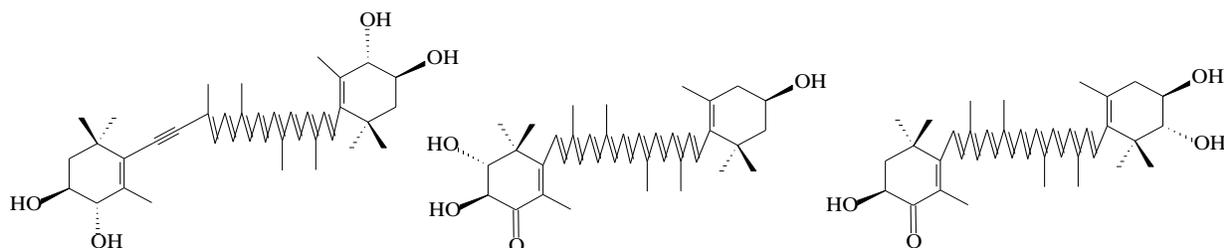




γ,ψ -Carotene [(6S)- γ,ψ -carotene] (CROM)

δ -Carotene [(6R)- ϵ,ψ -carotene] (CROM)

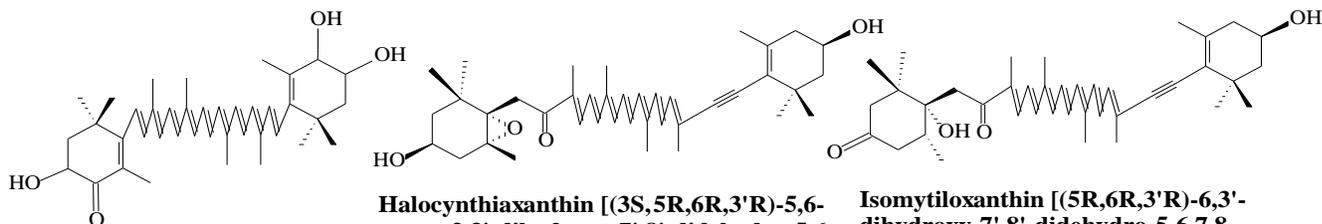
Figure 1.6D: C_{40} CROM γ,Ψ - and ϵ,Ψ -carotenes.



(4S,4'S)-4,4'-Dihydroxydiatoxanthin [(3S,4S,3'S,4'S)-7,8-didehydro- β,β -carotene-3,4,3',4'-tetrol] (irrechi)

2-Hydroxyadonixanthin [(2R,3S,3'R)-2,3,3'-trihydroxy- β,β -caroten-4-one] (irrechi)

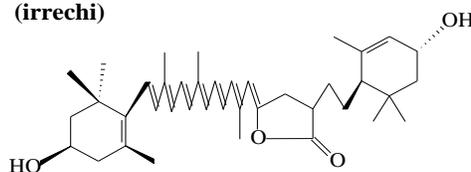
Erythroaxanthin [(3S,2'R,3'R)-3,2',3'-trihydroxy- β,β -caroten-4-one] (irrechi)



Idoxanthin [3,3',4'-trihydroxy- β,β -caroten-4-one] (irrechi)

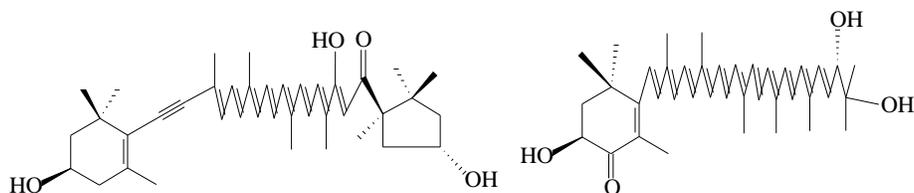
Halocynthiaxanthin [(3S,5R,6R,3'R)-5,6-epoxy-3,3'-dihydroxy-7',8'-didehydro-5,6,7,8-tetrahydro- β,β -caroten-8-one] (irrechi)

Isomytiloxanthin [(5R,6R,3'R)-6,3'-dihydroxy-7',8'-didehydro-5,6,7,8-tetrahydro- β,β -caroten-3,8-dione] (irrechi)



Deepoxyuriolide [(3R,3'R,6'R)-3,3'-dihydroxy-7',8'-dihydro- β,ϵ -caroten-19',11'-olide] (irrechi)

Figure 1.7C: C_{40} irrechic-Carotenoids of β,β - and β,ϵ -carotenes

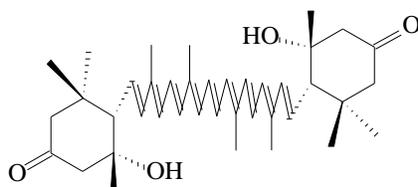


Mytiloxanthin [(3R,3'S,5'R)-3,3',8'-trihydroxy-7,8-didehydro- β,κ -caroten-6'-one] (CROM)

2'-Hydroxyflexixanthin [(3S,2'S)-3,1',2'-trihydroxy-3',4'-didehydro-1',2'-dihydro- β,ψ -caroten-4-one] (CROM)

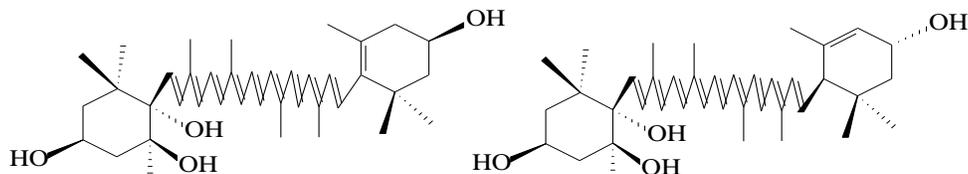
Figure 1.7D: C_{40} CROM-Carotenoids of β,κ - and β,Ψ -carotenes





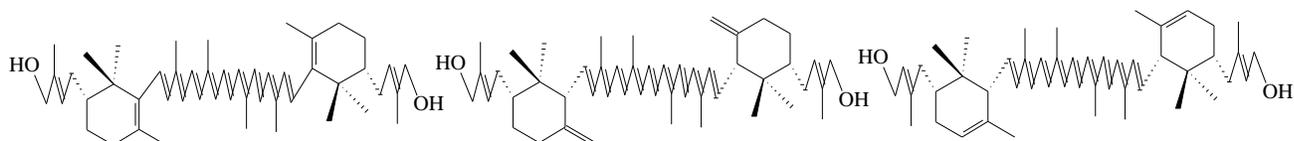
Webbiaxanthin [(5R,6S,5'R,6'S)-5,5'-dihydroxy-5,6,5',6'-tetrahydro-β,β-carotene-3,3'-dione] (chitwin)

Figure 1.8B: C₄₀ chitwin-Carotenoid of β,β-carotene



5,6-Diepikarpoaxanthin [(3S,5S,6S,3'S)-5,6-dihydro-β,β-carotene-3,5,6,3'-tetrol] (irrechi) **5,6-Dihydroxy 5,6-dihydrolutein [(3S,5S,6S,3'R)-5,6-dihydro-β,β-carotene-3,5,6,3'-tetrol] (irrechi)**

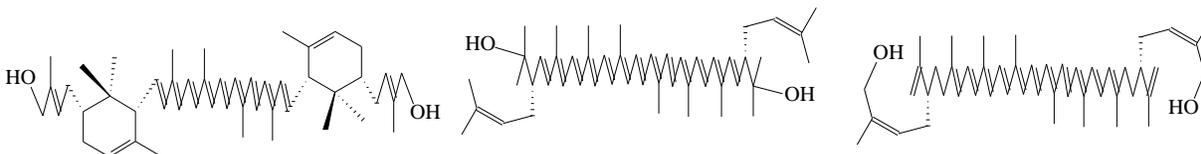
Figure 1.8C: C₄₀ irrechi-Carotenoids of β,β-carotenes



C. p. 450 [(2R,2'R)-2,2'-bis(4-hydroxy-3-methylbut-2-enyl)-β,β-carotene] (chitwin)

Sarcinaxanthin [(2R,6R,2'R,6'R)-2,2'-bis(4-hydroxy-3-methylbut-2-enyl)-γ,γ-carotene] (chitwin)

Okadaxanthin [(2R,6R,2'R,6'R)-2,2'-bis(4-hydroxy-2-methylbut-2-enyl)-ε,ε-carotene] (chitwin)

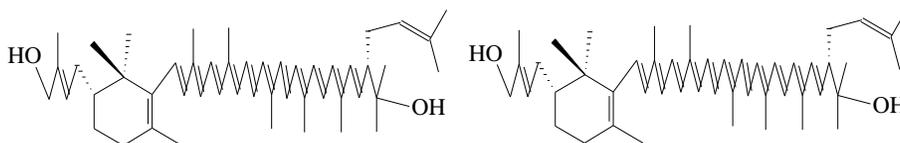


Decaprenoxanthin [(2R,6R,2'R,6'R)-2,2'-bis(4-hydroxy-3-methylbut-2-enyl)-ε,ε-carotene] (chitwin)

Bisanhydrobacterioruberin [(2S,2'S)-2,2'-bis(3-methylbut-2-enyl)-3,4,3',4'-tetrahydro-1,2,1',2'-tetrahydro-ψ,ψ-carotene-1,1'-diol] (chitwin)

Flavuxanthin [(2R,2'R)-2,2'-bis(4-hydroxy-3-methylbut-2-enyl)-1,16,1',16'-tetrahydro-1,2,1',2'-tetrahydro-ψ,ψ-carotene] (chitwin)

Figure 1.9B: C₅₀ chitwin-Carotenoids

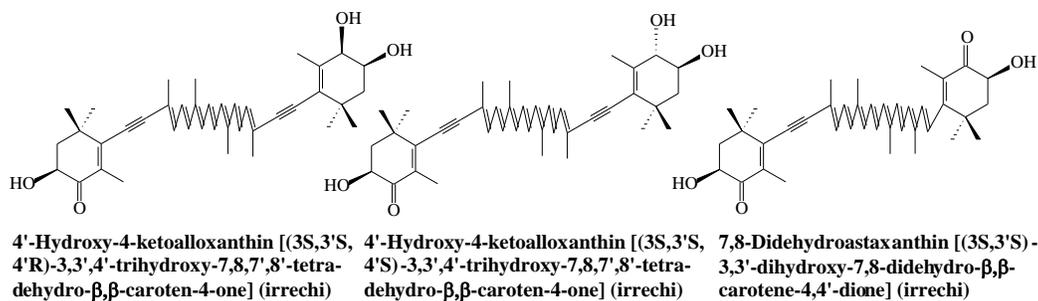
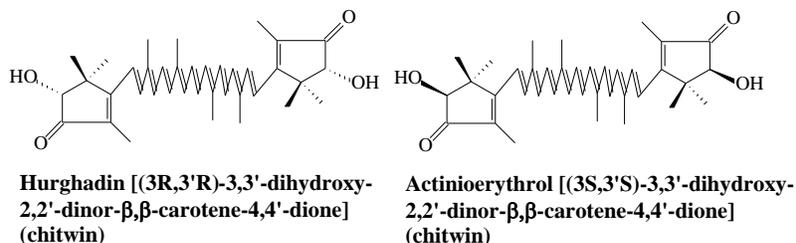


C. p. 473 [(2R,2'S)-2-(4-hydroxy-3-methylbut-2-enyl)-2'-(3-methylbut-2-enyl)-3',4'-didehydro-1',2'-dihydro-β,ψ-caroten-1'-ol] (CROM)

A. g. 471 [(2R,6R,2'S)-2-(4-hydroxy-3-methylbut-2-enyl)-2'-(3-methylbut-2-enyl)-3',4'-didehydro-1',2'-dihydro-ε,ψ-caroten-1'-ol] (CROM)

Figure 1.9D: C₅₀ CROM-Carotenoids



Figure 1.10C: C_{40} irrechi-Carotenoids of β,β -carotenes.Figure 1.11B: C_{38} chitwin-Carotenoids

Carotenoids possessing 2-hydroxylated β -rings i.e. β,ϵ -caroten-2-ol, β,β -caroten-2-ol and β,β -caroten-2,2'-diol have been isolated from the green alga *Trentepohlia iolithus* (L.) Wallroth [104]. A mixture of two isomers, β,ϵ -caroten-2-ol and β,β -caroten-2-ol, was acetylated, oxidized with NiO_2 and the products analyzed by GLC. Products as (+)- α -ionone and ϵ -apo-carotenal indicated 6'R configuration for β,ϵ -caroten-2-ol. 2R Configuration was indicated by a series of physical methods analyses in comparison with (3R,3'R)-zeaxanthin and lutein. Briefly, a modified Horeau method was used for the elucidation of configuration of 2-hydroxy group. This method is based on the partial resolution of racemic and *meso* α -phenylbutyric anhydride by means of an optically active alcohol, which reacts preferentially with one diastereomer, followed by hydrolysis and optical rotation measurement of the unreacted α -phenylbutyric acid. In fact, the racemic mixture of α -phenylbutyric anhydride consists of two *chitwin* isomers. *meso*-Dihydroxy- β -carotene [(2R,2'S)- β,β -carotene-2,2'-diol] has been isolated from the stick insect *Ectatosoma tiaratum* as a mixture with the other two isomers. Tunaxanthin D [(3R,6S,3'S,6'R)- ϵ,ϵ -carotene-3,3'-diol] was isolated as a major carotenoid from the yellow-tail rockfish *Sebastes flavidus* and the fresh-water fish *Siniperca scherzeri*. A HPLC chiral column was used for its purification. Tunaxanthin E [(3R,6R,3'S,6'S)- ϵ,ϵ -carotene-3,3'-diol] was isolated as a minor carotenoid from the fishes *Chaenogobius isaza* and *Siniperca scherzeri*. 2,2'-Dihydroxy- β,β -carotene [(2R,2'R)- β,β -carotene-2,2'-diol] was isolated as pure isomer from the green alga *Trentepohlia iolithus* (L.) Wallroth and from adults and eggs of the stick insect *Ectatosoma tiaratum* as a mixture with the (2R,2'S)- and (2S,2'S)-diastereomers.

Isozeaxanthin [(-)-(4R,4'R)- β,β -caroten-4,4'-diol] was also found and studied [103,105]. The absolute configuration of optically active isozeaxanthin was established by synthesis using (-)-(R)-4-hydroxy- β -ionone as starting material [106]. Lactucaxanthin [(3R,6R,3'R,6'R)- ϵ,ϵ -carotene-3,3'-diol] was found as a major carotenoid in leaves of lettuce (*Lactuca sativa*) and some other members of the Compositae, and as a minor carotenoid from the fish *Tilapia nilotica*. Tunaxanthin A [(3S,6S,3'S,6'S)- ϵ,ϵ -carotene-3,3'-diol] was separated from the skin of the fishes *Oxyjulis californica*, tilapia (*Tilapia nilotica*), the fresh-water fish *Siniperca scherzeri* and eggs of dolphin fish and flying fish. Tunaxanthin C [(3R,6S,3'R,6'S)- ϵ,ϵ -carotene-3,3'-diol] was found as a minor carotenoid from various fishes including *Oxyjulis californica*, the yellow-tail rockfish *Sebastes flavidus* and from eggs of dolphin fish and flying fish. Tunaxanthin J [(3S,6R,3'S,6'R)- ϵ,ϵ -carotene-3,3'-diol] was isolated from skin of the yellow Costa Rican frog *Atelopus chiriquiensis* and from the yellow-tail rockfish *Sebastes flavidus*. β -Carotene-diepoxy [(5R,6S,5'R,6'S)-5,6:5',6'-diepoxy-5,6,5',6'-tetrahydro- β,β -carotene] was found as a minor carotenoid in the white-fleshed sweet potato (*Ipomoea batatas*) and from cotyledons of bean (*Phaseolus vulgaris* var. Zlota Saxa). Cucumariaxanthin A [(5S,6S,5'S,6'S)-5,6,5',6'-tetrahydro- β,β -carotene-4,4'-dione] was found in relatively low amounts in the sea



cucumbers *Cucumaria japonica*, *C. echinata* and *Penctata australis*. 2,3-Dihydroxy- β -carotene [(2R,3R)- β , β -carotene-2,3-diol] was found as a minor carotenoid in the mutant 1-207 of the bacterium *Rhizobium lupini* [51]. 6'-Epilutein [(3R,3'R,6'S)- β , ϵ -carotene-3,3'-diol] was separated as a minor carotenoid from eggs of dolphin fish and of flying fish [51]. 3'-Epilutein [(3R,3'S,6'R)- β , ϵ -carotene-3,3'-diol] was isolated from flowers and anthers of *Caltha palustris*, *Rosa gallica officinalis* Thory, *R. odorata pseudindica* and *Paeonia officinalis*. 3',6'-Diepilutein [(3R,3'S,6'S)- β , ϵ -carotene-3,3'-diol] was isolated as a minor carotenoid from eggs of dolphin fish and of flying fish. Tunaxanthin B [(3R,6S,3'S,6'S)- ϵ , ϵ -carotene-3,3'-diol] was isolated as a minor carotenoid from the fishes *Oxyjulis californica*, *Amanses modestus*, *Thunnus thynnus*, *Seriola quinqueradiata*, *Cyprinus carpio* and *Siniperca scherzeri* as well as from eggs of dolphin fish and flying fish. Tunaxanthin I [(3R,6R,3'S,6'R)- ϵ , ϵ -carotene-3,3'-diol] was separated as a minor carotenoid from skin of the yellow Costa Rican frog *Atelopus chiriquiensis*, from carp (*Cyprinus carpio*) and the fresh-water fish *Siniperca scherzeri*. Tunaxanthin G [(3S,6R,3'S,6'S)- ϵ , ϵ -carotene-3,3'-diol] was purified as a minor carotenoid from carp (*Cyprinus carpio*) and the fresh-water fish *Siniperca scherzeri*. Tunaxanthin H [(3R,6R,3'R,6'S)- ϵ , ϵ -carotene-3,3'-diol] was separated as a minor carotenoid from carp (*Cyprinus carpio*) and the fresh-water fish *Siniperca scherzeri*. 2-Hydroxy- β -carotene-5,6-epoxide [(2R,5S,6R)-5,6-epoxy-5,6-dihydro- β , β -caroten-2-ol] was isolated as a minor carotenoid from the green alga *Trentepohlia iolithus*. Cryptoxanthin-5,6-epoxide [(3S,5R,6S)-5,6-epoxy-5,6-dihydro- β , β -caroten-3-ol] was isolated as a minor carotenoid from various citrus fruits. Antioxidants were needed for its protection during purification process.

Cryptoxanthin-5',6'-epoxide [(3R,5'R,6'S)-5',6'-epoxy-5',6'-dihydro- β , β -caroten-3-ol] was purified as a minor carotenoid from various citrus fruits in the presence of an antioxidant. 2-Hydroxy- α -carotene-5,6-epoxide [(2R,5S,6R,6'R)-5,6-epoxy-5,6-dihydro- β , ϵ -caroten-2-ol] was separated as a minor carotenoid from the green alga *Trentepohlia iolithus*. Cryptoflavin [(3S,5R,8S)-5,8-epoxy-5,8-dihydro- β , β -caroten-3-ol] was isolated from lyophilized fruit of red guava (*Psidium guajava*) and from other fruit such as star fruit (*Carambola*), papaya and plum. Luteochrome [(5R,6S,5'R,8'RS)-5,6:5',8'-diepoxy-5,6,5',8'-tetrahydro- β , β -carotene] was isolated as a minor carotenoid from pulp of banana (*Musa cavendishi*) and from the ornamental gourd *Cucurbita pepo* cv. ovifera, as well as from Brazilian sweet potato (*Ipomoea batatas*) as a mixture of the (5R,6S,5'R,8'R)- and (5R,6S,5'R,8'S)-isomers. 4'-Hydroxy-5',6'-dihydroechinenone [(4'S,5'S,6'S)-4'-hydroxy-5',6'-dihydro- β , β -caroten-4-one] was isolated as a minor carotenoid from muscles of the spindle shell mollusc *Fucinus perplexus*.

Saproxanthin (3',4'-Didehydro-1',2'-dihydro- β , ψ -carotene-3,1'-diol) was found as a major carotenoid in *Saprospira grandis*. Plectanixanthin [(2'R)-3',4'-Didehydro-1',2'-dihydro- β , ψ -carotene-1',2'-diol] was isolated as a major carotenoid in free and esterified form from the mushroom *Plectonia coccinea* and from saponified extracts of the asporogenous yeast *Cryptococcus laurentii*. 2,3-Dihydroxy- γ -carotene [(2R,3R)- β , ψ -carotene-2,3-diol] was isolated from cultures of *Rhizobium lupini*, strain 1-250, grown in the presence of a cyclization inhibitor, nicotine or CPTA. Cryptocapsin [(3'S,5'R)-3'-hydroxy- β , κ -caroten-6'-one] was isolated as a minor carotenoid, in free form, from mature red fruit of *Capsicum anuum*, paprika and its oleoresin, and from orange varieties of *C. anuum*. meso-Astaxanthin [(3R,3'S)-3,3'-dihydroxy- β , β -carotene-4,4'-dione] was isolated in a mixture with the two diastereomers (enantiomers) from eggs of lobster (*Homarus gammarus*) and other aquatic animals [107,108]. Astaxanthin is biosynthesized from zeaxanthin and since the latter exists as three isomers, astaxanthin subsists also as three isomers [109,110]. An astaxanthin protein complex has been found in the wings of migratory locust *Locusta migratoria migratorioides* R. & F., desert locust *Schistocerca gregaria* Forsk., and the red locust *Nomadacris septemfasciata* Serville [111]. (4S,4'S)-4,4'-Dihydroxyalloxanthin [(3S,4S,3'S,4'S)-7,8,7',8'-tetrahydro- β , β -carotene-3,4,3',4'-tetrol] was isolated as a minor carotenoid from the starfish *Asterina pectinifera* and *A. amurensis*. 4-Keto-4'-hydroxydiatoxanthin [(3S,3'S,4'R)-3,3',4'-trihydroxy-7',8'-didehydro- β , β -caroten-4-one] was isolated as a minor carotenoid from the goldfish *Carassius auratus*. 4-Keto-4'-hydroxydiatoxanthin [(3S,3'S,4'S)-3,3',4'-trihydroxy-7',8'-didehydro- β , β -caroten-4-one] was isolated as a minor carotenoid from the starfish *Asterina pectinifera* and *A. amurensis*. 2-Hydroxyadonirubin [(2R,3S)-2,3-dihydroxy- β , β -carotene-4,4'-dione] was isolated as a minor carotenoid from the mutant 1-207 *Rhizobium lupini*. Amarouciaxanthin B [(3R,6'S)-3,6'-dihydroxy-7,8-didehydro-7',8'-dihydro- β , ϵ -carotene-3,8'-dione] was isolated as a major carotenoid from the tunicates *Sydnium argus* and *Amaroucium pliciferum*. Anhydrouriolide [(3S,5R,6S,6'S)-5,6-epoxy-3-hydroxy-2',3'-didehydro-5,6,7',8'-



tetrahydro- β,ϵ -caroten-19',11'-olide] was isolated as a minor carotenoid from the prasinophyte algae *Mantoniella squamata* and *Micromonas pusilla*. Mytiloxanthinone (3,8'-Dihydroxy-7,8-didehydro- β,κ -carotene-3',6'-dione) was isolated from tissues of the sea squirt *Halocynthia roretzi* and from *Styela clava*, *S. plicata* and *Botryllus schlosseri*. Eschscholtzianthrin [(3S,3'S)-4,4'-didehydro-4,4'-retro- β,β -carotene-3,3'-diol] was isolated as a characteristic carotenoid from orange flowers of Californian poppy *Eschscholtzia californica* and as a minor carotenoid from the carapace and epidermis of the crab *Pagurus prideauxi*. 3-Hydroxyechinenone [(3S)-3-Hydroxy- β,β -caroten-4-one] was isolated as a minor carotenoid from a range of sources: a mutant of *Rhizobium lupini*, flowers of *Adonis annua*, the alga *Acetabularia mediterranea*, the cyanobacterium *Aphanocapsa*, the yeast *Xanthophyllomices* (formerly *Phaffiarhodozyma*), and eggs of three species of Cyprinidae fish. 2-Keto-2'-hydroxy- β -carotene [(2'S)-2'-hydroxy- β,β -caroten-2-one] was isolated from the stick insects *Neophirasea japonica*, *Carausius morosus* and *Ectatosoma tiaratum*. 3'-Hydroxyechinenone [(3'R)-3'-Hydroxy- β,β -caroten-4-one] was isolated from the cyanobacteria *Spirulina maxima*, *Oscillatoria rubescens* and *Arthrospira* sp. 4'-Hydroxyechinenone [(4'S)-4'-Hydroxy- β,β -caroten-4-one] was isolated from eggs of goldfish, the spindle shell mollusc *Fusinus perplexus* and the alga *Chlorococcum*. 3'-Dehydrolutein [(3R,6'R)-3-hydroxy- β,ϵ -caroten-3'-one] was isolated from flowers of *Caltha palustris* and from a number of sources, e.g. egg yolk, eggs of flying fish and dolphin fish, eggs of carp and oily gudgeon (*Sarcocheilichthys variegatus*) and the silkworm *Philosamia Cynthia pryri*. 2-Hydroxyechinenone [(2R)-2-Hydroxy- β,β -caroten-4-one] was separated as a major carotenoid from the zooplankton *Daphnia magna* fed with *Scenedesmus acutus* and from the sea louse *Ligia exotica*. 3-Keto-3'-hydroxy- ϵ -carotene [(6S,3'R,6'R)-3'-hydroxy- ϵ,ϵ -caroten-3-one] was isolated as a minor carotenoid from egg yolk of hens. 3-Keto-3'-hydroxy- ϵ -carotene [(6S,3'R,6'S)-3'-hydroxy- ϵ,ϵ -caroten-3-one] was isolated as a minor carotenoid from eggs of dolphin fish *Coryphaema hippurus* and of flying fish *Prognichtys agoo*. 3-Dehydrolactucaxanthin [(6R,3'R,6'R)-3'-hydroxy- ϵ,ϵ -caroten-3-one] was separated as a minor carotenoid from egg yolk of hens. 3-Hydroxy-4-keto- γ -carotene [(3S)-3-Hydroxy- β,Ψ -caroten-4-one] was isolated from illuminated cultures of *Rhizobium lupini*, strain 1-250, grown in the presence of nicotine or CPTA. Ternstroemiaxanthin [(3S)-3-hydroxy- β,ψ -caroten-18'-al] was isolated as a major carotenoid from the red seeds of *Ternstroemia japonica*. Nostoxanthin [(2R,3R,2'R,3'R)- β,β -carotene-2,3,2',3'-tetrol] was isolated as a major characteristic carotenoid from some cyanobacteria, especially of the Nostocales, e.g. *Anacystis nidulans* and from some non-phototrophic bacteria. Auroxanthin [(3S,5R,8R,3'S,5'R,8'R)-5,8:5',8'-diepoxy-5,8,5',8'-tetrahydro- β,β -carotene-3,3'-diol] and auroxanthin [(3S,5R,8S,3'S,5'R,8'S)-5,8:5',8'-diepoxy-5,8,5',8'-tetrahydro- β,β -carotene-3,3'-diol] are commonly encountered in plant and algal extracts that contain violaxanthin. Reported to be major carotenoids in egg yolk from hens fed seaweed meal. Acid-catalyzed epoxide-furanoid rearrangement of violaxanthin and isomerism dependence of C-8 have been evidenced [112]. Crustaxanthin [(3S,4S,3'S,4'S)- β,β -carotene-3,4,3',4'-tetrol and crustaxanthin [(3S,4R,3'S,4'R)- β,β -carotene-3,4,3',4'-tetrol were isolated as minor carotenoids from the copepod *Euchaeta russelli*, eggs of mackerel and flying fish, and from shrimps (*Penmaeus* sp). Crustaxanthins as metabolites of astaxanthins [(3S,3'S)-, (3R,3'S)-, (3R,3'R)] have been investigated in flesh, skin, and gonads of sexually immature and maturing Arctic charr (*Salvelinus alpinus* L.) [113]. Two diastereomers of crustaxanthins, (3S,4R,3'S,4'R) and (3S,4S,3'S,4'S), have been synthesized [114]. Mimulaxanthin [(3S,5R,3'S,5'R)-6,7,6',7'-tetrahydro-5,6,5',6'-tetrahydro- β,β -carotene-3,5,3',5'-tetrol] was isolated from flowers of *Mimulus guttatus* and of *Lamium montanum*. Violaxanthin [(3S,5R,6S,3'S,5'R,6'S)-5,6:5',6'-diepoxy-5,6,5',6'-tetrahydro- β,β -carotene-3,3'-diol] was found to occur in the yellow flowers of *Viola tricolor* as well as in all green leaves. Cycloviolaxanthin [(3S,5R,6R,3'S,5'R,6'R)-3,6:3',6'-diepoxy-5,6,5',6'-tetrahydro- β,β -carotene-5,5'-diol] was found as a minor carotenoid in red paprika (*Capsicum annuum* var. *longum nigrum*). Capsorubin [(3S,5R,3'S,5'R)-3,3'-dihydroxy- κ,κ -carotene-6,6'-dione] was isolated as a major carotenoid from red paprika (*Capsicum annuum*) and its oleoresin and from flowers of *Lilium tigrinum*. Heteroxanthin [(3S,5R,6R,3'R)-7',8'-didehydro-5,6-dihydro- β,β -carotene-3,5,6,3'-tetrol] was isolated as a major carotenoid from algae of the *Tribophyceae* and *Euglenophyceae* e.g. *Euglena gracilis*. Neoxanthin [(3S,5R,3'S,5'R,6'S)-5',6'-epoxy-6,7-didehydro-5,6,5',6'-tetrahydro- β,β -carotene-3,5,3'-triol] occurs as the (9'Z)-isomer as a major carotenoid in all green leaves and in many algae. The (all E)-isomer occurs in some yellow flowers e.g. laburnum. Salmoxanthin (5,6-epoxy-5,6-dihydro- β,ϵ -carotene-3,3',6'-triol] was isolated as a major carotenoid from chum



salmon *Oncorhynchus keta*. Neochrome [(3S,5R,6R,3'S,5'R,8'RS)-5',8'-epoxy-6,7-didehydro-5,6,5',8'-tetrahydro- β , β -carotene-3,5,3'-triole] is commonly found as a minor carotenoid in green leaves and algae, as an artefact formed from neoxanthin by acid catalysed rearrangement during isolation. Cucurbitaxanthin B [(3S,5R,6S,3'S,5'R,6'R)-5,6:3',6'-diepoxy-5,6,5',6'-tetrahydro- β , β -carotene-3,5'-diol] was isolated from *Cucurbita maxima* and as a minor carotenoid from red pepper (*Capsicum annuum* var. *longum*). Crustaxanthin (β , β -carotene-3,4,3',4'-tetrol) was isolated as a minor carotenoid from the copepod *Euchaeta russelli*, eggs of mackerel and flying fish, and from shrimps (*Penaeus* spp). Cucurbitachrome I [(3S,5R,8RS,3'S,5'R,6'R)-5,8:3',6'-diepoxy-5,8,5',6'-tetrahydro- β , β -carotene-3,5'-diol] was isolated as a minor carotenoid from red paprika (*Capsicum annuum* var. *longum*). Its partial synthesis was made from cucurbitaxanthin B. Siphonaxanthin [(3R,3'R,6'R)-3,19,3'-trihydroxy-7,8-dihydro- β , ϵ -caroten-8-one] was isolated as a major carotenoid from the green macroalga *Codium fragile* and from the prasinophyte *Pyramimonas amyliifera*. Prasinoxanthin [(3S,6R,3'R,6'R)-3,6,3'-trihydroxy-7,8-dihydro- γ , ϵ -caroten-8-one] was isolated as a major carotenoid from the prasinophyte algae. Preprasinoxanthin [(3S,5R,6S,3'R,6'R)-5,6-epoxy-3,3'-dihydroxy-5,6,7,8-tetrahydro- β , ϵ -caroten-8-one] was isolated as a minor carotenoid from the prasinophyte algae "IIA2" (suggested to be *Prasinococcus capsulatus* or *Prasinoderma coloniale*) and from *Prasinoderma coloniale*. Auroxanthin [(3S,5R,8R,3'S,5'R,8'S)-5,8:5',8'-diepoxy-5,8,5',8'-tetrahydro- β , β -carotene-3,3'-diol] is commonly encountered in plant and algal extracts that contain violaxanthin. Reported to be major carotenoids in egg yolk from hens fed seaweed meal. Acid-catalyzed epoxide-furanoid rearrangement of violaxanthin and isomerism dependence of C-8 have been evidenced [112]. Luteoxanthin [(3S,5R,6S,3'S,5'R,8'RS)-5,6:5',8'-diepoxy-5,6,5',8'-tetrahydro- β , β -carotene-3,3'-diol] was isolated as a minor carotenoid from petals of *Rosa foetida* and from flowers, e.g. *Narcissus* sp. and *Brassica napus*, and claimed to be a carotenoid in calamondin fruits (*Citrus madurensis*). Its partial synthesis was accomplished from violaxanthin. Lilixanthin [(3S,4R,3'S,5'R)-3,4,3'-trihydroxy- β , κ -caroten-6'-one] was isolated as a minor carotenoid from petals of *Lilium tigrinum* cv. Red Knight. Capsanthin 5,6-epoxide [(3S,5R,6S,3'S,5'R)-5,6-epoxy-3,3'-dihydroxy-5,6-dihydro- β , κ -caroten-6'-one] was isolated as a minor carotenoid from red paprika (*Capsicum annuum*) and from flowers of *Lilium tigrinum*. Partial synthesis was made. Capsanthin 3,6-epoxide [(3S,5R,6R,3'S,5'R)-3,6-epoxy-5,3'-dihydroxy-5,6-dihydro- β , κ -caroten-6'-one] was isolated as a minor carotenoid from red paprika (*Capsicum annuum* var. *longum*). Capstoneoxanthin [(3S,5R,6R,3'S,5'R)-3,5,3'-trihydroxy-6,7-didehydro-5,6-dihydro- β , κ -caroten-6'-one] was isolated as a minor carotenoid from the fruit of *Asparagus falcatus*. (6R,6'S)-3,3'-Diketo- ϵ -carotene [(6R,6'S)- ϵ , ϵ -carotene-3,3'-dione] was isolated as a minor carotenoid from the yellow-tail rockfish *Sebastes flavidus*. 3,3'-Diketo- ϵ -carotene [(6S,6'S)- ϵ , ϵ -carotene-3,3'-dione] was isolated as a major carotenoid from eggs of the dolphin fish *Coryphaena hippurus* and of flying fish *Prognichthys agoo* and as a minor carotenoid from the integument of the yellow-tail rockfish *Sebastes flavidus*. (6R,6'R)-3,3'-Diketo- ϵ -carotene [(6R,6'R)- ϵ , ϵ -carotene-3,3'-dione] was isolated as a minor carotenoid from the yellow-tail rockfish *Sebastes flavidus*. Eschscholtzanthone [(3'S)-3'-hydroxy-4',5'-didehydro-4,5'-retro- β , β -carotene-3-one] was isolated as a minor carotenoid from the arils (fruit) of yew (*Taxus baccata*) and *T. cuspidata*. Partial synthesis from rhodoxanthin was made. [S,S)- ϵ , ϵ -carotene] [(6S,6'S)- ϵ , ϵ -carotene] was isolated as a minor carotenoid from monoalgal cultures of the phytoplankton *Pelagococcus subviridis*, from avian retinas and the marine green alga *Ulva lactuca*. Its total synthesis was made. ϵ -Carotene [(6R,6'R)- ϵ , ϵ -carotene] was isolated as a minor carotenoid from fruit of the Delta tomato mutant, the marine diatom *Naviculata torquatum*, and the algae *Briopsis corticulans*, *Codium fragile* and *Cryptomonas ovata*. An equimolar mixture of *chitwin* enantiomers was synthesized. γ , γ -Carotene [(6R,6'R)- γ , γ -carotene] was isolated as a minor carotenoid from the aphid *Macrosiphum liriodendri* and from the ladybird beetle *Coccinella septempunctata*. Total synthesis was accomplished. β , γ -Carotene [(6'S)- β , γ -Carotene] was isolated as a minor carotenoid from the discomycete fungus *Caloscypha fulgens* and from the ladybird beetle *Coccinella septempunctata*. Mixtures enriched in (6'R) and (6'S) were synthesized. α -Carotene [(6'R)- β , ϵ -carotene] is widely distributed, but usually only in relatively low concentration (in green leaves). In carrots and red palm oil is found in considerable amount. Its total synthesis was made. γ , ψ -Carotene [(6S)- γ , ψ -carotene] was isolated as a minor carotenoid from the ladybird beetle *Coccinella septempunctata*. δ -Carotene [(6R)- ϵ , ψ -carotene] was isolated as a major carotenoid from fruit of the Delta tomato mutant, as a minor carotenoid from other plant sources, e.g. ripe fruits of *Rosa pomifera*.



(4S,4'S)-4,4'-Dihydroxydiatoxanthin [(3S,4S,3'S,4'S)-7,8-didehydro- β,β -carotene-3,4,3',4'-tetrol] was isolated as a minor carotenoid from the starfish *Asterina pectinifera* and *A. amurensis*. 2-Hydroxyadonixanthin [(2R,3S,3'R)-2,3,3'-trihydroxy- β,β -caroten-4-one] was isolated from a marine bacterium strain SD-212 from southern Japan. Erythroanthin [(3S,2'R,3'R)-3,2',3'-trihydroxy- β,β -caroten-4-one] was isolated from a marine bacterium strain SD-212 from southern Japan. Its partial synthesis from erythroanthin sulphate was made. Idoxanthin [(3,3',4'-trihydroxy- β,β -caroten-4-one)] was isolated as a major carotenoid from fancy red carp (*Cyprinus carpio*) from eggs of mackerel and flying fish, from wild Atlantic salmon fed astaxanthin. Partial synthesis from crustaxanthin was accomplished. Halocynthiaxanthin [(3S,5R,6S,3'R)-5,6-epoxy-3,3'-dihydroxy-7',8'-didehydro-5,6,7,8-tetrahydro- β,β -caroten-8-one] was isolated from the sea squirt *Halocynthia roretzi*, the edible mussel *Mytilus edulis*, the tunicate *Amaroucium pliciferum* and from other nine species of tunicates. Partial synthesis from fucoxanthin was made. Isomytiloxanthin [(5R,6R,3'R)-6,3'-dihydroxy-7',8'-didehydro-5,6,7,8-tetrahydro- β,β -carotene-3,8-dione] was isolated from the edible mussel *Mytilus edulis*. Deepoxyuriolide [(3R,3'R,6'R)-3,3'-dihydroxy-7',8'-dihydro- β,ϵ -caroten-19',11'-olide] was isolated as a minor carotenoid from the prasinophyte alga "PIA2" (suggested to be *Prasinococcus capsulatus* or *Prasinoderma coloniale*). Mytiloxanthin [(3R,3'S,5'R)-3,3',8'-trihydroxy-7,8-didehydro- β,κ -caroten-6'-one] was isolated as a major carotenoid from the edible mussel *Mytilus edulis* and *M. coriescus* and as a minor carotenoid from other marine invertebrate animals including *Halocynthia roretzi*, *Amaroucium pliciferum* and seven species of tunicates. Total synthesis was made. 2'-Hydroxyflexixanthin [(3S,2'S)-3,1',2'-trihydroxy-3',4'-didehydro-1',2'-dihydro- β,ψ -caroten-4-one] was isolated as a minor carotenoid from the bacteria *Myxococcus fulvus* strain Mxf2 and *Flexibacterium* sp. strain NIVA BR6-64. Webbiaxanthin [(5R,6S,5'R,6'S)-5,5'-dihydroxy-5,6,5',6'-tetrahydro- β,β -carotene-3,3'-dione] is an important carotenoid of red Lonicera berries (*Lonicera webbiana* und *Lonicera ruprechtiana*). Webbiaxanthin has about the same polarity as violaxanthin. Surprisingly, webbiaxanthin cannot be acetylated, hence it is devoid of primary and secondary OH groups. Exposed epoxidic groups also lacks, since the compound is stable to dil. HCl. Allyl OH groups are also excluded since in MeOH/HCl no ether is formed. However, webbiaxanthin produces a disilylether, a proof for the presence of two tertiary OH groups. It reacts with NaBH₄ and the reduction product can easily be acetylated and subsequently silylated [115]. 5,6-Diepikarpoxanthin [(3S,5S,6S,3'R)-5,6-dihydro- β,β -carotene-3,5,6,3'-tetrol] was found as a minor carotenoid in ripe red paprika fruit (*Capsicum annum* var. *longum*). 5,6-Dihydroxy 5,6-dihydrolutein [(3S,5S,6S,3'R)-5,6-dihydro- β,ϵ -carotene-3,5,6,3'-tetrol] was isolated as a minor carotenoid from flowers of buttercup *Ranunculus acer*. All C₅₀ presented in this paper, as well as their di- β -D-Glcp glycosides are *chitwin*. C. p. 450 [(2R,2'R)-2,2'-bis(4-hydroxy-3-methylbut-2-enyl)- β,β -carotene] was isolated as a major carotenoid, in crystalline form, from *Curtobacterium flaccumfaciens* cv. *poinsettiae* (formerly *Corynebacterium poinsettiae*) [116].

Sarcinaxanthin [(2R,6R,2'R,6'R)-2,2'-bis(4-hydroxy-3-methylbut-2-enyl)- γ,γ -carotene] was isolated in crystalline form [117] as the main carotenoid from *Micrococcus luteus* (formerly *Sarcina lutea*) [118] and from *Cellulomonas biazotea* [119]. It produces a diacetate. Okadaxanthin [(2R,6R,2'R,6'R)-2,2'-bis(4-hydroxy-2-methylbut-2-enyl)- ϵ,ϵ -carotene] was isolated as a major carotenoid from a bacterium (*Pseudomonas* sp.) recovered from the marine sponge *Halichondriaokadai* [120]. Okadaxanthin gives a diacetate and it is structurally similar to decaprenoxanthin, with the 5-carbon side chain at C2 reversed. This difference manifests itself only as small differences in the ¹NMR spectrum. The absolute configuration of okadaxanthin was assigned by comparison of the ¹NMR and CD data with those of decaprenoxanthin. Decaprenoxanthin [(2R,6R,2'R,6'R)-2,2'-bis(4-hydroxy-3-methylbut-2-enyl)- ϵ,ϵ -carotene] was isolated in crystalline form [121] as a major carotenoid from *Agromyces mediolans* (formerly *Flavobacterium dehydrogenans*) and it was recognized as the first C₅₀ carotenoid found in nature [122]. It was also found in *Arthrobacter* M3 [123,124]. Decaprenoxanthin gives a diacetate and its absolute configuration was determined by comparison of CD and NMR data with those of model compounds [125]. Bisanhydrobacterioruberin [(2S,2'S)-2,2'-bis(3-methylbut-2-enyl)-3,4,3',4'-tetrahydro-1,2,1',2'-tetrahydro- Ψ,Ψ -carotene-1,1'-diol] was separated in crystalline form [126] as a major carotenoid from *Curtobacterium flaccumfaciens* cvar *poinsettiae* (formerly *Corynebacterium poinsettiae*). Bisanhydrobacterioruberin cannot be acetylated but gives a diTMS ether [116]. Flavuxanthin [(2R,2'R)-2,2'-bis-(4-hydroxy-3-methylbut-2-enyl)-1,16,1',16'-tetrahydro-1,2,1',2'-tetrahydro-



Ψ,Ψ -carotene] was isolated from a pink transposon mutant MV70 of *Corynebacterium glutamicum* [127]. C. p. 473 [(2*R*,2'*S*)-2-(4-hydroxy-3-methylbut-2-enyl)-2'-(3-methylbut-2-enyl)-3',4'-didehydro-1',2'-dihydro- β,Ψ -caroten-1'-ol] was separated in crystalline form [116] as a major carotenoid from *Curtobacterium flaccumfaciens* pvar *poinsettiae* (formerly *Corynebacterium poinsettiae*). It gives a monoacetate, which gives a monoTMS ether. The initial structure has been corrected [128-130]. A. g. 471 [(2*R*,6*R*,2'*S*)-2-(4-hydroxy-3-methylbut-2-enyl)-2'-(3-methylbut-2-enyl)-3',4'-didehydro-1',2'-dihydro- ϵ,Ψ -caroten-1'-ol] was isolated as a major carotenoid from *Arthrobacter glacialis* [131]. It gives a monoacetate which gives a monoTMS ether. The structure was assigned by low-resolution NMR with Eu-shift experiments. Chirality was assigned by analogy and by CD comparison with decaprenoxanthin and bisanhydrobacterioruberin present in the same extract.

4'-Hydroxy-4-ketoalloxanthin [(3*S*,3'*S*,4'*R*)-3,3',4'-trihydroxy-7,8,7',8'-tetrahydro- β,β -caroten-4-one] was isolated as a minor carotenoid from the goldfish *Carassius auratus*. 4'-Hydroxy-4-ketoalloxanthin [(3*S*,3'*S*,4'*S*)-3,3',4'-trihydroxy-7,8,7',8'-tetrahydro- β,β -caroten-4-one] was isolated as a minor carotenoid from the starfish *Asterina pectinifera* and *A. amurensis*. 7,8-Didehydroastaxanthin [(3*S*,3'*S*)-3,3'-dihydroxy-7,8-didehydro- β,β -carotene-4,4'-dione] was isolated as a major carotenoid from four species of starfish, *Asterias rubens* and the crab *Paralithodes brevipes* and, as a minor carotenoid, from three species of *Cyprinidae* fish. Total synthesis was made. Hurghadin [(3*R*,3'*R*)-3,3'-dihydroxy-2,2'-dinor- β,β -carotene-4,4'-dione] was isolated in esterified form from the Red sea nudibranch *Hexabranhus sanguineus* [132]. Saponification should be omitted since it converted the hurghadin to violerythrin, an optically inactive compound. The absolute configuration of hurghadin was assigned as (2*R*,2'*R*) from the CD spectrum which was the opposite of that of actinioerythrin. For the (3*S*,3'*S*)-isomer, see actinioerythrol. Actinioerythrol [(3*S*,3'*S*)-3,3'-dihydroxy-2,2'-dinor- β,β -carotene-4,4'-dione] was isolated as diester (actinioerythrin) as the major carotenoid from the red variant of the sea anemones *Actinia equine* [133] and *A. tenebrosa* [134]. Saponification should be omitted since it converts actinioerythrol to violerythrin. However, actinioerythrol can be hydrolysed enzymically [135]. Chirality was proved by CD comparison with synthetic Enantiomers [136]. For the (3*R*,3'*R*)-isomer, see hurghadin.

Other three *meso* polyprenyl compounds are (3*R*,3'*S*)-alloxanthin, teurilene and glabrescol (Fig. 1.12).

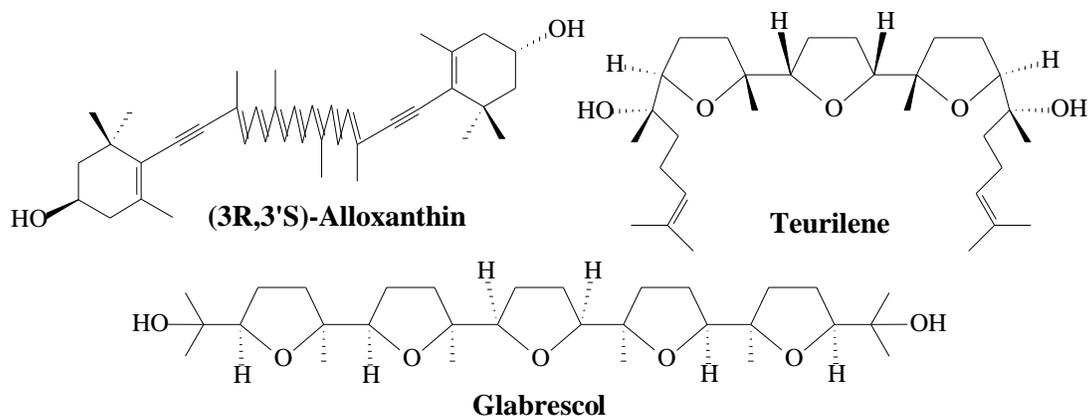
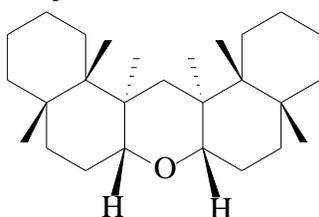


Figure 1.12: Other *meso* polyprenyl compounds presenting a unique *meso* isomer

Alloxanthin was isolated from the crab *Paralithodes brevipes* [103]. Both teurilene [137] and glabrescol [138] are *meso* polyisoprenoid compounds formed of two enantiomeric halves. Teurilene was isolated from the red alga *Laurencia obtusa* [139] and from the wood of *Eurycoma longifolia* [140]. Glabrescol was extracted from the branches and wood of *Spathelia glabrescens* (Rutaceae) [138]. The stereostructures of the two compounds have been elucidated by X-ray crystallographic analysis and spectroscopic methods, respectively. These unique polyethers are optically inactive *meso* molecules due to *C_s* symmetry despite possessing eight and ten asymmetric centers, respectively. Molecular formula of teurilene is $C_{30}H_{52}O_5$. The search of the chemical literature for isomers with the same molecular formula led us to the following compounds: (3*R*,6*R*,12*R*,20*S*,24*S*)-20,24-Epoxy-dammarane-3,6,12,25-tetraol dihydrate, cyclocanthogenin, sartortuosterol A, hosenkol A, siphonellinol B, cycloasgenin C [24(*R*)-cycloartane-3 β ,6 α ,16 β ,24,25-pentaol], trilocularol A [3 β ,6 α ,16 α ,20(*S*),27-

pentahydroxydammar-24(Z)-ene], (24S)-ergostane-3 β ,5 α ,6 β ,25-tetraol 25-monoacetate. The latter compounds are chiral steroids or chiral cyclic compounds. According to our systematization they are all *CROM*, since they are isomer to teurilene, a *meso* polyprenoid. Another polyprenyl compound is glabrescol. Molecular formula of glabrescol is C₃₀H₅₂O₇. Its *CROM* isomers are: concentricol B, pseudodehydrothysiferol, longilene, cubensic acid, serratane-3 α ,14 α ,15 α ,20 β ,21 β ,24,29-heptol,(3 α ,5 β ,7 α ,12 α)-3,7,12-tris(methoxymethoxy)cholan-24-al (synthetic). Let's make the following imaginary experiment: one designs (or synthesizes) a hypothetical *meso* combination having molecular formula C₂₇H₄₆O, i.e. an isomer of cholesterol and cholest-22-en-16- β -ol (Fig. 1.13). In this case the latter compounds are *CROM* isomers of the hypothetical combination, and we have an example of versatility of our systematization concerning new relationship between chiral dimeric compounds.



Hypothetical isomer (meso)

Figure 1.13: A hypothetical *meso* isomer of cholesterol

There is a superposition between some isomeric enantiomers and diastereomers, on one hand, and the four types of isomeric homodimeric compounds of our systematization – *meso*, *chitwin*, *irrechi*, *CROM*. (Diastereomers have been defined as stereoisomers that are not enantiomers). From our point of view, enantiomers are *chitwin* and diastereomers are *meso*, *irrechi* or *CROM*. Hence our systematization observes and uses details that are ignored by the preceding points of view. Here it's another example of versatility of our rationalization. A definition of diastereomers could be this one: compounds of maximum resemblance to enantiomers, however different. In our systematization, *meso* and *irrechi* are of maximum similarity to *chitwin* ones i.e. to enantiomers.

2. Conclusions

Heterodimeric compounds possessing a mirror plane of symmetry can be treated as homodimers due to the power of the mirror plane of symmetry, a physical instrument. The atom(s) cut by the mirror plane of symmetry is (are) imaginarily eliminated, and implicitly the envisaged structure is evaluated as a homodimeric one.

Our new systematization of homodimeric compounds consists in four types of isomers: *meso*, *chitwin*, *irrechi*, *CROM*. The latter four types constitute new and detailed physical chemical relationships between homodimeric compounds. An impressive number of natural compounds are characterized by the four types of isomers: (1) carbohydrates; (2) amino acids, their derivatives and chiral hydroxyacids; (3) carotenoids (polyprenyl or isoprenoid compounds) and perhydro isoprenoid hydrocarbons; (4) lignans and neolignans; (5) cyclobutane derivatives; (6) phenolic compounds; (7) alkaloids; (8) terpenoids; (9) lipids; (10) coenzymes based on cysteine and cysteamine, in oxidized state, or on nucleosides; (11) homodimeric proteins (12); palindromes [88-89]. However, the most spectacular and best illustration of our systematization belongs to carotenoids (polyprenyl or isoprenoids). The four types of isomers disclosed in this paper does not exclude other type of isomers, especially non-rotatory ones.

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