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Review

Superlative carotenoids*

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A selection of carotenoids beyond normal appearance or properties has been presented at the 16th International Symposium on Carotenoids. Some of the exceptional compounds shown at the conference cannot be reproduced in this proceeding since they have not yet been published. In addition, editorial space limitation does not allow illustrating all of the previously mentioned carotenoids.

Key words: carotenoids, polyenes, antioxidants, antireductants, polyunsaturated fatty acids, polyunsaturated lipids, aggregation, self-assembling

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INSTRODUCTION

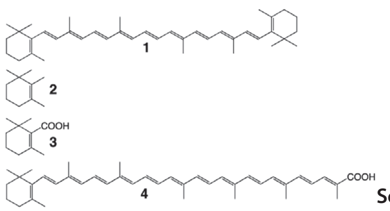
All compounds with the key structural elements of carotenoids (polyene chain connected to rings and functional groups) are considered carotenoids in the context of this presentation. Superlative is used to express "more than is normal." In other words, the presented carotenoids will normally not be found in the Carotenoids Handbook (Britton *et al.*, 2004).

THE SHORTEST CAROTENOID

The typical representative of carotenoids is β,β'-carotene **1** (Scheme 1). Downsizing this compound results in the shortest carotenoid 7-apo-β-carotene **2** (Naves, 1964). Adding an acid group generates the shortest carotenoic acid: C10:1 acid, cyclogeranic acid (**3**) (Kappeler *et al.*, 1953).

THE LONGEST CAROTENOIC ACID

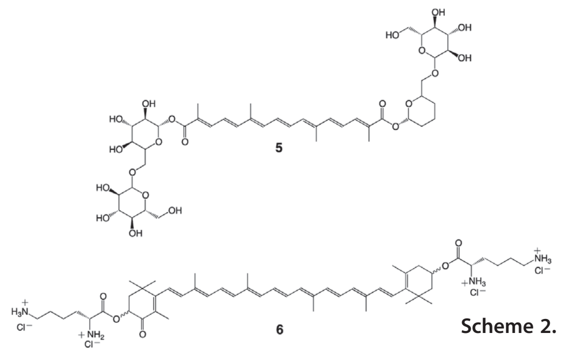
Subsequent elongation of C10:1 (**3**) provides a series of homologous carotenoic acids C12:2, C15:3, C17:4, C20:5 (retinoic acid), C22:6, C25:7, C27:8, C30:9 (C30-acid), C32:10 C35:11, C37:12 and finally results in the longest carotenoic acid so far detected in nature: torularhodin C40:13 (**4**), (Scheme 1) (Isler *et al.*, 1959). The natural limit has now been passed by synthesizing C45:15 acid (Zaidi, unpublished). The surface properties of the Na, K and Cs salts of these polyunsaturated fatty acids have been determined and compared with the data of saturated acids (Zaidi *et al.*, unpublished).



Scheme 1.

THE MOST WATER-SOLUBLE CAROTENOID

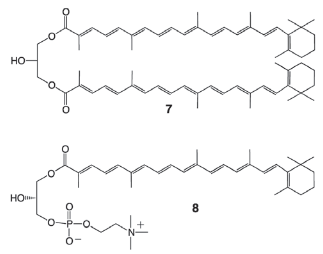
Carotenoids are commonly classified as hydrophobic pigments. It is, therefore, quite astonishing that the best known carotenoid since historical times is water-soluble. The water-solubility of crocin (**5**), the saffron constituent, is exceptional; there is no saturation point (Nalum Naess *et al.*, 2006). Some thousand years passed before a new water-soluble carotenoid emerged: astaxanthin-lysine **6** (Scheme 2) (Jackson *et al.*, 2004, Nalum Naess *et al.*, 2007). The distinct properties of hydrophilic carotenoids attract increasing interest (Lockwood *et al.*, 2006, Breukers *et al.*, 2009, Sliwka *et al.*, 2010).



Scheme 2.

THE MOST LIPOPHILIC CAROTENOID

Opposed to the few hydrophilic carotenoids are the numerous lipophilic ones. Consequently, the most lipophilic carotenoids would be carotenoid lipids. Dicarotenoid glycerol **7** (Partali *et al.*, 1996) and carotenoid phospholipid **8** (Foss *et al.*, 2003) are the most fatty ca-



Scheme 3.

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rotenoids described so far (Scheme 3). Nevertheless, the zwitterionic end group in phospholipid **8** confers some hydrophilicity to the molecule, it becomes amphiphilic. When in contact with water, phospholipid **8** self-assembles to aggregates.

THE SMALLEST CAROTENOID AGGREGATE

The aggregate morphology and size of the phospholipid **8** have been determined (Foss *et al.*, 2005b). In analogy to crystals, which are built of crystallization units, aggregates are expected to form basic aggregation units. The aggregation unit of phospholipid **8** is an octamer, representing the simplest repeating primary component expressing absorption and optical activity (Foss *et al.*, 2005a) (Scheme 4).

THE MOST OPTICAL ACTIVE CAROTENOID LIPID

Phospholipid **8**, although a pure enantiomer, is not optically active showing a flat line in the CD spectrum. Absence of optical activity is common for monomolecular solutions of glycerolipids. However, in water optical inactive enantiomer **8** assembles to optical active aggregates causing strong CD signals. Aggregation functions as an amplifier for the weak or absent optical activity in fats (Scheme 5). The advantages of carotenoids in fat research are evident. Carotenoid fatty acids transmit color to lipids, they become visible for eyes and detectable for instruments (Foss *et al.*, 2005a).

GOOD NEIGHBORS

The glycerolipid structure allowed combining three different antioxidants in triglyceride **9** (Scheme 6) (Naalsund *et al.*, 2001).

THE BEST ANTIOXIDANT

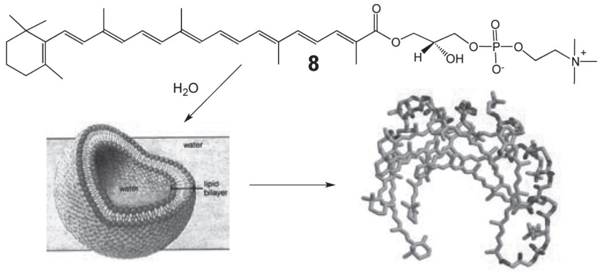
Carotenoids easily transfer electrons to noxious radicals transforming them to benign molecules. This property established the reputation of carotenoids as potent antioxidants. The best antioxidant is astaxanthin (**10**) (Scheme 7) (Miki, 1991; Lockwood & Gross, 2005).

THE BEST ANTIREDUCTANT

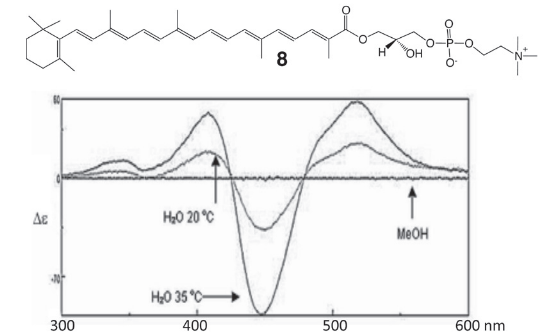
Carotenoids do not only release electrons they also capture electrons. Electron transfer from radicals to carotenoids has not yet been observed in nature but has recently been predicted (Martinez *et al.*, 2008). Usually, electron transfer to carotenoids is enforced with electrochemical methods, with laser or nuclear radiation (Mairanovsky *et al.*, 1975; Land *et al.*, 1978; Naqvi *et al.*, 2009). We have found a more convenient approach: carbonyl carotenoids take up electrons from alkaline DMSO (DMSO⁻, $CH_3(S{=}O)CH_2^-$). Thus, C20-dialdehyd **11** and other carotenoid dialdehydes (C10–C50) all react with similar activity as antireductants (Scheme 8) (Øpstad *et al.*, 2010) (Zeeshan, unpublished).

CAROTENOIDS AS GENE CARRIERS

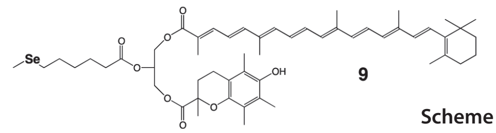
Cationic phospholipids, e.g. C30-6 **12** (Scheme 9), function as potential gene carriers. In these phospholipids, the rigid unsaturated carotenoid moiety is part



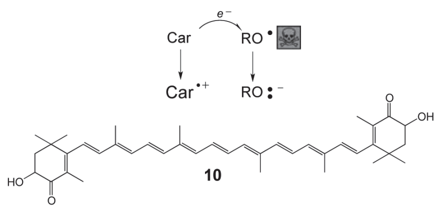
Scheme 4. Self-assembling of phospholipid 8 to aggregates with an octamer as aggregation unit.



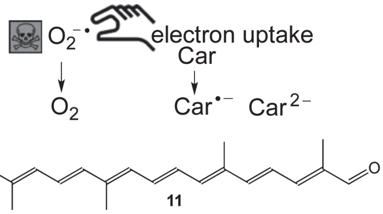
Scheme 5. No CD signals of 8 in MeOH, CD bands of 8 in water.



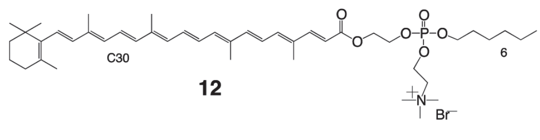
Scheme 6.



Scheme 7. Antioxidant function by electron transfer from carotenoid to radical.



Scheme 8. Antireductant function by electron transfer from radical to carotenoid.



Scheme 9. Cationic phospholipid C30-6.

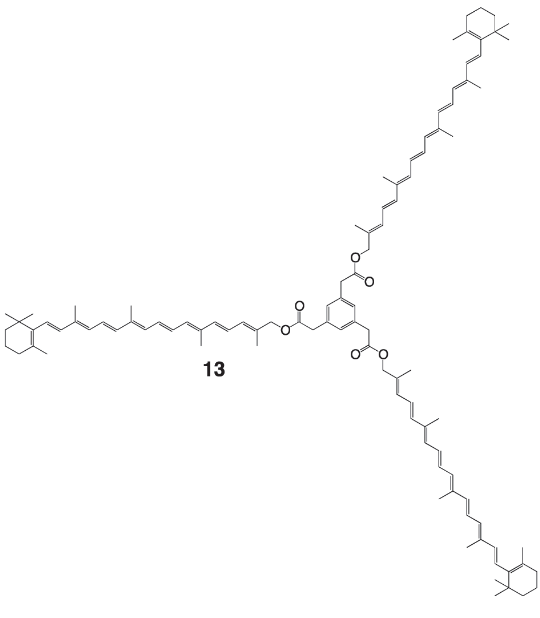
of a molecule with saturated flexible alkyl chains of different lengths. The length of the alkyl chain modifies the efficiency of the carrier. The results so far obtained confirm the validity of the concept (Popplewell *et al.*, 2012).

PROPELLER CAROTENOIDS

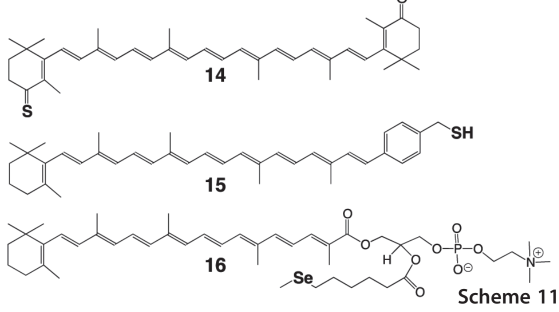
Carotenoids form propeller shaped molecules under certain circumstances. Propeller **13** has a benzene ring as hub and three C30-chain as wings (Scheme 10) (Háda *et al.*, 2010). Another propeller is build with trithia-cyclohexane as hub and C30-chains as wings (Sandru, unpublished).

THE MOST PRECIOUS CAROTENOIDS

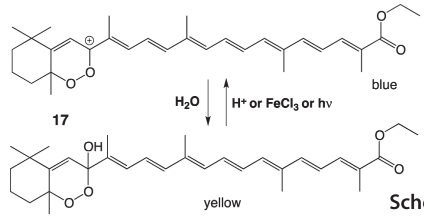
Hydrophilic carotenoids aggregate into several macromolecular structures; vesicles, rods, spheroids and cones have been observed (Sliwka *et al.*, 2010) (Øpstad unpublished). The size and morphology of the supramolecular assembly may change with time. Uncertainty on the aggregate architecture is avoided when carotenoids with an appropriate anchor self-assemble on metal surfaces. Previously, carotenoid thione **14**, carotenoid thiol **15** and carotenoid-selena phospholipid **16** formed strong molecular layers on gold surfaces (Scheme 11) (Ion *et al.*, 2002, Liu *et al.*, 2002; Foss *et al.*, 2006). The self-assembling effect was applied to attach carotenoid selena derivative **16** on gold nanoparticles. The selenacarotenoid-gold nanoparticles have a predefined size and morphology (Sandru, unpublished).



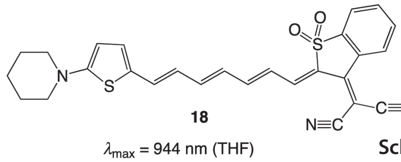
Scheme 10. Propeller carotenoid.



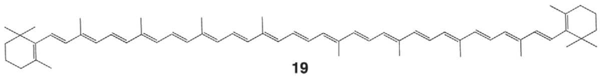
Scheme 11.



Scheme 12.



Scheme 13.



Scheme 14.

THE MOST EUROPEAN CAROTENOID

Adding water or acid to dioxane carotenoid **17** induces the molecule to display the blue and yellow color of the European flag (Scheme 12) (Li *et al.*, 2010). More European in character are carotenoid europium salts. These Eu-carotenoates will be used in photophysical investigations (Zaidi & Heng unpublished).

MAXIMUM λ_{max}

Push-pull compound **18** with only four double bonds displays the highest λ_{max} measured for a polyene (Scheme 13) (Blanchard-Desce *et al.*, 1997). However, polarization incommodes studies of absorption in relation to the number of conjugated double bonds. Such investigation must be based on unperturbed polyene chains.

THE LONGEST CAROTENOID

C60:19 carotenoid **19** represent since 1951 the ultimate length record (Scheme 14) (Karrer & Eugster, 1951). An attempt to go beyond C60 failed, C70:23 β,β-carotene was not stable (Broszeit *et al.*, 1997). Modifying the classical Wittig reaction has now allowed extending C40-zeaxanthin *via* C50-, C60- and C70- to stable C80-zeaxanthin with 27 conjugated double bonds (Zeeshan, unpublished).

CONCLUSION

Other superlative carotenoids are worth mentioning. Yet, superlative carotenoids may not be important. It is, however, advantageous to use ordinary, commercial carotenoids in the synthesis of superlative compounds.

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