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Latoxanthin, a minor carotenoid isolated from the fruits of yellow paprika (*Capsicum annuum* var. *lycopersiciforme flavum*)

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Abstract—Latoxanthin was isolated as a minor carotenoid from the ripe fruits of yellow tomato shaped paprika (*Capsicum annuum* var. *lycopersiciforme flavum*) and identified as (all-*E*,3*S*,5*R*,6*R*,3′*S*,5′*R*,6′*S*)-5′,6′-epoxy-5,6,5′,6′-tetrahydro-β,β-carotene-3,5,6,3′-tetrol based on spectral data.
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Naturally occurring carotenoids possessing a 3,5,6-trihydroxy-5,6-dihydro β-end group have been found in different sources, for example, heteroxanthin (**1**) was isolated from *Euglena gracilis*,[1] karpoxanthin (**2**) from the ripe hips of *Rosa pomifera*,[2] karpoxanthin (**2**) and 6-epikarpoxanthin (**3**) from the petals and pollen of *Lilium tigrinum*,[3] latoxanthin (**4**) from the petals of *Rosa foetida*[4] and neoflor (**5**) and 6-epineoflor (**6**) from the petals of *Trollius europaeus*.[5]

Structural elucidation of the 3,5,6-trihydroxy-end group was performed by Eugster.[6,7] Several ionone derivatives and carotenoids bearing this end group were prepared by partial synthesis and the 3,5,6-trihydroxy-5,6-dihydro β-end groups with (3*S*,5*R*,6*R*) (**A**), (3*S*,5*S*,6*S*) (**B**), (3*S*,5*R*,6*S*) (**C**) and (3*S*,5*S*,6*R*) (**D**) configurations have been established (Fig. 1). For structural elucidation of the 3,5,6-trihydroxy-5,6-dihydro-β-end groups, Eugster and co-workers successfully used acid-catalysed hydrolysis of 3-hydroxy-5,6-epoxy carotenoids.[6,7] It was demonstrated that during hydrolysis of the 5,6-epoxy carotenoids the configuration at C(5) was maintained whereas at C(6) both configurations were obtained. Based on these results the configuration of the 3,5,6-trihydroxy-5,6-dihydro-β-end group was 3*S*,5*R*,6*R* (**A**) in karpoxanthin (**2**),[2] latoxanthin (**4**)[4] and neoflor (**5**)[5] and 3*S*,5*R*,6*S* (**C**) in 6-epikarpoxanthin (**3**)[2] and 6-epineoflor (**6**).[5] On the other hand, it is remarkable that for karpoxanthin isolated from red paprika the 3*S*,5*S*,6*S*-configuration (**B**) was established.

As a continuation of our work on paprika carotenoids four carotenoids bearing the 3,5,6-trihydroxy-β-end group were isolated from the red spice paprika (*C. annuum* var. *longum*).[8] The structures of these compounds were unequivocally assigned from their spectroscopic data. One of the carotenoids was identical with 6-epikarpoxanthin (**3**).[2] The second carotenoid was identified as (all-*E*,3*S*,5*S*,6*S*,3′*R*)-5,6-dihydro-β,β-carotene-3,5,6,3′-tetrol. Since it was a diastereoisomer of karpoxanthin (**2**) with reversed configuration at C(5) and C(6), we proposed the trivial name 5,6-diepikarpoxanthin (**7**). The third compound was identified as (all-*E*,3*S*,5*S*,6*S*,3′*S*,5′*R*,6′*S*)-5′,6′-epoxy-5,6,5′,6′-dihydro-β,β-carotene-3,5,6,3′-tetrol and for this 5,6-diastereomer of latoxanthin (**4**) the name 5,6-diepilatoxanthin (**8**) was proposed. The fourth carotenoid was identified as (all-*E*,3*S*,5*S*,6*S*,3′*S*,5′*R*)-5,6-dihydro-3,5,6,3′-tetrahydroxy-β,κ-carotene-6′-one, and the name 5,6-diepicapsokarpoxanthin (**9**) was proposed.

During the separation of violaxanthin (**10**) and antheraxanthin (**11**) from a yellow paprika extract (1 g of hypophasic crystals was obtained from 15 kg of yellow tomato shaped paprika) several polar carotenoids were obtained by column chromatography. The compounds which were absorbed at the top of the silica gel column (Merck, Darmstadt, Germany), and could be eluted only with hexane/acetone 3:7 mixture, were further investigated. By repeated column chromatography on $CaCO_3$ columns (Biogal, Hungary) a minor carotenoid,

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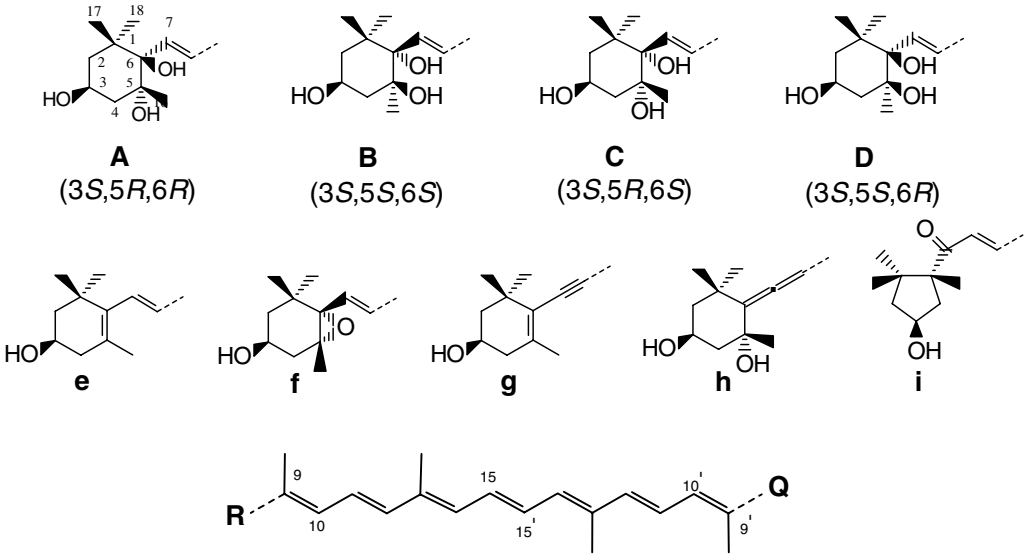

Figure 1. Compound **1**: Heteroxanthin R = **A**, Q = **g**; **2**: Karpoxanthin R = **A**, Q = **e**; **3**: 6-Epikarpoxanthin R = C, Q = **e**; **4**: Latoxanthin R = **A**, Q = **f**; **5**: Neoflor R = **A**, Q = **h**; **6**: 6-Epineoflor R = **C**, Q = **h**; **7**: 5,6-Diepikarpoxanthin R = **D**, Q = **e**; **8**: 5,6-Diepilatoxanthin R = **D**, Q = **f**; **9**: 5,6-Diepicapso-karpoxanthin R = **D**, Q = i; **10**: Violaxanthin R = Q = **f**; **11**: Antheraxanthin R = **f**, Q = **e**.

latoxanthin (**4**) was isolated and crystallised from benzene/hexane (0.5 mg red crystals). The UV/vis spectrum with maxima at 482, 452 and 428 nm (in benzene, no cis peak, $A_{III}/A_{II} = 0.98$) was identical with the spectra published in the literature.[8] Reaction with HCl/AcOH indicated that one 5,6-epoxy group was present (λ_{max} after acid treatment in benzene: 460, 431, 407 nm). The HPLC–MS showed the signal for the molecular ion at *m/z* 618 (100, M^+) which corresponds to $C_{40}H_{58}O_5$. Further characteristic signals were observed at 600 ($[M-H_2O]^+$), 582 ($[M-2H_2O]^+$) and 494.

Due to the small sample amount of the sample obtained detailed structure information about the configuration of the new compound was derived from a ^1H NMR experiment. The ^1H chemical shifts and the $J_{H,H}$ coupling constants correspond with chemical shifts from the literature.[8,9] The ^1H signals of the olefinic range could only be partially assigned. The identification of latoxanthin was based on NMR data previously published by Eugster for the corresponding trihydroxy and epoxy end groups.[6,7] These data were confirmed also by our group.[9,10] The shift patterns of the four epimers (**A**–**D**) including the δ values of H(3), H(7), CH_3(16), CH_3(17) and CH_3(18) differed enough to determine the 3,5,6-trihydroxy configuration. Protons H-3 (4.16 ppm), H-7 (6.14 ppm) and CH_3(18) (1.18 ppm) indicated the (3*S*,5*R*,6*R*) configuration for the 3,5,6-trihydroxy-end-group and protons H-3′ (3.91 ppm) and H-7′ (5.90 ppm) point to the (3*S*,5*R*,6*S*)-5,6-epoxy end-group as in violaxanthin (Table 1).[11]

Our investigation confirmed that the chirality of latoxanthin, similarly to karpoxanthin, differs depending on the natural source. In red paprika, the configuration of karpoxanthin and latoxanthin was established as (3*S*,5*S*,6*S*) and in other species such as yellow paprika as (3*S*,5*R*,6*R*). In addition 5,6-diepicapsokarpoxanthin,

Table 1. Significant ^1H NMR shifts (ppm, in $CDCl_3$) of trihydroxy end groups **A**–**D**

	A	**B**	**C**	**D**	Latoxanthin in yellow paprika
H-3	4.16	4.28	4.27	3.98	4.15
H-7	6.14	6.36	5.88	5.84	6.13
Me-16	1.18	1.12	1.10	1.36	1.17
Me-17	1.25	1.31	1.26	1.06	1.25
Me-18	0.87	0.89	0.81	1.02	0.87

which has been isolated for the first time from a natural source exhibits the (3*S*,5*S*,6*S*) configuration. In contrast, 6-epikarpoxanthin (**3**) possesses the (3*S*,5*R*,6*S*) chirality independently of the natural source. We assume that in nature, carotenoids with the 3,5,6-trihydroxy-β-end group are formed from the 3-hydroxy-5,6-epoxy-β-end group, the (3*S*,5*R*,6*S*)-3-hydroxy-5,6-epoxy-β-end group of violaxanthin being a possible precursor in all organisms. Therefore it is highly probable that in red paprika, compared to other organisms, the 3,5,6-trihydroxy-β-end group is formed from the corresponding 3-hydroxy-5,6-epoxy-β-end group following a different mechanism. In red paprika during the enzyme-catalysed hydrolysis of carotenoid-5,6-epoxides the configuration at C(5) may change but the configuration at C(6) remains the same. Either the (3*S*,5*S*,6*S*)- or the (3*S*,5*R*,6*S*)-end group may be formed via the carbocation at C(5). In plants (*Rosa foetida*, ripe hips of *Rosa pomifera*) that do not contain carotenoids with the κ-end group, the ring opening of carotenoid-5,6-epoxides may be acid catalysed. During the acid-catalysed hydrolysis of carotenoid-5,6-epoxides the configuration at C(6) may change, whereas that at C(5) remains unchanged. The different biosynthetic routes may explain the differences between the configurations of carotenoids possessing the 3,5,6-trihydroxy-β-end group isolated from different sources.

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11. ^{1}H NMR data for latoxanthin: $\delta = (400\ \text{MHz}, \text{CDCl}_3)$ 0.87 (s, 3H, H-18), 0.97 (s, 3H, H-16′), 1.15 (s, 3H, H-17′), 1.17 (s, 3H, H-16), 1.18 (s, 3H, H-18′), 1.25 (m, 5H, H-2′, H-4′, H-17), 1.60 (m, 3H, H-2, H-2′), 1.81 (s, 1H, H-4), 1.92 (s, 1H, H-4), 1.94 (m, 12H, H-19, H-20, H-19′, H-20′), 2.41 (s, 1H, H-4′), 3.91 (m, 1H, H-3′), 4.15 (m, 1H, H-3), 5.87 (d, 1H, H-7′, $J_{7',8'} = 16$ Hz), 6.13 (d, 1H, H-7, $J_{7,8} = 15.6$ Hz), 6.2–6.7 (2m, 12H, other olefinic protons).