Dietary zeaxanthin occurrence and bioaccessibility

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This entry provides a comprehensive and exhaustive overview of natural food sources of zeaxanthin and their respective zeaxanthin bioaccessibility, while also placing emphasis on the importance of this oxygenated carotenoid in human health. The content of zeaxanthin in foods of different origin (plant-, animal- and microalgal-based food sources) has been reviewed and the *in vitro* accessibility results obtained by various research groups through the standardized INFOGEST protocol were compared among the different zeaxanthin food sources.

Keywords: zeaxanthin ; bioaccessibility ; INFOGEST ; ocular health ; age-related macular degeneration

1. Introduction

Among the 1195 identified natural carotenoids [1], only lutein (β,ε-Carotene-3,3′-diol) and zeaxanthin (β,β-Carotene-3,3′-diol) have the ability to pass the blood–retina barrier and to accumulate in the macula lutea of the human eye. Here, the two dihydroxycarotenoids together with *meso*-zeaxanthin (a metabolite of lutein) exert their protection by filtrating high energy blue light and by limiting the oxidative stress, thus acting as powerful antioxidants [2].

Being lipophilic pigments, lutein and zeaxanthin follow the same absorption pathway as dietary lipids. After their release from the food matrix, the oxygenated carotenoids need to be solubilized into lipid emulsion particles in the stomach, incorporated into mixed micelles stabilized by the biliary salts in the duodenum before being taken up by the small intestinal cells and packaged in chylomicrons for secretion into the lymphatic system [3]. Despite the relatively low blood level of lutein (0.1–1.44 µmol/L in USA; 0.26–0.70 µmol/L in Europe) and especially of zeaxanthin (0.07–0.17 µmol/L in USA; 0.05–0.13 µmol/L in Europe), human retina accumulates high amounts of carotenoids (lutein, zeaxanthin and *meso*-zeaxanthin) in the macula, reaching as much as 1 mM [4][5][6].

The deposition form of carotenoids in plant and animal-based foods (solid-crystalline aggregates, lipid-dissolved forms or liquid-crystalline forms) exerts a strong influence on their liberation from the food matrix and consequently on their bioavailability [7]. Zeaxanthin, present (mainly as zeaxanthin dipalmitate) in liquid-crystalline form in the tubular chromoplasts of goji berries, showed an enhanced liberation and bioaccessibility compared to lutein, which is stored as protein-complexes in the thylakoids of chloroplasts [8]. Alongside the arduous liberation from foods, other factors such as the presence of co-ingested fat [9], fiber [10] or the processing level of the investigated food sample [11][12] can have a significant impact on carotenoid bioaccessibility.

Given the fact that a high amount of zeaxanthin in the micellar phase is associated with a potentially high absorption by the intestinal cells and transportation into plasma, data on the bioaccessibility of zeaxanthin from different food sources is a prerequisite for determining its bioavailability [13].

2. Dietary Sources of Zeaxanthin

As seen in Table 1, the overall occurrence of zeaxanthin in natural food products is low. The broad majority of xanthophyll-rich foods contain more lutein than zeaxanthin. Moreover, many of the zeaxanthin-containing products listed in Table 1 are not commercially available around the world. Consequently, the most predominant sources of zeaxanthin present in the human diet are corn-based foods along with pepper and egg yolk [14].

Table 1. Dietary sources of zeaxanthin (µg/g dry weight[a] or µg/g fresh weight[b]).

Plant sources	Zeaxanthin	Ref.
Einkorn wheat (*Triticum monococcum*)	0.94[a]	[15]

Khorasan wheat (*Triticum turgidum* subsp. *turanicum*)	0.71[a]	[15]
Durum wheat (*Triticum turgidum* subsp. *durum*)	0.49[a]	[15]
Corn (*Zea mays* L.)	10.31[a]	[15]
Corn flakes	1.02 - 2.97[a]	[16]
Corn chips	1.05[a]	[17]
Corn tortilla	0.93[a]	[17]
Corn masa	1.13[a]	[17]
Corn flour	9.4[a]	[18]
Boiled corn	3.7[a]	[18]
Potato (*Solanum tuberosum* L.)	7.7[a]	[18]
Sweet potato (*Ipomoea batatas*)	0.3[a]	[18]
Squash (*Cucurbita maxima*)	1.9[a]	[18]
Kidney been (*Phaseolus vulgaris* L.)	0.1[a]	[18]
Okra (*Abelmoschus esculentus*)	0.1[a]	[18]
Beet (*Beta vulgaris* L.)	0.7[a]	[18]
Tomato (*Solanum lycopersicum* L.)	1.3[a]	[18]
Hot chili peppers (*Capsicum frutescens* L.)	1230[a*]	[19]
Pepper (*Capsicum annuum* L.)		
red	55.0 - 97.0[a]	[20]
green	1.7 - 5.7[a]	[20]
orange	62.0[a]	[18]
yellow	4.4[a]	[18]
India mustard (*Brassica juncea*)	0.8[a]	[18]
Watercress (*Nasturtoum officinale*)	0.4[a]	[18]

Endive (*Cichorium endivia* L.)	0.5[a]	[18]
Romaine lettuce (*Lactuca sativa* L. var. *longifolia*)	0.7[a]	[18]
Lettuce (*Lactuca sativa* L.)	0.1[a]	[18]
Cabbage (*Brassica oleracea* L.)	0.1[a]	[18]
Spinach (*Spinacia oleracea* L.)	0.7[a]	[18]
Kale (*Brassica oleracea* L. var. *sabellica*)	163 - 2460[a]	[21]
Zucchini blossoms (*Cucurbita pepo* L.)	32.7[b*]	[22]
Artichoke heart (*Cynara cardunculus* L. var. *scolymus*)	0.18[b]	[14]
Avocado (*Persea americana*)	0.08 - 0.18[b]	[23]
Apple (*Malus domestica*)		
flesh	nd - 0.04[a]	[24]
peel	nd - 0.52[a]	[24]
Apricot (*Prunus armeniaca* L.)	nd - 0.39[b]	[25]
European plum (*Prunus domestica* L.)	0.1[a]	[18]
Nectarine (*Prunus persica*)	0.2[a]	[18]
Orange[‡] (*Citrus sinensis*)	0.3[a]	[18]
Orange juice[‡] (*Citrus sinensis*)	0.1[a]	[18]
Grafted orange[‡] (*Citrus sinensis*)	1.1[a]	[18]
Grafted orange (juice)[‡]	0.6[a]	[18]
Mandarin[‡] (*Citrus reticulata*)	2.1[a]	[18]
Mandarin juice[‡] (*Citrus reticulata*)	1.7[a]	[18]
Red grapefruit[‡] (*Citrus paradisi*)	0.2[a]	[18]
Peruvian groundcherry (*Physalis peruviana* L.)	0.4[a]	[18]
Strawberry tree (*Arbutus unedo* L.) fruits	0.7 - 2.0[a]	[26]

Raspberry (*Rubus idaeus* L.)	0.14 - 0.49[a]	[27]
Rose hip (*Rosa* spp.)	23 - 107[a*]	[28]
Wolfberry (goji berry) (*Lycium barbarum* L.)	1231.1[a*]	[29]
Red Chinese lantern fruit (*Physalis alkekengi* L.)	847 - 1035[a*]	[30]
Sea buckthorn (*Hippophae rhamnoides* L.)		
berries	193 - 424[a*]	[31]
oil (cold-pressed)	2312.2[b*]	[32]
Murici fruit (*Byrsonima crassifolia*)	5.4[a*]	[33]
Arazá fruit (*Eugenia stipitata*)		
peel	1.14[b]	[34]
pulp	0.17[b]	[34]
Astringent persimmon (*Diospyros kaki* Thunb. var. Rojo brillante)	10.2[b*]	[35]
Cashew apples (*Anacardium occidentale* L.)		
peel	0.51 - 2.69[b*]	[36]
pulp	0.04 - 0.58[b*]	[36]
Corozo[‡] (*Aiphanes aculeata*)	79.2[a]	[18]
South American sapote[‡] (*Quararibea cordata*)	46.2[a]	[18]
Passion fruit[‡] (*Passiflora edulis*)	0.2[a]	[18]
Mango[‡] (*Mangifera indica*)	0.5[a]	[18]
Red papaya[‡] (*Carica papaya*)	0.6[a]	[18]
Yellow guava[‡] (*Psidium guajava* L.)	0.2[a]	[18]
Pineapple[‡] (*Ananas comosus*)	0.1[a]	[18]
Melon[‡] (*Cucumis melo* L.)	0.1[a]	[18]
Tahitian apple[‡] (*Spondias dulcis*)	0.1[a]	[18]

Cassabanana[‡] (*Sicana odorífera*)	0.4[a]	[18]
Tree tomato[‡] (*Cyphomandra betacea*)	1.7[a]	[18]
Red tree tomato[‡] (*Cyphomandra betacea*)	2.4[a]	[18]
Roselle[‡] (*Hibiscus sabdariffa* L.)	0.8[a]	[18]
Membrillo[#] (*Gustavia superba*)	37.6[a]	[18]
Canistel[#] (*Pouteria campechiana*)	19.7[a]	[18]
Chinese passion fruit[#] (*Cionosicyos macranthus*)	2.8[a]	[18]
Sastra[#] (*Garcinia intermedia*)	84.7[a]	[18]
Yellow mombin[#] (*Spondias mombin* L.)	1.2[a]	[18]
Guanabana toreta[#] (*Annona purpurea*)	6.8[a]	[18]
Purple mombin[#] (*Spondias purpurea* L.)	0.8[a]	[18]
Chinese rose[#] (*Pereskia bleo*)	0.8[a]	[18]
Nance[#] (*Byrsonima crassiflora*)	0.2[a]	[18]
Lucuma fruit (*Pouteria lucuma*)		
Molina variety	3.44 - 5.76[b*]	[37]
Beltran variety	5.74 - 6.66[b*]	[37]
Sarsaparilla (*Smilax aspera* L.) berries	8.56[b*]	[38]
Animal sources		
Butter	nd - 0.02[b]	[39]
Marine crab (*Charybdis cruciata*)		
meat	0.02[b]	[40]
Freshwater crab (*Potamon potamon*)		
meat	1.72[b]	[40]
Eggs		

raw	1.5[a]	[41]
boiled	1.3[a]	[41]
poached	1.3[a]	[41]
omelette	1.14[a]	[41]
Microalgal sources		
Nannochloropsis sp.		
suspension	420[a]	[42]
oil	1930[b]	[42]
Chlorella ellipsoidea	1999[a]	[43]
Dunaliella salina	11270[a]	[44]
Phaeodactylum tricornutum	679.2[a]	[45]
Scenedesmus almeriensis	370[a]	[46]

In what concerns the origin of the zeaxanthin-containing foods, plant-based foods are unequivocally the most investigated foods, as they are also more abundant in nature. In vegetables, zeaxanthin is present in its free form, while in ripped fruits it usually occurs in a more stable and less soluble form, i.e., esterified with various fatty acids [47][48]. After the ingestion of these zeaxanthin-rich fruits, the mono- or di-esters need to be enzymatically hydrolyzed into their free form in the gastrointestinal tract before absorption by the intestinal cells [49]. Some fruits with distinguished zeaxanthin content such as goji (*Lycium barbarum* L.) berries and sea buckthorn (*Hippophae rhamnoides* L.) berries have been studied in terms of zeaxanthin content and bioaccessibility [8][29][31][32] but a large number of exotic fruits with a high content of zeaxanthin still remain uninvestigated.

Animal-based food sources of zeaxanthin are limited and fully dependent on the animal's diet. For instance, by supplementing the feed of laying hens, the content of both lutein and zeaxanthin in egg yolk can be enhanced [50][51][52]. Due to the high-lipid matrix, xanthophylls from egg yolk, present in a lipid-dissolved form, are more bioavailable than from plant-based sources [53].

Apart from plant and animal food sources, the dried edible biomass of microalgae constitutes a potential rich source of zeaxanthin. Several microalgae such as *Dunaliella* sp. and *Chlorella* sp. can accumulate impressive amounts of zeaxanthin (Table 1). Considering the steady increase in the human population and Earth's limited resources, microalgae could be regarded as reliable sources of zeaxanthin and other beneficial byproducts in the near future.

3. Zeaxanthin Bioaccessibility

Following the publication of the INFOGEST® harmonized simulated digestion method [54], various research groups investigated carotenoid bioaccessibility from different food sources, some of them containing zeaxanthin. Table 2 summarizes the bioaccessibility of zeaxanthin from dietary sources obtained through the above-mentioned protocol. It should pointed out that even though the bioaccessibility was obtained using the same simulated digestion technique, each study was amended with consideration to the particularities of the tested food samples (as can be seen in the observations section), having carotenoid bioaccessibility as their common research purpose.

The release from the food matrix (also known as liberation) represents one of the many factors that affect carotenoid bioaccessibility, and consequently their bioavailability. Thermal processing promotes the release of zeaxanthin [55], as well as its solubilization into the aqueous environment of the stomach. The use of energy-saving high-pressure homogenization on raw mandarin juice exhibited an approximately ten-fold increase in zeaxanthin bioaccessibility as opposed to traditional pasteurization methods [56]. Similar results were observed in the case of orange juice, with a five-fold increase in zeaxanthin bioaccessibility [57].

Zeaxanthin-containing foods co-ingested with a source of fat stand a higher chance of solubilization and incorporation into mixed micelles [58]. It is for this reason that, for example, the bioaccessibility of zeaxanthin from sea buckthorn oil (*Hippophae rhamnoides* L.) [32] is significantly higher than that from *Pouteria lucuma* fruits [37] (Table 2). The food matrix in which zeaxanthin is delivered to the gastrointestinal tract is of paramount importance. Indeed, oil and other food products that contain a high amount of lipids have a superior zeaxanthin bioaccessibility compared to fruits in which the xanthophyll deposition restrains its release. Including dietary fat in the simulated digestion along with the investigated food sample has been shown to enhance the bioaccessibility of zeaxanthin among other carotenoids. By way of example, the addition of coconut oil (1%) in the in vitro digestion of goji berries boosted zeaxanthin bioaccessibility from 6.7% to 13.3% [8]. In the same perspective, fruits that have a natural high content of lipids such as the fruit of murici (*Byrsonima crassifolia*) have a higher zeaxanthin bioaccessibility [33].

Corn (*Zea mays* L.), food source from which the name zeaxanthin is derived, is considered one of the best dietary contributors of this xanthophyll. However, in recent a study focusing on the in vitro digestion of corn-based products, the bioaccessibility of lutein from boiled kernels and porridge was similar to that of zeaxanthin and even higher in the case of tortilla (22.4% versus 18.5%) [59]. This is an important aspect considering that the content of lutein in tortilla was 6.5-fold higher than zeaxanthin and more than 7-fold higher in boiled kernels and porridge, thus making corn a more powerful source of lutein than zeaxanthin.

The superior bioaccessibility of zeaxanthin from egg yolk is widely acknowledged [60]. Nevertheless, the contribution of egg yolk to the dietary intake of zeaxanthin is rather low. Considering that the zeaxanthin content in a boiled egg yolk with an average weight of 17 g is 11.8 μg/g with 90% bioaccessibility [60], the actual zeaxanthin absorption after the ingestion of a single boiled egg yolk would be 180.54 μg. In order to cover the 2 mg of zeaxanthin needed for a significant reduction in the progression of age-related macular degeneration [61], the ingestion of 11 egg yolks would be required. An alternative approach for the enhancement of dietary zeaxanthin would be to consume food sources containing a high content of zeaxanthin with a moderate to high bioaccessibility rather than highly bioaccessible food products with low zeaxanthin content.

Investigation on zeaxanthin bioaccessibility from processed beverages is also worthwhile seeing that most of them are commercially available and ready for consumption. In a broad study including twenty-two commercial milk-fruit beverages the bioaccessibility of zeaxanthin was found in the range of approximately 10% to 90%, with a mean percentage of 45.3% [62]. This wide range can be explained by the vastly different characteristics of each beverage comprising various types of fruits. A range of 7.4%–15.2% was observed for zeaxanthin bioaccessibility from different homemade cajá frozen pulp based beverages depending on the presence of other ingredients such as sugar and fat in the matrix [63]. In this case, the bioaccessibility of zeaxanthin increased in accordance with the presence and the amount of both sugar and fat.

Limited data is available on the bioaccessibility of zeaxanthin from microalgal sources. These microorganisms can produce strikingly high amounts of natural high-value byproducts such as zeaxanthin and the evaluation of their bioaccessibility after human ingestion represents an interesting yet uninvestigated area of research. In addition to cell disruption, systems such as oil-in-water emulsions prepared from the extracted microalgal oil can provide an increased zeaxanthin bioaccessibility [42].

Table 2. Recent research (last 5 years) with regard to zeaxanthin bioaccessibility (%) from different food sources assessed through the internationally recognized in vitro digestion method [54].

Food Matrix	Bioaccessibility (%)	Ref.	Observations

Sea buckthorn (*Hippophae rhamnoides* L.)			
oil	61.5	[32]	The oral phase was not considered and porcine cholesterol esterase was included in the protocol.
oil-in-water (o/w) emulsion	64.6		

Plant sources	Goji berries (*Lycium barbarum* L.)	13.3	[8]	The tested food sample (dried goji berries) was supplemented with 1% (w/w) coconut fat.
	Astringent persimmon (*Diospyros kaki* Thunb, var. Rojo Brillante)	2.5	[35]	The persimmon samples were subjected to a high hydrostatic pressure treatment and the protocol was slightly amended as concerns the simulated digestion fluids.
	Cajá (*Spondias mombin* L.) water and milk based beverages	7.4–15.2	[63]	Six homemade cajá frozen pulp based beverages were analyzed through the slightly adjusted protocol.
	Ortanique mandarin juices (*Citrus reticulata* x *Citrus sinensis*)	8.8–82	[56]	Five mandarin juices subjected to traditional pasteurization and energy-saving high-pressure homogenization treatments were analyzed through the slightly adjusted protocol in which the oral phase was not considered.
	Orange juice (*Citrus sinensis* L. Osb.)	16–79	[57]	Five orange juices subjected to traditional pasteurization, energy-saving high-pressure homogenization and a combined centrifugation and homogenization technique were analyzed through the slightly adjusted protocol in which the oral phase was not considered.
	Commercial milk-fruit juice beverages	45.3	[62]	Twenty-two commercial milk-fruit juice beverages were analyzed through the slightly adjusted protocol. The oral phase was not considered and the bioaccessibility of zeaxanthin was expressed as mean percentage of the twenty-two commercial beverages investigated.
	Pouteria lucuma fruits			
	variety “Molina”	5.8	[37]	Two varieties of seedless lucuma fruit pulps were analyzed through the slightly adjusted protocol.
	variety “Beltran”	1.6		

	Murici (*Byrsonima crassifolia*) fruit	22	[33]	The freeze-dried murici fruit were rehydrated and analyzed through the slightly adjusted protocol along with other reported in vitro digestion methods.
	Maize (*Zea mays* L.)		[59]	After their preparation from maize, boiled kernels, porridge and tortilla were analyzed through the slightly adjusted protocol. In the case of porridge, the oral phase was not included.
	boiled kernels	2.4		
	porridge	7.8		
	tortilla	18.4		
	Egg yolk (hard boiled)	90	[60]	The yolk of hard-boiled commercial eggs was analyzed through the slightly adjusted protocol along with another in vitro digestion method.
Animal sources	Egg yolk		[41]	The protocol was amended so as to simulate the digestion conditions of exocrine pancreatic insufficiency patients.
	boiled	26–98		
	poached	28–103		
	omelette	31–111		
Microalgal sources	*Nannochloropsis* sp.		[42]	*Nannochloropsis* sp. (untreated biomass, high pressure homogenized biomass and oil-in-water emulsion) was analyzed through the slightly adjusted protocol. The oral phase was not considered and the results are expressed in terms of micellar incorporation (%).
	Untreated suspension	9		
	HPH suspension	19		
	o/w emulsion	54		

4. Zeaxanthin and Health Related Benefits

Due to its accumulation in the human retina, zeaxanthin is known primarily as one of the three macular pigments. Zeaxanthin and *meso*-zeaxanthin are predominantly distributed near the fovea, whereas lutein is more concentrated in the peripheral retina [4][64]. In recent decades, lutein and zeaxanthin have been associated with a reduced risk of developing several ocular diseases such as age-related macular degeneration and cataract [65][66].

Based on their preferential accumulation in the human brain and the acknowledged correlation between macular pigment optical density (MPOD) and brain carotenoids, lutein and combinations of lutein and zeaxanthin have been investigated for their contribution in cognitive function. Zeaxanthin concentration in the brain tissue of centenarians decedents was significantly correlated with premortem memory retention, verbal fluency and dementia [67]. In addition to a significant increase in MPOD, several cognitive parameters such as complex attention and cognitive flexibility were improved in both older women and men (mean age 72.51 years) after twelve months supplementation with 10 mg of lutein and 2 mg of zeaxanthin, with the composite memory being improved only in men [68].

Lutein and zeaxanthin were among the major carotenoids found in the infant brain and the detection of higher concentrations of lutein and zeaxanthin in almost all the brains of term infants as opposed to preterm infants may indicate an important role in cognition [69].

Henriksen et al. [70] found a correlation between zeaxanthin concentration in serum and MPOD in healthy term infants, as well as a correlation between the mother's zeaxanthin concentration in serum and infant MPOD. These results indicated that maternal zeaxanthin has a more relevant role in macular pigment deposition in utero than lutein.

5. Conclusions

As age-related macular degeneration (AMD) is one of the leading causes of blindness, seeking bioaccessible natural sources of macular xanthophylls represents the way forward in preventing and delaying the progression of this medical condition. The presence of lutein and zeaxanthin in the infant brain further indicates an important role of these dihydroxycarotenoids in cognitive function, also confirmed by the lower concentrations found in elderly with mild cognitive impairment.

Along with some zeaxanthin-rich exotic fruits, the edible biomass of microalgae emerges as a promising zeaxanthin source and deserves further investigation.

This brief overview of potentially bioaccessible food sources of zeaxanthin provides a valuable support not only for the industry in the development of functional foods designed so as to enhance the intake of this oxygenated carotenoid, but also for nutritionists and end-consumers in the wise selection of dietary sources with an elevated zeaxanthin absorption.

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