Lutein Esters are More Bioavailable than Free Lutein

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Abstract

Lutein is a carotenoid that has been shown to support vision health. Lutein is available in two forms – lutein esters, which is the form naturally found in plants, and free lutein. Both forms have been used for eye support products. In order to assess the relative bioavailability of these two forms, we used an animal model to compare absorption into the blood, and we measured the levels of lutein in plasma as a function of time. The commercial samples of lutein esters and free lutein were made from the same source of oleoresin and in the same form (oil), thus eliminating variability in the source. We found that the bioavailability of lutein esters was significantly greater than that of free lutein, as measured by Area Under The Curve. Bioavailability is an important measure of the efficacy of dietary ingredients.

Introduction

Lutein is a carotenoid (colored pigment) primarily found in plants, but also in fruits, cereals and some fats. Animals and humans obtain lutein primarily by ingesting plants. Lutein has strong anti-oxidant properties. In humans, lutein can scavenge peroxyl free radicals and promote direct antioxidant activity [1]. Because of its unique chemistry and structure, lutein can immerse itself in fatty brain cell membranes, crossing between the cell's exterior and interior environments. This stabilizes cell structures and protects against oxidative stress from inside and outside the cell [2].

The link between lutein and eye health was first reported in 1994 [3]. Since then, numerous studies, including the well-known AREDS II study [4], have shown a strong correlation between lutein intake and eye health. In particular, lutein is known to improve and even prevent age-related macular disease, which is the leading cause of vision impairment and blindness.

Lutein is a 40 carbon linked oxygenated carotenoid, known as an xanthophyll. There are two forms of lutein - lutein esters and free lutein. The natural form found in plants is the ester form. Lutein is extracted from the petals of the African marigold (*Tagetes erecta*) as the oleoresin. It can then be converted to the free lutein form by saponification [5].

Both forms are used interchangeably by the medical profession; however there are physiological differences that may manifest themselves in how they are absorbed by the body. Absorption (or bioavailability) seems to be controversial, with some studies showing that the lutein ester form is better absorbed [6], while others showing the free lutein form better absorbed [7], and yet others showing no difference [8].

We hypothesize that the bioavailability or absorbability of lutein esters or free lutein depends on the physical form of the lutein – for example oil vs powder. If these are not standardized and compared on an equivalent basis then any comparison between the free and ester forms is less useful. In this study we compare the bioavailability of lutein esters and free lutein in an animal model, both as oils, derived from the same oleoresin, diluted in sunflower oil.

Methods

Commercial samples of a lutein ester containing 40% lutein ester measured as lutein dipalmitate (equivalent to 20% free lutein) in sunflower oil, and free lutein containing 20% free lutein in sunflower oil, were used in this study.

Bioavailability was studied in an animal model. Male Wistar rats were fasted overnight and then fed a single dose of lutein at 40 mg/kg body weight. There were 6 rats in each group and the study was conducted under Good Laboratory Practices. 1.5 ml of blood was taken from each animal at 0, 1, 3, 6 and 12 hours. Plasma was separated and then extracted with n-hexane and the organic layer evaporated to dryness. The dried material was solubilized in mobile phase and then analyzed by LCMS. In the statistical analysis, the area under the curve [9] was used as the measure of relative bioavailability. T-test was used to determine significance. A T-test % <5% was used as a determination of significance.

Results

The mean and standard error results for the free lutein studies and the lutein ester studies are shown the tables below. The time course for plasma lutein from lutein esters and free lutein is shown in the chart below. Area Under Curve (AUC) is the integrated plasma concentration.

Maximum absorption occurred at 6 hours for both free lutein and lutein esters. Figure 1 shows the time course for mean plasma concentrations for both free lutein and lutein ester.

The %T-test is <5% which means a significant difference between the two areas under the curve. The amount of "available lutein" from the free lutein ingredient is significantly less than the amount of "available lutein" from the lutein ester ingredient.

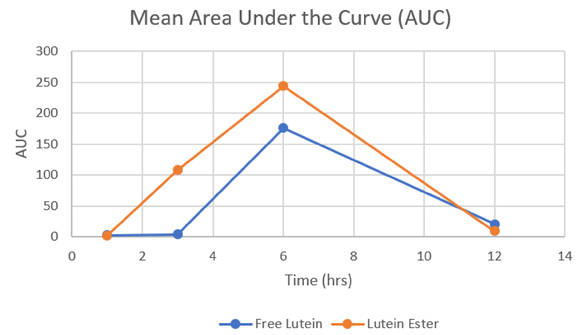
Table I: Free Lutein Data

Time (hrs.)	Plasma level (ppb)	Area Under Curve (AUC)	Cumulative Mean AUC
0	0	0	0
1	0.10 +/- 0.00	2.70 +/- 0.08	2.70
3	0.16 +/- 0.03	4.49 +/- 0.89	7.19
6	6.19 +/- 2.09	175.8 +/- 59.51	182.99
12	0.73 +/- 0.19	20.67 +/- 5.53	203.66

Table II: Lutein Ester Data

Time (hrs.)	Plasma level (ppb)	Area Under Curve (AUC)	Cumulative Mean AUC
0	0	0	0
1	0.12 +/- 0.00	3.34 +/- 0.07	3.34
3	3.80 +/- 2.84	108.00 +/- 80.71	111.34
6	8.60 +/- 0.01	244.1 +/- 20.14	355.44
12	0.35 +/- 0.04	9.82 +/- 1.28	365.26

Figure 1: Mean Area Under the Curve



Statistical analysis: The T-test was used to determine significance of the results. The T-test value for the AUC data was 0.96%. This is less than 5% which was used as a measure of significance. This means that the two AUC data sets are significantly different.

Discussion

Area Under the Curve is a standard method to compare bioavailability. The data is for plasma lutein concentration as a function of time. Relative areas under the curve give an indication of relative bioavailability or transport from the gut to the blood. Lutein ester bioavailability for these specific ingredients in this animal model is significantly greater than for free lutein. The ester tends to have greater solubility than the free lutein. This may partially explain the difference in bioavailability.

Testing ingredients made from the same oleoresin source and in the same form (oil in this case) takes these variable out of the picture and we are then left with a more accurate measure of bioavailability as it relates to the free lutein vs the lutein ester.

Conclusions

This bioavailability study was conducted to assess the relative bioavailability/absorption between lutein esters and free lutein. Lutein esters and free lutein are from the same source of oleoresin derived from marigold flowers. By fixing the source, this removes this variability, leaving only the ester vs the free form as the variable. Under these conditions, in an animal model, lutein ester bioavailability was measured to be significantly greater than free lutein bioavailability. Bioavailability is an important measure of the efficacy of dietary ingredients.

References

1. Gao, Shasha et al. "Lutein and zeaxanthin supplementation reduces H2O2-induced oxidative damage in human lens epithelial cells." *Molecular Vision* vol. 17 (2011): 3180-90

2. Widomska J, Zareba M, Subczynski WK. Can Xanthophyll-Membrane Interactions Explain Their Selective Presence in the Retina and Brain? Foods 2016;5(1)

3. https://www.ncbi.nlm.nih.gov/pubmed/7933422

4. Age-Related Eye Disease Study 2 (AREDS2) Research Group (2014). JAMA Ophthalmol. 132: 142-149

5. https://en.wikipedia.org/wiki/Lutein

6. https://academic.oup.com/jn/article/132/12/3668/4712124

7. https://www.ncbi.nlm.nih.gov/pubmed/21677121

8. https://www.ncbi.nlm.nih.gov/pubmed/27273910

9. https://www.excelforum.com/excel-formulas-and-functions/432855-how-do-i-calculate-the-area-under-the-curve-using-excel.html

Conflicts:

The author is an employee of NutriScience Innovations LLC, who markets and distributes lutein products.