Clinical and Scientific Evidence for the Safety and Efficacy of XanMax® Lutein/Zeaxanthin

Priya[1], M.K., M.Sc., Michael Lelah[2], Ph.D.

1. Katra Phytochem (India) Pvt. Ltd., Bangalore, India 2. NutriScience Innovations, LLC, Trumbull, CT, USA

ABSTRACT

We review the direct evidence for the safety and efficacy of XanMax® 2002 free lutein/zeaxanthin. Animal studies demonstrated that XanMax® 2002 lutein/zeaxanthin was well absorbed into the blood and with increased macular deposits of lutein and zeaxanthin, and increased antioxidant potential. In a human study, these increases in macular levels of lutein and zeaxanthin were demonstrated to improve macular pigment optical density (MPOD) by 40%. The three studies, when integrated together, demonstrate that supplementing the diet with XanMax® 2002 can be measured by absorption into the blood, deposition in the macular, and improvements in MPOD. No abnormalities or adverse events were reported. We conclude that supplementation with XanMax® 2002 lutein/zeaxanthin is a safe and effective means to increase macular pigmentation, therefore demonstrating benefits for healthy aging and improved eye health.

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 antioxidant 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]. Zeaxanthin is one of the most common carotenoid alcohols and is found in plants and some micro-organisms. Lutein and zeaxanthin have identical chemical formulas but are isomers, with the difference being the location of a double bond. There are 3 different isomers of zeaxanthin, trans-zeaxanthin and meso-zeaxanthin being the two primary ones. Both trans- and meso- zeaxanthin are taken up and found in the macula [3], and in general they are not distinguished for dietary supplement purposes.

The link between lutein / zeaxanthin and eye health was first reported in 1994 [4]. Since then, numerous studies, including the well-known AREDS2 study [5], have shown a strong correlation between lutein intake and eye health. Lutein / zeaxanthin is known to improve and even prevent age-related macular disease, which is the leading cause of vision impairment and blindness.

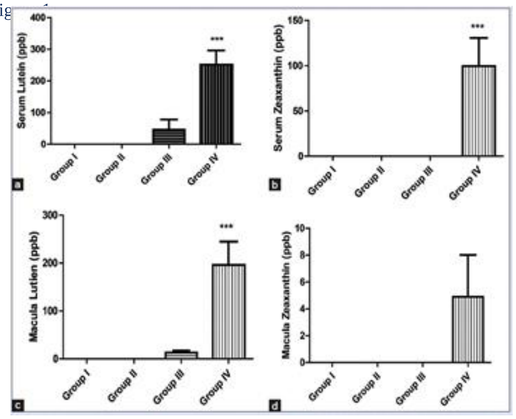
XanMax® is a portfolio of free lutein/zeaxanthin developed for optimum eye health and healthy eye aging. Lutein helps support eye health and may help reduce the risk of progression to advanced age-related macular degeneration (AMD) as demonstrated in the AREDS2 study. The macular pigment is a region of the retina that plays a vital role in vision. XanMax® free lutein/zeaxanthin helps to improve visual performance with prolonged screen use in healthy individuals. Lutein and zeaxanthin have also been found to improve cognitive function in all age groups, from infants to late adulthood.

XanMax® is extracted and purified from marigold flowers *Tagetes erecta*. XanMax® is available in several different lutein/zeaxanthin formulations and in various formats – oils, powders, beadlets and aqueous dispersions. XanMax® 2002 is a specific lutein/zeaxanthin formula consisting of 20% lutein and 2% zeaxanthin with a lutein:zeaxanthin ratio of 20:2. The oil form is dispersed in a matrix of sunflower oil. This formula is commercially available. It should be noted that this formula is different from the 20:4 ratio used in the AREDS2 study. This formula has been specifically studied in two animal studies, and one human clinical study. This paper summarizes and integrates these studies.

Animal Study on the effects of supplementing the diet with XanMax® 2002 on antioxidant and pigment levels in the macula

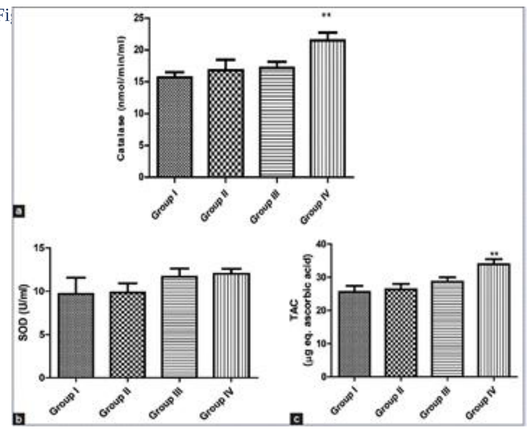
In a 2018 published study [6] XanMax® 2002 was evaluated for its modulatory effects on antioxidant enzymes and macular pigments in the serum and macula of rats. Male Swiss albino rats were treated with 0.514 mg/kg body weight twice daily (Group III), 1.028 mg/kg body weight twice daily (Group IV), and controls treated with carboxymethylcellulose (Group I) and 1.028 mg/kg bw sunflower oil (Group II). At the end of the 42-day test period, samples of serum and macula were collected for analysis for lutein and zeaxanthin, total antioxidant capacity (TAC), superoxide dismutase (SOD), and catalase activity (CAT). The lutein/zeaxanthin results are shown in Figure 1 below:

Fig



The results clearly demonstrate the dramatic increase in serum and macula lutein and zeaxanthin levels for the treatment with XanMax®, and the dose-response nature of the treatment. Serum lutein and zeaxanthin, and macular lutein increases were statistically significant (*** p<0.0001).

Fi



The results demonstrate significant elevations (** p<0.005) of CAT, TAC and SOD in serum for the treatment groups with XanMax®.

This study demonstrates that diet supplementation with XanMax® lutein and zeaxanthin helps maintain a healthy macula through increases in lutein and zeaxanthin in the macula and serum and increases in antioxidant activity.

Bioavailability of XanMax® 2002 compared with other lutein/zeaxanthin formulas in an animal model

In an unpublished 2019 animal study, bioavailability of XanMax® 2002 was compared with Optilut® 40% lutein ester oil (equivalent to 20% free lutein) and XanMax® 2004 lutein/zeaxanthin 20:4 oil. Bioavailability was determined by absorption of lutein in the serum of rats. All the formulations were using the same original source of lutein/zeaxanthin and dispersed in sunflower oil at similar lutein concentrations. Male Wistar rats were fasted overnight and then fed a single dose of lutein/zeaxanthin 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 for lutein. Zeaxanthin was not measured due to its low concentration in the blood. In the statistical analysis, the area under the curve (AUC) was used as the measure of relative bioavailability. Results are shown in Table I below.

Table I

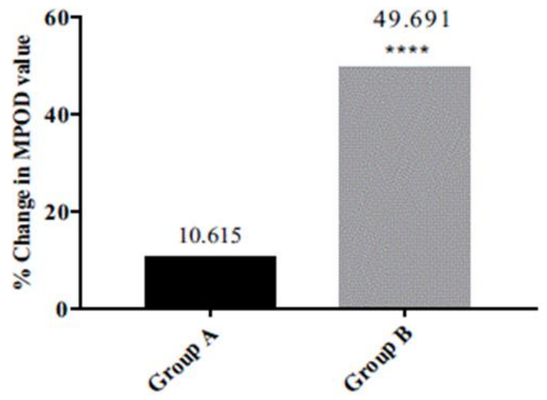
Formula	Lutein / zeaxanthin	Ave Cmax (ppb)	Tmax (hrs)	Average AUC
OptiLut® 40%	20:0	6.19	6	203.7
XanMax® 2002	20:2	5.78	6	201.0
XanMax® 2004	20:4	3.67	6	148.9

The results, although not statistically significant, demonstrate the dose-response where increasing the amount of zeaxanthin in the formula decreases the absorbability of lutein into the blood.

Human Clinical Study on XanMax® 2002 as measured by Macular Pigment Optical Density (MPOD)

A pilot human clinical was conducted in 2017 [7]. 60 healthy elderly volunteers with MPOD between 0.2 and 0.4 were given either 1 capsule placebo (Group A), or 1 capsule XanMax® 2002 (20 mg lutein/2 mg zeaxanthin) (Group B) once per day taken 30 minutes after a meal, for 180 days. The results are shown in Figure 3 for combined left and right eyes (separate left and right eye results similar).

Figure 3: Change in MPOD from first visit to last visit combined for both eyes (p<0.05)



The MPOD measurement results showed a statistically significant improvement in MPOD for the XanMax® group (A) vs. placebo (B). The average increase in macular optical density was 40%. The study also demonstrated the safety and tolerability of the product during the 6 months study. No adverse events were reported. Dilated fundus exams were performed on all subjects at each visit with no abnormalities observed, indicating the safe administration of these dietary nutrients.

DISCUSSION AND CONCLUSION

Discussion:

The animal studies demonstrated that XanMax® 2002 lutein/zeaxanthin was well absorbed into the blood and with increased macular deposits of lutein and zeaxanthin, and increased antioxidant potential. In the human study, these increases in macular levels of lutein and zeaxanthin were demonstrated to improve MPOD by 40%. The three studies, when integrated together, demonstrate that supplementing the diet with XanMax® 2002 lutein/zeaxanthin can be measured by absorption into the blood, deposition in the macular, and improvements in macular pigment optical density.

Conclusion:

Supplementation with XanMax® 2002 lutein/zeaxanthin is a safe and effective means to increase macular pigmentation, therefore demonstrating benefits for healthy aging and improved eye health.

REFERENCES

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

2. WidomskaJ, ZarebaM, SubczynskiWK. Can Xanthophyll-Membrane Interactions Explain Their Selective Presence in the Retina and Brain? Foods 2016;5(1)

3. https://www.nature.com/articles/eye201398

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

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

6. Pharmacognosy Magazine, Volume 14, Issue 54, April-June 2018, pp. 268-274

7. Study Protocol CTRI2016/10/007413 http://ctri.nic.in/Clinicaltrials/login.php

TRADEMARKS