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Bilberry Extract in Macular Pigment Density Improvement

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Abstract

Macular Pigments (MPs), by absorbing potentially toxic short-wavelength (400–500 nm) visible light, provide protection against photo-chemical damage. A new method of MPs levels screening analyzes polarization-dependent absorption of blue light by MPs, which results in the entoptic phenomenon called Haidinger's Brushes (HB). Subjects identify the direction of rotation of HB when presented with a circular stimulus illuminated with an even intensity of polarized white light in which the electric field vector was rotating either clockwise or anti-clockwise. The examination was performed at baseline and after 3 months of daily intake of 320 mg bilberry extract, from *Vaccinium myrtillus L.* and standardized to contain more than 36% of anthocyanins (anthocyanosides), in normal subjects and MPs improvement was recorded after 3 months of dietary supplements. The results suggest a challenging role of daily intake of 320 mg bilberry extract in macular pigment density improvement possibly due to a macular protection from oxidative damage by bilberry.

Keywords: Macular Pigment; Macula; Blue wavelength; Dietary supplementation; Bilberry extract; Polarized light

Introduction

Macular Pigments (MPs) are xanthophyll carotenoids of dietary origin. In nature, there are more than 600 carotenoids but only lutein, zeaxanthin and meso-zeaxanthin are present in the inner retina directly over the macula [1] in order to intercept the path of light before photoreceptors are involved in vision cycle. Thanks to their well-established antioxidant properties and their ability to decrease violet/blue wavelength impact on retina, MPs protect retina from oxidative damage [2]. Low levels of MPs have therefore been implicated in long-term accumulation of photochemical damage [3] and with increased likelihood of developing several macular diseases, such as Age-related Macular Degeneration (AMD) [4-10]. Smoking, light exposure and obesity [11-14] are known risk factors.

A method of assessing Macular Pigment Density (MPD) suitable for mass screening would be very useful to provide a valuable tool to understand the natural levels of protection; if low MPD is present, several precautions, light eye protection, smoking and obesity reduction, or supplementation of macular pigments with natural substances would be useful to prevent degeneration [11-13]. In particular, bilberry was traditionally utilized since the Middle Ages for its positive effects on ocular health by bolstering capillaries and improving eye blood circulation [15,16].

Several techniques have been developed to assess MPD in vivo [17] with different disadvantages. Recently, a new method of assessing MPD was proposed [5,18] that is based on the differential absorbance of polarized light by the MPs [19], which is central to the underlying mechanism responsible for the perception of the entoptic phenomenon known as Haidinger's Brushes (HB) [20-22]. This psychophysical approach uses the subjects' threshold for detecting Haidinger's brushes as the degree of polarization (DoP) is decreased to assess the total amount of MPs in the macula. The technique does not require pupil dilation and can be performed on anyone with normal vision without taking into consideration refractive errors/defects or accommodation. The technology required to deliver the test is relatively inexpensive and can be suitable even for both optometric and clinical use. Furthermore, the repeatability and time requirements for different testing protocols for measuring the degree of polarization threshold in both research and a clinical setting have been tested with excellent result. The primary aim of these observations was to evaluate if 3-months of a bilberry extract, standardized to containing 36% anthocyanosides, supplementation would increase the density of macular pigments in healthy subjects.

Methods

Population

30 healthy subjects (12 male and 18 female) aged 22–63 years, without any pathological eye condition were included

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as case reports. Subjects underwent MPD at baseline, before supplementation, and after 3 months supplementation. Following demographic page indications presented by MP-eye before starting the examination, several parameters were considered and ranked (see Results).

Exclusion criteria were: amblyopia, any ocular pathology or vitamin and/or minerals supplement intake. Endpoints: The primary outcome was the evolution of MPD after 3 months of bilberry supplementation assessed by a new instrument measuring the macular pigment density; the second endpoint was to evaluate the speed of identification of spinning bowtie appearance.

Apparatus

The MP-eye (www.azulOptics.com, Azul Optics 102 Hill View Henleaze Bristol, UK) is based on an exclusively new procedure to assess the density of macular pigments in the eye, based on an idea first introduced by Temple and colleagues [18] (Figure 1). The approach utilizes polarized light to create a visual effect inside the eye called Haidinger's brushes, which looks like a faint yellow bowtie figure (Figure 2). The effect is in fact a shadow on the retina created by the macular pigments absorbing the blue wavelengths from the white light source, leaving yellow light to reach the photoreceptors. The macular pigments absorb light when the polarization is aligned with the long axis of the pigment molecules, which are lutein, zeaxanthin and meso-zeaxanthin. Because macular pigments are attached at 90 degrees to the photoreceptor axons that exit the fovea like thspokes of a wheel, when the polarized light in the MP-eye rotates the yellow bowtie also rotates. The MP-eye decreases the percent of light that is polarized, thereby making it harder and harder to see the yellow bowtie (Figure 2) with each step. At first, the subject will see a faint yellow bowtie quite clearly but as it gets harder, the effect will become more difficult until they can just make out the direction of rotation by subtle wisps of movement. The test ends when the subject can no longer determine the direction of rotation; the last step they get correct is their threshold.

The parameters calculated by the MP-eye analysis were two: the score, where a higher score means a high presence of macular pigment, while a low score is due to a low presence of macular pigments; and the time measuring the speed of identification of the spinning Yellow bowtie: a shorter time represents a normal macular pigments presence, while longer time means low MDP.

Supplementation

All subjects received a daily intake of 320 mg (2 capsules of 160 mg each) for 3 months of a standardized bilberry *Vaccinium myrtillus* L. extract (Indena SpA, Italy), containing more than 36% of anthocyanins (anthocyanosides) by HPLC [16]. Before supplementation (Basal) and after 3 months supplementation, macular pigment density was analyzed by MP-eye.

Statistical Analysis

For each variable (score and time) the comparison was made between data obtained at the end of supplementation and data collected at basal time. Data were expressed as means ± Standard Error (SEM) of 30 subjects. D'Agostino-Pearson's test was utilized to assess normality, followed by a two-tail Wilcoxon test.

A possible relation with sex, age, smoke, physical activity, solar filter, BMI or dietary fruits and vegetables intake were analyzed by 2-way ANOVA with repeated measures.

Results

Demographic parameters of the subjects are summarized and scored in Table 1.

After 3 months of bilberry supplementation, significant differences in respect to the basal values were observed when score and time were analyzed. A significant, about 50% increase ($p<0.001$) in score after 3 months supplementation by bilberry was detected, together with a 45% reduction in time score (Figure 3).

However, no ocular morpho-functional characteristics were modified in relation to the parameters described in Table 1, i.e. sex, age, smoke, physical activity, solar filter use, BMI or dietary fruits and vegetables intake (data not shown).

Table 1: Demographic parameters.

Sex	
Male Female	12 18
Age range	22-63
BMI	
Normal weight Overweight	21 9
Smoking habit	
Never Frequent Ex-frequent	15 3 12
Dietary Fruit and vegetable intake	
Low	4
Medium	17
High	9
Exercise	
Never	11
Occasional	11
Frequent	8
Sunglasses wearing	
Never	5
Occasional	9
Frequent	16

Figure 1: MP-Eye Device Model (www.azulOptics.com, Azul Optics 102 Hill View Henleaze Bristol, UK).

Figure 2: Spinning Yellow bowtie figure presented by MP-Eye during examination.

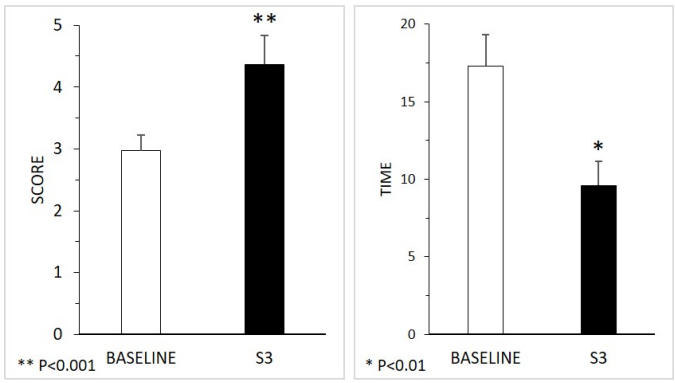

Figure 3: Score and time parameters at baseline and after 3 months Supplementation (S3).
Data are expressed as means ± SEM, n=30, *p<0.01 and **p<0.001 3-month supplementation (S3, black bars) vs baseline (white bars) by Wilcoxon t test.

All subjects completed 3 months of follow-up with no drop-outs, indicating the excellent tolerability of the supplementation and a good quality of life of participants, with follow-up visits consistently showing overall subjects well-being.

Discussion and Conclusion

The present study highlights the beneficial effects of a standardized bilberry extract supplementation on Macular Pigments (MPs) protection against photo-chemical damage, through MP density improvement. The clinical observation included a new method of MPs levels screening, by analyzing the polarization-dependent absorption of blue light by macular pigments, which results in the entoptic phenomenon called Haidinger's Brushes (HB).

The speed and simplicity of measurement of degree of polarization threshold utilized in the present study makes it well suited for large-scale screening of macular pigmentation. Indeed, the MP-eye use was very recently shown in a cross-sectional study involving 484 Indian subjects, confirming the effectiveness of that method to screen macular pigment density [23].

The bilberry extract supplemented in the present study previously proved beneficial activity on vascular health and ophthalmology [15,24] and it was produced by respecting the natural environment. Though, this bilberry extraction process used biodegradable and eco-compatible solvents, instead of other more hazardous organic and toxic solvents frequently utilized. Moreover, the bilberry extract was verified by on-site DNA plant analysis (Hyris Ltd), in order to assure high quality and avoid any adulteration issues. Metabolomic analysis of that extract highlighted its unicity in respect to other natural bilberry extracts [25].

Results obtained showed that the daily intake of 320 mg bilberry extract has great potential in improving macular health, confirming the activities reported in literature, where beneficial effects on ocular vascular circulation was shown to improve oxygen and blood delivery to the eye [24,26]. Bilberry extracts also exerted positive effects on accomodation [27], on preventing eye aging for its antioxidant properties [28]. Previous favorable effects on vascular circulation and glycemic levels in diabetic models were reported [26,29,30] by bilberry supplementation.

Our study may have several limitations in common with other trials, i.e., the small number of subjects, or the lack of a well-defined and widely accepted protocol of macular pigments evaluation, and a control group. Despite these issues, the present study suggests a clear improvement of macular pigment in a otherwise healthy population after a 3-month supplementation of a standardized bilberry extract.

Overall, we consider our findings promising and worthy of investigation in a future placebo-controlled study involving a larger number of subjects.

Author Statements

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