The effect of anthocyanosides on night vision

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CLINICAL STUDY

Abstract

Purpose **In view of research demonstrating the ability of anthocyanosides in a single oral dose to improve night vision in normal individuals, it was decided to evaluate their effect on three night vision tests: full-field scotopic retinal threshold (SRT), dark adaptation rate (DAR) and mesopic contrast sensitivity (MCS).**
Methods **In a double-masked, placebo-controlled, cross-over study, 16 young normal volunteers were randomly assigned to one of four different regimens of single oral administrations of 12, 24 and 36 mg of anthocyanosides, and a placebo, with a 2 week washout period between doses. SRT, DAR and MCS were measured immediately before, and 4, 8 and 24 h after treatment.**
Results **No significant effect was found on any of the three night vision tests during the 24 h following a single oral administration of 12, 24 or 36 mg anthocyanosides. The study had a power of 0.95 to detect a 0.1 log unit improvement in SRT and 0.5 log unit improvement in MCS.**
Conclusions **Single oral administration of 12–36 mg of anthocyanosides appears to lack significant effect on militarily relevant night vision tests.**

Key words Anthocyanosides, Dark adaptation rate, Mesopic contrast sensitivity, Night vision, Scotopic retinal threshold

Anthocyanosides are water-soluble pigments that appear in nature predominantly as glycosides. The richest source is the blueberry plant (*Vaccinium myrtillus*). Compounds extracted from blueberries that contain predominantly anthocyanosides were reported to improve night vision functions in human subjects even after a single oral administration.[1–3]

We undertook to determine the effect of single doses of oral anthocyanosides on full-field absolute scotopic retinal threshold (SRT), full-field dark adaptation rate (DAR) and mesopic contrast sensitivity (MCS) in human subjects. SRT, DAR and MCS were chosen for a number of reasons. Standard visual acuity testing using a high-contrast chart with Sloan letters does not always predict how well observers will see a target in an operational setting.[4] Especially under scotopic conditions, contrast sensitivity proved to be a more reliable measure of visual performance than visual acuity. Scotopic contrast sensitivity can predict the ability of pilots to detect a small, semi-isolated, air-to-ground target in a visual flight simulator.[4] We recently found SRT, DAR and MCS to be directly related to the ability to identify field targets at night.[5] It appeared, therefore, that a combination of these tests could reliably predict global night vision capability. To the best of our knowledge, there is no published double-masked placebo-controlled, cross-over study on the effects of single oral administration of different doses of anthocyanosides on night vision tests.

Subjects and methods

Subjects were 16 healthy male volunteers, 21–28 years of age (mean 25 ± 1.8 years), who had a best corrected mesopic (1 foot-lambert) visual acuity of 20/25 or better (mean 20/22.5 ± 2.5). Thirteen subjects were emmetropic, and 3 had ametropia with −2.25 D to +2 D, the greatest cylinder being 1.25 D in one case.

After their informed consent had been obtained (approved by the Tel Aviv University Helsinki Committee), subjects were randomly assigned to one of four groups. Each group was given a different regimen of single oral administrations of 12, 24 and 36 mg of anthocyanosides, and a placebo, as detailed in Table 1. A 2 week washout period intervened between doses.

The double-masked, placebo-controlled, cross-over study was carried out in the summer (August–September 1995). MCS, DAR and SRT were tested in that order immediately before drug administration (between 09:00 and 10:00), and 4, 8 and 24 h thereafter. Tablets of Strix, which are freely available as a health food supplement (Halsoprodukter, Forserum, Sweden), containing 12 mg anthocyanosides (blueberry extract) and 2 mg beta-carotene, and placebo tablets (CTS, Israel) were used. Each consumption of Strix or placebo was visually

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Table 1. *Treatment regimens of anthocyanosides (12, 24 or 36 mg) and placebo*

Group	Week 0	Week 2	Week 4	Week 6
1 (n = 4)	12 mg	24 mg	36 mg	Placebo
2 (n = 4)	24 mg	36 mg	Placebo	12 mg
3 (n = 4)	36 mg	Placebo	12 mg	24 mg
4 (n = 4)	Placebo	12 mg	24 mg	36 mg

confirmed by one of us (Y.L.). Blood or urine drug levels were not evaluated.

MCS was measured with the MCT 8000 (Vistech Consultants, Dayton, OH), which consists of circular patches of sine-wave gratings varying in spatial frequency, contrast and orientation. Each target has seven circular discs, each one with a sine-wave grating of a fixed spatial frequency. The gratings are vertical or tilted 15° to the right or left, and the contrast of the gratings progressively decreases from disc 1 to 7. The contrast sensitivity score is the last consecutive disc whose orientation is correctly identified (using a spatial three-alternative forced choice method).[6] The spatial frequencies displayed are 1.5, 3, 6, 12 and 18 cycles/degree (cpd). MCS was measured in the right eye of each subject using a mesopic background luminance of 1 foot-lambert with corrections for distance worn as needed.

SRT and DAR were measured binocularly following bleaching for 5 min (3000 asb). A Goldmann-Weekers dark adaptometer (Haag-Streit, Bern, Switzerland) was employed, which presents flickering (0.5 Hz), diffuse, white-light, ganzfeld stimuli.[7] The instrument was calibrated for stimulus illuminance and bleaching luminance before each session. No fixation light was used for retinal sensitivity measurements; the subject was instructed to look straight ahead into the centre of the bowl as the luminance of the whole-field flickering stimulus was increased progressively at a fixed rate until detected. Following a response, the luminance was reduced to its lowest level and retinal sensitivity determined two more times. The DAR score was the average of three consecutive measurements of retinal threshold at 10 min after dark adaptation. SRT was determined in the same way, after 30 min of dark adaptation.

Data were stored and processed by the SAS statistical package for personal computers.[8] Spearman rank correlations were used to evaluate the net correlations between repeated test results. The general linear models procedure (within-subject repeated measures analysis of variance, ANOVA) was used to compare the effect of the various doses of anthocyanosides.

Table 2. *Mean full-field scotopic retinal threshold (SRT) values (log units ± SD) after 30 min of dark adaptation* (n = 16)

	Anthocyanosides			
Time (h)	12 mg	24 mg	36 mg	Placebo
0	1.85 ± 0.28	1.85 ± 0.27	1.8 ± 0.26	1.8 ± 0.26
4	1.88 ± 0.22	1.86 ± 0.26	1.84 ± 0.27	1.8 ± 0.27
8	1.86 ± 0.29	1.78 ± 0.28	1.8 ± 0.24	1.77 ± 0.24
24	1.83 ± 0.25	1.77 ± 0.28	1.8 ± 0.28	1.73 ± 0.30

Table 3. *Mean dark adaptation rate (DAR) values (log units ± SD) after 10 min of dark adaptation* (n = 16)

	Anthocyanosides			
Time (h)	12 mg	24 mg	36 mg	Placebo
0	2.92 ± 0.26	2.95 ± 0.19	2.9 ± 0.19	2.85 ± 0.27
4	2.92 ± 0.23	2.94 ± 0.19	2.93 ± 0.22	2.88 ± 0.24
8	2.93 ± 0.23	2.86 ± 0.23	2.92 ± 0.28	2.83 ± 0.26
24	2.86 ± 0.27	2.89 ± 0.21	2.95 ± 0.19	2.82 ± 0.32

Results

There were no significant differences in the mean SRT (Table 2) or DAR (Table 3) values between the anthocyanoside-treated groups and the control group during the 24 h following drug administration (within-subject repeated measures ANOVA). Nor were there significant differences in the mean values of MCS (average of 1.5, 3, 6 and 12 cpd) (Table 4) between the anthocyanoside-treated groups and the control group during the 24 h after drug administration (within-subject repeated measures ANOVA). Similar results (data not shown) were obtained for each of the 4 cpd rates of MCS: 1.5, 3, 6 and 12 cpd.

The study had a power of 0.95 to detect a 0.1 log unit improvement in SRT and 0.5 log unit improvement in MCS.[9]

Discussion

The rumour that French and British pilots in World War II ate blueberry jellies or jams to improve their ability to see during night operations probably initiated the development and marketing of pharmacological preparations of extracts of *Vaccinium myrtillus* following the war. Several scientific publications in the 1960s and early 1970s reported improvement of night vision functions after a single oral administration of anthocyanosides.[1,10,11] This dosage improved scotopic and mesopic retinal sensitivity in normal human volunteers for a few hours; the effect disappeared after 24 h.[1] The tests that were used, namely absolute scotopic threshold and dark adaptation rate, are similar to those we used in our study. Adaptoelectroretinographic studies demonstrated improved dark adaptation rate in humans 1.5 h after single oral administration of anthocyanosides.[10] Similar results in humans were observed after single sublingual administration of anthocyanosides.[11]

The ability to improve night vision functions of normal persons with anthocyanosides is attractive in

Table 4. *Mean values (log units ± SD) of mesopic contrast sensitivity (MCS): average of 1.5, 3, 6 and 12 cpd* (n = 16)

	Anthocyanosides			
Time (h)	12 mg	24 mg	36 mg	Placebo
0	5.2 ± 0.67	5.17 ± 0.79	4.9 ± 0.79	5.12 ± 0.6
4	5.2 ± 0.64	5.02 ± 0.69	5.1 ± 0.77	5.05 ± 0.69
8	5.2 ± 0.86	5.2 ± 0.54	5.22 ± 0.74	5.6 ± 0.62
24	5.2 ± 0.68	5.3 ± 0.76	5.37 ± 0.85	5.22 ± 0.79

view of the many complaints of difficulty driving or walking at night in subjects with no ocular disease. In the present study we found no effect of single-dose anthocyanosides on any of the three night vision tests previously found by us to be good predictors of actual night performance.[5]

Our findings contrast with those of studies carried out 20–30 years ago,[1,10,11] probably because of differences in study design and populations. Our double-masked, placebo-controlled, cross-over study enabled more accurate evaluation of the parameters being tested. Moreover, anthocyanosides might have had no effect on the young subjects in our study who had excellent night vision, while they may improve the scores in individuals with low or moderate night vision ability. The discrepancy in results could also be due to differences in extracts of blueberries from different parts of the world, which might contain unequal amounts of active ingredients other than anthocyanosides.

The exact biochemical influence of anthocyanosides on the neurosensory retina is not known. It has been speculated that anthocyanosides accelerate the resynthesis of rhodopsin,[11] and modulate retinal enzymatic activity[12] – mechanisms that may require longer administration to produce a measurable effect. Further study is required to evaluate the effect of anthocyanosides on night vision: various doses of the compound should be tested for several days to weeks in subjects with moderate to low night vision ability.

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