The Effect of Bilberry Nutritional Supplementation on Night Visual Acuity and Contrast Sensitivity

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Abstract

PURPOSE: The purpose of this study was to investigate the effect of bilberry on night visual acuity (VA) and night contrast sensitivity (CS). METHODS: This study utilized a double-blind, placebo-controlled, crossover design. The subjects were young males with good vision; eight received placebo and seven received active capsules for three weeks. Active capsules contained 160 mg of bilberry extract (25-percent anthocyanosides), and the placebo capsules contained only inactive ingredients. Subjects ingested one active or placebo capsule three times daily for 21 days. After the three-week treatment period, a one-month washout period was employed to allow any effect of bilberry on night vision to dissipate. In the second three-week treatment period, the eight subjects who first received placebo were given active capsules, and the seven who first received active capsules were given placebo. Night VA and night CS was tested throughout the three-month experiment. RESULTS: There was no difference in night VA during any of the measurement periods when examining the average night VA or the last night VA measurement during active and placebo treatments. In addition, there was no difference in night CS during any of the measurement periods when examining the average night CS or the last night CS measurement during active and placebo treatments. CONCLUSION: The current study failed to find an effect of bilberry on night VA or night CS for a high dose of bilberry taken for a significant duration. Hence, the current study casts doubt on the proposition that bilberry supplementation, in the forms currently available and in the doses recommended, is an effective treatment for the improvement of night vision in this population.

(*Altern Med Rev* 2000;5(2):164 -173)

Introduction

Bilberry,*Vaccinium myrtillus*, a berry related to the blueberry, grows on a shrubby plant in Europe. It is similar to one of many varieties of North American huckleberries. Europeans have used the bilberry fruit for many years to make jams and jellies. The notion that bilberry can be used to enhance night vision arose from anecdotal reports of British Royal Air Force (RAF) aviators in World War II eating bilberry jam to improve their night vision.[1] A number of European studies have

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reportedly shown an improvement in night vision with a variety of bilberry supplements.[2-6] Although bilberry is widely available as a nutritional supplement in the United States, there are very few scientific references for bilberry research available in English.

The therapeutic properties of bilberry are attributed to the presence of anthocyanosides, a class of water-soluble chemicals (anthocyanin glucosides) belonging to a larger class of substances known as plant bioflavonoids. Pharmacologically, anthocyanosides are thought to have a stabilizing effect on collagen, prevent capillary fragility, and improve microcirculation.[7,8] They are also thought to have antioxidant activity.[7,8] Aside from its purported role in improving night vision, bilberry has been used to help in the treatment of glaucoma, cataracts, retinopathy, diabetes mellitus, and arthritis.[8] The *Physician's Desk Reference (PDR) for Herbal Medicine, Facts and Comparisons' The Review of Natural Products*, and the *The Complete German Commission E Monograph: Therapeutic Guide to Herbal Medicines* all list diarrhea and inflammation of the mouth and throat as indications for the use of bilberry, but none lists impaired night vision as an indication.[9-11]

The concentration of anthocyanosides in raw bilberry fruit is estimated to be 0.1- 0.25 percent by weight, while concentrated bilberry extracts can contain 25-percent anthocyanosides.[8] The current study selected the concentration of anthocyanosides in most bilberry preparations currently on the market. *A Textbook of Natural Medicine* listed a normal dosage range of 80-160 mg of a standardized bilberry extract containing 25-percent anthocyanosides, taken three times daily.[8] The current study chose to use the maximum recommended dose of 480 mg daily of the 25-percent extract to maximize the likelihood of observing a measurable improvement in night vision. Hence, the final protocol in the current study called for three capsules daily, each containing 160 mg bilberry extract with 25-percent anthocyanosides. This is the equivalent of eating approximately 1/3 cup of raw bilberries daily.

The treatment time for the onset of an observable therapeutic effect is not well defined in the literature. Anecdotal reports of the RAF aviators indicated an improvement in night vision less than 24 hours after ingesting an unknown quantity of bilberry jam. One French study[2] examined the effects of bilberry on light sensitivity threshold, administering two 100 mg tablets of bilberry extract four hours before an experiment and another two tablets (four total) 1.5 hours before the experiment. Another study by the same investigators examined the effects of bilberry on light sensitivity threshold, administering four 100 mg tablets daily for eight days.[3] Both studies reported positive results.[2,3] A more recent investigation examined the effects of bilberry on whole field scotopic retinal threshold, mesopic contrast sensitivity, and dark adaptation rate, administering dosages of either 24 mg or 48 mg of anthocyanosides daily for four days and found no effect on night vision testing.[12] These dosages are equivalent to 96 mg or 192 mg of the bilberry extract used in the current study. Based on previous positive results, the amount of bilberry extract taken daily in the current study (480 mg) would be expected to show a measurable improvement in night vision within days and certainly within two weeks of treatment. Due to the uncertainty of time to measurable improvement, a supplementation period of 21 days was chosen for the current study, with testing throughout the dosage period.

The night vision tests used by previous investigators studying the effects of bilberry supplementation have included scotopic light thresholds, electroretinograms (ERGs), changes in the dark adaptation rate, scotopic perimetry, and mesopic contrast sensitivity.[2-5,12] A number of these tests are used in the research community, but most of them are time consuming, require expensive laboratory equipment, are difficult to administer correctly, and may even require patient/subject training to obtain valid measurements.

The current study utilized two tests: night visual acuity (VA) and night contrast sensitivity (CS). Visual acuity was selected partly because it has been an accepted vision standard for clinical and legal purposes for many years. A previous study conducted at this laboratory has also shown VA is related to nighttime performance: "Visual acuity can be used to accurately predict performance in a marksmanship task at low light levels."[13] Since one of the goals of this study was to investigate the possible enhancement of night vision relevant to military operations, the demonstrated correlation between night VA and marksmanship was considered significant. A modified version of contrast sensitivity testing was also selected to evaluate a secondary component of night vision believed to provide additional information about visual function more relevant to "real-world" targets, which are often not of the high contrast level typical of standard VA charts.[14]

Figure 1: Study Design Timeline

Session	Pre-trt	Treatment1			Washout				Treatment 2			Post treatment			
Week	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15

Methods

Subjects:

Subjects were 15 males (age range 25 to 47 years) recruited from personnel working at Naval Air Station Pensacola, Florida. Only male subjects were recruited because the data were collected from the Navy SEAL community, which currently only utilizes male personnel. All subjects had visual acuity correctable to 20/20 or better. All subjects were given a thorough explanation of the study, and they reviewed and signed an informed consent form that was approved by Protection of Human Subjects Committees at the Naval Aerospace Medical Research Laboratory and the Naval Medical Research and Development Command.

Experimental Design:

This study was a double-blind, placebo-controlled, crossover. Eight subjects received placebo and seven received active capsules for three weeks. Subjects ingested one active or placebo capsule three times daily for the 21-day period. Analysis of the active treatment by an independent laboratory (Thorne Research, Dover, ID) verified that the active capsules contained 160 mg bilberry extract of which 25 percent were anthocyanosides, and that the placebo capsule contained only inactive ingredients (magnesium aspartate and coloring). The active and placebo capsules were identical in appearance. The capsules were dispensed in seven-day "Pill Minder" dispensers to make it easier for subjects to remember to take them. One week's dosage was distributed at a time. Monitoring pill count helped ensure compliance with the dosage protocol. After the three-week treatment period, a one-month washout period occurred to allow any effect of bilberry on night vision to dissipate. In the second three-week treatment period, the eight subjects who first received placebo were given active capsules. The seven subjects who first received active capsules were then given placebo (see Figure 1).

During week 1 of the study (Pretreatment), subjects had one daylight VA measure taken and three pretreatment night VA and night CS measurements taken. Subjects then began

Table 1: Sizes of the Landolt Cs used for night visual acuity testing. Sizes given in log minimum angle of resolution (MAR) units with the Snellen equivalent and diameter of the letter in millimeters. (The size of the opening in the C is 1/5 of the diameter.)

log MAR	Snellen	Letter Size (mm)
-0.6	20/05	2.2
-0.5	20/06	2.8
-0.4	20/08	3.5
-0.3	20/10	4.5
-0.2	20/13	5.6
-0.1	20/15	7.1
0	20/20	8.9
0.1	20/25	11.2
0.2	20/32	14.1
0.3	20/40	17.7
0.4	20/50	22.3
0.5	20/63	28.1
0.6	20/80	35.5
0.7	20/100	44.5
0.8	20/126	56.0
0.9	20/159	70.5
1.0	20/200	88.7
1.1	20/252	111.7
1.2	20/317	140.6
1.3	20/399	177.0

either the bilberry or placebo treatment for 21 days (Treatment 1). During Treatment 1, subjects had their night VA and night CS measured at the following intervals: twice during week 2 (once between 24-36 hours and once between days 4-6), once during week 3 (between days 12-14), and once during week 4 (between days 19-21). Subjects then had a four-week washout period (weeks 5-8) with night VA and night CS measurements taken once each week (washout). Subjects then began the second treatment phase (Treatment 2, weeks 9-11), following the same testing intervals as Treatment 1 with the subjects receiving the opposite treatment from Treatment 1. Following Treatment 2, subjects had a four-week (weeks 12-15) post-treatment phase with visual measurements taken once weekly.

Testing Protocol:

Testing took place in a light-proof room. With the exception of the pretreatment daylight VA measurement, the light level used for this project was in the scotopic region, below cone threshold. This light level has been shown to be relevant to night marksmanship while enhancing the ability to detect differences between individuals.[13] The light source used, the Hoffman Night Sky Projector (Hoffman Engineering, model # LM-33-80A, Stamford, CT), was capable of providing four different representative night-sky conditions, based on work done by the Army Night Vision Lab, Fort Belvoir, Virginia.[15] For the current study, testing was conducted at the "full moonlight" setting, resulting in a target luminance of 0.005 candelas/meter^2 (cd/m^2). Subjects were dark-adapted in complete darkness for a minimum of 30 minutes. Order of testing was always night VA first and night CS second.

Visual acuity was tested with individual Landolt C targets, where the size of the opening in the C and the thickness of the letter corresponded to the size of the spaces and bars in the more familiar Snellen letter E.[16] The Landolt C targets used in this study were computer-generated black letters on a white background, sized in 0.1-log minimum angle of resolution (MAR) steps. The minimum angle of resolution was measured in minutes of arc, and can be compared to a Snellen letter E where the spaces and bars of the E are similarly specified in minutes of arc. For example, the spaces and bars on a 20/20 Snellen E each have a visual angle of 1 minute of arc, making 20/20 VA equal to a log MAR of zero (log 1 = 0). A Snellen 20/

200 letter with spaces and bars subtending 10 minutes of arc is equivalent to a log MAR of one (log 10 = 1). A set of Landolt C targets corresponding to the sizes in Table 1 was used in testing.

Individual Landolt C targets were presented at a distance of 20 feet with the opening of the C facing one of eight possible directions (using a clock analogy the positions were: 3:00, 6:00, 9:00, 12:00, 1:30, 4:30, 7:30, and 10:30). The order of presentation for the different orientations was randomized. Targets were presented in a large-to-small size sequence, with three correct responses (out of a maximum of five tries) required for a given letter size to be considered identified before presenting the next smaller size. Three incorrect responses for a given letter size ended the test, with the next larger letter size deemed to be the final score.

Night contrast sensitivity was tested under the same conditions used for the night VA testing. As with the Army Small Letter Contrast Test,[17] the size of the target did not change, but the contrast between the target and the background was decreased in steps of 0.1 log units. Contrast was calculated with the formula: C = Lmax – Lmin/Lmax + Lmin, where Lmax = background luminance and Lmin = target letter luminance. With this formula, the range of possible contrasts extends from 0 = 0% to 1 = 100%.[16] Contrast sensitivity is the reciprocal of the contrast: CS = 1/C. A series of 1.3 log MAR (20/399) Landolt C targets were used with the contrast levels found in Table 2. Similar to the night VA testing protocol, three correct responses were required for a given letter contrast to be considered identified before presenting the next letter of decreased contrast. Three incorrect responses for a given contrast were required to end the test, with the next higher contrast (smaller CS) deemed to be the final test measurement.

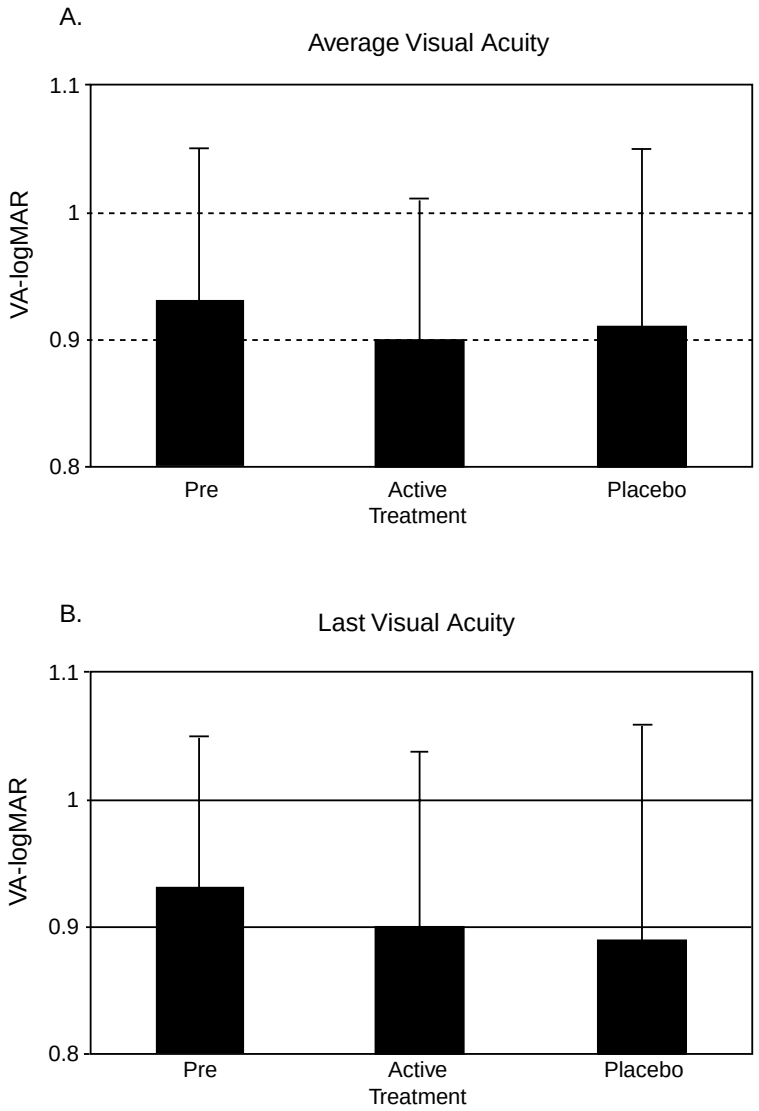
Statistical Analyses:

The baseline night VA and night CS were calculated by taking the median of the three pretreatment measurements. The average night VA and night CS measurements were calculated for each subject for the active and placebo treatments. In addition, the last night VA and night CS measurements taken during the active and placebo treatments were examined for each subject. Four repeated-measures analyses of variance were performed, comparing pretreatment measurements with those obtained in active- and placebo-treatment phases using: (1) average night VA; (2) average night CS; (3) last night VA; and (4) last night CS. In addition to the above parametric analyses, a nonparametric approach was taken for both the average data and the last measurement data. In this approach, each subject was placed into one of four categories: im-

Table 2: Contrast levels for the Cs used for contrast sensitivity testing. The size of the C was held constant at 1.3 log MAR (Snellen 20/399, 177mm). Contrast increments were made in tenth log contrast sensitivity steps. Contrast was calculated with the formula: C=Lmax - Lmin/Lmax + Lmin, where Lmax = background luminance and Lmin = target letter luminance. Contrast sensitivity is the reciprocal of the contrast: CS = 1/C.

Contrast	CS	log CS
0.79	1.26	0.1
0.63	1.58	0.2
0.50	2.00	0.3
0.40	2.51	0.4
0.32	3.16	0.5
0.25	3.98	0.6
0.20	5.01	0.7
0.16	6.31	0.8
0.13	7.94	0.9
0.10	10.00	1.0
0.08	12.66	1.1
0.06	16.67	1.2
0.05	20.00	1.3

Figure 2: Result for average (A) and last (B) visual acuity measurements for the active and placebo treatments. Individual pretreatment values were the median of the three pretreatment measurements. All values shown are group means plus one standard deviation.



provement on both active and placebo treatment, no improvement on either active or placebo treatment, improvement on active treatment only, improvement on placebo treatment only. A McNemar's test was performed on these data. For the active treatment to be more effective than placebo, the count needed to be high in the active-only category and low in the placebo-only category. The other two categories did not directly affect the analysis.

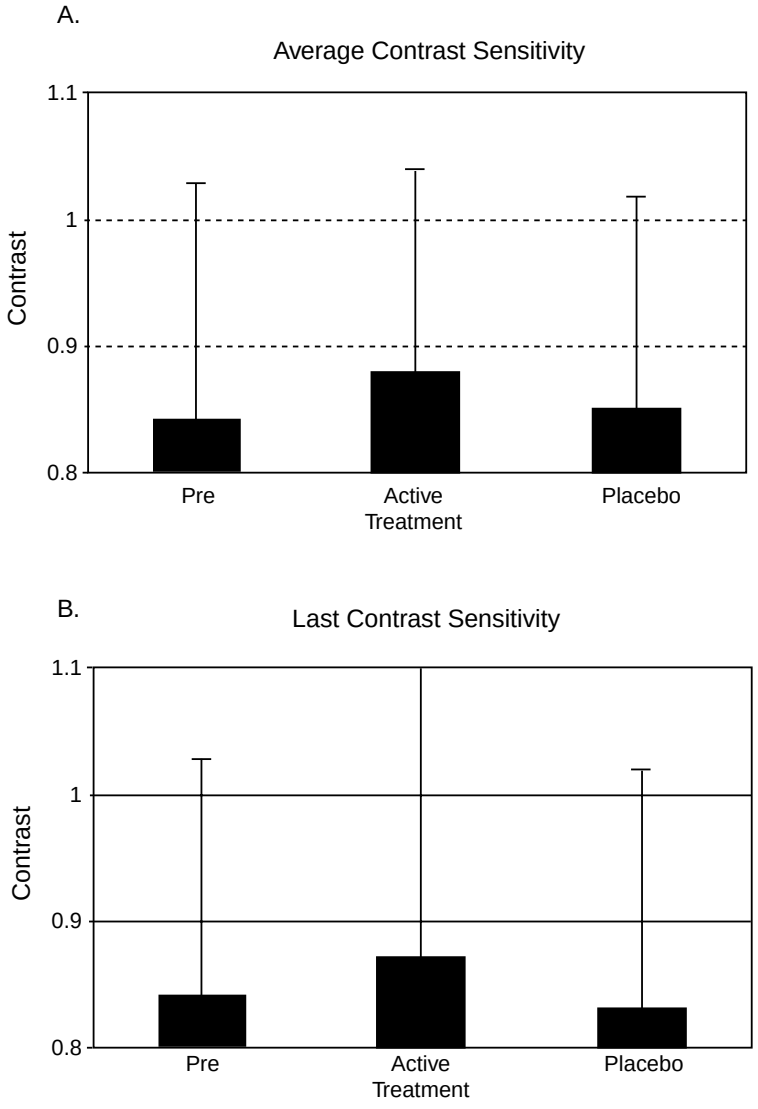
Results

As can be seen in Figure 2A, there were no differences in night VA during any of the measurement periods when examining the average night VA during active treatment and the average night VA during placebo ($F[2/28] = 1.8$, $p > 0.15$). Likewise as seen in Figure 2B, examination of the last night VA measurement during active treatment and the last night VA measurement during placebo did not reveal any differences in night VA ($F[2/28] = 0.7$, $p > 0.50$).

As seen in Figure 3A, there were no differences in night CS during any of the measurement periods when comparing the average night CS during active treatment with the average night CS during placebo ($F[2/28] = 1.0$, $p > 0.35$). Likewise, as seen in Figure 3B, examining the last night CS measurement during active treatment and the last night CS measurement during the placebo treatment did not reveal any difference in night CS ($F[2/28] = 0.8$, $p > 0.45$).

Nonparametric analyses confirmed the lack of difference between the active and placebo treatments. For the active treatment to be more effective than the placebo, there must be significantly higher numbers in the "improvement on active-only" category compared to the "improvement on placebo-only category." As can be seen in Tables 3 and 4, the number of improvements on active compared to placebo was not significantly higher for night VA. In fact, for the last night VA measurement,

Figure 3: Result for average (A) and last (B) contrast sensitivity acuity measurements for the active and placebo treatments. Individual pretreatment values were the median of the three pretreatment measurements. All values shown are group means plus one standard deviation.



the outcome was in the opposite direction from that expected. Results for night CS were similar (see Tables 5 and 6).

Discussion

This study failed to reveal a significant effect of bilberry treatment on either night visual acuity or night contrast sensitivity. One could argue that using the *average* night VA and night CS measurements from the active treatment period serves to hide the effect of the bilberry, since such an effect might be minimal in the early part of the treatment period. However, by comparing the *last* night VA and night CS measurements while on active treatment to the *last* night VA and night CS measurements on placebo, this concern is addressed. The last night VA and night CS measurements were taken after three weeks on active- or three weeks on placebo-treatment. Any effect of bilberry on VA or CS should have been detectable by that point. A French study found five of 14 subjects had significant improvement in their scotopic light thresholds after eight days of bilberry supplementation. The authors noted that all five subjects showing improvement had poor night vision initially and seemed to have improved to the level of the others after eight days of bilberry supplementation.[3]

A possible criticism of the present study could be the limited subject population: i.e., young males with good vision, although two of the subjects had below-average night VA and night CS in pretreatment testing. An examination of these two subjects, however, found no measurable change in either the bilberry- or placebo-treatment phases.

Most of the published investigations finding bilberry improved night vision were European studies conducted in the 1960s and 1970s

Table 3: Number of individuals showing an improvement/no improvement in average visual acuity while on either active or placebo treatment compared to baseline. McNemar's test results were not significant, x^2 = 0.80, critical value = 3.841.

Average Visual Acuity

Bilberry \ Placebo	Improvement	No Improvement
Improvement	8	**4**
No Improvement	**1**	2

8 subjects improved on bilberry and placebo; 4 improved on bilberry but not placebo; 1 improved on placebo but not bilberry; and 2 experienced no improvement on either protocol.

Table 4: Number of individuals showing an improvement/no improvement in visual acuity on the last day measured while on either active or placebo treatment compared to baseline. McNemar's rest results were not significant, x^2 = 0.13, critical value = 3.841.

Last Day Visual Acuity

Bilberry \ Placebo	Improvement	No Improvement
Improvement	3	**3**
No Improvement	**5**	4

3 subjects improved on bilberry and placebo; 3 improved on bilberry but not placebo; 5 improved on placebo but not bilberry; and 4 experienced no improvement on either protocol.

Table 5: Number of individuals showing an improvement/no improvement in average contrast sensitivity while on either active or placebo treatment compared to baseline. McNemar's test results were not significant, $x^2 = 0.80$, critical value = 3.841.

Average Contrast Sensitivity

Bilberry \ Placebo	Improvement	No Improvement
Improvement	6	**4**
No Improvement	**1**	4

6 subjects improved on bilberry and placebo; 4 improved on bilberry but not placebo; 1 improved on placebo but not bilberry; and 4 experienced no improvement on either protocol.

(see references). There has been very little scientific literature on bilberry published in the United States. This may be due to the fact that preparations like bilberry, or other herbal medicines, are not regulated by the U.S. Food and Drug Administration (FDA), may not be patentable like pharmaceutical medicines, and consequently, may not attract financial interest for research. However, in Europe, the German Federal Institute for Drugs and Medical Devices established an expert committee, the Commission E, in 1978 to evaluate the safety and efficacy of many herbs and herbal combinations. The published monographs of the Commission E have recently been translated into English and have been made widely available in the United States.[11] The Commission E does not mention night vision improvement as a use for bilberry. In the United States, both the *Physician's Desk Reference (PDR)* and the similar drug reference, *Drug Facts and Comparisons*, have published natural medicine editions.[9,10] Neither publication mentions night vision improvement in their entries for bilberry.

The 1997 Israeli investigation of bilberry and night vision also reported negative results.[12] Although the investigators used a lower dose of bilberry extract for a shorter period of time, the study was in many ways similar to the current study, i.e., it was a double-blind, placebo-controlled, crossover study with 18 subjects. The current study failed to find any effect of bilberry on night visual acuity or night contrast sensitivity using a high dose of bilberry taken for a significant duration. Hence, the current study casts additional doubt that bilberry supplementation, in the forms currently available and in the doses recommended, is an effective treatment for the improvement of night vision in a population of people with good vision and primarily normal night vision.

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Table 6: Number of individuals showing an improvement/no improvement in average contrast sensitivity while on either active or placebo treatment compared to baseline. McNemar's test results were not significant, x^2 = 0.17, critical value = 3.841.

Last Day Contrast Sensitivity

Bilberry	Placebo: Improvement	Placebo: No Improvement
Improvement	3	**4**
No Improvement	**2**	6

3 subjects improved on bilberry and placebo; 4 improved on bilberry but not placebo; 2 improved on placebo but not bilberry; and 6 experienced no improvement on either protocol.

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