Nor. Afr. J. Food Nutr. Res. 2021; 5(12): 130-138

https://doi.org/10.51745/najfnr.5.12.130-138

https://www.najfnr.com

ORIGINAL ARTICLE

Beetroot juice: effects on blood pressure, intraocular pressure, and ocular vessel density in healthy adults

Brian Randolph, Patricia M. Cisarik *

1 Southern College of Optometry (1245 Madison Avenue, Memphis, Tennessee 38104, United States of America)

Abstract

Background: The blood pressure (BP)-lowering effect of beetroot is attributed to its high nitrate concentration, which converts to the vasodilator nitric oxide. Nitric oxide may also mediate ocular aqueous outflow to regulate intraocular pressure (IOP). **Aims:** We investigated the effect of beetroot juice on IOP and ocular vessel density. **Subjects and Methods:** With a single-blind, crossover design, 19 healthy young adults participated on 2 days 1 week apart. On Visit 1, baseline IOP, BP, and ocular vessel density (optical coherence tomography angiography, disc, and macula) were measured. Three hours after consumption of 16 ounces of beetroot juice or water (randomly assigned), all measurements were repeated. On Visit 2, baseline and 3-hour post-consumption measurements were assessed, with each subject consuming the drink not ingested on Visit 1. **Results:** Paired-samples t-test showed 1) no difference in IOP change post-water vs post-beet root juice (P = 0.27), and 2) mean systolic and diastolic BPs were lower only post-beet root juice (systolic: -4.8 (SEM ± 2.1) mm Hg, P = 0.032, 95% CI (0.47, 9.11); diastolic: -6.2 (SEM± 1.4) mm Hg, P <0.001, 95% CI (3.27, 9.15)). Superficial vessel density was significantly lower in several macular regions post-beet root juice, but not post-water (Wilcoxon signed ranks test, immediately superior, inferior, and temporal to center; respective P values of 0.016, 0.035, and 0.046). **Conclusions:** Beetroot juice lowers BP and macular vessel density, but does not lower IOP in young, healthy adults. Further investigation into its effect on IOP and vessel density in glaucomatous eyes is warranted.

Keywords: beetroot, blood pressure, intraocular pressure, vessel density.

Received: August 19, 2021 / Accepted: December 19, 2021 / Published: December 29, 2021

1 Introduction

Beetroot (*Beta vulgaris*) recently has attracted significant attention from the "superfood" movement for its touted health benefits, from lowering blood pressure (BP) to improved athletic performance [1]. These effects are attributed to beet root's high inorganic nitrate content, although beetroot also contains anti-inflammatory betalains and other phytonutrients [1]. Beetroot has been studied as a potential adjunct treatment for many systemic conditions associated with elevated BP, endothelial dysfunction, inflammation, and oxidative stress, including cardiovascular disease, diabetes, and dementia [1]. In particular, beetroot has a demonstrated ability to lower systolic and diastolic BP [1, 2].

About 80% of dietary nitrates come from vegetables [3]. Beetroot is one of many vegetables known for high inorganic nitrate content, consumption of which is thought to increase nitric oxide production *in vivo* [1]. While the traditional pathway for nitric oxide production is enzymatic mediation through the action of nitric oxide synthase on L-arginine [4], recent evidence has shown that dietary nitrites and nitrates also form nitrogen oxides within blood and tissues, particularly under hypoxic conditions [5]. Nitric oxide is a ubiquitous endogenous signaling molecule that mediates many processes, including BP regulation, vascular homeostasis, control of smooth muscle tone, antimicrobial defense, learning, and memory [6].

Intraocular pressure (IOP), the main modifiable risk factor for glaucoma and the current target of all glaucoma medications, is determined by the balance between aqueous humor production and outflow [7]. Nitric oxide is thought to be an important mediator of trabecular meshwork aqueous outflow [7]. Another vital function of nitric oxide is the mediation of retinal and uveal blood flow, including optic nerve perfusion, which may be altered in glaucoma [8]. Certain ocular diseases, such as diabetic retinopathy and glaucoma, have been associated with reduction and dysregulation of nitric oxide [8].

Topical nitric oxide has been shown to significantly reduce IOP in animal models, and the recently available glaucoma topical eye drop latanoprostene bunod 0.024% contains a prostaglandin analog with a moiety that breaks down into nitric oxide within the eye [6, 8]. This nitric oxide is hypothesized to increase trabecular meshwork outflow through the conventional outflow pathway and to boost optic nerve perfusion [6]. Previous research has also shown that increased dietary nitrate intake and leafy green vegetable consumption are associated with a lower risk of visual field loss from primary open-angle glaucoma, particularly in early paracentral visual field loss, which is most associated with vascular disease [9]. Unclear is the effect of increased dietary nitrate intake on intraocular pressure. An understanding of the effect of dietary nitrate intake on intraocular pressure could influence clinical decision-making for those clinicians who employ dietary and lifestyle modifications in addition to pharmaceutical and surgical management of glaucoma.

A literature review identified no study that has measured the direct effect of dietary nitrate on IOP or superficial retinal vessel density.

* **Corresponding author:** Patricia M. Cisarik, Southern College of Optometry. E-mail: pcisarik@sco.edu

Research may lack due to the assumption that the blood-aqueous and blood-retinal barriers, consisting of tight junctions that limit the passage of ions and solutes [10], impede the ability of ingested molecules to reach action sites in the eye. However, a literature review did not unearth any information on the permeability of these vascular barriers to nitric oxide. This study explored the effect of beetroot juice consumption on BP, IOP, and superficial retinal vessel density in young, healthy adults.

2 Subjects and Methods

The research protocol conformed to the Declaration of Helsinki tenets and was approved by the Institutional Review Board of the Southern College of Optometry. Subjects gave informed consent prior to participation.

2.1 Subjects

Nineteen healthy adult participants (13 female and 6 male), with a mean age of 25.1 (± 2.2) years, participated. Exclusion criteria were: allergies to beetroot or other ingredients in Lakewood Organic beet juice; glaucoma, retinopathy, or papillopathy of any origin; recent ocular infection; current or past systemic hypotension (systolic < 90 mm Hg *or* diastolic < 60 mm Hg); current or past history of orthostatic hypotension; current use of BP-lowering medications; current nutritional supplementation; pregnancy or intention to become pregnant; history of kidney stones or disease.

2.2 Procedures

After establishing subject eligibility, data was collected using a single-blinded, crossover design. Investigator 1 measured and recorded the following baseline data on Day 1, Visit 1: date and time of the data collection session; BP (right arm, sitting) using an arm cuff sphygmomanometer and stethoscope, after the subject rested for 5 or more minutes; IOP, right eye (iCare ic100 tonometer, Icare USA, with the 6-measurement series setting); and optical coherence tomography angiography (macula and optic nerve) of the (undilated) right eye (Avanti AngioVue, Optovue: HD scans 6.0 x 6.0 mm for macula, 4.5 x 4.5 mm for optic disc).

After baseline measurements, subjects met Investigator 2, who dispensed 16 fluid ounces (473 ml) of the randomly-assigned beverage (beetroot juice -Lakewood Organic, or water). Investigator 2 watched each subject consume the entire fluid within 15 minutes and advised subjects to avoid both exercises until after Visit 2 of Day 1 and disclosure of the beverage consumed to Investigator 1.

Three hours post-beverage consumption (Day 1, Visit 2), which is the time at which plasma nitrate levels and blood pressure effects of beetroot consumption previously have been shown to reach their peaks [11], Investigator 1 repeated the IOP and BP measurements and obtained repeat optical coherence tomography angiography scans. Subjects returned for Day 2 of data collection, scheduled at least 1 week after the Day 1 collection. All baseline (Day 2 Visit 1) and post-beverage consumption (Day 2 visit 2) measurements were repeated, with each subject consuming 16 fluid ounces of the beverage (water or beetroot juice) not consumed on Day 1.

2.3 Sample size calculation

To achieve a power of 80% for the primary outcome variable of intraocular pressure at 5% significance and to detect a change in the intraocular pressure of at least 3.5 mm Hg (which is 20% of the mean baseline intraocular pressure of 17.4 mm Hg in our sample), the estimated number of subjects needed is 18.

2.4 Data analysis

All-optical coherence tomography angiography scans used for analysis demonstrated at least 8.0 on scan quality, except for the 6.0 quality for one subject with congenital nystagmus. No change in results occurred with vs without this subject's data. Hence, the reported data include this subject. IBM SPSS (v 26) was used for statistical analysis. Either a paired samples t-test or Wilcoxon's signed ranks test (depending on data distribution) was used to compare pre- and post-beverage consumption measurements on Day 1 and pre- and post-beverage consumption measurements on Day 2 for the following: systolic BP, diastolic BP, IOP, macular vessel density (central, 2 paracentral sectors in each region: superior, temporal, nasal, inferior), and radial peripapillary capillary density (whole image, inside disc, peripapillary, superior hemi-, inferior hemi-). All reported P values are 2-tailed.

3 Results

3.1 BP

Systolic and diastolic baseline BP distributions were approximately normal for both visits. Mean baseline and post-beverage consumption systolic and diastolic BPs are shown in Table 1. No significant difference between the means of the two baseline systolic BP distributions (P = 0.41) or the means of the two baseline diastolic BP distributions (P = 0.22) was found.

Post-consumption BP distributions also were approximately normal for both beverages. No significant difference between the means of the post-consumption systolic BP (P = 0.28) or diastolic BP (P = 0.92) distributions across beverage conditions was found. However, the means of the pre- versus post-beet root juice consumption BP measurements were significantly different for both systolic and diastolic measurements, whereas the means of the pre- versus post-water consumption systolic and diastolic BP measurements did not differ (Table 1 and Figure 1).

With fewer than 20 subjects, linear regression analysis was not appropriate; therefore, Spearman's rho correlations were calculated to evaluate the relationship between baseline BP measurement and the magnitude of the change in the measurement post-beverage consumption. Correlations were statistically significant for baseline versus change in diastolic measurement post- water consumption (correlation coefficient = 0.63, P = 0.004) and baseline versus change in diastolic measurement post-beet root juice consumption (correlation coefficient = 0.632, P = 0.004), but not for baseline versus change in systolic measurement for either beverage (water: correlation coefficient = 0.43, P = 0.07; beet root juice: correlation coefficient = 0.40, P = 0.09).

Table 1: Summary of baseline and post-beverage consumption measures, BP and IOP

Measurement	Beverage Consumed	Baseline (mean ± SD)	Post Beverage Consumption (mean ± SD)	Significance of Baseline versus Post-consumption comparison (P)	Significance of Baseline versus Post-consumption comparison (95% CI)
Systolic BP (mm Hg)	Water	114.5 ± 13.2	113.4 ± 12.3	0.34	-1.26, 3.47
	Beetroot juice	116.0 ± 12.4	111.2 ± 10.6	0.03	0.47, 9.11
Diastolic BP (mm Hg)	Water	75.2 ± 8.5	72.7 ± 6.8	0.25	-1.89, 6.73
	Beetroot juice	78.7 ± 11.9	72.5 ± 9.6	<0.001	3.27, 9.15
IOP, right eye (mm Hg)	Water	17.4 ± 2.9	15.6 ± 3.0	0.001	0.87, 2.81
	Beetroot juice	17.2 ± 3.7	16.0 ± 3.1	0.039	0.07, 2.25

BP; blood pressure, IOP; intraocular pressure, SD; standard deviation, CI; confidence interval, mm Hg; millimeters of mercury.

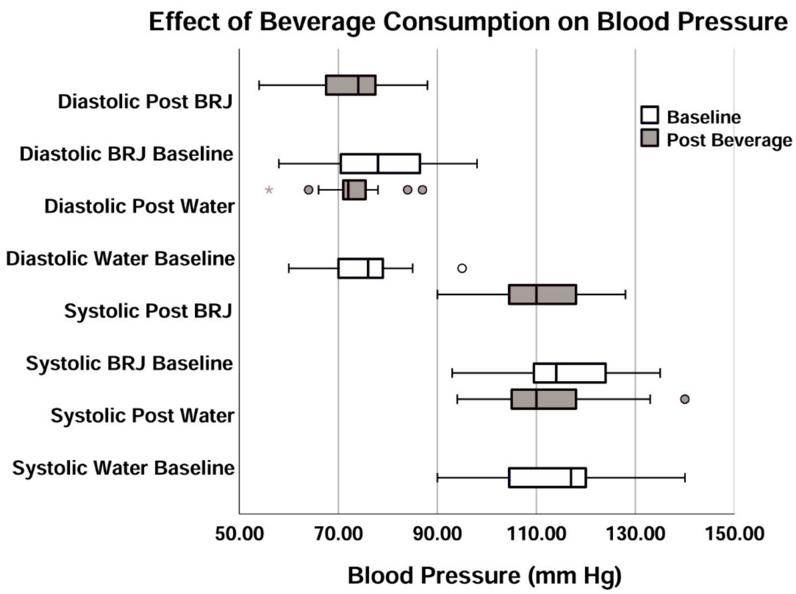

Figure 1: Box plots of systolic and diastolic blood pressures at baseline and three hours after beverage consumption

The means of the systolic and of the diastolic blood pressure measurements pre- versus post-beet root juice consumption were statistically significantly different (see Table 1), whereas the means of the systolic and of the diastolic blood pressure measurements pre- versus post-water consumption did not differ.

3.2 IOP

Mean IOPs baseline and post-beverage consumption are shown in Table 1. Both distributions of baseline IOP prior to consumption of beetroot juice or water were approximately normal. No significant difference between the baseline mean IOPs was found (P= 0.610).

The distributions of IOP after beverage consumption also were approximately normal. No significant difference between post-beverage consumption mean IOPs was found across beverages (P = 0.424). The distributions of the change in IOP between baseline and post-beverage consumption were approximately normal for both beverages. The mean change in IOP pre- versus post-water consumption was 1.8 ± 2.0 mm Hg, and the mean change in IOP pre- versus post-BRJ consumption was 1.2 ±2.3 mm Hg. One sample t-test showed that both mean changes were significantly different from zero (with water: P = 0.001, 95% CI (0.87, 2.81); with beetroot juice: P = 0.039, 95% CI (0.07,2.25)) (Figure 2).

3.3 Retinal vessel density – optic disc

The retinal peripapillary capillary densities [(%) percent] for the small vessels and for all vessels calculated using the instrument's built-in algorithm are indicated on the optic disc scan for 3 regions: whole image, inside disc, and peripapillary (Figure 3). Additionally, the peripapillary capillary densities are separately measured for the superior and inferior hemi regions. The distributions of these density values, at baseline and both post-water and post-beet root juice consumption, were approximately normal, except for one parameter in each category.

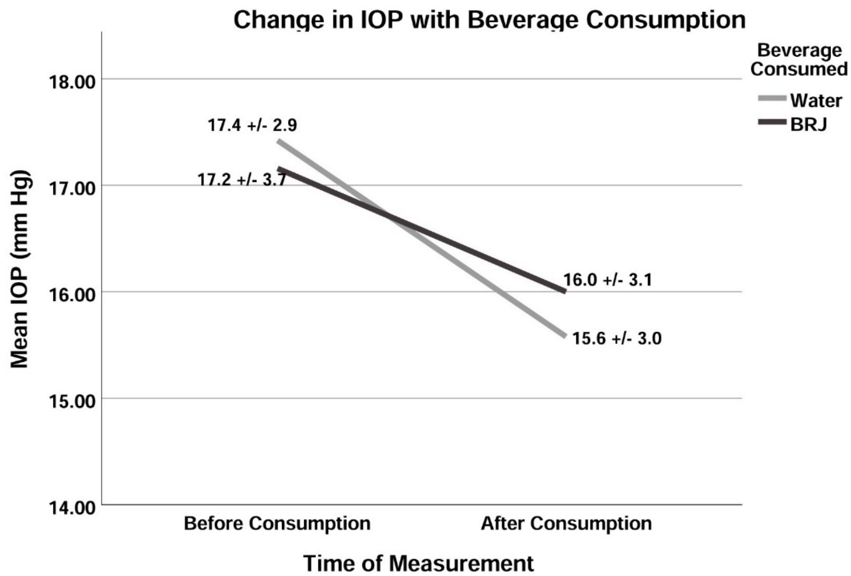

Figure 2: Change in mean IOP 3 hours after water and BRJ consumption

Although mean baseline IOP did not differ and post-beverage consumption IOP did not differ across beverage type, the change from baseline IOP was significantly different from zero for both beverages. See Table 1 for statistics.

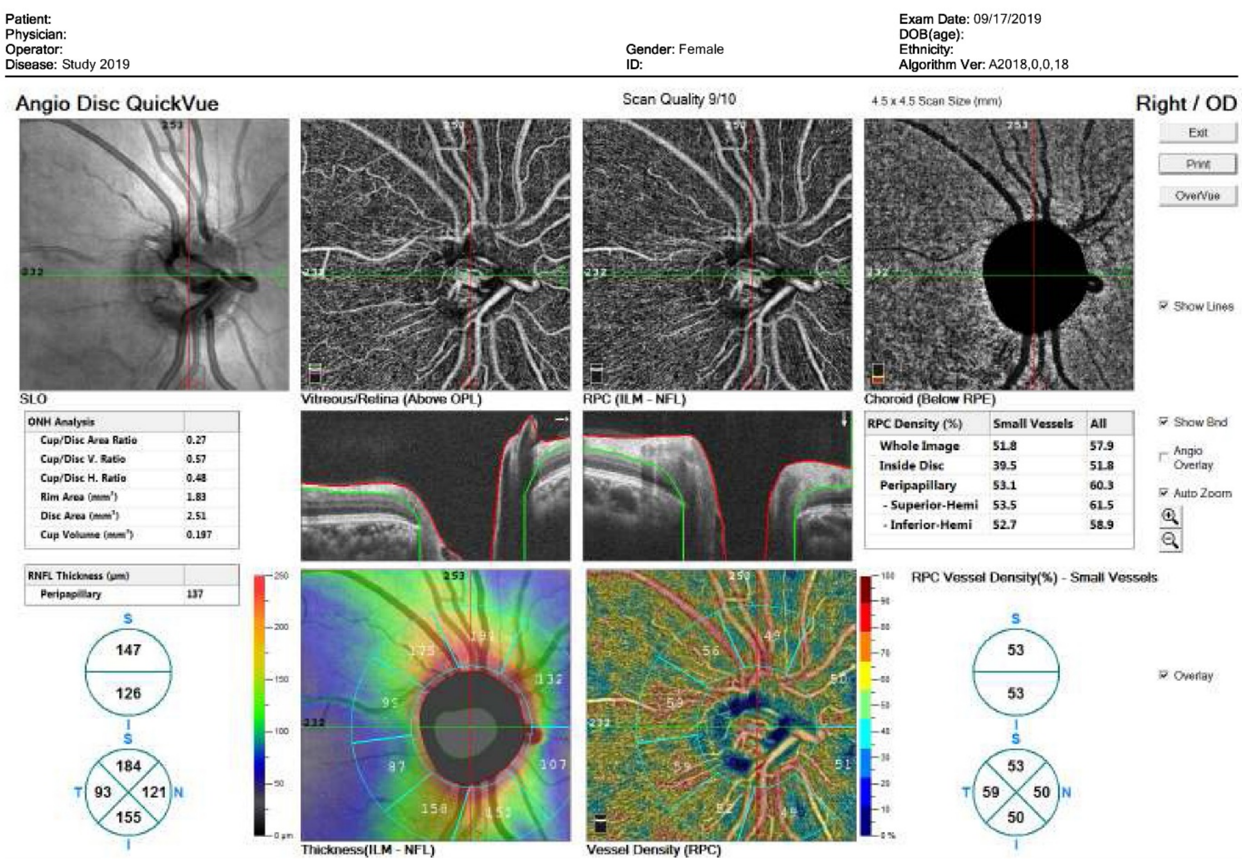

Figure 3: Representative 4.5 mm x 4.5 mm optical coherence tomography angiography scan of right eye optic nerve, captured using Avanti AngioVue HD (Optovue, Inc)

The vessel density values used for data analysis are located in the table on the right side of the figure.

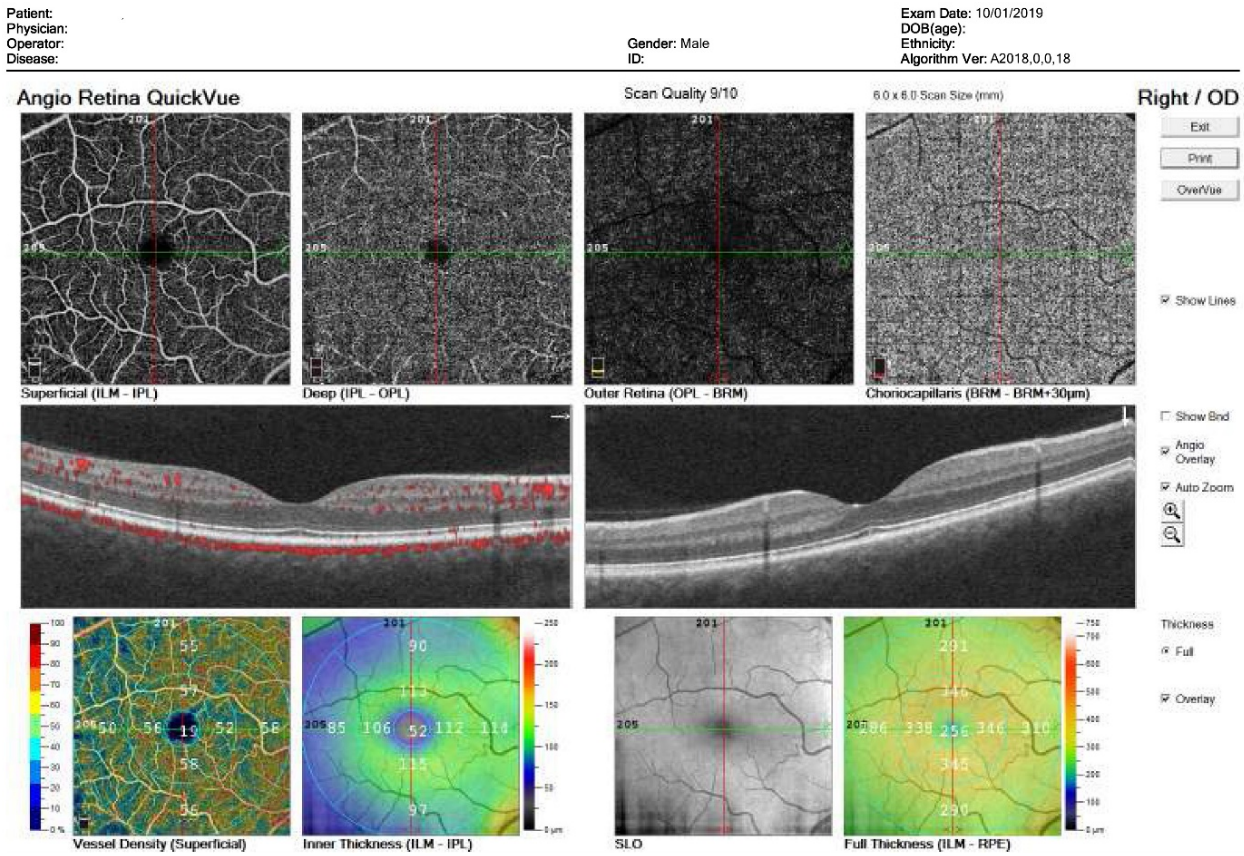

Figure 4: Representative 6.0 mm x 6.0 mm optical coherence tomography angiography scan of right eye macula, captured using Avanti AngioVue HD (Optovue, Inc)

The vessel density values are indicated in the bottom left image in the figure. For data analysis, the vessel density values from the innermost ring around the central fovea were labeled by their location relative to the central area (superior, inferior, nasal, temporal) and assigned to region 1. The vessel density values from the 2nd innermost ring around the central fovea were labeled by their location relative to the central area and assigned to region 2.

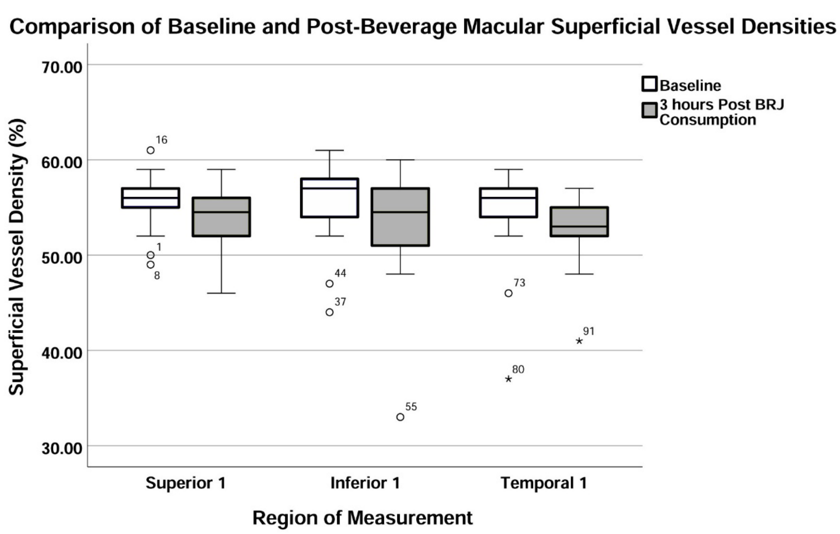

Figure 5: Comparison of mean superficial macular capillary density values before and after beet root juice (BRJ) consumption for the 3 regions that demonstrated significant changes (identified on the x-axis)

The related-samples Wilcoxon signed ranks test indicated significant differences before versus after beet root juice consumption for zones Superior 1 ($Z = -2.41$, $P = 0.016$), Inferior 1 ($Z = -2.11$, $P = 0.035$), and Temporal 1 ($Z = -2.00$, $P = 0.046$).

The same parameter was not normally distributed for baseline versus post-beet root juice consumption, but not for baseline versus post-water consumption. Thus, except for the non-normally distributed parameters, paired t-tests were used to compare the retinal peripapillary capillary densities. No significant differences in baseline densities were found for any region across the two visits (P > 0.05 for all). For the baseline and post-consumption of each beverage, no significant differences in retinal peripapillary capillary densities were found for any region (P > 0.05 for all). For the non-normally distributed data, the Wilcoxon signed ranks test indicated no significant differences in the distributions of the density values baseline versus post-beverage consumption for either beverage.

3.4 Retinal vessel density – macula

Superficial vessel density measurements from nine regions in the macula (Figure 4) were compared between baseline and post-beverage consumption. The distributions of these measurements were different from normal for most regions. No significant differences in the baseline density distributions were found for any region across the two visits (P > 0.05 for all). The Wilcoxon signed ranks test indicated significant differences in data distribution baseline versus post-beet root juice consumption for 3 of the innermost paracentral regions: Superior 1, Inferior 1, and Temporal 1 (Figure 5).

To determine whether vessel density changes for the 3 significant regions were related to their baseline density values, the magnitudes of the density changes were calculated. The distributions of these changes were approximately normal for region Superior 1 and region Inferior 1, but not for region Temporal 1. Pearson correlation coefficients were not significant for the comparison between baseline density and density change for region Superior 1 (r = 0.188, P = 0.45) or for region Inferior 1 (r = -0.02; P = 0.93). Spearman's correlation coefficient was not significant for the comparison between baseline density and density change for region Temporal 1 (r = 0.336, P = 0.17).

4 Discussion

This study confirmed the BP-lowering effect of beetroot juice found by numerous previous studies, including a 2013 meta-analysis [10]. Statistically significant decreases occurred in both systolic and diastolic BP following beetroot juice, but not water, consumption. Although the 4.8 mm Hg change in systolic BP observed is similar to the 4.4 mm Hg reduction found in the Siervo *et al.* meta-analysis [10], the larger drop in diastolic BP (6.2 mm Hg) in this study differed from their findings (1.1 mm Hg)[10]. However, more recent studies also have found a significant decrease in diastolic BP with beetroot supplementation. In a randomized, controlled, cross-over trial with healthy subjects, Hobbs *et al.* [11] provided beetroot supplementation baked into bread. Compared to when they consumed bread baked without the supplement, subjects demonstrated significantly lower diastolic, but not systolic, BP, as measured over a 6-hour period after bread consumption [11]. The same researchers conducted a different dose-dependent study in which BP was measured over 24 hours after the study product (either beetroot juice or beetroot baked into bread) was consumed [12]. Their healthy subjects showed significant lowering of both systolic and diastolic BP following beetroot supplementation compared to the control condition [12]. Additionally, their subjects showed increased microvascular vasodilation, measured with laser doppler imaging, after consuming the beetroot product compared to after consumption of the control product [12]. A more recent study showed that beetroot juice supplementation's effect on BP was greater in older compared to younger adults [13]. Reasons for the varying results across studies include different doses of beetroot juice, differences in ages of study subjects, different times and frequencies of BP measurements, and different baseline BP measurements. Finally, in individuals with healthy BP, the degree to which BP can be further reduced with nitrate supplementation from a food source is likely limited, due to the autoregulation of vascular diameter to maintain homeostasis [14]. Although we do not know the blood plasma levels of nitrate in our subjects, the blood pressure-lowering observed post-BRJ in our subjects suggests their plasma levels were comparable to responses that previously have been reported [11].

We did not find a significant difference in the change in IOP at 3 hours following beetroot juice vs water consumption. Interestingly, both groups saw significant decreases of IOP 3 hours after beverage consumption: a mean of -1.2 mm Hg for beetroot juice and -1.8 mm Hg for water. Previous research into the water drinking test has suggested that IOP temporarily spikes about 1-hour post-water consumption before returning to baseline [15]. One theory for this effect is that decreased blood osmolality after water consumption promotes increased aqueous production until osmolality rises again [15]. Based on this research, the 3-hour drop in IOP observed in both groups likely reflected average diurnal variation in IOP, rather than the effect of beverage consumption. Baseline measurements were taken in the late morning, between 10:00 AM and 12:00 PM, with 3-hour post-consumption measurements taken between 1:00 PM and 3:00 PM.

Although broad agreement exists on the presence of a nocturnal acrophase in which IOP peaks for most healthy and glaucomatous individuals, significant variation in the shape of diurnal IOP curves between individuals has been demonstrated [16, 17]. However, in a study of diurnal variation in IOP from 8 AM to 6:30 PM in 690 healthy eyes, the mean range of fluctuation was 5.0 mm Hg, with the highest values found in the morning [17]. Thus, the normal fluctuation of IOP over a 3-hour time period in healthy eyes is expected to be smaller. The present study's results are consistent with the diurnal variation in IOP described in Agnifili *et al.*, in which the researchers used a Triggerfish contact lens sensor to continuously monitor IOP over a 24-hour period [16]. Although the contact lens produces an output in mV that does not yet have a standardized conversion to mm Hg, the device has been validated to closely correlate with IOP measurements taken through noncontact tonometry [18]. The curve produced by Agnifili *et al.* shows a mild decrease in IOP as measured by the contact lens sensor over the late morning to afternoon [16], which corresponds to the mild decrease in IOP that we observed in our subjects at both post-prandial visits.

Topical intraocular pressure-lowering medications have been shown to produce significant effects in healthy eyes [19-21]; the failure of this study to find a significantly lower IOP after BRJ ingestion in healthy eyes may be due to the oral route leading to insufficient nitrate delivery to the mechanisms involved in intraocular fluid drainage. Alternatively, the single post-prandial IOP measurement time may have precluded detection of a significant reduction in IOP that may have occurred at an earlier time. Our study visits took place at a time of day when IOP is generally trending downward. Our results cannot preclude an IOP-lowering effect of BRJ if administered during a time when the IOP is trending upward.

Optical coherence tomography angiography has been shown to be capable of reproducible and repeatable measurements of retinal vessel density in both healthy subjects and in ocular disease [22, 23]. In support of previous work, the vessel density measurements for our subjects' pre-beverage consumption visits did not differ across study days. In our study, optical coherence tomography angiography of the optic disc showed no significant difference in retinal peripapillary capillary density between visits or following either beverage consumption. Optical coherence tomography angiography of the macular region showed no significant changes in superficial vessel density in any region following water consumption, but 3 regions showed significantly decreased vessel density following beetroot juice consumption. This result is unexpected, as an increase in nitric oxide would generally be expected to cause vasodilation. The mild drop in BP that was observed should also cause the autoregulated retinal vessels to dilate to maintain constant ocular perfusion pressure as BP drops [24]. One hypothesis for the finding in this study is that a concomitant increase in choroidal blood flow occurred, lessening the blood supply-demand to the macula, thereby causing the superficial retinal vessels in those regions to constrict [25]. Alternatively, the local vascular regulatory mechanisms in the macula may have passively constricted slightly in response to the small reduction in blood volume passing through them [26]. A third possibility is that the vessels underwent initial vasodilation after beetroot juice consumption, but were already demonstrating rebound constriction at 3 hours post-consumption. Other studies that have evaluated change in retinal vessel caliber with changes in BP have induced a large acute change in BP and monitored blood vessel caliber changes over a shorter period than in this study [24, 27]. Further investigation into the changes in retinal vessel caliber with a gradual change in BP, using more frequent assessment than in this study, may help explain the results.

One limitation of this study is the inclusion of only young, healthy volunteers. Glaucomatous patients may react differently to beetroot supplementation than did the subjects in this study, either with respect to IOP or retinal and optic nerve blood flow. Dysregulation of nitric oxide has been implicated in glaucoma [8]; thus, the possibility exists that glaucomatous eyes may experience a significant and/or more long-lasting change in IOP in response to increased blood concentrations of nitric oxide that was not seen in healthy volunteers. Glaucoma is also associated with poor blood flow to the optic nerve [8]. Therefore, glaucoma patients may experience a benefit from beetroot supplementation that was not seen in healthy volunteers. Additionally, plasma nitrate concentrations and diastolic BP lowering from beetroot supplementation have been shown to be greater for older than for younger adults [14]. Thus, the effect of beetroot supplementation on the ocular vasculature in older adults remains to be explored.

Another limitation of this study is the failure to instruct our subjects to avoid spitting, brushing their teeth, and using an antibacterial mouthwash after ingesting the beetroot juice, all of which have been shown to reduce the amount of nitrate-nitrite conversion by interfering with bacterial species at the back of the tongue involved in the reduction of salivary nitrate to nitrite [14, 28]. Some subjects did comment on the "earthy" taste of the beetroot juice and may have sought to alleviate the lingering taste. While failure to provide these instructions to the subjects did not prohibit demonstration of beetroot juice supplementation's effect on BP or superficial vessel density in some regions of the macula, whether the data for any of the parameters measured were affected by such actions taken by any of the subjects is unknown.

Two additional limitations of this study were the limited number of subjects and the limited number of data collection periods. The 19 subjects were sufficient for a power of 0.8 with respect to finding a 20% reduction from the mean pre-consumption IOP, but additional subjects would strengthen the study results. Had data been collected every 30-60 minutes post-beverage consumption for several hours, the time to onset for the BP changes and determination of when the peak changes occurred could have been reported. Identification of whether the superficial retinal capillary density in the macula had actually experienced an expected increase (if an increase in retinal nitric oxide had been achieved with beetroot juice consumption) at an earlier time post-beet root juice consumption before the decrease in density that was observed at the 3-hour time point also could have been determined. Finally, more frequent measurements could have identified whether a larger decrease in intraocular pressure had occurred prior to the 3-hour post-consumption measurement.

5 Conclusions

This study confirmed the BP-lowering effect of beetroot juice over a 3-hour period in young, healthy adults. Although IOP was not differentially affected post-beet root juice compared to post-water consumption in these subjects, differences in superficial retinal vessel density in the macula post-beet root juice consumption were significant. The time span over which the effect is measured, the duration of supplementation, the form of the beetroot, and the age and health of subjects may contribute to the variability of effects on these parameters. Further exploration of the effects of beetroot supplementation on retinal vasculature is warranted.

Acknowledgments: None.
Author contribution: (Randolph: study idea, data collection, writing. Cisarik: study design, statistics, writing and editing.)
Funding: This research received no external funding.
Conflict of interest: The authors declare no conflicts of interest.

References

[1] Clifford, T., Howatson, G., West, D., & Stevenson, E. (2015). The potential benefits of red beetroot supplementation in health and disease. *Nutrients*, *7*(4), 2801-2822. https://doi.org/10.3390/nu7042801

[2] Lundberg, J. O., Gladwin, M. T., Ahluwalia, A., Benjamin, N., Bryan, N. S., Butler, A., Cabrales, P., Fago, A., Feelisch, M., Ford, P. C., Freeman, B. A., Frenneaux, M., Friedman, J., Kelm, M., Kevil, C. G., Kim-Shapiro, D. B., Kozlov, A. V., Lancaster, J. R., Lefer, D. J., … Weitzberg, E. (2009). Nitrate and nitrite in biology, nutrition and therapeutics. *Nature Chemical Biology*, *5*(12), 865-869. https://doi.org/10.1038/nchembio.260

[3] Goldstein, I. M., Ostwald, P., & Roth, S. (1996). Nitric oxide: A review of its role in retinal function and disease. *Vision Research*, *36*(18), 2979-2994. https://doi.org/10.1016/0042-6989(96)00017-x

[4] Salloum, F. N., Sturz, G. R., Yin, C., Rehman, S., Hoke, N. N., Kukreja, R. C., & Xi, L. (2014). Beetroot juice reduces infarct size and improves cardiac function following ischemia-reperfusion injury: Possible involvement of endogenous H2S. *Experimental Biology and Medicine*, *240*(5), 669-681. https://doi.org/10.1177/1535370214558024

[5] Tsai, J. C., Gray, M. J., & Cavallerano, T. NITRIC OXIDE IN GLAUCOMA: What Clinicians Need to Know. Available at http://www.candeoscience.com/nitric-oxide-in-glaucoma

[6] Stamper, R. L., Lieberman, M. F., & Drake, M. V. (2009). Aqueous Humor Formation. In *Becker-Shaffer's diagnosis and therapy of the glaucomas* (8th ed., pp. 8-24). Elsevier Health Sciences.

[7] Schmetterer, L. (2001). Role of nitric oxide in the control of ocular blood flow. *Progress in Retinal and Eye Research*, *20*(6), 823-847. https://doi.org/10.1016/s1350-9462(01)00014-3

[8] Kang, J. H., Willett, W. C., Rosner, B. A., Buys, E., Wiggs, J. L., & Pasquale, L. R. (2016). Association of dietary nitrate intake with primary open-angle glaucoma. *JAMA Ophthalmology*, *134*(3), 294. https://doi.org/10.1001/jamaophthalmol.2015.5601

[9] Coca-Prados, M. (2014). The blood-aqueous barrier in health and disease. *Journal of Glaucoma*, *23*, S36-S38. https://doi.org/10.1097/ijg.0000000000000107

[10] Siervo, M., Lara, J., Ogbonmwan, I., & Mathers, J. C. (2013). Inorganic nitrate and beetroot juice supplementation reduces blood pressure in adults: A systematic review and meta-analysis. *The Journal of Nutrition*, *143*(6), 818-826. https://doi.org/10.3945/jn.112.170233

[11] Hobbs, D. A., Goulding, M. G., Nguyen, A., Malaver, T., Walker, C. F., George, T. W., Methven, L., & Lovegrove, J. A. (2013). Acute ingestion of beetroot bread increases endothelium-independent vasodilation and lowers diastolic blood pressure in healthy men: A randomized controlled trial. *The Journal of Nutrition*, *143*(9), 1399-1405. https://doi.org/10.3945/jn.113.175778

[12] Hobbs, D. A., Kaffa, N., George, T. W., Methven, L., & Lovegrove, J. A. (2012). Blood pressure-lowering effects of beetroot juice and novel beetroot-enriched bread products in normotensive male subjects. *British Journal of Nutrition*, *108*(11), 2066-2074. https://doi.org/10.1017/s0007114512000190

[13] Stanaway, L., Rutherfurd-Markwick, K., Page, R., Wong, M., Jirangrat, W., Teh, K. H., & Ali, A. (2019). Acute supplementation with nitrate-rich beetroot juice causes a greater increase in plasma nitrite and reduction in blood pressure of older compared to younger adults. *Nutrients*, *11*(7), 1683. https://doi.org/10.3390/nu11071683

[14] Badrick, A. (2018). Control of blood pressure [monograph on the Internet]. England and Wales: Teach Me Physiology. [Cited 17 Jul 2020]. Available at https://teachmephysiology.com/cardiovascular-system/circulation/control-blood-pressure/

[15] Lai, I., Poon, Y., Teng, M., Lin, P., & Tsai, J. (2016). Intraocular pressure fluctuation after water drinking test in primary angle-closure glaucoma and primary open-angle glaucoma. *Indian Journal of Ophthalmology*, *64*(12), 919. https://doi.org/10.4103/0301-4738.198851

[16] Agnifili, L., Mastropasqua, R., Frezzotti, P., Fasanella, V., Motolese, I., Pedrotti, E., Iorio, A. D., Mattei, P. A., Motolese, E., & Mastropasqua, L. (2014). Circadian intraocular pressure patterns in healthy subjects, primary open angle and normal tension glaucoma patients with a contact lens sensor. *Acta Ophthalmologica*, *93*(1), e14-e21. https://doi.org/10.1111/aos.12408

[17] David, R., Zangwill, L., Briscoe, D., Dagan, M., Yagev, R., & Yassur, Y. (1992). Diurnal intraocular pressure variations: An analysis of 690 diurnal curves. *British Journal of Ophthalmology*, *76*(5), 280-283. https://doi.org/10.1136/bjo.76.5.280

[18] Mottet, B., Aptel, F., Romanet, J., Hubanova, R., Pépin, J., & Chiquet, C. (2013). 24-Hour Intraocular pressure rhythm in young healthy subjects evaluated with continuous monitoring using a contact lens sensor. *JAMA Ophthalmology*, *131*(12), 1507. https://doi.org/10.1001/jamaophthalmol.2013.5297

[19] Kazemi, A., McLaren, J. W., Trese, M. G., Toris, C. B., Gulati, V., Fan, S., Reed, D. M., Kristoff, T., Gilbert, J., Moroi, S. E., & Sit, A. J. (2019). Effect of Timolol on aqueous humor outflow facility in healthy human eyes. *American Journal of*

Ophthalmology, *202*, 126-132. https://doi.org/10.1016/j.ajo.2019.02.014

[20] Larsson, L. (2001). Intraocular pressure over 24 hours after single-dose administration of latanoprost 0.005% in healthy volunteers. A randomized, double-masked, placebo controlled, cross-over single center study. *Acta Ophthalmologica Scandinavica*, *79*(6), 567-571. https://doi.org/10.1034/j.1600-0420.2001.790604.x

[21] Liu, Y.-T. (2021). Effect of Brimonidine 0.025% Ophthalmic Solution on Contrast Sensitivity, Pupil Size, and Intraocular Pressure: A Pilot Study. Thesis for Master of Science in Vision Science at Pacific University, Oregon, USA.

[22] You, Q., Freeman, W. R., Weinreb, R. N., Zangwill, L., Manalastas, P. I., Saunders, L. J., & Nudleman, E. (2017). Reproducibility of vessel density measurement with optical coherence tomography angiography in eyes with and without retinopathy. *Retina*, *37*(8), 1475-1482. https://doi.org/10.1097/iae.0000000000001407

[23] Kee, A. R., Yip, V. C., Tay, E. L., Lim, C. W., Cheng, J., Teo, H. Y., Chua, C. H., & Yip, L. W. (2020). Comparison of two different optical coherence tomography angiography devices in detecting healthy versus glaucomatous eyes – an observational cross-sectional study. *BMC Ophthalmology*, *20*(1). https://doi.org/10.1186/s12886-020-01701-9

[24] Jeppesen, P., Sanye-Hajari, J., & Bek, T. (2007). Increased blood pressure induces a diameter response of retinal arterioles that increases with decreasing Arteriolar diameter. *Investigative Opthalmology & Visual Science*, *48*(1), 328. https://doi.org/10.1167/iovs.06-0360

[25] Huemer, K., Garhofer, G., Aggermann, T., Kolodjaschna, J., Schmetterer, L., & Fuchsja¨ger-Mayrl, G. (2007). Role of nitric oxide in Choroidal blood flow regulation during light/dark transitions. *Investigative Opthalmology & Visual Science*, *48*(9), 4215. https://doi.org/10.1167/iovs.07-0176

[26] Shepro, D., D'Amore, P.A., eds. (2006). *Microvascular Research: Biology and Pathology*. Burlington, MA: Elsevier Academic Press.

[27] Tani, T., Nagaoka, T., Nakabayashi, S., Yoshioka, T., & Yoshida, A. (2014). Autoregulation of retinal blood flow in response to decreased ocular perfusion pressure in cats: Comparison of the effects of increased Intraocular pressure and systemic hypotension. *Investigative Opthalmology & Visual Science*, *55*(1), 360. https://doi.org/10.1167/iovs.13-12591

[28] Petersson, J., Carlström, M., Schreiber, O., Phillipson, M., Christoffersson, G., Jägare, A., Roos, S., Jansson, E. Å., Persson, A. E., Lundberg, J. O., & Holm, L. (2009). Gastroprotective and blood pressure lowering effects of dietary nitrate are abolished by an antiseptic mouthwash. *Free Radical Biology and Medicine*, *46*(8), 1068-1075. https://doi.org/10.1016/j.freeradbiomed.2009.01.011

Cite this article as: Randolph, B., Cisarik, P. M. (2021). Beetroot juice: effects on blood pressure, intraocular pressure, and ocular vessel density in healthy adults. *The North African Journal of Food and Nutrition Research,* 5(12): 130-138. https://doi.org/10.51745/najfnr.5.12.130-138