Acute Effects of Sugar-Sweetened Beverage Consumption on Hemodynamics and Reactive Hyperemia in Young, Healthy Humans

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Background: Previously, the consumption of sugar-sweetened beverages (SSBs) has been associated with the onset of cardiovascular disease. In addition, reactive hyperemia (RH), a measure of microvascular function, has been associated with cardiovascular disease risk.

Purpose: Therefore, the purpose of this study was to test the hypothesis that consumption of a SSB would acutely mitigate microvascular responses.

Methods: Thirteen subjects consumed 24 fluid ounces of water or SSB (68g mixture of fructose and dextrose). Prior to, immediately after, and 1-hr post beverage consumption, venous occlusion plethysmography was used to measure the forearm blood flow (FBF) during baseline and post-ischemia (5 min) RH conditions. Whole blood [glucose] was determined via finger-stick samples with rapid glucometry. Heart rate and blood pressure were monitored throughout the experiment.

Results: Despite significant elevations in blood glucose levels, there was no significant change in forearm blood flow at rest or during reactive hyperemia in any of the conditions (p=0.823). Slight elevations in heart rate and mean arterial pressure were observed immediately following consumption of SSB.

Conclusions: The present findings indicated that young, healthy humans maintained microvascular function following acute consumption of a SSB. Future studies should address whether the ability to maintain microvascular function following acute SSB consumption persists in at-risk populations as well as whether chronic SSB consumption can attenuate RH responses.

Conflict of Interest: No conflicts declared.

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Therefore, the purpose of the present study was to test the hypothesis that the acute consumption of a glucose-fructose beverage would impair microvascular function as assessed by reactive hyperemia.

2. Methods

2.1 Subjects

Thirteen (6 men, 7 women) healthy adults (mean ± SEM: 21.5 ± 0.4 yrs) volunteered to participate in the present study. The subjects were non-smokers, non-obese (24.5 ± 0.8 BMI), normotensive (<140/90 mmHg), sedentary to moderately active, and not taking any medications were used for investigation. The study was approved by the University of Dayton’s Institutional Review Board for Human Subjects and all subjects completed a health history questionnaire and signed a written informed consent prior to testing. During the initial screening visit, the subjects were assessed for body composition via air displacement technique (Bod Pod, CosMed, Chicago, IL) as seen in Table 1.

Table 1. Thirteen subjects’ anthropometric and resting hemodynamic values are presented as mean ± S.E.M.

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Mean ± S.E.M</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>13 (6 males, 7 females)</td>
</tr>
<tr>
<td>Age</td>
<td>21.5 ± 0.4</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>173.0 ± 2.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73.7 ± 3.6</td>
</tr>
<tr>
<td>BMI</td>
<td>24.5 ± 0.8</td>
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<tr>
<td>Body Fat (%)</td>
<td>16.7 ± 1.9</td>
</tr>
<tr>
<td>Fasted Glucose (mg/dL)</td>
<td>69.0 ± 2.2</td>
</tr>
<tr>
<td>Fasted Cholesterol (mg/dL)</td>
<td>112 ± 2.6</td>
</tr>
<tr>
<td>Resting Systolic Pressure (mmHg)</td>
<td>112.0 ± 2.5</td>
</tr>
<tr>
<td>Resting Diastolic Pressure (mmHg)</td>
<td>67.0 ± 1.9</td>
</tr>
<tr>
<td>Resting MAP (mmHg)</td>
<td>84.0 ± 2.0</td>
</tr>
<tr>
<td>Resting Heart Rate (BPM)</td>
<td>58.0 ± 3.0</td>
</tr>
</tbody>
</table>

2.2 Procedures

The day preceding an experimental trial, the subjects were instructed to fast overnight (at least 8 hours), refrain from vigorous exercise for 24 hours, and abstain from caffeine consumption for 12 hours. The female subjects were studied in the supine position. Each experimental day began with subjects quietly resting for 30 minutes. After a basal state was reached, the baseline RH trial was conducted. The procedure included three RH trials, baseline, immediate, and 1-hr post. Each of the trials was divided into three timepoints (initial, RH, and recovery), and heart rate and mean arterial pressure were recorded during these timepoints. After the first trial (baseline RH), the subjects were permitted to assume a sitting position and given either the control or intervention beverage adhering to counterbalance design. The second RH trial (immediate trial) was conducted immediately following beverage ingestion. Prior to the 60-min post ingestion RH trial (1-hr post trial), heart rate, blood pressure, and mean arterial pressure were recorded in 5-min intervals.

Blood Glucose and Cholesterol

Whole blood cholesterol and glucose were measured once basal state was reached via finger-stick samples. Blood glucose was assessed again at 5- and 60-min post beverage ingestion. Values were determined using a CardioChek Plus (Polymer Technology Systems, Indianapolis, Ind) (17).

Systemic hemodynamics

Heart rate was recorded continuously using a 3-lead electrocardiogram (Powerlab, AD Instruments). During each RH trial, blood pressure and mean arterial pressure were recorded during baseline FBF (initial timepoint), RH occlusion (RH timepoint), and post occlusion (recovery timepoint) using a Datascope Passport 2 patient monitor (Mahwah, NJ, USA). Mean arterial pressure was recorded directly from the Datascope, which utilized a well-accepted preset equation.

Beverage

In both the control and intervention trials, subjects were given 24 fluid ounces of water flavored with 1 serving (~4 drops) of lemon juice (Italia Lemon Juice, Brockton, MA) The intervention beverage consisted of 68 grams of sugar (37.4 grams fructose and 30.6 grams dextrose from Modernist Pantry, York, ME) to mimic high fructose corn syrup-55 (13). For each condition, the subjects were given two cups with an equal distribution of fluid and five minutes to finish both cups (total of 24 fluid ounces of beverage).

Forearm Blood Flow

Forearm blood flow was measured utilizing VOP with mercury-in-salistic strain gauges (18). A blood pressure cuff was placed around the subject’s wrist and rapidly inflated to a suprasystolic value (~200 mmHg) to occlude all inward and outward flow of the hand, thus isolating the forearm vasculature. Another cuff was positioned superior to the antecubital fossa on the same arm. This upper cuff cycled rapidly to inflate to approximately 50 mmHg for 7 seconds and to completely deflate for 8 seconds, which produced one FBF value every 15 seconds. Values were expressed as milliliters per deciliter of forearm volume (FAV) per minute (ml · dl FAV⁻¹ · min⁻¹). Mean arterial pressure was accounted for with forearm vascular conductance (FVC), which is an indicator of vascular tone. Forearm vascular conductance was calculated by FBF/MAP x 100 with values expressed as ml · dl FAV⁻¹ · mmHg⁻¹ · 100 mmHg⁻² (19).

Reactive Hyperemia

Utilizing the same cuff placement as FBF, the upper cuff was used to occlude arterial flow during the RH trials. Following the resting FBF measurements, the upper cuff was rapidly inflated to ~200 mmHg for 5 minutes to induce transient ischemia. Previously, this design has been utilized to investigate various endothelial – derived vasodilator pathways (19, 20). Following the 5 minutes of transient ischemia, the cuffs cycled between inflation (4 seconds) and deflation (3 seconds) for 56 seconds before returning to the resting FBF procedure, 7:8 seconds for approximately 2 minutes.

2.3 Statistical Analyses

The data were reported as mean ± S.E.M. Intraclass correlation coefficients were calculated using the 2, k model (21). Two separate 1-way repeated measures ANOVAs were used to analyze blood glucose values. Two separate 2 (Condition [Control, SSB]) × 13 (Time [Initial, 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60-min]) repeated measures ANOVAs were used to analyze the hemodynamic values resulting from the intervention RH trials. Three separate 2 (Condition [Control, SSB]) × 3 (Trial [Baseline, Immediate, Post]) repeated measures ANOVAs were used to analyze Peak FBF, Peak FVC, and total AUC. Significant interactions were decomposed with follow-up repeated measures ANOVAs and paired samples t-tests. Greenhouse-Geisser
corrections were applied when sphericity was not met according to Mauchly’s Test of Sphericity, and partial eta squared effect sizes (\(\eta^2_p\)) were calculated for each ANOVA. All statistical analyses were performed using IBM SPSS v. 25 (Armonk, NY) and an alpha of \(p \leq 0.05\) considered statistically significant for all comparisons.

3. Results

3.1 Reliability
During the resting baseline trial, there were no systematic mean differences (\(p>0.05\)) between the control and SSB conditions for FBF, blood glucose, mean arterial pressure, and heart rate. The intraclass class coefficients for FBF, blood glucose, mean arterial pressure heart rate were 0.84, 0.77, 0.88, and 0.86, respectively.

3.2 Blood Glucose
For the control condition, the 1-way repeated measures ANOVA was not significant (\(p=0.218\)). For the SSB condition, there was a significant (\(p<0.015; \eta^2_p = 0.86\)) difference in blood glucose. Pairwise comparisons indicated that immediate values were significantly elevated compared to baseline valued (69.1 ± 2.2 vs. 108.3 ± 3.7 mg/dL). Blood glucose remained elevated following the 1-hr quiet rest (76 ± 3.8 mg/dL), but this was not statistically significant (\(p=0.056\)) at an alpha of \(p \leq 0.05\).

3.3 Hemodynamic Measurements
During the RH trials, for the control condition’s heart rate values, there was not a significant (\(p=0.538\)) Trial × Timepoint interaction, but a significant (\(p=0.011; \eta^2_p = 0.33\)) main effect for Trial. Pairwise comparisons indicated that baseline heart rate values were significantly elevated compared to baseline value (69.1 ± 2.2 vs. 108.3 ± 3.7 mg/dL). Blood glucose remained elevated following the 1-hr quiet rest (76 ± 3.8 mg/dL), but this was not statistically significant (\(p=0.056\)) at an alpha of \(p \leq 0.05\).

3.4 Blood Flow Measurements

Peak Reactive Hyperemia
For all subjects, the peak flow was observed in either the first or second time point post occlusion. There was not a significant (\(p=0.823\)) Condition × Trial interaction or significant main effects for Peak Flow. Individual values are presented in Figure 1.

Peak Forearm Vascular Conductance
For Peak FVC, there was not a significant Condition × Trial interaction (\(p=0.324\)), but there was a significant (\(p=0.015; \eta^2_p = 0.31\)) main effect for Trial. Pairwise comparisons indicated that baseline Peak FVC was significantly (\(p=0.001\)) greater than Immediate Peak FVC (34.7 ± 2.3 vs 30.6 ± 2.4 ml dlFAV^{-1} · min^{-1} · 100 mmHg^{-1}). Individual values are presented in Figure 2.

Total Area Under the Curve
For Total AUC FBF, there was a significant Condition × Trial interaction (\(p=0.029; \eta^2_p = 0.27\)). The follow-up 1-way repeated measures ANOVA (collapsed across Trial) indicated that the conditions were not significantly (\(p=0.724\)) different. Individual values are presented in Figure 3.

Table 2. n=13; Hemodynamic values during quiet rest following beverage consumption

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Control Heart Rate (BPM)</th>
<th>MAP (mmHg)</th>
<th>Control Heart Rate (BPM)</th>
<th>MAP (mmHg)</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>61 ± 2.7</td>
<td>87 ± 2.4</td>
<td>60 ± 2.1</td>
<td>86 ± 1.9</td>
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<tr>
<td>0</td>
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<td>5</td>
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<td>91 ± 3.1</td>
<td>62 ± 3.6</td>
<td>88 ± 2.6</td>
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<tr>
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<td>59 ± 2.8</td>
<td>88 ± 2.6</td>
<td>64 ± 4.0</td>
<td>91 ± 2.9</td>
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<tr>
<td>15</td>
<td>59 ± 2.8</td>
<td>89 ± 3.4</td>
<td>66 ± 3.9</td>
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</tr>
<tr>
<td>20</td>
<td>61 ± 3.2</td>
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<td>87 ± 2.8</td>
<td>65 ± 3.1</td>
<td>89 ± 2.9</td>
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</table>
Figure 1. The individual values are represented for the control condition (white circles) and for the SSB condition (black circles). Mean values for each condition are represented with solid black bars for each condition. There were no reported significant differences observed in the mean peak forearm blood flow values.

Figure 2. The individual values are represented for the control condition (white circles) and for the SSB condition (black circles). Mean values for each condition are represented with solid black bars for each condition. There was a significant reduction in peak forearm vascular conductance (collapsed across condition) during the immediate trial compared to baseline, as described in the results section.
4. Discussion

The results of the present study suggested that the acute consumption of the SSB compared to the control beverage did not impair microvascular function in young, healthy humans, as measured by RH. As expected, only the SSB condition increased blood glucose levels. In addition, the current study was consistent with previous findings (9) and reported that the consumption of a SSB increased systemic hemodynamics (HR and MAP).

Recently, Charrière and colleagues (22) reported that the consumption 500 mL of water containing 60 g of fructose by healthy, young adults elicited the greatest increase in heart rate (+7 beats · min⁻¹) 45-min post beverage consumption. Furthermore, the authors (22) reported that the consumption of the fructose beverage increased mean arterial pressure 10-min following consumption, and mean arterial pressure remained elevated for the remainder of the study (~120-min). Consistent with Charrière et al. (22), the current study reported that heart rate was elevated following the consumption of the SSB compared to the control beverage. However, the current study was not consistent with the nearly immediate increase in mean arterial pressure. Perhaps, this discrepancy was due to the current study’s sugar mixture (55% fructose, 45% glucose), Charrière et al. (22) did report that glucose alone initially decreased mean arterial pressure.

As previously mentioned, individual monosaccharides (glucose, fructose, etc.) have been reported to influence the hemodynamics of humans (9, 14, 22). In addition, high fructose corn syrup (mixture of monosaccharides) has been shown to increase hemodynamics as well (23). Comparable to the present study, Le et al. (23) reported that when 40 healthy adults consumed 24 fluid ounces with 68.0 grams of high fructose corn syrup, there was an increase in both heart rate and blood pressure. However, the current study did not find an increase in FVC despite the elevated heart rate during the 1-hr quiet rest for the SSB condition. Perhaps, this difference was due to the magnitude of percent change in heart rate. The current study reported that following the consumption of the SSB, heart rate was approximately increased 12.5% on average from baseline; however, Pike et al. (24) reported approximately a 34% increase in heart rate from baseline. Another explanation may be that the SSB effected the microvascular system on a local level (25).

As previously stated, the consumption of glucose and/or fructose, more specifically SSBs, has been linked to adverse health events such as oxidative stress (7–9, 26). Furthermore, Loader et al. (16) was reportedly the first group to investigate the acute vascular consequences to the consumption of commercially available SSB. Specifically, this seminal study found that the cutaneous blood flux increased following iontophoresis of acetylcholine and sodium nitroprusside, but that the relative increase was significantly lower during the SSB mediated hyperglycemia as compared to water trial (normoglycemia). Thus, this suggests that in a healthy adult population, SSB-mediated microvascular dysfunction is at least partly due to increased oxidative stress. In addition, Mah and Bruno (25) stated that oral glucose tolerance tests (75 grams glucose) have routinely succeeded in attenuating vascular responses in healthy humans. The discrepancy in the attenuation of microvascular function between these previous reports (16, 25) and the current study may be partially due to a difference in the way subjects responded to the sugar load. For example, Loader et al. (16) reported a 75% increase in blood glucose following the consumption of the a commercially available SSB, whereas the present study only reported a 56% increase. Concomitantly with the smaller change in blood glucose, young healthy humans are known to have adequate antioxidant capabilities that have the potential to mitigate the external stress of the consumption of sugars (16). Perhaps, the current study’s subjects had sufficiently robust antioxidant capabilities that could manage the given sugar load without compromising nitric oxide bioavailability.
While FBF is the relevant measurement when considering RH responses, it can also be valuable to look at FVC as this accounts for changes in MAP. For example, during the immediate trial and for both the SSB and control conditions, there was a slight attenuation in peak FVC that was likely driven by an increase in MAP. Although this change was observed in both conditions, therefore this finding does not impact our conclusions that SSB consumption does not impair RH responses.

Limitations
There were no direct measures of sympathetic nervous system activity plasma insulin levels, antioxidant status or nitric oxide bioavailability. Thus, our potential mechanistic insight is limited; however, the present study did measure plasma glucose levels and systemic hemodynamic responses, which provided some insight to sympathoexcitation. Consequently, we are confident that the SSB intervention elicited the appropriate systemic responses.

Conclusions
Young, healthy individuals maintain microvascular function assessed with RH following the consumption of a commercially-like SSB. It is possible that with an increased sugar load, there could be an effect of acute consumption; however, the aim of the present study was to mimic a typical serving of a common, commercially available SSB. Given this investigation examined young, healthy humans who have preserved microvascular function to a variety of physiological challenges, it would be of interest to examine how the impact of acute SSB consumption might change in populations at-risk for CVD or with established vascular dysfunction. Finally, the direct impact of chronic SSB consumption at a given dosage on RH responses is also yet to be determined.

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