

## Clinical Trials Study

**Consumption of energy beverage is associated with attenuation of arterial endothelial flow-mediated dilatation**

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**Abstract****AIM**

To investigate whether consumption of an energy drink will acutely impair endothelial function in young healthy adults.

**METHODS**

Energy drinks are being consumed more and more worldwide, and have been associated with some deaths in adolescents and young adults, especially when consumed while exercising. After fasting and not smoking for at least 8 h prior, eleven medical students (9 males) received an electrocardiogram, blood pressure and pulse check, and underwent baseline testing (BL) of endothelial function using the technique of endothelium-dependent flow mediated dilatation (FMD) with high-resolution ultrasound

(according to recommended guidelines of the University of Wisconsin Atherosclerosis Imaging Research Program Core Laboratory). The subjects then drank an energy beverage (EB), a 24-oz can of Monster Energy, and the above was repeated at 90 min after consumption. The relative FMD (%) was calculated as the ratio between the average post-cuff release and the baseline diameter. Each image was checked for quality control, and each artery diameter was measured from the media to media points by two experts, 3 measurements at the QRS complex, repeated on 3 separate beats, and then all were averaged.

## RESULTS

Subjects characteristics averages (given with standard deviations) include: Age  $24.5 \pm 1.5$  years, sex 9 male and 2 female, weight  $71.0 \pm 9.1$  kg, height  $176.4 \pm 6.0$  cm, BMI  $22.8 \pm 2.7$  kg/m<sup>2</sup>. The hemodynamics were as follows, BL *vs* EB group respectively (mean  $\pm$  SD): Heart rate  $65.2 \pm 11.3$  *vs*  $68.2 \pm 11.8$  beats per minute, systolic blood pressure  $114.0 \pm 10.4$  mmHg *vs*  $114.1 \pm 10.4$  mmHg, diastolic blood pressure  $68.8 \pm 9.3$  mmHg *vs*  $70.6 \pm 7.1$  mmHg; all were not significantly different. However after drinking the EB, a significantly attenuated peak FMD response was measured (mean  $\pm$  SD): BL group  $5.9\% \pm 4.6\%$  *vs* EB group  $1.9\% \pm 2.1\%$ ;  $P = 0.03$ ). Given the increased consumption of energy beverages associated with exercise in young adults, more research is needed.

## CONCLUSION

Energy beverage consumption has a negative impact on arterial endothelial function in young healthy adults.

**Key words:** Energy drinks; Endothelial function; Exercise; Flow mediated dilatation; Blood pressure

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**Core tip:** Energy drinks are being consumed worldwide, and are gaining in popularity, especially amongst youth. We studied the acute effects that one energy drink has on endothelial function, a measure of vascular health. We found that consumption of a single 24-oz can of Monster Energy resulted in attenuation of brachial artery endothelium-dependent flow mediated dilatation in 11 healthy volunteers.

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## INTRODUCTION

Energy beverages are being consumed increasingly

worldwide, and have been associated with deaths in adolescents and young adults, especially when consumed while exercising<sup>[1]</sup>.

What effect these energy drinks have on endothelial cells could help explain its effect on the cardiovascular system. These cells are part of the inner lining of blood vessels and have metabolic and also synthetic functions<sup>[2]</sup>. When endothelial cells are functioning abnormally or "endothelial dysfunction", it is associated with poor vascular reactivity, pro-thrombosis, pro-adhesion, pro-inflammation, and growth promotion<sup>[1,3]</sup>.

Several recent reviews on cardiovascular complications associated with energy drink consumption suggest that the impact on endothelial function could be a factor in subsequent cardiac events<sup>[1,4]</sup>. Some of their ingredients individually or in combination may be associated with reduced endothelial function<sup>[5-7]</sup>.

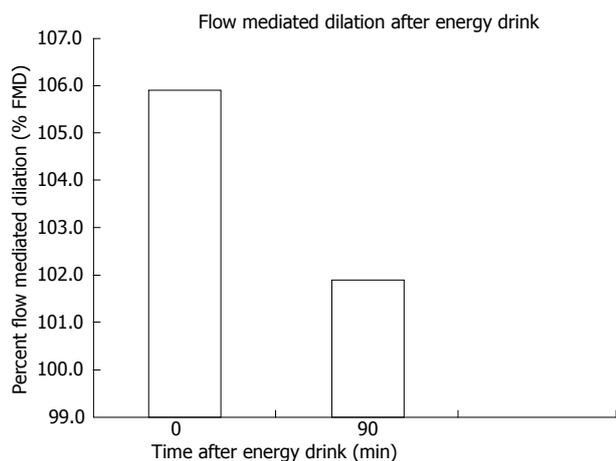
Mechanistically, endothelial dysfunction, where the endothelium's ability in regulating vascular resistance is impaired, may be related to reduced coronary blood flow<sup>[6,8]</sup>. Following exposure to stress such as exposure to cold, mental arithmetic, anger, exercise, cigarette smoking, cocaine, excess food or alcohol, the impaired ability to dilate the coronary arteries could result in supply-demand imbalance or coronary spasm, potentially leading to myocardial ischemia, coronary vasospasm, thrombosis and/or cardiac arrhythmia<sup>[6,9]</sup>. Importantly, this acute endothelial dysfunction could lead to ischemia, which in turn could lead to serious arrhythmia, coronary vasospasm, and myocardial infarction<sup>[1,6,10]</sup>.

This study describes the acute changes of normal endothelial function after consumption of a single can of a popular energy drink<sup>[11]</sup>.

## MATERIALS AND METHODS

After fasting from caffeine for at least 24 h and food for at least 8 h prior, eleven healthy non-smoker medical students (9 males), average age 24.5 years (range 23-27 years), average BMI 22.8, received an electrocardiogram (ECG), blood pressure and pulse check, and underwent baseline testing (BL) of endothelial function using the technique of endothelium-dependent flow-mediated dilatation (FMD) with high-resolution ultrasound according to recommended guidelines of the University of Wisconsin Atherosclerosis Imaging Research Program Core Laboratory by a single registered vascular ultrasonographer who was certified by the University of Wisconsin Atherosclerosis Imaging Research Program Core Laboratory<sup>[12]</sup>.

After resting supine for 10-min in a temperature-controlled room, a blood pressure cuff was placed on the widest part of proximal right forearm approximately 1 cm distal to the antecubital fossa. Using a 10 MHz resolution linear array vascular ultrasound transducer with a Philips iE33 ultrasound machine, the brachial artery was located above the elbow and scanned in longitudinal sections. After recording baseline B-mode digital images of the brachial artery and spectral Doppler images of



**Figure 1** Flow mediated dilation at baseline (0 min) and after energy drink (90 min). Consumption of the EB resulted in a significantly attenuated peak FMD response (mean ± SD): BL group 5.9% ± 4.6% vs EB group 1.9% ± 2.1%;  $P = 0.03$ . FMD: Flow mediated dilatation; BL: Baseline testing; EB: Energy beverage.

flow, the forearm cuff was inflated to 250 mmHg for 5 min to induce reactive hyperemia. Immediately after deflation, spectral Doppler images are obtained to verify hyperemia. FMD of the brachial artery was measured 60 and 90 s after cuff deflation. The relative FMD (%) was calculated as the ratio between the largest post-cuff release and the baseline diameter. Each image was checked for quality control, and each artery diameter was measured from the media to media points by two experts, 3 measurements at the QRS complex, repeated on 3 separate beats, and then averaged.

The subjects then drank an energy beverage (EB), a 24-oz can of Monster Energy Drink® in approximately 1 min. The contents of this can include 54 g Sucrose, glucose, sucralose, maltodextrin, Sodium 360 mg Sodium Citrate Sodium Chloride, Caffeine 240 mg, Taurine 2000 mg, Niacin 40 mg 200% RDA Niacinamide, Pyridoxine 4 mg 200% RDA, Cyanocobalamin (B12) 12 mcg 200% RDA, Riboflavin (B2) 3.4 mg 200% RDA, Ginseng Extract 400 mg, Glucuronolactone, Inositol (B8), Guarana Extract, and L-Carnitine all listed as a part of a 5000 mg "Energy Blend", and Sodium Benzoate.

The subjects had FMD repeated at 90 min after consumption of the EB. The subjects were in the supine position for all ECGs and FMD measurements.

### Statistical analysis

Statistical analyses were performed by John P Higgins and the statistical methods of this study were reviewed by Benjamin Yang using Microsoft Excel 2010 and the Data Analysis ToolPak. We used the *t*-test: Paired Two Sample for Means, and significance was defined as a *P*-value of 0.05 or less.

## RESULTS

Subjects characteristics averages (given with standard deviations) include: Age 24.5 ± 1.5 years, sex 9 male

and 2 female, weight 71.0 ± 9.1 kg, height 176.4 ± 6.0 cm, BMI 22.8 ± 2.7 kg/m<sup>2</sup>.

The hemodynamics were as follows, BL vs EB group respectively (mean ± SD): Heart rate 65.2 ± 11.3 vs 68.2 ± 11.8 beats per minute, systolic blood pressure 114.0 ± 10.4 mmHg vs 114.1 ± 10.4 mmHg, Diastolic blood pressure 68.8 ± 9.3 mmHg vs 70.6 ± 7.1 mmHg; all were not significantly different.

With drinking the energy beverage, a significantly attenuated peak FMD response was found (mean ± SD): BL group 5.9% ± 4.6% vs EB group 1.9% ± 2.1%;  $P = 0.03$  (Figure 1).

## DISCUSSION

There are few studies exploring the effects on endothelial function following consumption of energy drinks.

In one study, fifty healthy volunteers (34 male, aged 22 ± 2 years) consumed either a 250-mL sugar-free energy drink or 250 mL carbonated water (control)<sup>[13]</sup>. They found that an hour after consumption of an energy drink, there was an acute decreased in endothelial function and increased platelet aggregation<sup>[7,13]</sup>.

Another study involving 25 healthy young adults (13 male, aged 22.5 ± 0.6 years) who consumed either 355-mL Red Bull or 355-ml tap water noted that 2 h later, while blood pressure, heart rate and cardiac output were significantly increased, there was no reduction in endothelial function *via* finger skin microcirculation<sup>[14]</sup>.

A 47-year-old healthy Caucasian male was noted to have a progressive attenuation of peak flow-mediated dilatation at 45 and 90 min following consumption of a 24-oz can of Monster Energy Drink®<sup>[7]</sup>.

Energy drinks likely increase myocardial oxygen demand, and this may be increased under stress. For example, one study has noted that the combination of Red Bull and mental stress results in greater increases in heart rate and blood pressure, *i.e.*, a greater cardiovascular load<sup>[15]</sup>.

While our study has noted a change in endothelial function after consumption of energy drinks, which is consistent with some of the previous studies, it still however conflicts with other studies. A possible explanation for these contrasting results on endothelial function, blood pressure, and heart rate in response to energy drinks include difference in methods of assessing endothelial function, difference in methods of monitoring blood pressure, difference in types of energy drinks consumed, difference in study participant profiles, and varying environmental stimuli<sup>[15,16]</sup>. Further investigations should take in account these differences, and also investigate how energy drink consumption in stress conditions affect endothelial function, as it would help simulate conditions in which energy drinks are used in real-life.

Weaknesses of our study include the fact that human measurement was performed on the arterial segments, which may be less accurate than automated detection methods. However one study analyzing variability and

reproducibility of FMD found that the mean absolute difference in %FMD from baseline FMD assessment was 1.04% and 0.99% for short-term (48 h) and medium-term (3 mo) repeat measurements, respectively<sup>[17]</sup>. Potential improvements in the future include a water load as a control, and having FMD baseline measurements performed on one day, followed by the FMD measurements with energy beverage consumption on the next day. In addition, this was a small sample, and such medical student volunteers may be healthier than the normal population.

Consumption of energy drinks may lead to an acute attenuation of endothelial function. Given the popularity of energy drinks, especially among youth, the combination of their consumption and exercise/extreme sports, and the rise in emergency room visits associated with their consumption, it is important that the specific physiological effects they are having be elucidated. Due to the potential endothelial dysfunction that may occur with energy drinks and the potential morbidity when consumed with exercise, further research is needed to explore these mechanisms and significance of their effects.

## COMMENTS

### Background

Energy drinks are being consumed more and more worldwide, and have been associated with deaths in adolescents and young adults, especially when consumed while exercising. Adverse cardiovascular events can be caused by abnormal endothelial cell function or "endothelial dysfunction". Endothelial cells form the inner lining of blood vessels and have metabolic as well as synthetic functions, which allow them to carry out multiple important tasks such as regulating vascular resistance. Mechanistically, reduced coronary blood flow may be a symptom of endothelial dysfunction, and is associated with poor vascular reactivity, pro-thrombosis, pro-adhesion, pro-inflammation, and growth promotion.

### Research frontiers

There is a paucity of studies describing the effects on endothelial function following consumption of energy drinks. Several recent reviews on cardiovascular complications associated with energy drink consumption suggest that effects on endothelial function may play a role in subsequent cardiac events. Some of their ingredients individually or in combination may be associated with reduced endothelial function.

### Innovations and breakthroughs

The current study describes the acute changes of normal endothelial function following consumption of a single can of a popular energy drink. While the study has noted a change in endothelial function after consumption of energy drinks, which is consistent with some of the previous studies, it still however conflicts with other studies. A possible explanation into these contrasting results on endothelial function, blood pressure, and heart rate in response to energy drinks include a difference in study methods and energy drink types. Further investigations should take in account these differences, and also investigate how energy drink consumption in stress conditions affect endothelial function, as it would help simulate conditions in which energy drinks are used in real-life.

### Applications

Consumption of energy drinks may lead to an acute attenuation of endothelial function. Given the popularity of energy drinks, especially among youth, the combination of their consumption and exercise/extreme sports, and the rise in emergency room visits associated with their consumption, it is important that

the specific physiological effects they are having be elucidated. Further, due to the possibility that endothelial dysfunction may play a role in morbidity with concomitant energy drink intake and exercise, more research is recommended to clarify the mechanisms of and significance of these effects.

### Terminology

Energy drinks are also known as energy beverages. Popular brand names include Monster Energy Drink® and Red Bull Energy Drink® that contain high caffeine content, along with other ingredients. Flow-mediated dilatation is a non-invasive technique using high-resolution ultrasound to assess a vessel's endothelium-dependent (nitric oxide release) vasomotor function.

### Peer-review

In this study, Dr. Higgins and his colleagues have done a very interesting investigation even though the report is very brief. They show a significant result that one kind of the "energy beverage" is associated with endothelial dysfunction. The study is well designed and outcome is enough to warn the lovers of those drinks.

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