

Review

Energy drink consumption: a rising public health issue

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Abstract

Energy drink (ED) consumption has become a growing public health issue over the past few decades. Despite claims of being safe and beneficial, EDs have been linked to particularly fatal outcomes associated with the cardiovascular system which include atrial and ventricular arrhythmias, myocardial infarctions, cardiomyopathies, and sudden cardiac death. Large quantities of caffeine, taurine, sugars, and B-vitamins may be contributing to these outcomes by increasing the heart rate, blood pressure (BP), and contractility of the heart in addition to prolonging the QTc. There is still a substantial amount of unknown information on EDs that warrants more research and a dire need for age regulations, transparency of ingredients, clear labeling of adverse effects, and most importantly, education of consumers.

Keywords: energy drinks; caffeine; taurine; arrhythmia; red bull; monster energy

1. Introduction

Energy drink consumption has increased worldwide with its use becoming a norm in society. Many of these EDs advertise claims of increasing physical stamina, focus, cognition, and wakefulness in individuals who consume them. Combined with aggressive marketing from ED companies, these claims may be the very reason these beverages appeal to young adults, athletes, students, and military personnel. In addition to containing large quantities of caffeine, they also contain high concentrations of ingredients such as taurine, sucrose, B-vitamins, ginseng, and other herbal extracts [1]. According to recent data which evaluated caffeinated beverage consumption through volume sales in countries around the world, it was found that the United States consumed the most EDs, sports drinks, and carbonated soda per capita than in any other country [2]. The consumption of these beverages in the United States is most prevalent in men, especially between the ages of 18–34. Additionally, about one-third of teens from the ages of 12–17 also consume these beverages regularly [3]. Co-ingestion of other drugs and substances, particularly alcohol, with EDs has also become a widespread practice amongst adolescents and young adults [4]. Being highly unregulated, EDs are showing increasing scientific evidence of their detrimental health effects on various organ systems of the body. The organ systems affected by ED consumption include the gastrointestinal, renal, endocrine, and psychiatric systems [5] along with the cardiovascular and neurological systems being the most common [5,6]. The American Association of Poison

Control Centers (AAPCC) reported 1764 single exposures to caffeine-containing energy drinks in 2019 alone with 10 major outcomes and 1 death [7]. From 2009 to 2013, a total of 43 fatalities were linked to Monster Energy and 5-hour Energy as reported by the FDA's Center for Food and Safety and Applied Nutrition (CFSAN) Adverse Event Reporting System (CAERS) [8]. In 2018, the FDA issued a guidance on dietary supplements being sold in bulk that contained pure or highly concentrated levels of caffeine as being unlawful, however, they have yet to issue regulations on the consumption or availability of EDs [9]. Currently, EDs and energy shots exceed and even double or triple the FDA's official soft drink caffeine concentration limit that is regarded as safe, which is 71 milligrams (mg) per 12-ounce beverage [10]. The main ingredients of these beverages (caffeine, taurine, sucrose, and B-vitamins [1]) alter the cardiovascular parameters through various mechanisms and contribute to hemodynamic changes and raise the overall risks for short and long-term cardiovascular outcomes.

2. Pathophysiology

The adverse effects of EDs on the cardiovascular system are due to its many different ingredients that have the ability to individually and collectively change the physiology of the cardiovascular system. The main ingredients contributing to the stimulatory effects of these beverages are caffeine, taurine, sugars, and B-vitamins [1]. Currently, some of the top selling brands of EDs, Red Bull, Monster Energy, and Bang Energy all include these ingredients, in



Table 1. ED drink ingredients and their pathophysiological effects on the cardiovascular system.

Caffeine	<ul style="list-style-type: none"> • Blocks vasodilation of vascular beds • Increase in catecholamine levels, peripheral vascular resistance and renin secretion • Positive inotropic action on myocardium • Decreased myocardial perfusion
Taurine	<ul style="list-style-type: none"> • Positive inotropic action on myocardium
Sugars	<ul style="list-style-type: none"> • Increased heart rate, cardiac output and blood pressure • Obesity, insulin resistance and diabetes
B-vitamins	<ul style="list-style-type: none"> • Reduce homocysteine levels
Guarana and Yerba mate	<ul style="list-style-type: none"> • Same as caffeine
Ginkgo biloba	<ul style="list-style-type: none"> • Platelet-activating factor antagonism

addition to various other additives and elements. Red Bull and Monster Energy (original green) contain around 32 mg [11] to 34 mg [12] of caffeine per 100 mL, respectively. Per can, there is 80 mg of caffeine in an 8.4 fluid (fl) ounce can of Red Bull [11] and 160 mg of caffeine in a 16 fl ounce can of Monster Energy [12]. Moreover, Bang Energy contains around 300 mg of caffeine in its 16 ounce can (smallest can available) [13], which is just 100 mg less than the FDA approved safe limit of 400 mg of caffeine per day [14]. Red Bull and Monster Energy (original green) contain around 11 grams of added sugar per 100 mL [15,16], which is a total of 27 grams of sugar in an 8.4 fl ounce can of Red Bull [15] and 54 grams of sugar in a 16 fl ounce can of Monster Energy [16]. In addition to caffeine and sugar, most energy drinks also contain large amounts of taurine and B-vitamins [1]. All these ingredients have a certain mechanism of action through which they affect the cardiovascular system (Table 1). In the following sections, we will discuss the possible pathophysiologies behind these effects.

2.1 Caffeine

Caffeine acts on the cardiovascular system through various mechanisms (Fig. 1). It acts as an antagonist of adenosine A1, A2A, and A2B receptors mainly [17]. Adenosine acts on the local vascular receptors (mainly A2A in vascular tissues) causing vasodilation of vascular beds. Caffeine, by acting as an antagonist, blocks its vasodilatory effect. Moreover, the inhibition of adenosine receptors by caffeine causes an increase in plasma adenosine levels, which in turn increases the sympathetic tone, catecholamine levels, peripheral vascular resistance, and renin secretion. This is due to the systemic effects of adenosine as it stimulates the chemoreceptors in the circulatory system [18]. This could be the possible mechanism by which EDs acutely increases heart rate and blood pressure.

Another mechanism of caffeine is dependent on its competitive inhibition of phosphodiesterase, which in turn results in the elevation of myocardial cyclic adenosine monophosphate (AMP) and leads to a positive inotropic action on the myocardium [10]. The vasodilatory action

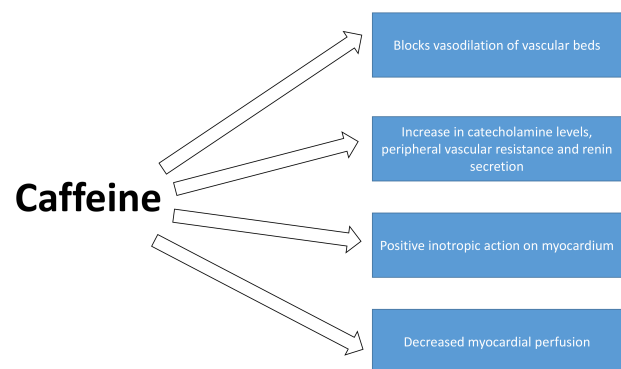


Fig. 1. Effects of caffeine on the cardiovascular system. These effects such as blocking the vasodilation of vascular beds, increase in sympathetic tone, and positive inotropic action on the myocardium brings about the acute increase in heart rate and blood pressure that is exhibited by caffeine consumption.

of adenosine also causes coronary arteries to dilate. Caffeine, by blocking adenosine receptors, inhibits this action. A study done on 47 patients showed that caffeine can attenuate the intravenous adenosine induced hyperemia in Fractional Flow Reserve (FFR) measurements [19]. Hence, caffeine can also decrease myocardial perfusion by blocking adenosine induced hyperemia.

2.2 Taurine

Taurine (2-aminoethane-sulfonic acid), another common ingredient in EDs, is one of the most abundant amino acids in the body. It is present in most tissues throughout the body including the brain, spinal cord, retina, heart cells, muscle cells, and leukocytes [20]. Short-term treatment using taurine causes an increase in intracellular sodium resulting from the influx of taurine and sodium via the taurine-sodium co-transporter. This increase in sodium causes a calcium influx via the sodium-calcium exchanger. Therefore, short term exposure to taurine increases intracellular levels of calcium in vascular smooth muscle cells and the heart, leading to a positive inotropic effect (Fig. 2). On the other hand, long-term taurine intake decreases intracellu-

lar sodium and calcium overload. Hence, with short term use, it contributes to caffeine induced intracellular calcium release while in the long term, it protects cells from the caffeine induced calcium overload [21].

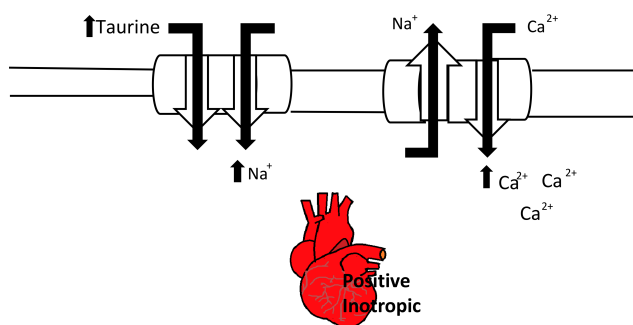


Fig. 2. Short-term treatment with taurine causes an increase in intracellular sodium and taurine via the taurine-sodium cotransporter. This causes a calcium influx via the sodium-calcium exchanger leading to increased intracellular calcium in vascular smooth muscle cells and the heart, resulting in a positive inotropic effect.

There are many cardiovascular benefits of taurine. It increases the transcription of CYP7A1, an important enzyme in bile conjugation along with increasing the liver's low-density lipoprotein (LDL) uptake and up-regulation of LDL receptors. Hence, it improves the lipid profile [10]. It also increases vascular relaxation, although the exact mechanism is unclear, it could be due to its ability to decrease angiotensin II-mediated vasoconstriction, opening of potassium channels, reducing calcium mobilization, or increasing nitric oxide levels as an antioxidant [22].

2.3 Sugars

EDs contain around 21 grams (g) to 34 g per 8 ounces of sugar, which is in the form of sucrose, glucose, or high fructose corn syrup [23]. A randomized crossover study showed that consuming sucrose and glucose together reduced total peripheral resistance but increased cardiac output, while fructose increased total peripheral resistance. Moreover, glucose, fructose, and sucrose also increased heart rate after 60 minutes [24]. According to studies done on rats, sucrose stimulates the sympathetic nervous system, leading to an increase in renin secretion, heart rate, renal sodium retention and vascular resistance, which in turn elevates blood pressure [25]. Similarly, glucose increases cardiac output by a combination of an increase in sympathetic activity and vasodilation associated with glucose-induced insulin secretion [26].

According to a review article on the content and safety of EDs, the amount of sugar in one can (or 500 mL) is typically about 13 teaspoons (slightly more than ¼ cup of sugar)

[27]. Sugar and caffeine have been noted to have synergistic effects causing a significantly high increase in blood glucose and insulin after its consumption [28]. Long-term consumption of these EDs containing excessive amounts of simple sugars can lead to obesity and insulin resistance. Reduction in insulin sensitivity causes pancreas beta cells to increase insulin secretion. Over time, beta cells are not able to secrete sufficient insulin to maintain normal blood glucose levels, causing diabetes [27]. And diabetes is a major risk factor and one of the most common causes of cardiovascular disease [29].

2.4 B-vitamins

B-vitamins comprise of a group of eight water soluble vitamins that perform essential roles in cellular functioning. These vitamins play a vital role in many catabolic and anabolic enzymatic reactions by acting as coenzymes [30]. They include thiamine, riboflavin, pantothenic acid, niacin, pyridoxine hydrochloride, inositol, cyanocobalamin, and biotin [27]. Vitamin B12 (cyanocobalamin) and folic acid can reduce homocysteine levels. The enzyme Methionine Synthase catalyzes the reaction of remethylation of homocysteine to methionine, requiring 5-methyltetrahydrofolate (circulating form of folate) and Vitamin B12 [31]. Hence, folate and vitamin B12 reduce homocysteine levels, which is a risk factor for cardiovascular diseases [32]. Despite B-vitamins being regarded as generally beneficial to the human body, large quantities of B-vitamins may likely be included in EDs due to their function as cofactors for energy utilization and metabolism, therefore possibly augmenting the stimulatory effects of the other ingredients present in these beverages. Most individuals however consume sufficient amounts of B-vitamins through their diets [33].

2.5 Other ingredients

Guarana is a plant used in some EDs and is rich in caffeine. Likewise, Yerba mate also contains a high caffeine concentration. Hence, these ingredients could also add to the adverse effects of caffeine on the cardiovascular system, as previously discussed. Ginkgo biloba is another herb used in some energy drinks. Some case reports describe serious bleeding events due to Ginkgo biloba extracts, probably due to its platelet-activating factor antagonism effect [34].

Ginseng is commonly used in energy drinks, and reports show that its prolonged use is associated with cardiovascular side effects, such as increased BP, long QT syndrome, or atrial fibrillation [34]. Therefore, there is an urgent need to study these ingredients in more detail, especially when they are combined with each other.

Additional mechanisms contributing to cardiovascular pathology include platelet aggregation and prolongation of the QTc. ED consumption has been shown to acutely increase platelet aggregation and decrease endothelial cell function [1]. Furthermore, EDs have also been found to prolong the QTc when compared to an equivalent amount

of isolated caffeine consumption without the additive ingredients present in EDs. A randomized, double-blind, controlled, crossover study showed that participants who consumed the commercial ED had significant prolongation of the QTc interval 2 hours after its consumption when compared to participants who consumed an equivalent amount of isolated caffeine. The prolongation of QTc is a known risk factor for fatal arrhythmias and may likely be a contributor to the adverse cardiovascular outcomes experienced by ED consumers. Although both the ED and caffeine drink caused initial elevations in systolic BP, the participants who consumed the ED showed significantly elevated BP even 6 hours after its consumption, indicating that other substances in the ED were hemodynamically active and contributing to this elevation [35]. The changes in cardiovascular parameters that have been observed thus far warrant further investigation as many of them can act synergistically and lead to detrimental outcomes.

3. Clinical outcomes

Because of the effects that EDs have on various cardiovascular parameters, there have been a variety of adverse clinical outcomes associated with their consumption (Table 2). High consumption of these beverages is associated with an acute hemodynamic and adrenergic state causing elevated glucose and norepinephrine levels, along with palpitations and increased blood pressure. This increases the cardiovascular risk, even in healthy young adults without any cardiovascular risk factors, reinforcing the critical need to advise the young population about the adverse cardiovascular effects [36].

Some of the adverse cardiovascular outcomes that have been reported include supraventricular and ventricular arrhythmias, coronary vasospasms, myocardial ischemia/infarctions, and sudden cardiac death in otherwise healthy patients [37,38]. The presenting symptoms in these patients were often chest pain, palpitations, nausea, and vomiting [37]. Reports of patients who have presented with these symptoms have indeed shown various cardiovascular markers indicating adverse or fatal outcomes. These markers include ST-segment changes, PR interval changes, and the prolongation of QT and QTc on the electrocardiogram (ECG), with many patients showing evidence of fatal arrhythmias [37] on presentation along with elevations in heart rate and blood pressure [1]. Other less common cardiovascular clinical outcomes include documented cases of dilated cardiomyopathies [39,40], Takotsubo cardiomyopathy [37], and aortic dissections [38] in otherwise healthy and young patients. Lastly, the deadliest of these cardiovascular outcomes that have been reported was sudden cardiac death [1,38]. The risk of detrimental outcomes increases in those who may have pre-existing structural or inherited cardiac abnormalities [38]. For example, a patient with a repaired structural abnormality due to Tetralogy of Fallot experienced ventricular fibrillation after the consumption of

three to four EDs [41]. Furthermore, these beverages can also be affecting those who may have heart conditions that they are unaware of. For example, a patient was discovered to have Brugada Syndrome (a mutation in the sodium channels of myocytes) after experiencing a ventricular arrhythmia following the ingestion of Red Bull [42]. There have also been reports of adverse cardiovascular effects with co-ingestion of other substances such as alcohol, methylenedioxymethamphetamine (MDMA), and amphetamine salts with EDs. Some clinical outcomes of co-ingestion included supraventricular arrhythmias, ventricular arrhythmias, and ST segment changes [37].

Besides the dangerous cardiovascular consequences which have been reported, many other systems of the human body are also affected negatively due to the consumption of EDs. Acute side effects associated with EDs are headache, discomfort, irritability, excitability, malaise, dehydration, nervousness, insomnia, nausea/vomiting, abdominal pain, and xerostomia [28]. Some other more serious and even fatal consequences that have been reported from ED consumption include epileptic seizures, intracerebral hemorrhage, acute hepatitis, rhabdomyolysis [5], acute renal failure [5,43], and psychosis [43,44].

4. Treatment

Patient education is highly necessary for overcoming this public health issue. Although statistics show otherwise, the American Academy of Pediatrics states that there should be no place for caffeine in the diets of children and adolescents [45]. In fact, the American College of Sports Medicine also stands by this and stated that energy should not be consumed by any children or adolescents, while also encouraging further education about the adverse effects of these beverages in schools, universities and by healthcare providers and athletic/personal trainers [46]. Because many children and adolescents under the age of 18 currently have access to these beverages, it is imperative that parents are also educated on the safety and potential hazards of EDs. It is important for healthcare providers to educate themselves and their patients on the detrimental effects of EDs. Lifestyle changes such as alternatives for caffeine consumption (coffee, tea), adequate hydration, and proper sleep, should be encouraged to help decrease the need for EDs. Individuals should also be advised to appropriately read and examine labels before consuming EDs. They should also be informed on the ingredients of these EDs and how they affect the human body and should be urged to do their own research as well. Due to the widespread use of EDs and their correlation with adverse outcomes, there is a dire need for tighter regulation on their availability and consumption. Although we understand the physiological effects of the main ingredients in these EDs, there are also additional stimulating ingredients and additives which may be contributing to these negative adverse effects. This combined with the large quantities of

Table 2. List of cardiac outcomes observed from the consumption of ED's.

Clinical outcomes observed after energy drink consumption	
EKG changes	QT and QTc prolongation
	ST segment elevation and depression
	PR interval changes
	QRS tachycardia with delta waves
	PVC and ST changes
	T waves
Arrhythmias	NSR with subtle J point elevation
	Atrial flutter
	Atrial fibrillation
	Ventricular fibrillation
	Torsades de Pointes
	Narrow complex tachycardia
	Ventricular Tachycardia
Wolf Parkinson White Syndrome	
Ischemia/Infarction	Myocardial infarction
	Coronary vasospasm
Myopathies	Takotsubo cardiomyopathy
	Dilated Cardiomyopathy
Exacerbation of pre-existing cardiac conditions	Brugada Syndrome
	Tetralogy of Fallot
	Long QT Syndrome 1
Others	Sudden Cardiac Death
	Aortic Dissection

ingredients that are being used in EDs, make these drinks increasingly dangerous. There is a need for age regulation, an increase in surveillance of EDs currently on the market, clear warning labels that include acute and long-term adverse effects, and clear instructions on lethal doses of these products to decrease and prevent fatal outcomes.

5. Conclusions

EDs have detrimental effects on the cardiovascular system, due to the collective effects of their ingredients. Caffeine, the major ingredient of these beverages, has several mechanisms through which it adversely affects the cardiovascular system, yet large cans containing excessive amounts of caffeine are being sold in the market. This indicates a need to regulate the contents in EDs and ensure their conformity to limits prescribed by the FDA. Recently, European Cardiac Arrhythmia Society released some recommendations to draw attention on the possible danger of EDs like not allowing children under 14 years or those children with known heart disease to consume EDs, only allowing children and adolescents to consume EDs after consideration of the amount of caffeine, carbohydrates and other nutrients, and not allowing mixing of EDs with alcohol and other drugs along with recommending not to use EDs before or during sports or heavy exercise. Moreover, it stated

that total caffeine content should be less than 400 mg/day for young adults and less than 2.5 mg/kg body weight for children over 14 [47]. This warrants an immediate need to issue proper legislation and regulate the sale of EDs.

Effects like QTc prolongation, increased blood pressure and heart rate, decreased myocardial perfusion, platelet aggregation, and endothelial dysfunction are dangerous and even fatal. As discussed, EDs have led to many adverse outcomes and will continue to do so, until and unless they are regulated. Ingredients like guarana, yerba mate, ginkgo biloba and ginseng are commonly included in the EDs without any major studies discussing their effects on the cardiovascular system. The current literature mostly discusses the effects of the major ingredients in EDs and although these ingredients may have benefits when consumed in isolation and in appropriate quantities, they have been contributing to dangerous side effects when consumed in EDs, which therefore warrants a need for more research. The mechanism of action of all the elements in EDs and their interaction with one another, along with the effects of co-ingestion of alcohol and other drugs with EDs is yet to be thoroughly investigated. Once fully understood, it may be possible to design a better blend of EDs that has maximum benefits and minimum risks.

Abbreviations

ED, Energy drink; BP, Blood pressure; LDL, Low-density lipoprotein; ECG, Electrocardiogram; AMP, Adenosine Monophosphate; FFR, Fractional Flow Reserve; Mg, milligram; G, gram; mL, milliliter; fl, fluid.

Author contributions

AK, HY, DR-M, RahJ, RohJ—made substantial contributions to analyze and interpret the research data available, drafted and revised the manuscript critically for important intellectual content, and gave their final approval of the version to be published. Each author sufficiently takes public responsibility for the content and agrees to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

Not applicable.

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Conflict of interest

The authors declare no conflict of interest.

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