

## REVIEW

## Energy Beverages: Content and Safety

JOHN P. HIGGINS, MD, MPhil; TROY D. TUTTLE, MS; AND CHRISTOPHER L. HIGGINS, BHMS (ExSc)

Exercise is making a resurgence in many countries, given its benefits for fitness as well as prevention of obesity. This trend has spawned many supplements that purport to aid performance, muscle growth, and recovery. Initially, sports drinks were developed to provide electrolyte and carbohydrate replacement. Subsequently, energy beverages (EBs) containing stimulants and additives have appeared in most gyms and grocery stores and are being used increasingly by “weekend warriors” and those seeking an edge in an endurance event. Long-term exposure to the various components of EBs may result in significant alterations in the cardiovascular system, and the safety of EBs has not been fully established. For this review, we searched the MEDLINE and EMBASE databases from 1976 through May 2010, using the following keywords: *energy beverage, energy drink, power drink, exercise, caffeine, red bull, bitter orange, glucose, ginseng, guarana, and taurine*. Evidence regarding the effects of EBs is summarized, and practical recommendations are made to help in answering the patient who asks, “Is it safe for me to drink an energy beverage when I exercise?”

*Mayo Clin Proc.* 2010;85(11):1033-1041

EB = energy beverage; ECG = electrocardiogram; SD = sport drink

Red Bull was introduced in Austria in 1987 and in the United States in 1997. Since then, the energy beverage (EB) market has grown exponentially.<sup>1</sup> Hundreds of different brands are now marketed, with caffeine content ranging from a modest 50 mg to an alarming 505 mg per can or bottle.<sup>2</sup> In the United States, Red Bull enjoyed a 65% share of the \$650-million energy/power drink market in 2005, and its sales are growing at about 35% per year.<sup>3</sup> The United States is the world’s largest consumer of EBs by volume, roughly 290 million gallons in 2007, or 3.8 qt per person per year.<sup>2</sup> Consumption of EBs is most common among those aged 11 to 35 years, and 24% to 57% of this age group reported that they drank an EB within the past few months.<sup>4</sup>

Regulation of EBs, including content labeling and health warnings, differs across countries, with some of the laxest requirements existing in the United States.<sup>2</sup> For instance, no EBs are banned in the United States, and EB companies can say whatever they want regarding energy and performance effects. This is in stark contrast to countries in which some EBs have been banned, and companies are not allowed to outline the performance effects that their products may or may not provide.<sup>4</sup> This absence of oversight has resulted in aggressive marketing of EBs, targeted primarily toward young men and openly promoting psychoactive, performance-enhancing, and stimulatory effects.<sup>1,4</sup>

Alarming, EB consumption has been shown to be positively associated with high-risk behavior, including

marijuana use, sexual risk taking, fighting, failure to use seat belts, and taking risks on a dare, as well as with smoking, drinking, problems stemming from alcohol abuse, and illicit drug use.<sup>5,6</sup>

In an era in which Gatorade and Powerade, termed *sport drinks* (SDs) for the purposes of this article, have paved the way as optimal hydration fluids that boast superiority to water, uncertainty is growing with regard to where EBs fit and how they are consumed.<sup>7</sup> Convenience stores now display EBs next to the SDs, which can mislead the consumer into thinking that they are similar products. Whereas SDs can indeed provide hydration and replenishment of electrolytes and carbohydrates, the elevated levels of caffeine in EBs have diuretic effects, more pronounced in the first-time user, that increase urinary output and natriuresis.<sup>8</sup> Additionally, EBs may have thermogenic effects.<sup>9</sup> Moreover, EBs supply an amount of carbohydrate far beyond that recommended for physically active people, which can slow the rate at which fluid is absorbed into the bloodstream or lead to gastrointestinal distress.<sup>10</sup> Finally, the effects due to the interaction of substances on which little research has been done (eg, glucuronolactone) are not well understood.

This review of EBs describes the various ingredients, discusses their safety, and provides recommendations regarding their use. Although most research studies and observational data have come from athletics, our research query included studies and information involving nonathlete consumers. Also, the review differentiates between these populations and offers recommendations specific to each group.

## METHODS

A search of the English-language scientific literature was performed primarily by searching the MEDLINE and EMBASE databases and using the Google Internet search

From the Division of Cardiology, Lyndon B. Johnson General Hospital, and Memorial Hermann Sports Medicine Institute, The University of Texas Medical School at Houston (J.P.H.); Noninvasive Cardiovascular Laboratory, University of Texas Health Science Center at Houston (T.D.T.); and School of Human Movements Studies, University of Queensland, St Lucia, Queensland, Australia (C.L.H.).

Individual reprints of this article are not available. Address correspondence to John P. Higgins, MD, MPhil, The University of Texas Medical School at Houston, LBJ General Hospital, 5656 Kelley St, UT Annex-Room 104, Houston, TX 77026-1967 (john.p.higgins@uth.tmc.edu).

© 2010 Mayo Foundation for Medical Education and Research

engine for the period January 1976 through May 2010. For this search, we used keywords found in lead peer-reviewed articles and research outlining the current body of knowledge on EBs. Keywords used in the search are *energy beverage*, *energy drink*, *power drink*, *exercise*, *caffeine*, *red bull*, *bitter orange*, *glucose*, *ginseng*, *guarana*, and *taurine*. The bibliographies of articles were searched for relevant articles; links on Web sites containing published articles were searched for pertinent information. This review endeavored to bring the most pertinent research to light in order to present real-world recommendations to both the athletic community and the general population.

### INGREDIENTS OF EBs

The most common ingredient in EBs is caffeine, which is often combined with taurine, glucuronolactone, guarana, and B vitamins to form what manufacturers have called an “energy blend.”<sup>11</sup> When higher doses of caffeine are combined with these other substances currently blended in EBs, the subsequent effect cannot always be predicted; adverse effects have been reported, including cardiac arrest.<sup>11,12</sup> The components of the 4 best-selling EBs are given in Table 1, and the specific ingredients are subsequently discussed in more detail.

Well-performed research indicates that some of these substances are important for proper body function, but this does not mean that a person has a deficiency. Moreover, important questions regarding overall intake and subsequent adverse effects should come to mind as the reader progresses through this review. We have also included information on the bioavailability of each substance if the necessary research has been completed.

#### CAFFEINE

Caffeine, an adenosine receptor antagonist, is a stimulant that can influence the activity of neuronal control pathways in the central and peripheral nervous systems.<sup>13</sup> It is the most common stimulant in EBs, with most EBs containing between 70 and 200 mg of caffeine per 16-oz serving. In comparison, an 8-oz cup of coffee contains 110 to 150 mg for drip, 65 to 125 mg for percolated, and 40 to 80 mg for instant; caffeinated beverages contain about 50 to 100 mg of caffeine.<sup>14</sup> Caffeine is known as an ergogenic compound that raises the heart rate and blood pressure. Adverse effects typically manifest with ingestion higher than 200 mg of caffeine and include insomnia, nervousness, headache, tachycardia, arrhythmia, and nausea.<sup>14,15</sup> The ergogenic effects of caffeine on athletic performance have been shown, and its broad range of metabolic, hormonal, and physiologic effects has been described.<sup>16,17</sup> Caffeine has been shown to be an effective ergogenic aid for endurance ath-

letes when ingested before and/or during exercise in moderate quantities (3-6 mg/kg of body mass); abstaining from caffeine for at least 7 days before use will optimize the effect.<sup>16</sup> Of note, caffeine appears on the list of substances banned by the International Olympic Committee.<sup>18</sup> Of all the compounds analyzed in this review, caffeine is by far the most-researched in the literature.<sup>16</sup>

The absolute bioavailability of orally administered caffeine was investigated in 10 healthy adult male volunteers aged 19 to 30 years.<sup>19</sup> Participants received a 5-mg/kg dose of caffeine as either an aqueous oral solution or an intravenous infusion on separate occasions about 1 week apart in a randomized crossover fashion. Plasma samples were collected during the 24-hour period after each dose and assayed for their caffeine content using a high-performance liquid chromatographic technique. The oral absorption was very rapid, with caffeine reaching a peak plasma concentration after 29.8 minutes, and the variation in the maximum plasma concentration was low at 10.0 µg/mL. The absolute bioavailability was assessed by comparing the areas under the plasma concentration vs time curves for the intravenous and oral doses of caffeine. The rapid absorption resulted in essentially complete bioavailability of the oral caffeine, with a plasma half-life varying from 2.7 to 9.9 hours, indicating substantial variability in its elimination between participants.<sup>19</sup>

Caffeine mobilizes fat stores and stimulates working muscles to use fat as a fuel, which delays depletion of muscle glycogen and allows for prolonged exercise.<sup>20</sup> The critical period in glycogen sparing appears to occur during the first 15 minutes of exercise, when caffeine has been shown to decrease glycogen utilization by as much as 50%. Thus, glycogen saved at the beginning is available during the later stages of exercise. Although the exact mechanism is still unclear, caffeine caused sparing in all the human studies in which muscle glycogen levels were measured. The effect on performance, which was observed in most experimental studies, was that participants were able to exercise longer before exhaustion occurred.<sup>20</sup>

Caffeine binds to the adenosine class of G protein-coupled receptors on the surface of heart muscle cells, which begins a second messenger system with cyclic adenosine monophosphate inside the cells and mimics the effects of epinephrine.<sup>21</sup> The rate of glycolysis increases, which increases the amount of adenosine triphosphate available for muscle contraction and relaxation.<sup>22</sup> This can result in a positive inotropy and chronotropy, ie, a stronger and faster heartbeat. Caffeine immediately increases blood pressure and peripheral vascular resistance, in part because of sympathetic stimulation. One group of investigators showed a significant effect of drinking caffeinated coffee on arterial tone and function, suggesting that caffeine immediately

TABLE 1. Comparison of Ingredients in Energy Beverages<sup>a</sup>

	Red Bull	Rockstar	Monster	Full Throttle
Calories	220	280	200	220
Carbohydrates	54 g Sucrose, glucose	62 g Sucrose, glucose	54 g Sucrose, glucose, sucralose, maltodextrin	57 g High-fructose corn syrup, sucrose
Sodium	Only listed as sodium citrate	80 mg sodium citrate	360 mg 16% RDA Sodium citrate, sodium chloride	160 mg Sodium citrate
Caffeine	160 mg	160 mg Part of a 1.35-g “energy blend”	Only listed as part of a 5000-mg “energy blend”	141 mg Part of a 3000-mg “energy blend”
Taurine	2000 mg	2000 mg Part of a 1.35-g “energy blend”	2000 mg Part of a 5000-mg “energy blend”	Only listed as part of a 3000-mg “energy blend”
Glucuronolactone	Only listed (1200 mg) <sup>b</sup>	None listed	Only listed as part of a 5000-mg “energy blend”	None listed
Niacin (B <sub>3</sub> )	200% RDA Niacinamide (40 mg) <sup>b</sup>	40 mg 200% RDA Niacinamide	40 mg 200% RDA Niacinamide	100% RDA Niacinamide
Inositol (B <sub>8</sub> )	Only listed	50 mg Part of a 1.35-g “energy blend”	Only listed as part of a 5000-mg “energy blend”	None listed
Pyridoxine hydrochloride (B <sub>6</sub> )	500% RDA (10 mg) <sup>b</sup>	4 mg 200% RDA	4 mg 200% RDA	200% RDA
Cyanocobalamin (B <sub>12</sub> )	160% RDA Listed as vitamin B <sub>12</sub> (10 µg) <sup>b</sup>	12 µg 200% RDA	12 µg 200% RDA	200% RDA
Riboflavin (B <sub>2</sub> )	None listed	6.8 mg 400% RDA	3.4 mg 200% RDA	None listed
Pantothenic acid (B <sub>5</sub> )	100% RDA Calcium pantothenate (10 mg) <sup>b</sup>	20 mg 200% RDA Calcium pantothenate	None listed	None listed
Ginseng extract	None listed	50 mg Part of a 1.35-g “energy blend”	400 mg	Only listed as part of a 3000-mg “energy blend”
Guarana extract	None listed	50 mg Part of a 1.35-g “energy blend”	Only listed as part of a 5000-mg “energy blend”	Only listed as part of a 3000-mg “energy blend”
Ginkgo biloba leaf extract	None listed	300 mg Part of a 1.35-g “energy blend”	None listed	None listed
Milk thistle extract	None listed	40 mg Part of a 1.35-g “energy blend”	None listed	None listed
L-carnitine	None listed	50 mg Part of a 1.35-g “energy blend”	Only listed as part of a 5000-mg “energy blend”	Only listed as part of a 3000-mg “energy blend” Carnitine fumarate
Sorbic acid	None listed	Yes	Yes	No
Sodium benzoate	None listed	Yes Benzoic acid	Yes Benzoic acid	Yes
Citric acid	None listed	Yes	Yes	Yes
Natural flavors	Yes	Yes	Yes	Yes
Artificial flavors	Yes	Yes	None listed	None listed
Coloring	“Colors”	“Caramel”	“Color added”	Blue 1, Red 40

<sup>a</sup> As listed on 16-oz can unless otherwise noted. RDA = recommended daily allowance.

<sup>b</sup> This amount is not listed on the can; the corporate office was called and this was all the information given.

increases arterial stiffness, with the effect being more pronounced on aortic systolic and diastolic blood pressures than on the brachial artery.<sup>23</sup>

The discussion on caffeine and hydration continues to evolve. A number of studies have examined the effects of ingesting a large dose of caffeine and found that urine output was increased.<sup>24</sup> Yet, the long-held conclusion that caffeine increases 24-hour urine output has been challenged, because most of the studies that established this conclusion involved persons who refrained from caffeine consumption before the analysis.<sup>25,26</sup> The human body develops a tolerance to caffeine quickly, usually 3 to 5 days after regular use, and when this happens, it noticeably weakens the already limited diuretic effect of caffeine.<sup>26,27</sup> Moreover, the human kidneys are masters at ensuring that proper homeostatic conditions are maintained. Recent research now leans toward the ability of the body to maintain proper water levels and overcome the mild diuretic effects of caffeine in long-term users.<sup>25,28</sup>

As the rest of the ingredients are reviewed herein, please note that in comparison with caffeine, each has had far fewer research studies performed.

#### TAURINE

Taurine, a sulfur-containing amino acid, is the most abundant intracellular amino acid in humans and a normal constituent of the human diet.<sup>29</sup>

A study of the pharmacokinetics of taurine was conducted in 8 healthy male volunteers with a median age of 28 years. After oral administration of 4 g of taurine in the fasting state, blood samples were taken at regular intervals, and plasma taurine concentration was measured by a modified high-performance liquid chromatographic technique. Maximum plasma taurine concentration was 86 mg/L 1.5 hours after administration. Plasma elimination half-life and the ratio of clearance to bioavailability were 1.0 hour and 21 L/h, respectively.<sup>30</sup>

Taurine modulates skeletal muscle contractile function and may attenuate exercise-induced DNA damage, with some evidence showing the ability to improve exercise capacity and performance; however, this has not been definitively demonstrated.<sup>4</sup> Taurine has numerous other biological and physiologic functions, including bile acid conjugation and cholestasis prevention; antiarrhythmic, inotropic, and chronotropic effects; central nervous system neuromodulation; retinal development and function; endocrine or metabolic effects; and antioxidant and anti-inflammatory properties.<sup>31</sup> Taurine also assists in cell membrane stabilization, osmoregulation, and detoxification.<sup>32</sup> However, the amounts of taurine found in popular EBs are far below the amounts expected to deliver either therapeutic benefits or adverse events.<sup>14</sup>

#### GLUCURONOLACTONE

This is a naturally occurring substance produced in small amounts within the body. Supplementation with D-glucarates, including glucuronolactone, may favor the body's natural defense mechanism for eliminating carcinogens and tumor promoters and their effects.<sup>33</sup> Toxicokinetic data on glucuronolactone in rats, which show bioavailability and lack of accumulation, with peak plasma levels 1 to 2 hours after oral administration, are in accordance with the limited human data.<sup>34</sup> Unfortunately, little research has been done in humans, and the current body of knowledge on this substance is scant. Therefore, conclusions on whether this compound is harmful or beneficial cannot be made.

#### B VITAMINS

The B vitamins are water-soluble vitamins required as coenzymes for proper cell function, especially mitochondrial function and energy production.<sup>35</sup> B vitamins include thiamine, riboflavin, niacin, pantothenic acid, pyridoxine hydrochloride, biotin, inositol, and cyanocobalamin. Because EBs contain large amounts of sugar, these vitamins are touted as ingredients necessary to convert the added sugar to energy. Hence, the B vitamins are the "key" needed to unlock all the energy provided by the simple sugars in EBs, and this is the extra energy that EB companies claim their product can provide. An expansive amount of research has been done on the B vitamins, and we outline the specific functions each major B vitamin plays in the human body.

Thiamine (vitamin B<sub>1</sub>) is essential for the oxidative decarboxylation of the multienzyme branched-chain  $\alpha$ -keto acid dehydrogenase complexes of the citric acid cycle and thus serves as a coenzyme precursor of some key enzymes of carbohydrate metabolism.<sup>36</sup> Riboflavin (vitamin B<sub>2</sub>) is required for the flavoenzymes of the respiratory chain and thus also supports energy metabolism involving fats, carbohydrates, and proteins.<sup>37</sup>

The reduced form of nicotinamide adenine dinucleotide (NADH) is synthesized from niacin (vitamin B<sub>3</sub>). This coenzyme is required to supply protons for oxidative phosphorylation and plays a major part in energy production in cells.<sup>38</sup> It also stimulates the production of such neurotransmitters as L-dopa, dopamine, serotonin, and norepinephrine.

Pantothenic acid (vitamin B<sub>5</sub>) is required for coenzyme A,  $\alpha$ -ketoglutarate, and pyruvate dehydrogenase formation, as well as fatty acid oxidation.<sup>35</sup>

Pyridoxine hydrochloride (vitamin B<sub>6</sub>) is a coenzyme involved in amino acid and homocysteine metabolism, glucose and lipid metabolism, neurotransmitter production, and DNA and RNA synthesis.<sup>39</sup> Specifically, pyridoxine hydrochloride is involved in protein and red blood cell me-

tabolism, is important for immune system function, and is needed to convert tryptophan to niacin.

Biotin (vitamin B<sub>7</sub>) is the coenzyme of decarboxylases required for gluconeogenesis and fatty acid oxidation.<sup>35</sup> Inositol (formerly vitamin B<sub>8</sub> but declassified as a vitamin because it is synthesized by the human body) exists in 9 possible stereoisomers, of which the most common form is myo-inositol. It is part of cell membranes, plays a role in helping the liver process fats, and contributes to the function of muscles and nerves.<sup>40</sup>

Cyanocobalamin (vitamin B<sub>12</sub>) helps maintain nerve cell function, is needed for production of DNA, and is important in red blood cell formation.<sup>35</sup>

### GUARANA

Also known as guaranine, *Paullinia cupana*, and Sapindaceae, guarana is a rainforest vine that was domesticated in the Amazon for its caffeine-rich fruits and has long been used by the Amazonians to increase awareness and energy.<sup>41</sup> Guarana seeds contain more caffeine than any other plant in the world, with levels ranging from 2% to 8%; guarana also contains the stimulants theobromine and theophylline.<sup>42</sup> The amounts of guarana found in popular EBs are below the amounts expected to deliver therapeutic benefits or cause adverse events.<sup>14</sup> However, some young adults have been admitted to emergency departments with overdoses of caffeine after overindulging in guarana-based EBs.<sup>42</sup>

### GINSENG

Ginseng is one of the most popular herbal supplements in the world and is used for treatment and prevention of many ailments. This adaptogen (a natural herb product said to increase the body's resistance to stress, trauma, anxiety, and fatigue) is purported to increase energy, relieve stress, and increase memory by stimulating the hypothalamic and pituitary glands to secrete corticotropin. Athletes use ginseng for its alleged performance-enhancing attributes; however, a recent review concluded that enhanced physical performance after ginseng administration remains to be demonstrated.<sup>43</sup> Adverse effects associated with ginseng include hypotension, edema, palpitations, tachycardia, cerebral arteritis, vertigo, headache, insomnia, mania, vaginal bleeding, amenorrhea, fever, appetite suppression, pruritus, cholestatic hepatitis, mastalgia, euphoria, and neonatal death.<sup>4</sup> However, the amounts of ginseng found in EBs are far below the amounts expected to deliver therapeutic benefits or cause adverse events.<sup>14</sup>

### GINKGO BILOBA

Ginkgo biloba extract is derived from the leaves of the Ginkgo biloba tree and has been used in traditional Chinese medicine for centuries.<sup>44</sup> Ginkgo biloba extract has been

reported to have antioxidant properties, modify vasomotor function, reduce adhesion of blood cells to endothelium, inhibit activation of platelets and smooth muscle cells, affect ion channels, and alter signal transduction.<sup>45</sup> However, to date, no large, well-conducted randomized controlled trials have shown that it has important clinical effects in healthy or ill persons.<sup>44</sup>

### L-CARNITINE

This amino acid is made predominantly by the liver and kidneys to increase metabolism. Dietary supplementation with L-carnitine has been shown to increase maximal oxygen consumption and lower the respiratory quotient, indicating stimulation of lipid metabolism.<sup>46</sup> Recent evidence indicates that L-carnitine plays a decisive role in preventing cellular damage and favorably affects recovery from exercise stress. Uptake of L-carnitine by blood cells may promote (1) stimulation of hematopoiesis, (2) inhibition of collagen-induced platelet aggregation, and (3) prevention of programmed cell death in immune cells. There is evidence of a beneficial effect of L-carnitine supplementation in training, competition, and recovery from strenuous exercise and in regenerative athletics.<sup>46</sup> No advantage appears to exist in giving an oral dose greater than 2 g at one time, because absorption studies indicate saturation at this dose.<sup>47</sup>

### SUGARS

Sugars are the basic currency for energy in the body, with glucose being the key carbohydrate that can readily be oxidized by skeletal muscle for energy production. Often, EBs contain sugar (high-fructose corn syrup or sucrose). Administration of glucose or other carbohydrates before, during, and after prolonged exercise (>1 hour) has been shown to postpone fatigue, conserve muscle glycogen, and improve performance.<sup>48,49</sup> Ingestion of moderately concentrated carbohydrate solutions (4%-8%) with the aim of achieving a carbohydrate intake of 60 to 70 g/h enhances prolonged exercise performance and is appropriate for optimizing energy and fluid delivery without causing adverse effects.<sup>50</sup> However, the ergogenic effects of carbohydrate ingestion on performance during intermittent exercise such as competitive sports are less well established, although the evidence to date suggests diminished performance when carbohydrates are limited.<sup>48</sup> The amount of sugar provided in one can (or 500 mL) of an EB is typically about 54 g. A teaspoon of sugar weighs about 4 g, so a typical EB contains about 13 teaspoons, or just more than ¼ cup, of sugar.

Long-term exposure of the body to excesses of simple sugars is associated with the development of obesity and insulin resistance. Pancreatic beta cells increase insulin

secretion in response to this reduction in insulin sensitivity. Over time, in many individuals, the beta cells become unable to secrete sufficient insulin to maintain normal blood glucose levels, leading to the development of diabetes.<sup>51</sup>

### ANTIOXIDANTS

During exercise, inflammation and oxidative stress are linked by means of muscle metabolism and muscle damage.<sup>52</sup> Antioxidants are purported to aid the body in the recovery phase and reduce damage to muscle cells.<sup>53</sup> However, there is no convincing evidence that short-term or long-term exercise modifies antioxidant requirements, nor have significant effects been shown for supplementation in well-trained athletes.<sup>54</sup>

## DO EBs WORK AND ARE THEY SAFE?

### RESEARCH ISSUES

A number of factors relating to EB consumption may make good morbidity and mortality data difficult to ascertain. These include the following.

- The target market for EBs is people between 15 and 30 years of age. This population is typically healthy and involved in activities and includes a higher proportion of sports enthusiasts and high-risk takers.
- Because of the many ingredients in EBs, cause and effect is difficult to assign to one specific ingredient. Indeed, it may be the combination of ingredients that augments the effect.
- Most of the ingredients are available over the counter and are unregulated in the United States. Thus, EBs are not under the jurisdiction of the US Food and Drug Administration and therefore are not subject to the stringent requirements for safety and efficacy data before approval for human use.
- Binge drinking of EBs combined with alcohol is common practice, again making causation difficult to assign.
- Many people consume more than the recommended daily allowance of EBs. (Recommended daily allowance is one can.)

### SHORT-TERM EFFECTS

In addressing the question of safety, it is important to consider both short-term and long-term effects of ingestion of EBs. Physiologic effects occur immediately after drinking the first dose.

In one study, 15 healthy persons aged 18 to 40 years consumed 2 cans (500 mL) of a commercially available EB containing 1000 mg of taurine and 100 mg of caffeine, as well as vitamins B<sub>5</sub>, B<sub>6</sub>, and B<sub>12</sub>, glucuronolactone, and niacinamide, daily for 1 week; effects of the EB on their

blood pressure, pulse, and electrocardiogram (ECG) were measured.<sup>55</sup> The key effects were as follows.

- Within 4 hours of EB consumption, the maximum systolic blood pressure increased by 8% on day 1 and 10% on day 7.
- Within 2 hours of EB consumption, the maximum diastolic blood pressure increased by 7% on day 1 and 8% on day 7.
- Heart rate increased by 8% on day 1 and 11% on day 7.
- Throughout the study, heart rates increased between 5 and 7 beats/min, and systolic blood pressure increased by 10 mm Hg after EB consumption.
- No clinically important ECG changes were observed.

The authors concluded that, although no clinically important ECG changes occurred, there were significant increases in heart rate and blood pressure, and thus patients with hypertension should not consume this type of drink.<sup>55</sup>

In a double-blind crossover study, 13 endurance-trained participants performed an exhaustive bout of endurance exercise at 3 different times.<sup>56</sup> Before the exercise, they ingested the original Red Bull drink, a similar drink without taurine but containing caffeine, and a placebo drink without caffeine or taurine. Echocardiography was performed before ingestion of the drinks, before exercise, 40 minutes after ingestion, and in the recovery period after exercise. Stroke volume was significantly influenced only in the Red Bull group (80±21 mL before ingestion vs 98±26 mL in the recovery period), mainly because of reduced end-systolic volume. Thus, this study shows that the original Red Bull increases cardiac contractility.<sup>56</sup>

A double-blind study of 68 healthy college-aged students showed that Red Bull reduced the changes in blood pressure during a stressful experience (cold pressor test) and increased participants' pain threshold.<sup>57</sup>

In a study of the effects of EBs on high-intensity run time-to-exhaustion in physically active university students (n=17; 9 men; mean age, 21±4 years), sugar-free Red Bull did not influence high-intensity run time-to-exhaustion.<sup>58</sup> However, in a study of 6 male and 6 female trained cyclists (mean age, 27.3 years), improved cycling time-trial performance was noted after ingestion of a caffeinated EB.<sup>59</sup>

In addition to these studies, several case reports on the immediate effects of EB ingestion have been published.

- Four documented cases of caffeine-associated death have been reported, as well as 5 separate cases of seizures associated with consumption of energy/power drinks.<sup>4,14</sup>
- An otherwise healthy 28-year-old man had cardiac arrest after a day of motocross racing.<sup>11</sup>
- A healthy 18-year-old man died playing basketball after drinking 2 cans of Red Bull.<sup>60</sup>

- Postural tachycardia syndrome associated with a vasovagal reaction was recorded in a young volleyball player after an excess intake of Red Bull as a refreshing energy/power drink, leading experts to suspect the drink as a possible cause of orthostatic intolerance.<sup>61</sup>

- Four cases of psychiatric effects on patients with known psychiatric illness were reported.<sup>4</sup>

- One case of suspected anaphylaxis was reported.<sup>62</sup>

Regarding fluid replacement in persons who do not typically ingest large amounts of caffeine, EBs deliver a considerable amount of caffeine, which can stimulate the kidneys to produce more urine. Thus, EBs can have a net dehydrating effect.<sup>63</sup>

### LONG-TERM EFFECTS

Unfortunately, there are no long-term studies of the effects of caffeine, taurine, and glucuronolactone on the body.<sup>4</sup> Energy beverages may exacerbate risk factors for heart disease because studies suggest that EBs may serve as a gateway to other forms of drug dependence.<sup>1</sup> Norway, Denmark, and France have banned the sale of Red Bull, partly in response to a study on rats that were fed taurine and exhibited bizarre behavior, including anxiety and self-mutilation.<sup>64</sup>

Whether caffeine can cause hypertension and coronary artery disease is still controversial, but questions have been raised about its safety in patients with heart failure and arrhythmia.<sup>65</sup> However, no clear association between coffee and the risk of hypertension, myocardial infarction, or other cardiovascular diseases has been demonstrated.<sup>66</sup>

### COMBINING EBs AND ALCOHOL

Many consumers are combining EBs with alcoholic drinks. These individuals are typically white men and intramural athletes, a group now termed “toxic jocks.”<sup>74</sup> The consequences can be tragic, as illustrated recently by Cleveland Browns wide receiver Donté Stallworth, who told police that he drank up to 4 shots of premium tequila and a can of Red Bull while partying with friends at a Miami Beach club, but did not feel drunk in the hours before he struck and killed a pedestrian with his car.<sup>67</sup> The combination of EBs with alcohol can impair cognitive function and reduce symptoms of alcohol intoxication, including the depressant effects, thus increasing the probability of accidents and/or favoring the possibility of development of alcohol dependence.<sup>68,69</sup> The combination might also increase important arrhythmia in patients with underlying heart disease.<sup>70</sup>

In late 2009, 100 scientists and physicians signed a petition that was delivered to the US Food and Drug Administration asking for more regulation of increasingly popular EBs because their high caffeine content puts young drink-

TABLE 2. **Recommendations Regarding Energy Beverage Consumption**

For the nonathlete consumer
Limit your consumption of EBs to no more than 500 mL, or 1 can per day
Do not mix EBs with alcohol; this can mask intoxication and may be extremely dehydrating
Rehydrate with water or an appropriately formulated SD after exercise or intense physical activity
If you experience an adverse reaction to an EB, report it to your health care professional or organization
If you are being treated for hypertension, avoid using EBs
If you have a serious underlying medical condition, including coronary artery disease, heart failure, or arrhythmia, consult with your physician before using EBs
For the athlete participating in exercise lasting <1 h
Do not use EBs
SDs appear safe, but we recommend against EBs while exercising because of the possibility of dehydration, elevation of blood pressure, and lack of equivocal benefits vs water or SDs
For the athlete participating in exercise lasting ≥1 h
Do not use EBs
SDs containing carbohydrates and electrolytes help prevent dehydration and restore important minerals lost through perspiration, and they produce better hydration than water

EB = energy beverage; SD = sport drink.

ers at possible risk of caffeine intoxication and higher rates of alcohol-related injuries.<sup>2,5</sup>

Clearly, more research is needed concerning the combined effects of the substances listed in this report and, specifically, at the doses EBs provide. Teens and young adults, both athletes and nonathletes, are consuming EBs at an alarming rate; thus, we need to determine whether long-term use of EBs by this population will translate into deleterious effects later.

## RECOMMENDATIONS

On the basis of this review, we make the recommendations listed in Table 2.

In summary, one can of an EB during one session is safe for most healthy individuals. However, excess consumption and consumption with other caffeine-containing beverages or alcohol may lead to adverse effects and possibly death. Patients with clinically relevant underlying medical conditions, including heart disease and hypertension, should consult with their physician before drinking EBs.

## CONCLUSION

Coaches and athletic departments should take the initiative in addressing the issue of EBs with student athletes and in educating them about the effects and risks. The main ingredients of energy/power drinks are caffeine, taurine, glucuronolactone, B vitamins, guarana, ginseng, ginkgo bi-

loba, L-carnitine, sugars, antioxidants, and trace minerals. The negative effects of excess caffeine have been proven, but the positive effects of many of the other additives, such as taurine and glucuronolactone, remain unproven, as does the combined effect of these ingredients in EBs.

Ingestion of EBs before an event or during training can have serious adverse effects, most notably restlessness and irritability; can increase blood pressure; and may result in dehydration. The long-term effects of EBs on the human body have not been established.

Limited ingestion of EBs by healthy people is not likely to cause major adverse effects, but binge consumption or consumption with alcohol may lead to adverse events. Individuals with medical illnesses, especially underlying heart disease, should check with their physician before using EBs, because they may exacerbate their condition.

## REFERENCES

- Reissig CJ, Strain EC, Griffiths RR. Caffeinated energy drinks—a growing problem. *Drug Alcohol Depend*. 2009;99(1-3):1-10.
- Weise E. Petition calls for FDA to regulate energy drinks. *USA Today*. October 22, 2008. [http://www.usatoday.com/news/health/2008-10-21-energy-drinks\\_N.htm](http://www.usatoday.com/news/health/2008-10-21-energy-drinks_N.htm). Accessed September 3, 2010.
- Bryce DJ, Dyer JH. Strategies to crack well-guarded markets. *Harv Bus Rev*. 2007;85(5):84-92.
- Ballard SL, Wellborn-Kim JJ, Clauson KA. Effects of commercial energy drink consumption on athletic performance and body composition. *Phys Sportsmed*. 2010;38(1):107-117.
- Thombs DL, O'Mara RJ, Tsukamoto M, et al. Event-level analyses of energy drink consumption and alcohol intoxication in bar patrons. *Addict Behav*. 2009;35(4):325-330.
- Miller KE. Energy drinks, race, and problem behaviors among college students. *J Adolesc Health*. 2008;43(5):490-497.
- Howarth KR, Moreau NA, Phillips SM, Gibala MJ. Coingestion of protein with carbohydrate during recovery from endurance exercise stimulates skeletal muscle protein synthesis in humans. *J Appl Physiol*. 2009;106(4):1394-1402.
- Riesenhuber A, Boehm M, Posch M, Aufricht C. Diuretic potential of energy drinks. *Amino Acids*. 2006;31(1):81-83.
- Rashti SL, Ratamesh NA, Kang J, Faigenbaum AD, Chilakos A, Hoffman JR. Thermogenic effect of meltdown RTD energy drink in young healthy women: a double blind, cross-over design study. *Lipids Health Dis*. 2009;8:57.
- Davis JM, Burgess WA, Slentz CA, Bartoli WP, Pate RR. Effects of ingesting 6% and 12% glucose/electrolyte beverages during prolonged intermittent cycling in the heat. *Eur J Appl Physiol Occup Physiol*. 1988;57(5):563-569.
- Berger AJ, Alford K. Cardiac arrest in a young man following excess consumption of caffeinated “energy drinks.” *Med J Aust*. 2009;190(1):41-43.
- Nagajothi N, Khraisat A, Velazquez-Cecena JL, et al. Energy drink-related supraventricular tachycardia. *Am J Med*. 2008;121(4):e3-e4.
- Jones G. Caffeine and other sympathomimetic stimulants: modes of action and effects on sports performance. *Essays Biochem*. 2008;44(1):109-123.
- Clauson KA, Shields KM, McQueen CE, Persad N. Safety issues associated with commercially available energy drinks. *J Am Pharm Assoc*. (2003). 2008;48(3):e55-e63.
- Calamaro CJ, Mason TB, Ratcliffe SJ. Adolescents living the 24/7 lifestyle: effects of caffeine and technology on sleep duration and daytime functioning. *Pediatrics*. 2009;123(6):e1005-e1010.
- Ganio MS, Klau JF, Casa DJ, Armstrong LE, Maresh CM. Effect of caffeine on sport-specific endurance performance: a systematic review. *J Strength Cond Res*. 2009;23(1):315-324.
- Sokmen B, Armstrong LE, Kraemer WJ, et al. Caffeine use in sports: considerations for the athlete. *J Strength Cond Res*. 2008;22(3):978-986.
- Clarkson PM. Nutrition for improved sports performance: current issues on ergogenic aids. *Sports Med*. 1996;21(6):393-401.
- Blanchard J, Sawers SJ. The absolute bioavailability of caffeine in man. *Eur J Clin Pharmacol*. 1983;24(1):93-98.
- Laurent D, Schneider KE, Prusaczyk WK, et al. Effects of caffeine on muscle glycogen utilization and the neuroendocrine axis during exercise. *J Clin Endocrinol Metab*. 2000;85(6):2170-2175.
- Piirainen H, Ashok Y, Nanekar RT, Jaakola VP. Structural features of adenosine receptors: from crystal to function [published online ahead of print June 2, 2010]. *Biochim Biophys Acta*. doi:10.1016/j.bbame.2010.05.021.
- Mayo Clinic Staff. Nutrition and healthy eating: caffeine: how much is too much? MayoClinic.com Web site. Published March 24, 2009. <http://www.mayoclinic.com/health/caffeine/NU00600#>. Accessed September 3, 2010.
- Mahmud A, Feely J. Acute effect of caffeine on arterial stiffness and aortic pressure waveform. *Hypertension*. 2001;38(2):227-231.
- Neuhäuser-Berthold B, Beine S, Verwied SC, Lüthmann PM. Coffee consumption and total body water homeostasis as measured by fluid balance and bioelectrical impedance analysis. *Ann Nutr Metab*. 1997;41(1):29-36.
- Maughan RJ, Griffin J. Caffeine ingestion and fluid balance: a review. *J Hum Nutr Diet*. 2003;16(6):411-420.
- Robertson D, Wade D, Workman R, Woosley RL, Oates JA. Tolerance to the humoral and hemodynamic effects of caffeine in man. *J Clin Invest*. 1981;67(4):1111-1117.
- Fisher SM, McMurray RG, Berry M, Mar MH, Forsythe WA. Influence of caffeine on exercise performance in habitual caffeine users. *Int J Sports Med*. 1986;7(5):276-280.
- Armstrong LE, Pumerantz AC, Roti MW, et al. Fluid, electrolyte, and renal indices of hydration during 11 days of controlled caffeine consumption. *Int J Sport Nutr Exerc Metab*. 2005;15(3):252-265.
- Gaull GE. Taurine in pediatric nutrition: review and update. *Pediatrics*. 1989;83(3):433-442.
- Ghandforoush-Sattari M, Mashayekhi S, Krishna CV, Thompson JP, Routledge PA. Pharmacokinetics of oral taurine in healthy volunteers. *J Amino Acids*. 2010;10. <http://www.sage-hindawi.com/journals/jaa/2010/346237.html>. Accessed September 3, 2010.
- Lourenço R, Camilo ME. Taurine: a conditionally essential amino acid in humans? An overview in health and disease. *Nutr Hosp*. 2002;17(6):262-270.
- Sato S, Kurasaki M. The physiological role of taurine in tissues and organs, especially in the liver and kidney. *Foods Food Ingrid J Jpn*. 2003;208(2):133-139.
- Zóltaszek R, Hanausek M, Kiliańska ZM, Walaszek Z. The biological role of D-glucuric acid and its derivatives: potential use in medicine [in Polish]. *Postepy Hig Med Dosw (Online)*. 2008; 62:451-462.
- Scientific Committee on Food. European Commission, Health & Consumer Protection Directorate-General. Opinion of the Scientific Committee on Food on additional information on “energy” drinks. Published March 5, 2003. [http://ec.europa.eu/food/fs/sc/scf/out169\\_en.pdf](http://ec.europa.eu/food/fs/sc/scf/out169_en.pdf). Accessed September 3, 2010.
- Depeint F, Bruce WR, Shangari N, Mehta R, O'Brien PJ. Mitochondrial function and toxicity: role of the B vitamin family on mitochondrial energy metabolism. *Chem Biol Interact*. 2006;163(1-2):94-112.
- Ba A. Metabolic and structural role of thiamine in nervous tissues. *Cell Mol Neurobiol*. 2008;28(7):923-931.
- Lakshmi AV. Riboflavin metabolism—relevance to human nutrition. *Indian J Med Res*. 1998;108(1):182-190.
- Sauve AA. NAD+ and vitamin B3: from metabolism to therapies. *J Pharmacol Exp Ther*. 2008;324(3):883-893.
- Spinneker A, Sola R, Lemmen V, Castillo MJ, Pietrzik K, Gonzalez-Gross M. Vitamin B6 status, deficiency and its consequences—an overview. *Nutr Hosp*. 2007;22(1):7-24.
- Balla T. Regulation of Ca<sup>2+</sup> entry by inositol lipids in mammalian cells by multiple mechanisms. *Cell Calcium*. 2009;45(6):527-534.
- da Costa Miranda V, Truffelli DC, Santos J, et al. Effectiveness of guarana (*Paullinia cupana*) for postradiation fatigue and depression: results of a pilot double-blind randomized study. *J Altern Complement Med*. 2009;15(4):431-433.
- Smith N, Atroch AL. Guarana's journey from regional tonic to aphrodisiac and global energy drink. *Evid Based Complement Alternat Med*. 2007;5(10):5.
- Bahrke MS, Morgan WP, Stegner A. Is ginseng an ergogenic aid? *Int J Sport Nutr Exerc Metab*. 2009;19(3):298-322.
- Nicolai SP, Kruidenier LM, Bendermacher BL, Prins MH, Teijink JA. Ginkgo biloba for intermittent claudication. *Cochrane Database Syst Rev*. 2009;(2):CD006888.



45. Zhou W, Chai H, Lin PH, Lumsden AB, Yao Q, Chen C. Clinical use and molecular mechanisms of action of extract of Ginkgo biloba leaves in cardiovascular diseases. *Cardiovasc Drug Rev.* 2004;22(4):309-319.
46. Karlic H, Lohninger A. Supplementation of L-carnitine in athletes: does it make sense? *Nutrition.* 2004;20(7-8):709-715.
47. Bain MA, Milne RW, Evans AM. Disposition and metabolite kinetics of oral L-carnitine in humans. *J Clin Pharmacol.* 2006;46(10):1163-1170.
48. el-Sayed MS, MacLaren D, Rattu AJ. Exogenous carbohydrate utilisation: effects on metabolism and exercise performance. *Comp Biochem Physiol Physiol.* 1997;118(3):789-803.
49. Burke LM, Millet G, Tarnopolsky MA; International Association of Athletics Federations. Nutrition for distance events [published correction appears in *J Sports Sci.* 2009;27(6):667]. *J Sports Sci.* 2007; 25(suppl 1):S29-S38.
50. Jeukendrup AE, Jentjens RL, Moseley L. Nutritional considerations in triathlon. *Sports Med.* 2005;35(2):163-181.
51. Tappy L, Lê KA, Tran C, Paquot N. Fructose and metabolic diseases: new findings, new questions [published online ahead of print May 13, 2010]. *Nutrition.* doi:10.1016/j.nut.2010.02.014.
52. Peake JM, Suzuki K, Coombes JS. The influence of antioxidant supplementation on markers of inflammation and the relationship to oxidative stress after exercise. *J Nutr Biochem.* 2007;18(6):357-371.
53. Williams SL, Strobel NA, Lexis LA, Coombes JS. Antioxidant requirements of endurance athletes: implications for health. *Nutr Rev.* 2006;64(3):93-108.
54. Margaritis I, Rousseau AS. Does physical exercise modify antioxidant requirements? *Nutr Res Rev.* 2008;21(1):3-12.
55. Steinke L, Lanfear DE, Dhanapal V, Kalus JS. Effect of "energy drink" consumption on hemodynamic and electrocardiographic parameters in healthy young adults. *Ann Pharmacother.* 2009;43(4):596-602.
56. Baum M, Weiss M. The influence of a taurine containing drink on cardiac parameters before and after exercise measured by echocardiography. *Amino Acids.* 2001;20(1):75-82.
57. Ragsdale FR, Gronli TD, Batoool N, et al. Effect of Red Bull energy drink on cardiovascular and renal function. *Amino Acids.* 2010;38(4):1193-1200.
58. Candow DG, Kleisinger AK, Grenier S, Dorsch KD. Effect of sugar-free Red Bull energy drink on high-intensity run time-to-exhaustion in young adults. *J Strength Cond Res.* 2009;23(4):1271-1275.
59. Ivy JL, Kammer L, Ding Z, et al. Improved cycling time-trial performance after ingestion of a caffeine energy drink. *Int J Sport Nutr Exerc Metab.* 2009;19(1):61-78.
60. Independent.ie. Red Bull, alcohol and drugs 'can spark violence.' Published February 21, 2007. <http://www.independent.ie/national-news/red-bull-alcohol-and-drugs-can-spark-violence-56088.html>. Accessed September 3, 2010.
61. Terlizzi R, Rocchi C, Serra M, Solieri L, Cortelli P. Reversible postural tachycardia syndrome due to inadvertent overuse of Red Bull. *Clin Auton Res.* 2008;18(4):221-223.
62. Masuda K, Katoh N, Mizutani H, Kishimoto S. Anaphylaxis to vitamin B2 added to an energy drink. *Clin Exp Dermatol.* 2009;34(7):e263-e264.
63. Hew-Butler T, Verbalis JG, Noakes TD. Updated fluid recommendation: position statement from the International Marathon Medical Directors Association (IMMDA). *Clin J Sport Med.* 2006;16(4):283-292.
64. CBC News. Red Bull promotion near Halifax schools halted: energy drink maker tells province promotion was a mistake. Updated September 27, 2007. <http://www.cbc.ca/canada/novascotia/story/2007/09/27/redbull-schools.html>. Accessed September 3, 2010.
65. Frishman WH, Del Vecchio A, Sanal S, Ismail A. Cardiovascular manifestations of substance abuse: part 2: alcohol, amphetamines, heroin, cannabis, and caffeine. *Heart Dis.* 2003;5(4):253-271.
66. Sudano I, Binggeli C, Spieker L, et al. Cardiovascular effects of coffee: is it a risk factor? *Prog Cardiovasc Nurs.* 2005;20(2):65-69.
67. Jones B. Tapes reveal Stallworth had tequila, shots before fatal accident. *USA Today.* July 8, 2009. [http://www.usatoday.com/sports/football/nfl/browns/2009-07-07-stallworth-tapes\\_N.htm](http://www.usatoday.com/sports/football/nfl/browns/2009-07-07-stallworth-tapes_N.htm). Accessed September 3, 2010.
68. Curry K, Stasio MJ. The effects of energy drinks alone and with alcohol on neuropsychological functioning. *Hum Psychopharmacol.* 2009;24(6):473-481.
69. Oteri A, Salvo F, Caputi AP, Calapai G. Intake of energy drinks in association with alcoholic beverages in a cohort of students of the School of Medicine of the University of Messina. *Alcohol Clin Exp Res.* 2007;31(10):1677-1680.
70. Wiklund U, Karlsson M, Ostrom M, Messner T. Influence of energy drinks and alcohol on post-exercise heart rate recovery and heart rate variability. *Clin Physiol Funct Imaging.* 2009;29(1):74-80.