Nutrition Reviews

Supplement Article

Performance outcomes and unwanted side effects associated with energy drinks

Ricardo Mora-Rodriguez and Jesús G Pallarés

Energy drinks are increasingly popular among athletes and others. Advertising for these products typically features images conjuring great muscle power and endurance; however, the scientific literature provides sparse evidence for an ergogenic role of energy drinks. Although the composition of energy drinks varies, most contain caffeine; carbohydrates, amino acids, herbs, and vitamins are other typical ingredients. This report analyzes the effects of energy drink ingredients on prolonged submaximal (endurance) exercise as well as on short-term strength and power (neuromuscular performance). It also analyzes the effects of energy drink ingredients on the fluid and electrolyte deficit during prolonged exercise. In several studies, energy drinks have been found to improve endurance performance, although the effects could be attributable to the caffeine and/or carbohydrate content. In contrast, fewer studies find an ergogenic effect of energy drinks on muscle strength and power. The existing data suggest that the caffeine dose given in studies of energy drinks is insufficient to enhance neuromuscular performance. Finally, it is unclear if energy drinks are the optimal vehicle to deliver caffeine when high doses are needed to improve neuromuscular performance.

INTRODUCTION

Carbonated drinks, sports drinks, and energy drinks are different beverage categories that consumers can find in any convenience or large store. While most people can distinguish between a soda and the other two beverage categories, sport and energy drinks could easily be confused. Sports drinks originated in the early 1960s with the formulation of Gatorade by Dr. Robert Cade to aid the summer performance of the collegiate football team at the University of Florida.[1] Several countries have since regulated the ingredients and labeling of beverages that are marketed as sports drinks. For instance, the European Food Safety Authority[2] advises a narrow range of osmolalities (200–330 mOsm·kg/H_2O) as well as sodium (20–50 mmol/L), and carbohydrate (2–8% w/v) concentrations when defining a sports drink's composition. Most sports drinks manufacturers formulate their products following the advice of scientific panels of experts in sports nutrition (e.g., the European Food Safety Authority and the US Food and Drug Administration); thus, the composition of these beverages is quite similar given that the common aim is to aid performance during prolonged exercise, especially in a hot environment.

Energy drinks appeared on the Western market 20 years later when the company Red Bull GmbH started selling their energy beverage products in Austria. In contrast with the relatively similar formulations of sports drinks, the composition of energy drinks is highly variable. Nevertheless, all energy drinks include one or several stimulants, with caffeine being the most common. The lack of uniformity in the formulations of energy drinks most probably originates from the fact that these drinks lack a unified purpose. Generally, manufacturers claim that energy drinks will benefit consumers by enhancing their physical capacity and cognitive performance.

Affiliations: *R Mora-Rodriguez* and *JG Pallarés* are with the Exercise Physiology Laboratory at Toledo, University of Castilla-La Mancha, Toledo, Spain.

Correspondence: *R Mora-Rodríguez*, Exercise Physiology Laboratory at Toledo, Universidad de Castilla-La Mancha, Avda, Carlos III, s/n, 45071 Toledo, Spain. E-mail: Ricardo.Mora@uclm.es. Phone: +34-925-26-88-00 (Ext. 5510). Fax: +34-925-26-88-46.

Key words: caffeine, endurance performance, energy drinks, neuromuscular performance, Red Bull, side effects, taurine

doi:10.1111/nure.12132

However, it is not clear if the aim is to enhance short, high-intensity bursts of exercise or to fuel and stimulate the body during prolonged aerobic exercise. Energy drinks seem to be marketed to improve performance in extreme sports requiring peak neuromuscular power and a high degree of athletic ability and coordination. However, energy drink advertisements may also feature long-duration sports like car and mountain bike racing or freestyle windsurfing that require a high degree of whole-body and local muscle endurance.

This review updates the current scientific information on the positive effects that energy drinks may have on exercise performance, and balances that with information on the possible negative side effects derived from their consumption. Due to the wide variability in the composition of energy drinks, this review analyzes the most common ingredients from the original energy drink, Red Bull, which are as follows: caffeine, taurine, glucuronolactone, glucose, and B vitamins. The review's focus is restricted to the claimed benefits that energy drinks provide for physical performance, since other reviews in this issue of the journal and elsewhere provide information on claims related to cognitive improvements[3] and weight loss.[4] Studies in humans are preferentially presented. Only laboratory studies in which variables were tightly controlled were included.

EVIDENCE FOR PROLONGED EXERCISE ENDURANCE

Energy drinks and prolonged muscle contraction

Complex carbohydrates and water are nutrients that have been repeatedly shown to delay fatigue during prolonged[5] dehydrating[6] exercise. However, energy drinks do not seem to be formulated to maximize the incorporation of glucose or water into the blood during exercise. One liter of Red Bull (i.e., 4 cans containing 250 mL each) contains 4 g of taurine (an amino acid), 2.4 g of glucuronolactone, 0.32 g of caffeine, 108 g of carbohydrates, and 0.14 g of B vitamins. The carbohydrate concentration is 11% and osmolality is 601 mOsm·kg/H_2O.[7] In contrast, a sports drink (e.g., Gatorade Orange) has a lower carbohydrate concentration (6%) and osmolality (297 mOsm·kg/H_2O). Carbohydrates comprise the main macronutrient in both drinks and determine the beverage's caloric content.

It has been reported that the caloric content of a beverage influences the rate of gastric emptying at rest[8] and when ingested during exercise.[9] High gastric emptying rates are important to ensure bioavailability of the ingested drink. Thus, ingestion of a drink with a carbohydrate concentration of 8% or higher could result in delayed incorporation into the bloodstream and reduced availability of the ingredients to the contracting musculature. Furthermore, increasing the osmolality of a 6% carbohydrate solution to 414 mOsm·kg/H_2O, reduced the absorption of the ingested fluid from 82% to 68% in comparison to water placebo.[10] The combination of high osmolality and carbohydrate concentration of Red Bull (601 mOsm kg/H_2O and 11%, respectively) probably reduces its absorption in comparison to a commercial sports drink.

In addition, energy drinks do not include salts in their formulation. Salt (sodium and chloride) is lost in sweat during exercise in amounts proportional to the exercise intensity.[11] Thus, the salt ingested in a beverage prior to or during prolonged exercise has an important role in maintaining cardiovascular stability, fluid balance, and even exercise performance.[12] In their favor, energy drinks contain caffeine, which has an ergogenic effect during prolonged exercise.[13,14] Caffeine ingestion increases endurance performance by delaying central nervous system fatigue,[15] and could increase neuromuscular performance through a direct effect on the muscle,[16] resulting, in both situations, in increased energy expenditure during exercise.

Recently, companies have introduced sugar-free versions of energy drinks. These beverages have zero calories and low osmolality (140 mOsmol·kg/H_2O for Red Bull Sugarfree), which solves the reduced absorption problems of the regular sugar-containing version. On the other hand, the caffeine in these drinks leads to extra energy expenditure, energy that is not provided by the sugar-free drink. Thus, the sugar-free drink may result in a faster drainage of endogenous energy stores (muscle glycogen, phosphocreatine, and ATP) counteracting its ergogenic actions. Hence, energy drinks containing stimulants and fluid but no carbohydrate (e.g., sugar-free versions) may improve endurance performance due to more extensive use of endogenous energy stores.

Energy drinks and rehydration

During prolonged exercise in warm environments, beverages are consumed in an attempt to maintain fluid balance by replacing the fluid lost via sweating. Fluid deficit (dehydration) increases the cardiovascular and thermal strain of exercise.[17] Even dehydration levels of less than 2% (e.g., 1.4 L fluid loss for a 70-kg man) increase core temperature and could decrease cycling performance.[18] The kidneys determine a body's fluid balance over the long term. Kidney function may be affected by the amount and composition of the rehydration fluid used during prolonged exercise. In addition, the kidneys help regulate blood pressure and acid-base balance, which are also important for performance during endurance exercise.

It is estimated that all our extracellular fluid passes through our kidneys 16 times per day. However, most of the fluid that is filtered at the glomerulus is reabsorbed and less than 1% ends up in the bladder (1 mL/min of urine formation rate). Renal blood flow, pressure, and hormones (mainly vasopressin and aldosterone) dictate the rates of glomerulus filtration and renal tubule reabsorption, respectively. Any component of a drink that induces vasoconstriction or alters the actions of the fluid-regulating hormones to reduce renal tubule reabsorption (i.e., diuretic effect) will negatively affect fluid balance and could, thus, impair endurance performance. Potentially, a beverage that contains a diuretic substance could increase body water loss through urine, reduce plasma volume, and negatively affect thermoregulation and cardiovascular function. Caffeine-containing drinks have been shown to increase urine production when ingested prior to[19] and after[20] exercise.

In addition to being diuretic, caffeine enhances urine sodium losses (i.e., natriuretic). Sodium has been deemed to be a key element in the maintenance of plasma volume during prolonged dehydrating exercise. This has recently been illustrated in a study comparing control subjects with patients that excrete a lot of sodium (cystic fibrosis) during prolonged dehydrating exercise.[21] The authors observed larger plasma volume reductions in the cystic fibrosis patients for the same level of dehydration. Likewise, the loss of sodium induced by caffeine ingestion could potentially alter cardiovascular performance during exercise. In addition, a negative sodium balance during prolonged exercise could weaken leg isometric strength.[22] Therefore, despite the fact that energy beverages are popularly associated with prolonged exercise, it is unclear if they can be recommended to rehydrate during long-duration physical activity due to their relatively high caffeine content and lack of added sodium.

DIURETIC EFFECT OF THE MOST COMMON ENERGY DRINK INGREDIENTS

B vitamins and glucose

B vitamins are water soluble and are, thus, distributed in the ample pool of body water. One liter of Red Bull contains 150 mg of B vitamins, any excess of which could be readily excreted by a normally functioning renal system. Upon ingestion, glucose is either utilized as an energy substrate or stored in the liver and muscles. The ingestion of 108 g of carbohydrate (4 cans of Red Bull) should not represent a problem for the kidneys. The exception is with the diabetic population for whom this amount of glucose could cause glycosuria (presence of glucose in urine) and the accompanying excessive water loss into the urine with resultant dehydration (i.e., osmotic diuresis).

Glucuronolactone

This naturally occurring metabolite of glucose is formed in the liver. Glucuronolactone is rapidly absorbed, metabolized, and excreted in urine as glucaric acid, xylitol, and L-xylulose. Glucuronic acid is an important constituent of fibrous and connective tissues. In 2003, the European Food Safety Authority raised concerns about the safety of its inclusion in energy drinks.[23] Their concerns were based on the finding of unspecified kidney lesions (inflammation in the papilla of the kidney) after 13 weeks of supplementation in rats. However, rats differ from humans in the way they metabolize glucuronolactone. In a follow-up study, which included a larger sample of rats, no effects on kidneys were reported, leading researchers to conclude that a dose of 1 g·day·kg/BW was safe.[24] It is estimated that the population with the highest energy drink exposure (i.e., 95% percentile) could be ingesting 1.5 cans per day of a Red Bull–like product, which will amount to 840 mg/day of glucuronolactone. Although this amount of glucuronolactone is much higher than the typical exposure in omnivore diets (1–2 mg/day), it is still well below the level that would trigger food safety concerns.[23] With regard to humans, no studies were found describing the effects of glucuronolactone on fluid regulation or in exercise performance.

Taurine

Taurine is present in high concentrations in skeletal muscle, the heart, and the central nervous system. It has been proposed that taurine participates in osmoregulation, stabilizes membrane potential in skeletal muscle, affects calcium ion kinetics, has an antioxidant and anti-inflammatory effect, and acts as a neurotransmitter.[25] One clinical study even suggests that oral treatment with taurine improves cardiac performance in humans with congestive heart failure.[26] However, in one study of healthy individuals, chronic supplementation with taurine (5 g/day for 7 days) had no effect on exercise heart rate or oxygen consumption during prolonged submaximal exercise.[27] Furthermore, muscle energy stores (e.g., glycogen, ATP, creatine, phosphocreatine) were not affected by a week of supplementation. Repeated taurine ingestion over 7 days had no effect on muscle metabolic responses to 120 min of exercise at moderate intensity.[27]

In one study, taurine infusion in cirrhotic patients resulted in transient diuresis and natriuresis, apparently through the inhibition of the renin-aldosterone axis.[28]

Based on this study, it could be hypothesized that taurine ingestion may also have a diuretic effect on healthy individuals. Furthermore, the combination of taurine and caffeine in energy drinks could result in a summation of their diuretic effects. Riesenhuber et al.[29] investigated the additive diuretic effects of caffeine and taurine in a cross-over design using 12 healthy male volunteers. Participants received 750 mL of four different test drinks in a blinded fashion after a 12 h overnight fluid restriction. One drink was regular Red Bull containing caffeine and taurine and the other drinks lacked caffeine, taurine, or both, but were otherwise identical. Urine volume and urine sodium concentration were measured for 6 h after drink ingestion. Caffeine treatment elevated urine output and urine sodium concentration, while taurine did not add to the effect of caffeine on urine production. On the contrary, there was a tendency for taurine to reduce diuresis and natriuresis. Thus, the currently available information does not support a diuretic role of taurine at the dose typically contained in energy drinks.

Caffeine

Caffeine is the most widely consumed drug in the world. This tri-methylxanthine antagonizes adenosine receptors and inhibits phosphodiesterase actions. Of all the methylxantines, caffeine has been found to increase urine output with a diuretic potency that is exceeded only by that of theophylline.[30] Administration of 400 mg of caffeine to healthy humans reduces kidney sodium reabsorption and increases the fractional excretion of water.[31] These effects do not seem to be mediated either by reduction in renal plasma blood flow[32] or by increases in plasma renin and vasopressin,[33] both of which remain unaltered by caffeine ingestion. Studies in mice show that the antagonism of A1 adenosine receptors is responsible for the diuretic and natriuretic actions of caffeine.[34]

Given this diuretic effect of caffeine, some water balance studies have proposed the ingestion of 1.2 mL of fluid per mg of caffeine to compensate its diuretic actions.[35] In the case of Red Bull, a 250 mL can has 80 mg of caffeine and thus surpasses that ratio by 2.5-fold. In addition, the effects of caffeine on increasing water excretion are dose-dependent and blunted when studying subjects that are in negative water balance (e.g., after an overnight fast). A review of the diuretic effects of caffeine in humans at rest proposes that there is a threshold of around 250–300 mg of caffeine, below which caffeine ingestion has no noticeable diuretic effect. This threshold could be even higher than 250 mg in habitual caffeine users.[36]

Ragsdale et al.[37] found that the ingestion of 250 mL of Red Bull (i.e., 1 can) had no measurable diuretic effect in comparison to the same volume of a glucose placebo solution. However, subjects were exposed to only 80 mg of caffeine and they started the trial mildly dehydrated (urine specific gravity ≥ 1.020). Ingestion of high volumes of energy drinks (i.e., 4 cans of Red Bull) or of energy drinks with higher caffeine concentrations (e.g., Monster Energy Drink, and Rockstar 2x Energy Drink) could have a diuretic effect and result in fluid deficit. Low levels of fluid deficit while at rest are rarely problematic, but during prolonged exercise, dehydration at a level of 1.5% raises core temperature and heart rate, and increases the perceived rate of exertion.[17] Thus, further study of the diuretic effects of caffeine during exercise is of interest.

EFFECTS OF CAFFEINE INGESTION DURING EXERCISE IN HOT ENVIRONMENTS

During exercise, blood flow is redistributed to the muscles, and the sympathetic nervous system lowers blood flow to the kidneys to 1% of cardiac output (~250 mL/min). The extent of the reduction in renal blood flow depends on the exercise intensity and duration. In fact, there is an inverse relationship between renal flow and heart rate, with progressive reductions in renal flow as the heart rate increases.[38] Renal blood flow parallels the glomerular filtration rate, explaining the reduction in urine formation during exercise.

Although exercise reduces urine formation, if fluid ingestion during prolonged exercise in the heat is enough to prevent dehydration, urine flow during exercise could reach the same levels as when at rest.[39] Some investigators have wondered whether the inclusion of caffeine in a rehydration drink could negatively affect fluid balance and, hence, thermoregulation during exercise. During prolonged exercise in a controlled hot environment (i.e., 33°C), male cyclists were invited to replace fluid losses (3.6 L) by consuming one of the following drinks: 1) water, 2) water + caffeine, 3) sports drink, 4) or sports drink + caffeine (Figure 1).[39] Trials were compared to no fluid replacement (NF) with or without caffeine pills. When dehydration was not prevented (NF trials), urine production was found to be very low and adding caffeine had no diuretic effect. When subjects drank the sports drink, urine production increased, but caffeine added to the sports drink had no diuretic effect either. It is possible that the salt included in the sports drink counteracted the diuretic effects of the caffeine. However, when caffeine was added to water, urine production increased by 37% (Figure 1).[39]

This increase in fluid losses via urine did not affect whole-body fluid balance, since urination represented a small percentage of total fluid loss (mostly sweat). Nevertheless, caffeine tended to increase core temperature when it was combined with the sports drink. This study is not alone in showing that caffeine has a mild thermogenic effect during[40] and even prior to exercise.[41] Finally, sweat

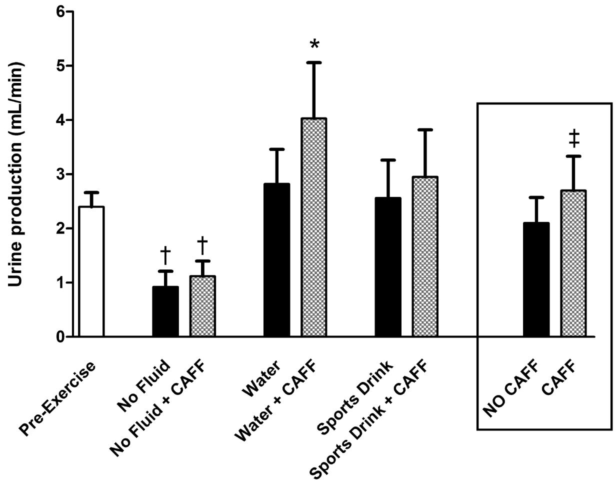

Figure 1 **Urine flow (UF) prior to and during 120 min of exercise in the heat at 63% VO_{2max}; without rehydration (NF), rehydrating 97% of sweat losses with water (WAT), with a carbohydrate-electrolyte solution (CES), or combining these treatments with caffeine ingestion (CAFF + NF, CAFF + WAT, and CAFF + CES).** Data for seven subjects are presented as mean ± SEM. *Different from NF trial ($P \leq 0.05$). †Different from preexercise ($P \leq 0.05$). The right inserts display the main effects of caffeine ingestion. ‡Different from noncaffeine trials ($P \leq 0.05$).
Reproduced from Del Coso et al.[39] with permission.

composition was measured and increased sweat sodium excretion was observed when trials with caffeine consumption were pooled together.[39] This suggests that caffeine may alter fluid and mineral balance during prolonged exercise in the heat.

It is unknown if these adverse effects of beverages containing caffeine on urine output, thermoregulation, and mineral balance could be replicated when using energy drinks as a source of caffeine. The amount of caffeine ingested in this study (6 mg/kg body weight) was equivalent to drinking 5–6 regular cans of Red Bull (1.25–1.5 liters); however, if that amount of caffeine were to replicated using the energy drink, only 50% of sweat losses would have been replaced while providing no salt. That level of rehydration (50%) is insufficient during exercise in a hot environment and results in core temperature elevations and cardiovascular strain[17] that may limit endurance performance. Conversely, full replacement of fluid losses (2.5 liters) with an energy drink (i.e., Red Bull) would have resulted in a caffeine dose of 11 mg/kg of body weight. That dose of caffeine is triple the amount that has been shown to be ergogenic for endurance performance (i.e., 3–4 mg/kg).[13] Thus, ingestion of energy drinks at high volumes with the aim of rehydration during prolonged exercise in the heat could potentially result in all the adverse effects reported for caffeine ingestion.

EFFECTS OF ENERGY DRINKS DURING PROLONGED EXERCISE IN A NEUTRAL ENVIRONMENT

Several studies have reported the effects of energy drink consumption before endurance exercise in a neutral environment (18–22°C, ~64–72°F) in which fluid deficit is not a concern for performance (Table 1). The earliest report to support a role for energy drinks in endurance performance enhancement is the one by Geiß et al.[42] In that study, 10 endurance-trained young males cycled for 60 min at 70% of VO_{2max}, after which they increased the workload by 50 watts every 3 min until exhaustion. Using a double-blind method and three trials, 500 mL of three different beverages were consumed 30 min into the 60 min submaximal ride. One of the drinks was regular Red Bull (~2 mg/kg caffeine and ~26 mg/kg taurine), another contained only the carbohydrate content of Red Bull, and a third drink contained the carbohydrate and caffeine content of Red Bull (~2 mg/kg caffeine) only (no taurine or glucuronolactone). Endurance time was increased when ingesting regular Red Bull, above the carbohydrates only beverage and above the carbohydrates and caffeine beverage. Since the beverage containing the caffeine and carbohydrate content of Red Bull resulted in the poorest performance, the authors suggest the ergogenic effect of Red Bull may be due to taurine (Table 1).

Taurine derives from the Latin word *taurus*, meaning bull, because it was first isolated in the bile acid of bulls.[47] The association between the strength of the bull and a possible ergogenic effect of taurine is not supported by data. Galloway et al.[27] could not find any cardiovascular or metabolic difference related to exercising for 2 h after a week of taurine supplementation in comparison to placebo ingestion. Furthermore, in a recent study, Pettitt et al.[48] showed that taurine and B vitamins at the levels present in a can of Red Bull do not affect aerobic metabolism during two bouts of intense exercise. In contrast to the view of Geiß et al.[42] supporting an ergogenic role for taurine, a recent meta-analysis of the literature suggests that caffeine ingestion at the dose administered in this study (2 mg/kg CAFF) increases endurance performance.[49] Thus, it is unclear which of the energy drink components could be behind the improvement in performance observed in the study by Geiß et al.,[42] although caffeine seems a likely candidate. In fact, it is intriguing that the trial investigating the effect of caffeine and glucose demonstrated the worst performance results of the three trials.

The performance effects related to the ingestion of 500 mL of Red Bull (i.e., 2 cans) has also been explored by Ivy et al.[43] In their study, well-trained cyclists simulated a cycling time trial to complete a load equivalent to a ride for 60 min at 70% of each participant's maximal aerobic

Table 1 **Summary of studies with double-blind, randomized, crossover designs examining the effects of energy drinks on endurance performance.**

Reference	Subjects	Habitual caffeine consumption	Dose	Protocol	Findings	Improvements (%; ES)
Geiß et al., (1994)[42]	10 endurance athletes	Not reported	3 Treatments: 1) A: 500 mL regular Red Bull 2) B: 500 mL Red Bull only CHO and caffeine without taurine 3) C: 500 mL Red Bull only CHO without caffeine or taurine (Caffeine dose in A and B treatments ~2.0 mg/kg)	60 min cycling at 70% VO_{2max} followed by an incremental test to exhaustion	↑ Endurance time in A compared to B treatment ↑ Endurance time in C compared to B treatment	14.9% and 0.74 ES* 24.5% and 1.03 ES; 8.3% and 0.31, respectively*
Ivy et al., (2009)[43]	12 young trained cyclists	Not reported	2 Treatments: 1) 500 mL Red Bull® (~2.0 mg/kg caffeine) 2) 500 mL of flavored water pacebo	Time to complete an amount of work equivalent to 1 h cycling at 70% Wmax	↓ Time required to complete the work	4.7% and ES not available*
Candow et al., (2009)[44]	17 moderately trained subjects	Range, 50–200 mg/day	2 Treatments: 1) Volume of sugar-free Red Bull to deliver 2.0 mg/kg caffeine 2) Same volume of flavored water placebo available energy drink	Time to exhaustion at 80% VO_{2max} running on a treadmill	No significant effect on performance	6.3% and 0.22 ES
Walsh et al., (2010)[45]	15 recreationally active subjects	Not reported	2 Treatments: 1) 500 mL of Amino Impact with 2.05 g of a mix of caffeine, taurine and glucuronolactone 2) 500 mL of flavored water placebo	Time to exhaustion at 70% VO_{2max} running on a treadmill	↑ Time to exhaustion	12.5% and ES not available*
Schubert et al., (2013)[46]	6 endurance-trained runners	80 mg/day	3 Treatments: 1) 59 mL Red Bull Energy Shot (~1.2 mg/kg caffeine) 2) 59 mL Yerba maté shot (2 mg/kg caffeine) 3) 59 mL placebo	Time to complete 5 km on a treadmill	No significant effect on performance	1.8–2.4% 0.24–0.30 ES

* Significant differences ($P < 0.05$).

Abbreviations: CHO, carbohydrates; ES, effect size.

power. In this study, the placebo drink contained only water with artificial color and sweetener. Performance improved in the Red Bull time trial by 3 min (~5%) in most (83%) of the participants. Either the carbohydrate or the caffeine content in Red Bull could have been responsible for the improved performance. Subjects ingested 2.3 mg of caffeine per kilogram of weight, and similar doses have been found to be ergogenic when ingested without the other energy drink ingredients.[14] Ingestion of an energy drink 40 min before exercise elevated blood glucose, insulin, and blood lactate, reduced plasma free fatty acids, and maintained higher rates of carbohydrate oxidation in the latter stages of exercise.[43] All these responses are compatible with an increased glucose supply to the working muscles, which may allow higher rates of ATP production. Thus, it is also possible that ingestion of the 54 g of carbohydrates contained in the 2 cans of Red Bull had some role in the improved endurance performance. Of note, in the study of Ivy et al.,[43] the rate of perceived exertion tended to be lower on the energy drink trial and β-endorphin levels tended to be higher than on the control trial.

Not only cycling, but running time to exhaustion at 70% VO_{2max} is also improved after ingestion of an energy drink containing high levels of caffeine (2 g each of caffeine, taurine, and glucuronolactone) when compared to a placebo without caffeine.[45] In contrast, when running intensity is higher (i.e., 80% VO_{2max}) and running time to exhaustion is, therefore, reduced, (12–17 min), ingestion of sugar-free energy drinks that deliver either a low (1.2 mg/kg) or a moderate (2 mg/kg) caffeine dose has no effect on performance.[46]

In summary, the available literature on the effects of energy drinks on endurance supports an ergogenic effect when performance is prolonged (~60 min) and ingestion of the energy drink provides at least 2 mg/kg body weight of caffeine. Due to the lack of a proper caffeine placebo control, there is no information about whether comparable effects could be found when similar amounts of fluid with only caffeine and carbohydrates are consumed. Data from Kovacs et al.[14] suggest this may be the case; however, when exercise intensity is increased and exercise duration falls below 20 min, energy drink consumption to provide up to 2 mg/kg of caffeine does not seem to result in an ergogenic effect.

EFFECTS OF ENERGY DRINK INGESTION ON SHORT-TERM HIGH-INTENSITY EXERCISE PERFORMANCE

Compared to the literature on endurance performance, a relatively larger number of studies are available on the effects of energy drinks during high-intensity exercises. Within this category are the following different performance durations: 1) trials lasting beyond 1 min to the point of muscle failure[50–55]; 2) efforts lasting below 1 min, such as the Wingate test and 20-meter sprints[51,52,56–59]; and 3) single maximal isometric, isokinetic, or isoinertial contractions[55] lasting only a few seconds.

All the literature is very recent, but Forbes et al.,[51] in 2007, appear to be the first research group to have examined the ergogenic effects of a marketed energy drink on neuromuscular performance. They found that a 500 mL serving of Red Bull (2.0 mg/kg caffeine) significantly increased the total number of bench press (BP) repetitions over 3 sets at 70% of one-repetition maximum (RM) in 15 young adults (with 1RM being the maximum amount of weight lifted while completing a full range of motion). In this study, during the Red Bull trial participants achieved 34 repetitions versus 32 repetitions when they received the placebo (5.9% and 0.24 effect size). However, no differences were reported for peak or average power during three consecutive 30-second leg cycling Wingate tests spaced by 2 minutes of recovery.

In two similar studies,[50,56] a commercially available energy drink (unreported brand; 2.1 mg/kg of caffeine) was provided to recreationally active subjects and resulted in a significant increase in total leg press lifting volume (12.3% and 0.24 effect size). However, it had no effect on bench press weight lifted[50] or on 2 × 20-second Wingate test.[56] Duncan et al.,[54] using a noncommercial self-prepared sugar-free energy drink (5 mg/kg of caffeine diluted into 250 mL of sugar-free artificially sweetened water), found a significant increase in bench press repetitions to failure with 60% of 1RM in 13 moderately trained athletes. Similar to Duncan et al.,[54] Woolf et al.[52] formulated their own noncommercial sugar-free energy drink (5 mg/kg caffeine and 0.125 g/kg carbohydrate) to determine its effect on a single dash, repeated sprint ability and local muscle endurance tests. They found no ergogenic effect on 40-yd dash, 20-yd shuttle run, or bench press repetitions to failure using a fixed load (84 or 102 kg) in 17 college football players.

Gwacham and Wagner[58] found no ergogenic effects of an AdvoCare Spark pouch of 120 mL (1.2 mg/kg caffeine) on the Running-based Anaerobic Sprint Test (6 × 35 meters) in a sample of American college football players. Similarly, Astorino et al.[59] did not find any ergogenic effects of a can of Red Bull (1.3 mg/kg caffeine) on repeated sprint performance (*t* test – 3 × 8 sprints) in female soccer players. Hoffman et al.[57] also reported that 120 mL of Redline Extreme (2.0 mg/kg caffeine) ingested 10 minutes before exercise had no effect on anaerobic power measured by 3 repeated 20-second Wingate tests separated by a 10-minute rest in 12 male strength-trained athletes. In the only study that has addressed the isolated effects of both caffeine and taurine on neuromuscular performance, Eckerson et al.[55] found that neither 500 mL of sugar-free Red Bull (2.0 mg/kg caffeine + 24 mg/kg taurine) nor 500 mL of sugar and taurine-free Red Bull (2.0 mg/kg caffeine) had an ergogenic effect compared to a sugar-free caffeine-free placebo when testing 1RM strength or repetitions to failure at 70% of 1RM for bench press exercise.

Despite the fact that all these studies have been conducted with appropriate double-blind, randomized, and crossover designs on well-trained subjects, only 5 of the 11 studies evaluated revealed significant energy drink-mediated improvements in neuromuscular performance. Of note, the performance enhancement was always on the number of repetitions to muscle failure[50–54] (5.1–15.5% and 0.24–0.69 effect size; Table 2). In addition, 2 of the 5 studies that found significant ergogenic effects of energy drinks on local muscle endurance used a study-specific, specially prepared energy drink with 5 mg/kg of caffeine. Given that caffeine has been suggested to be the only ergogenic ingredient of energy drinks,[3] this lack of positive effects on neuromuscular performance could be related to the low caffeine dose administered in the 8 studies using commercial energy drinks (range 1.2–2.1 mg/kg).

Recent findings indicate that the minimum caffeine dose needed to significantly improve muscle strength and power output in highly trained athletes is dependent on the resistance that the musculature has to overcome (% 1RM). A dose of 3 mg/kg was enough to improve high-velocity muscle actions against low loads (i.e., 25–50% 1RM), whereas a higher caffeine dose (9 mg/kg) was necessary against high loads (90% 1RM) (Figure 2).[61] The muscle actions involved in the testing protocols of the aforementioned studies that used energy drinks as an ergogenic aid required a different percentage of the athletes' maximum strength. For instance, the first pedal strokes on a Wingate test or the first strides of a running 20-meter shuttle test require 90–100% 1RM. However, as the event proceeds and the body accelerates, muscle recruitment frequency (cadence) is greatly increased while the percentage of the maximum force required is drastically reduced (20–30% 1RM).[62] The absence of ergogenic effects on neuromuscular performance when testing single actions near 1 RM may be explained by the insufficient caffeine dose (range, 1.0–2.0 mg/kg) that a single can of a commercial energy drink normally contains (Table 2).

These findings are consistent with previous studies in which caffeine doses above 5 mg/kg tended to produce ergogenic effects on neuromuscular performance,[63,64] while doses below 3 mg/kg usually did not promote significant improvements.[63,65] From a practical point of view, data suggest that if an athlete wishes to improve short-term, high-intensity exercise performance via energy drinks the minimum amount consumed must be the equivalent of 3–4 cans of Red Bull per 60 kg of body weight, or 4–5 cans for a subject weighing approximately 80 kg (~5 mg/kg of caffeine). However, when ingesting that amount of Red Bull (5 cans) to achieve a caffeine ergogenic dose for neuromuscular performance, subjects would also be ingesting 135 g of carbohydrate, 5 g of taurine, 3 g of glucuronolactone, and 0.175 g of B vitamins. The interaction of these components at these high concentrations is still unknown. In addition, energy drinks are not formulated to speed up fluid absorption, and different rates of incorporation of different components into the blood could result in unwanted side effects. Thus, when high doses of caffeine are needed, energy drinks may not be the optimal choice.

CONFOUNDING FACTORS IN THE PERFORMANCE EFFECTS OF ENERGY DRINKS

Besides the volume of energy drinks and, thus, caffeine ingested, other confounding variables may be behind the absence of significant effects on neuromuscular and endurance performance among studies that follow similar protocols and energy drink consumption volumes. Among these confounding variables, the following stand out: 1) the timing of energy drink ingestion relative to the time of testing, 2) the role of caffeine habituation, and 3) the time-of-day and circadian rhythm effect on the ergogenic potential of energy drinks.

Studies assessing the ergogenic effect of energy drinks report different elapsed times between drink intake and the beginning of the testing protocols. For instance, 10–20 min,[57] 30–40 min,[43,48,50,56] and 50–60 min.[44,46,51,52,60] In most people, the plasma caffeine concentration peaks 30–60 min after ingestion,[66,67] with an elimination half-life ranging between 2.5 and 10 hours.[68] However, the absorption rate constant of caffeine is influenced by the physicochemical properties of the dose formulation, including pH, volume, and composition.[69] For example, caffeine absorption is faster from chewing gum than from a capsule,[70] and from a capsule than from coffee.[71] Thus, it is not clear what amount of time should elapse between energy drink ingestion and performance testing to optimize results.

Since no other ingredient of energy drinks has been consistently reported to be ergogenic,[3] it seems reasonable to standardize the time between energy drink ingestion and the beginning of the testing protocols or sports events to 60 min to allow caffeine to reach peak plasma concentration. Moreover, although the caffeine half-life normally exceeds 2.5 hours, the potential ergogenic effect of caffeine in athletic efforts exceeding 1 hour is presently being questioned.[72] However, caffeine seems to maintain its ergogenic properties when ingestion is repeated during long-term, exhaustive endurance exercise.[73] In

Table 2 **Summary of studies with double-blind, randomized, crossover designs examining the effects of energy drinks on power-based performance.**

Reference	Subjects	Habitual caffeine consumption	Energy drink dose	Protocol	Findings	Improvements (%; ES)
Forbes et al., (2007)[51]	15 healthy physically active subjects	From naive to >200 mg/day	2 Treatments: 1) 500 mL of Red Bull(~2.0 mg/kg caffeine) 2) 500 mL of isoenergetic, isovolumetric, noncaffeinated placebo	Total number of BP repetitions over 3 sets at 70% 1RM Peak and mean power during repeated Wingate tests	↑ total repetitions No significant effect on Wingate peak or mean power	5.9% and 0.24 ES* 0.1–1.7% and 0.01–0.11 ES
Wolf et al., (2008)[60]	18 male highly trained athletes	40.8 ± 51.0 mg/day	2 Treatments: 1) Self-prepared beverage with 5 mg/kg caffeine + 125 mg/kg of CHO 2) CHO placebo drink	Total weight lifted in BP and leg press to muscle failure 30 s Wingate test	↑ total weight lifted in BP ↑ Wingate peak power	15.5% and 0.69 ES* 5.1% and 0.56 ES*
Wolf et al., (2009)[52]	17 male collegiate football players	<50 mg/day	2 Treatments: 1) Self-prepared beverage with 5 mg/kg caffeine + 125 mg/kg of CHO 2) CHO placebo drink	40-yd dash test 20-yd shuttle test Total number of BP repetitions with a fixed absolute load (84 or 102 kg)	No significant effect on performance	<0.5% and ES < 0.1
Hoffman et al., (2009)[57]	12 male strength-trained athletes	Not reported	2 Treatments: 1) 120 mL of Redline Xtreme (~2.0 mg/kg caffeine) 2) 120 mL of flavored water placebo	20-s Wingate test	No significant effect on Wingate peak or mean power	<1.5% and ES <0.2
Campbell et al., (2010)[56]	15 recreationally active subjects	Not reported	2 Treatments: 1) marketed energy drink (~2.1 mg/kg caffeine) 2) CHO placebo drink	2 × 20-s Wingate tests, separated by 150 s	No significant effect on performance	1.0% and 0.03 ES
Campbell et al., (2010)[50]	18 recreationally active subjects	Not reported	2 Treatments: 1) marketed energy drink (~2.1 mg/kg caffeine) 2) CHO placebo drink	Total weight lifted in 4 sets of BP and leg press repetitions to failure at an intensity of 80% 1RM	↑ total weight lifted in leg press	12.3% and 0.24 ES*
Duncan and Oxford, (2011)[53]	13 moderately trained athletes	Range 169–250 mg/day	2 Treatments: 1) Self-prepared beverage with 5 mg/kg caffeine diluted into 250 mL of sugar-free artificially sweetened water 2) 250 mL of flavored water placebo	BP repetitions to failure at 60% of 1RM	↑ total repetitions and total weight lifted	8.9 to 9.4% 0.44 to 0.62 ES*
Duncan et al, (2012)[54]	13 strength-trained athletes	211 mg/day; range, 120–400 mg/day	2 Treatments: 1) 250 mL of diluted Quick Energy (~3.0 mg/kg caffeine) 2) 250 mL of flavored water placebo	BP, deadlift, prone row and back squat repetitions to failure at 60% of 1RM	↑ total repetitions in all exercises	Average of 7.5% and 0.25 ES*
Gwacham and Wagner, (2012)[58]	20 football players	Significant interaction effect between caffeine use and the beverage treatment	2 Treatments: 1) 237 mL of AdvoCare Spark (~1.2 mg/kg caffeine) 2) 237 mL of flavored water placebo	Running-based anaerobic sprint test (RAST) 6 × 35m/10 s	No significant effect on performance	0% and 0.0 ES
Astorino et al., (2012)[59]	15 young healthy female soccer players	Habitual consumers	2 Treatments: 1) 255 mL of Red Bull (~1.3 mg/kg caffeine) 2) 255 mL of Canada Dry Ginger Ale placebo drink (caffeine and taurine free)	Repeated sprint performance (test – 3 × 8 sprints)	No significant effect on performance	<1% and <0.1 ES
Eckerson et al., (2013)[55]	17 resistance-trained athletes	<50 mg/day	3 Treatments 1) 500 mL of sugar-free Red Bull (~2.0 mg/kg caffeine + ~24 mg/kg of taurine) 2) 500 mL of sugar-free Red Bull (~2.0 mg/kg caffeine without taurine) 3) 500 mL placebo without placebo nor taurine	BP 1RM strength and repetitions to failure at 70% of 1RM	No significant effect on performance	<0.5% and ES < 0.1

* Significant differences ($P < 0.05$).
Abbreviations: 1RM, 1 repetition maximum; CHO, carbohydrates; ES, effect size.

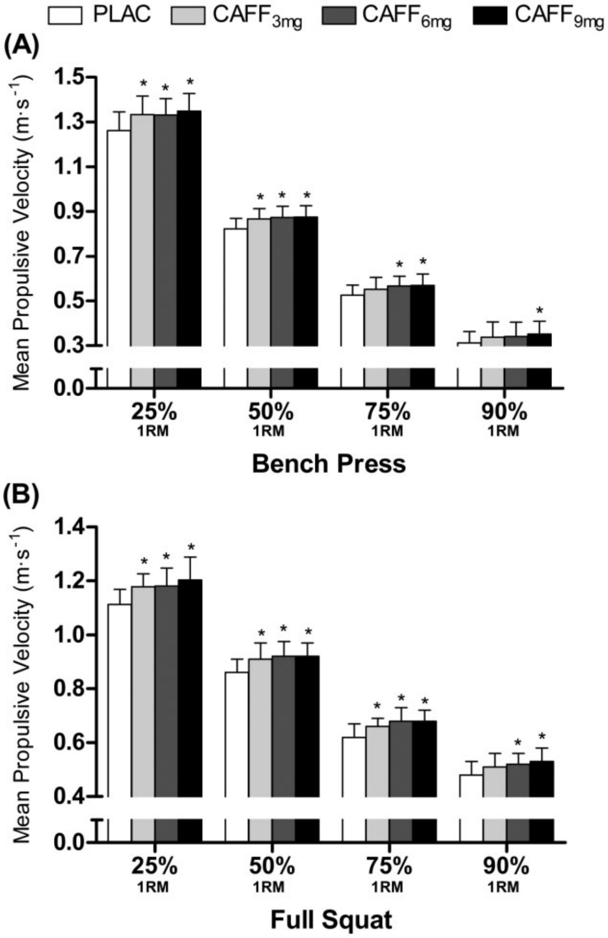

Figure 2 **Dose-response effects of caffeine ingestion on load-velocity relationship for bench press (A) and full squat (B) exercises.** Data are means ± SD. *Significant differences ($P \leq 0.05$) compared to the PLAC trial within each load.
Reproduced from Pallarés et al.[61] with permission.

addition, the dose of caffeine required for an ergogenic effect may differ if the ingestion takes place once the exercise has begun.[66] The effects of these different combinations of timing and dose need to be better studied if we are to reach a better understanding of the ergogenic effects of energy drinks.

To date, very little information is available regarding the potential relationship between caffeine habituation and the magnitude of endurance or neuromuscular performance improvement following energy drink ingestion. Although Gwacham and Wagner[58] did not detect significant ergogenic effects of energy drinks (~1.2 mg/kg caffeine) on repeated sprint performance, they found a significant interaction effect between caffeine habituation and the beverage treatment (energy drink versus placebo), suggesting that athletes not habituated to caffeine were more likely to improve performance when consuming energy drinks than those who regularly consumed caffeine. In animal models, chronic caffeine consumption resulted in an increase in the affinity of adenosine receptors within the central nervous system and, therefore, an increase in the amount of caffeine needed to have the same antagonist activity on the receptors.[74,75] In humans, Van Soeren and Graham[76] measured the time-to-exhaustion after subjects abstained from caffeine ingestion for 0, 2, and 4 days. Although nonsignificant, there was a trend towards greater improvement following 2 and 4 days of abstinence. Bell and McLellan,[77] using a similar time-to-exhaustion protocol, showed that improvements in performance were greater for caffeine-naive (<50 mg/day) compared to habitual caffeine consumers (≥300 mg/day).

In contrast, both Wiles et al.[78] and Tarnopolsky and Cupido[79] found no relationships between caffeine habituation and 1,500-meter running time and muscle force development, respectively. All these data suggest that caffeine habituation and its relationship to the effects of energy drinks needs further study. Meanwhile, to avoid the possible contaminating effects of this variable, it is recommended that researchers use participants who report similar regular caffeine consumption. Furthermore, as suggested by Ganio et al.,[75] athletes should abstain from caffeine ingestion for no fewer than 7 days before the experimental trials or competition events. In addition, it is strongly recommended that each manuscript report the mean, standard deviation, and confidence interval for the athletes' regular caffeine ingestion.

Most of the studies that assessed the potential of energy drinks to enhance endurance or short-term, high-intensity exercise performance have been conducted in the mornings[43,52–54–60] and a minority in the afternoons,[44] while the rest do not detail the time-of-day of testing.[46,48,50,51,55–58] To date, no study has addressed the possible implications of circadian rhythm for the ergogenic potential of energy drinks. It was recently found that the ergogenic effect of a 6 mg/kg caffeine dose on the neuromuscular performance in the morning (8:00 a.m.) (5.4–9.4%; 0.75–1.15 effect size; $P < 0.05$) was completely lost in the afternoon (18:00 p.m.) with the same caffeine dose administered.[80] The mechanisms behind this time-of-day-related effect of caffeine on muscle performance are not clear. One plausible explanation is that neural activation is almost complete in the afternoon, and caffeine may have minimal room for improvement at that hour.[16] These data suggest that the time of day at which an energy drink or caffeine is ingested is a confounding variable that should be taken into consideration when studying the ergogenic effects of these beverages.

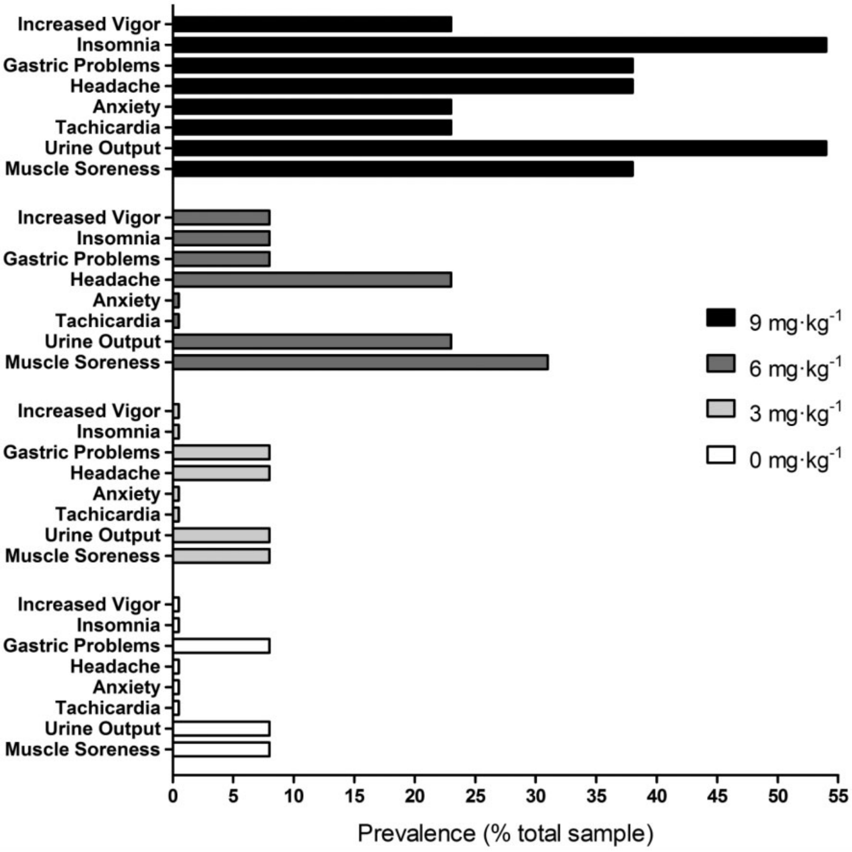

Figure 3 **Dose-response on side effects of caffeine ingestion.** Data are presented as percent of prevalence. Reproduced from Pallarés et al.[61] with permission.

SIDE EFFECTS OF ENERGY DRINKS

Although various studies[81,82] and several reports from international institutions[23,83] have described the possible negative effects that the habitual consumption of energy drinks may have on health, to date there is little information on the side effects that acute ingestion of energy drinks may have on the physical performance and perceived fatigue of athletes. For instance, when analyzing endurance performance, several studies have reported positive effects on the rate of perceived exertion (RPE) after the ingestion of one or two cans of commercial energy drinks (2.0–3.0 mg/kg of caffeine),[43,54] while others did not find any effect on this outcome.[44,46,48] Thus, a reduction in the perception of physical fatigue is not a consistent effect of energy drink ingestion when performing endurance exercise.

Using questionnaires to evaluate the side effects of energy drinks, Hoffman et al.[57] found that 120 mL of the marketed Redline Xtreme energy drink (~2.0 mg/kg of caffeine) significantly improved the participants' subjective feelings of energy and focus, while no differences were detected for the feelings of fatigue and alertness. These data are consistent with the findings of Walsh et al.,[45] who found that recreationally active subjects consuming a commercial energy drink (caffeine dose not reported) felt greater focus and energy as well as less fatigue (compared to a placebo treatment) before and during a time-to-exhaustion test. These positive effects disappeared immediately after exercise. Similarly, the mood state scores for vigor were significantly greater and fatigue scores significantly lower 60 min after the ingestion of a noncommercial, self-prepared, sugar-free energy drink (5 mg/kg of caffeine) compared to a placebo beverage.[53]

Astorino et al.[59] found that only 2 of 15 female participants felt adverse side effects (i.e., stomach ache and feelings of mild tremor) following the ingestion of a can of Red Bull (~1.3 mg/kg caffeine). In a descriptive cross-sectional study, Desbrow and Leveritt[84] found that an average caffeine dose of 3.8 ± 3 mg/kg produced very minor and infrequent adverse symptoms during the Ironman triathlon events. In a recent study, the caffeine dose was systematically raised (0–3–6 and 9 mg/kg) while monitoring participants' positive and adverse caffeine effects through a validated questionnaire. Although the positive feelings such us increased vigor/activeness and perception of performance improvement were already clearly present with the 3 and 6 mg/kg doses, the presence of negative side effects (i.e., gastrointestinal problems, headaches, and insomnia) increased markedly with the 9 mg/kg caffeine dose (Figure 3).[61] Furthermore, when a moderate dose of caffeine (6 mg/kg) is ingested in the evening (18:00 p.m.), the negative side effects felt by the participants drastically increase compared to the same dose of caffeine ingested in the morning.[80] In summary, in sports events lasting longer than half a day, the negative side effects generated by the ingestion of a sufficient amount of energy drink to provide caffeine doses higher than 6 mg/kg in the mornings, and 3 mg/kg in the afternoons, could counteract the ergogenic effects of caffeine and result in reduced physical performance.

CONCLUSION

Energy drinks are difficult to evaluate from the nutritional and ergogenic perspective due to the variety of ingredients they contain (e.g., water, sugars, caffeine, other stimulants, amino acids, herbs, and vitamins), which is further complicated by the introduction of calorie-free and concentrated (shot) versions to the marketplace. While the latter versions are formulated for fast delivery of their main stimulant (typically caffeine), the regular versions deliver other nutrients that have not been proven to be ergogenic (e.g., taurine, glucuronolactone, vitamins). Due to their high carbohydrate concentration and lack of salts, energy drinks are not a good beverage choice when prolonged exercise in a warm environment is likely to require rehydration. Short-term, high-intensity performance could be improved by energy drinks, but achieving this improvement requires the ingestion of high volumes to deliver enough caffeine. Ingestion of high doses of caffeine, although ergogenic, could result in negative side effects that could counteract the caffeine's ergogenic effect.

Acknowledgments

Funding. The authors received no external funding relevant to this review.

Declaration of interest. The authors have no relevant interests to declare.

REFERENCES

1. Applegate EA, Grivetti LE. Search for the competitive edge: a history of dietary fads and supplements. J Nutr. 1997;127:869S–873S.
2. European Food Safety Authority. Scientific opinion on the substantiation of health claims related to carbohydrate-electrolyte solutions. EFSA J. 2011;9:1–29.
3. McLellan TM, Lieberman HR. Do energy drinks contain active components other than caffeine? Nutr Rev. 2012;70:730–744.
4. Campbell B, Wilborn C, La Bounty P, et al. International society of sports nutrition position stand: energy drinks. J Int Soc Sports Nutr. 2013;10:1.
5. Sherman WM, Brodowicz G, Wright DA, et al. Effects of 4 h preexercise carbohydrate feedings on cycling performance. Med Sci Sports Exerc. 1989;21:598–604.
6. Dennis SC, Noakes TD, Hawley JA. Nutritional strategies to minimize fatigue during prolonged exercise: fluid, electrolyte and energy replacement. J Sports Sci. 1997;15:305–313.
7. Mettler S, Rusch C, Colombani P. Osmolality and pH of sport and other drinks available in Switzerland. Sportmed Sporttraumatol. 2006;54:92–95.
8. Vist GE, Maughan RJ. The effect of osmolality and carbohydrate content on the rate of gastric emptying of liquids in man. J Physiol. 1995;486(Pt 2):523–531.
9. Murray R, Bartoli W, Stofan J, et al. A comparison of the gastric emptying characteristics of selected sports drinks. Int J Sport Nutr. 1999;9:263–274.
10. Gisolfi CV, Summers RW, Lambert GP, et al. Effect of beverage osmolality on intestinal fluid absorption during exercise. J Appl Physiol. 1998;85:1941–1948.
11. Hamouti N, Del Coso J, Ortega JF, et al. Sweat sodium concentration during exercise in the heat in aerobically trained and untrained humans. Eur J Appl Physiol. 2011;111:2873–2881.
12. Hamouti N, Fernández-Elías VE, Ortega JF, et al. Ingestion of sodium plus water improves cardiovascular function and performance during dehydrating cycling in the heat. Scand J Med Sci Sports. 2014;24:507–518.
13. Graham TE. Caffeine and exercise – metabolism, endurance and performance. Sports Med. 2001;31:785–807.
14. Kovacs EMR, Stegen J, Brouns F. Effect of caffeinated drinks on substrate metabolism, caffeine excretion, and performance. J Appl Physiol. 1998;85:709–715.
15. Davis JM, Zhao ZW, Stock HS, et al. Central nervous system effects of caffeine and adenosine on fatigue. Am J Physiol Regul Integr Comp Physiol. 2003;284:R399–R404.
16. Mora-Rodriguez R, Garcia Pallares J, Lopez-Samanes A, et al. Caffeine ingestion reverses the circadian rhythm effects on neuromuscular performance in highly resistance-trained men. Plos One. 2012;7:e33807.
17. Montain SJ, Coyle EF. Influence of graded dehydration on hyperthermia and cardiovascular drift during exercise. J Appl Physiol. 1992;73:1340–1350.
18. Bardis CN, Kavouras SA, Kosti L, et al. Mild hypohydration decreases cycling performance in the heat. Med Sci Sports Exerc. 2013;45:1782–1789.
19. Wemple RD, Lamb DR, McKeever KH. Caffeine vs caffeine-free sports drinks: effects on urine production at rest and during prolonged exercise. Int J Sports Med. 1997;18:40–46.
20. Gonzalez-Alonso J, Heaps CL, Coyle EF. Rehydration after exercise with common beverages and water. Int J Sports Med. 1992;13:399–406.
21. Brown MB, McCarty NA, Millard-Stafford M. High-sweat Na+ in cystic fibrosis and healthy individuals does not diminish thirst during exercise in the heat. Am J Physiol Regul Integr Comp Physiol. 2011;301:R1177–R1185.
22. Coso JD, Estevez E, Baquero RA, et al. Anaerobic performance when rehydrating with water or commercially available sports drinks during prolonged exercise in the heat. Appl Physiol Nutr Metab. 2008;33:290–298.
23. European Commission Scientific Committee on Food. *Opinion of the Scientific Committee on Food on Additional Information on "Energy" Drinks*. 2003; Available at: http://ec.europa.eu/food/fs/sc/scf/out169_en.pdf. Accessed: December 2013.
24. European Food Safety Authority. The use of taurine and d-glucurono-γ-lactone as constituents of the so-called "energy" drinks. EFSA J. 2009;935:1–31.
25. Huxtable RJ. Physiological actions of taurine. Physiol Rev. 1992;72:101–163.
26. Beyranvand MR, Khalafi MK, Roshan VD, et al. Effect of taurine supplementation on exercise capacity of patients with heart failure. J Cardiol. 2011;57:333–337.
27. Galloway SD, Talanian JL, Shoveller AK, et al. Seven days of oral taurine supplementation does not increase muscle taurine content or alter substrate metabolism during prolonged exercise in humans. J Appl Physiol. 2008;105:643–651.
28. Gentile S, Bologna E, Terracina D, et al. Taurine-induced diuresis and natriuresis in cirrhotic patients with ascites. Life Sci. 1994;54:1585–1593.
29. Riesenhuber A, Boehm M, Posch M, et al. Diuretic potential of energy drinks. Amino Acids. 2006;31:81–83.
30. Fulgraff G. Xanthinderivate als diuretika. In: Herken H, ed. *Handbuch der experimentellen pharmakologie*. Berlin: Springer Verlag; 1969:596–640.
31. Shirley DG, Walter SJ, Noormohamed FH. Natriuretic effect of caffeine: assessment of segmental sodium reabsorption in humans. Clin Sci (Lond). 2002;103:461–466.
32. Beutler JJ, Koomans HA, Bijlsma JA, et al. Renal actions of theophylline and atrial natriuretic peptide in humans: a comparison by means of clearance studies. J Pharmacol Exp Ther. 1990;255:1314–1319.
33. Izzo JL, Jr, Ghosal A, Kwong T, et al. Age and prior caffeine use alter the cardiovascular and adrenomedullary responses to oral caffeine. Am J Cardiol. 1983;52:769–773.
34. Rieg T, Steigele H, Schnermann J, et al. Requirement of intact adenosine A1 receptors for the diuretic and natriuretic action of the methylxanthines theophylline and caffeine. J Pharmacol Exp Ther. 2005;313:403–409.

35. Stookey JD. The diuretic effects of alcohol and caffeine and total water intake misclassification. Eur J Epidemiol. 1999;15:181–188.
36. Maughan RJ, Griffin J. Caffeine ingestion and fluid balance: a review. J Hum Nutr Diet. 2003;16:411–420.
37. Ragsdale FR, Gronli TD, Batool N, et al. Effect of Red Bull energy drink on cardiovascular and renal function. Amino Acids. 2010;38:1193–1200.
38. Rowell LB. Human cardiovascular adjustments to exercise and thermal stress. Physiol Rev. 1974;54:75–159.
39. Del Coso J, Estevez E, Mora-Rodriguez R. Caffeine during exercise in the heat: thermoregulation and fluid-electrolyte balance. Med Sci Sports Exerc. 2009;41:164–173.
40. Millard-Stafford ML, Cureton KJ, Wingo JE, et al. Hydration during exercise in warm, humid conditions: effect of a caffeinated sports drink. Int J Sport Nutr Exerc Metab. 2007;17:163–177.
41. Ely BR, Ely MR, Cheuvront SN. Marginal effects of a large caffeine dose on heat balance during exercise-heat stress. Int J Sport Nutr Exerc Metab. 2011;21:65–70.
42. Geiß KR, Jester I, Falke W, et al. The effect of a taurine-containing drink on performance in 10 endurance athletes. Amino Acids. 1994;7:45–56.
43. 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;19:61–78.
44. Candow DG, Kleisinger AK, Grenier S, et al. Effect of sugar-free Red Bull energy drink on high-intensity run time-to-exhaustion in young adults. J Strength Cond Res. 2009;23:1271–1275.
45. Walsh AL, Gonzalez AM, Ratamess NA, et al. Improved time to exhaustion following ingestion of the energy drink amino impact. J Int Soc Sports Nutr. 2010;7:14.
46. Schubert MM, Astorino TA, Azevedo JL, Jr. The effects of caffeinated "energy shots" on time trial performance. Nutrients. 2013;5:2062–2075.
47. Tiedemann F, Gmelin L. Einige neue bestandtheile der galle des ochsen. Ann Phys. 1827;85:326–337.
48. Pettitt RW, Niemeyer JD, Sexton PJ, et al. Do the noncaffeine ingredients of energy drinks affect metabolic responses to heavy exercise? J Strength Cond Res. 2013;27:1994–1999.
49. Warren GL, Park ND, Maresca RD, et al. Effect of caffeine ingestion on muscular strength and endurance: a meta-analysis. Med Sci Sports Exerc. 2010;42:1375–1387.
50. Campbell B, Downing J, Kilpatrick M, et al. The effects of a commercially available energy drink on resistance training performance. Med Sci Sports Exerc. 2010;42:448.
51. Forbes SC, Candow DG, Little JP, et al. Effect of Red Bull energy drink on repeated Wingate cycle performance and bench-press muscle endurance. Int J Sport Nutr Exerc Metab. 2007;17:433–444.
52. Woolf K, Bidwell WK, Carlson AG. Effect of caffeine as an ergogenic aid during anaerobic exercise performance in caffeine naive collegiate football players. J Strength Cond Res. 2009;23:1363–1369.
53. Duncan MJ, Oxford SW. The effect of caffeine ingestion on mood state and bench press performance to failure. J Strength Cond Res. 2011;25:178–185.
54. Duncan MJ, Smith M, Cook K, et al. The acute effect of a caffeine-containing energy drink on mood state, readiness to invest effort, and resistance exercise to failure. J Strength Cond Res. 2012;26:2858–2865.
55. Eckerson JM, Bull AJ, Baechle TR, et al. Acute ingestion of sugar-free Red Bull energy drink has no effect on upper body strength and muscular endurance in resistance trained men. J Strength Cond Res. 2013;27:2248–2254.
56. Campbell B, Kilpatrick M, Wilborn C, et al. A commercially available energy drink does not improve peak power production on multiple 20-second Wingate tests. J Int Soc Sports Nutr. 2010;7:10.
57. Hoffman JR, Kang J, Ratamess NA, et al. Examination of a pre-exercise, high energy supplement on exercise performance. J Int Soc Sports Nutr. 2009;6:2.
58. Gwacham N, Wagner DR. Acute effects of a caffeine-taurine energy drink on repeated sprint performance of American college football players. Int J Sport Nutr Exerc Metab. 2012;22:109–116.
59. Astorino TA, Matera AJ, Basinger J, et al. Effects of Red Bull energy drink on repeated sprint performance in women athletes. Amino Acids. 2012;42:1803–1808.
60. Woolf K, Bidwell WK, Carlson AG. The effect of caffeine as an ergogenic aid in anaerobic exercise. Int J Sport Nutr Exerc Metab. 2008;18:412–429.
61. Pallares JG, Fernandez-Elias VE, Ortega JF, et al. Neuromuscular responses to incremental caffeine doses: performance and side-effects. Med Sci Sports Exerc. 2013;45:2184–2192.
62. Izquierdo M, Hakkinen K, Gonzalez-Badillo JJ, et al. Effects of long-term training specificity on maximal strength and power of the upper and lower extremities in athletes from different sports. Eur J Appl Physiol. 2002;87:264–271.
63. Astorino TA, Terzi MN, Roberson DW, et al. Effect of two doses of caffeine on muscular function during isokinetic exercise. Med Sci Sports Exerc. 2010;42:2205–2210.
64. Glaister M, Howatson G, Abraham CS, et al. Caffeine supplementation and multiple sprint running performance. Med Sci Sports Exerc. 2008;40:1835–1840.
65. Beck TW, Housh TJ, Malek MH, et al. The acute effects of a caffeine-containing supplement on bench press strength and time to running exhaustion. J Strength Cond Res. 2008;22:1654–1658.
66. Cox GR, Desbrow B, Montgomery PG, et al. Effect of different protocols of caffeine intake on metabolism and endurance performance. J Appl Physiol. 2002;93:990–999.
67. Conway KJ, Orr R, Stannard SR. Effect of a divided caffeine dose on endurance cycling performance, postexercise urinary caffeine concentration, and plasma paraxanthine. J Appl Physiol. 2003;94:1557–1562.
68. Magkos F, Kavouras SA. Caffeine use in sports, pharmacokinetics in man, and cellular mechanisms of action. Crit Rev Food Sci Nutr. 2005;45:535–562.
69. Bonati M, Latini R, Galletti F, et al. Caffeine disposition after oral doses. Clin Pharmacol Ther. 1982;32:98–106.
70. Kamimori GH, Karyekar CS, Otterstetter R, et al. The rate of absorption and relative bioavailability of caffeine administered in chewing gum versus capsules to normal healthy volunteers. Int J Pharm. 2002;234:159–167.
71. Fredholm BB, Battig K, Holmen J, et al. Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. Pharmacol Rev. 1999;51:83–133.
72. Peters EM. Nutritional aspects in ultra-endurance exercise. Curr Opin Clin Nutr Metab Care. 2003;6:427–434.
73. Bell DG, McLellan TM. Effect of repeated caffeine ingestion on repeated exhaustive exercise endurance. Med Sci Sports Exerc. 2003;35:1348–1354.
74. Chou DT, Khan S, Forde J, et al. Caffeine tolerance: behavioral, electrophysiological and neurochemical evidence. Life Sci. 1985;36:2347–2358.
75. Ganio MS, Klau JF, Casa DJ, et al. Effect of caffeine on sport-specific endurance performance: a systematic review. J Strength Cond Res. 2009;23:315–324.
76. Van Soeren MH, Graham TE. Effect of caffeine on metabolism, exercise endurance, and catecholamine responses after withdrawal. J Appl Physiol. 1998;85:1493–1501.
77. Bell DG, McLellan TM. Exercise endurance 1, 3, and 6 h after caffeine ingestion in caffeine users and nonusers. J Appl Physiol. 2002;93:1227–1234.
78. Wiles JD, Bird SR, Hopkins J, et al. Effect of caffeinated coffee on running speed, respiratory factors, blood lactate and perceived exertion during 1500-m treadmill running. Br J Sports Med. 1992;26:116–120.
79. Tarnopolsky M, Cupido C. Caffeine potentiates low frequency skeletal muscle force in habitual and nonhabitual caffeine consumers. J Appl Physiol. 2000;89:1719–1724.
80. Mora-Rodríguez R, Pallarés JG, López-Gullón JM, et al. Improvements on neuromuscular performance with caffeine ingestion depend on the time-of-day. J Sci Med Sport. 2014 Apr 26 [e-pub ahead of print].
81. Gunja N, Brown JA. Energy drinks: health risks and toxicity. Med J Aust. 2012;196:46–49.
82. Seifert SM, Seifert SA, Schaechter JL, et al. An analysis of energy-drink toxicity in the national poison data system. Clin Toxicol (Phila). 2013;51:566–574.
83. Zucconi S, Volpato C, Adinolfi F, et al. Gathering consumption data on specific consumer groups of energy drinks. Supporting Publications. 2013;EN-394:190.
84. Desbrow B, Leveritt M. Well-trained endurance athletes' knowledge, insight, and experience of caffeine use. Int J Sport Nutr Exerc Metab. 2007;17:328–339.