Special Article

Do energy drinks contain active components other than caffeine?

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Energy drinks (EDs) contain caffeine and are a new, popular category of beverage. It has been suggested that EDs enhance physical and cognitive performance; however, it is unclear whether the claimed benefits are attributable to components other than caffeine. A typical 235 mL ED provides between 40 and 250 mg of caffeine, equating to doses that improve cognitive and, at the higher levels, physical performance. EDs often contain taurine, guaraná, ginseng, glucuronolactone, B-vitamins, and other compounds. A literature search using PubMed, Psych Info, and Google Scholar identified 32 articles that examined the effects of ED ingredients alone and/or in combination with caffeine on physical or cognitive performance. A systematic evaluation of the evidence-based findings in these articles was then conducted. With the exception of some weak evidence for glucose and guaraná extract, there is an overwhelming lack of evidence to substantiate claims that components of EDs, other than caffeine, contribute to the enhancement of physical or cognitive performance. Additional well-designed, randomized, placebo-controlled studies replicated across laboratories are needed in order to assess claims made for these products.

INTRODUCTION

Energy drinks (EDs) represented a $6.7 billion industry in 2010,[1] with more than 50% of the consumer market consisting of adolescents and young adults under the age of 35 years.[2] In the United States, most ED manufacturers package and market their products so as to ensure the EDs are classified as dietary supplements. By doing so, manufacturers are not required to disclose the quantities of active ingredients in their products.[3] In addition, unlike manufacturers of soft drinks, which, in the United States, are classified as a food product and regulated by the Food and Drug Administration, manufacturers of EDs are not limited to a maximum dose of caffeine in a given volume or serving.[3] Several case reports[4–10] have associated the consumption of high volumes of EDs with manic, seizure, or cardiac episodes that resolved following cessation of the product's ingestion. It has also become increasingly common for younger adults to mix EDs and alcohol[11–13]; while this reportedly leads to high-risk behavior,[13] the association does not necessarily imply a cause-and-effect relationship since caffeine and EDs have been shown to antagonize some, but not all, of the depressant effects of alcohol.[14–17] Several reviews are available that address the potential adverse risks associated with EDs.[18–25]

By its classic physiologic definition, energy represents work performed per unit of time and is a purely physical concept. More recently, however, the concept of mental energy has been introduced to define a uniquely cognitive domain of energy that refers to cognitive performance and mood.[26–30] Energy drinks are marketed to improve physical or cognitive performance as well as to promote weight loss through increased energy expenditure. Table 1 provides a summary of the ingredients found in several of the more common EDs. It is apparent

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Table 1 **Some common energy drinks and their ingredients.**

Energy drink	Serving size (mL)	Ingredients (amount/serving size)					
		Caffeine (mg)	Taurine (mg)	Glucuronolactone (mg)	Sugar (g)	Vitamins	Herbal supplements and other ingredients
Amp®	237	71	ND	0	28	B_2, B_3, B_5, B_6, B_{12}	Guaraná (ND), ginseng (ND)
Cocaine®	248	280	750	0	18	B_6, B_{12}	Guaraná (25 mg), carnitine (50 mg)
Full Throttle®	237	100	ND	0	29	B_3, B_6, B_{12}	Guaraná (ND), ginseng (ND), carnitine (ND)
Go Girl® Sugar Free	355	100	800	ND	0	B_2, B_3, B_5, B_6, B_{12}	*Garcinia cambogia* (200 mg), inositol (100 mg)
Monster®	237	80	1,000	5	27	B_2, B_3, B_5, B_{12}	Guaraná (5 mg), ginseng (200 mg)
No Fear®	237	87	1,000	0	33	B_6, B_9, B_{12}	Guaraná (ND), ginseng (50 mg), carnitine (ND)
Red Bull®	245	80	1,000	600	27	B_3, B_5, B_6, B_{12}	None
Red Bull® Sugarfree	245	80	1,000	600	0	B_3, B_5, B_6, B_{12}	None
Rockstar®	237	80	1,000	0	31	B_2, B_3, B_5, B_6, B_{12}	Guaraná (25 mg), ginseng (25 mg), carnitine (25 mg), *Ginkgo biloba* (150 mg), milk thistle (20 mg)
Rockstar® Sugar Free	237	80	1,000	0	0	B_2, B_3,B_5, B_6, B_{12}	Guaraná (25 mg), ginseng (25 mg), carnitine (25 mg), *Ginkgo biloba* (150 mg), milk thistle (20 mg)
Tab® Energy	310	95	785	0	0	B_3, B_6, B_{12}	Guaraná (0.9 mg), ginseng (116 mg), carnitine (19 mg)
Venom® Energy	237	80	ND	0	28	B_2, B_3, B_6, B_{12}	Guaraná (ND), ginseng (ND), carnitine (ND)

Modified from Heckman et al. (2010)[2] and Milunsky et al. (1989).[87]
Abbreviation: ND, not disclosed.

that these drinks contain many common ingredients, such as caffeine, taurine, glucuronolactone, glucose, vitamins, and herbal supplements such as ginseng, guaraná, and yerba maté. However, the exact amounts of these ingredients are often not disclosed.

Many randomized, placebo-controlled, crossover studies have documented the effectiveness of EDs as thermogenic, ergogenic, or cognitive aids.[31,32] However, the predominant experimental design that has been used to establish the evidence-based support for EDs has involved a drink and placebo comparison. Given the varied composition of individual EDs (Table 1), however, this design does not make it possible to ascribe any positive effects to a single ingredient or to an interactive effect between ingredients. Moreover, many of these studies were sponsored by the manufacturer of the product being evaluated. One could assume it is probably in the manufacturer's best interest to determine whether their product is efficacious, but not necessarily to determine which ingredients, when given alone, are effective. However, it is certainly of scientific and regulatory interest to review the evidence indicating that the effects of EDs containing a variety of ingredients are greater than the effects of caffeine alone.

It is well documented that caffeine can act as a thermogenic, ergogenic, and cognitive aid,[33–36] effects which are consistent with the claims of ED manufacturers. It has been suggested that caffeine is the active component of EDs and is therefore responsible for their physiological and behavioral effects.[37] However, a key question is whether these purported effects of EDs are any greater than would be expected given the dose of caffeine the drinks contain.[28,34,38–40]

METHODS

For the present review, literature searches were conducted using PubMed, Psych Info, and Google Scholar with keywords that included caffeine with the other common ingredients listed in Table 1, either alone or in combination. An example of the keywords used in a search is caffeine AND taurine AND glucuronolactone. Searches of these databases were also performed using the same combination of keywords together with the phrases "physical performance" or "cognitive performance." Only English-language articles or abstracts were retrieved. The search primarily sought peer-reviewed publications, but some government reports and non-peer-reviewed publications were also evaluated.

RESULTS

The literature search identified 243 articles, of which 63 were reviews dealing with adverse events and the safety

and efficacy of the use of EDs as well as herbal, nutritional, and dietary supplements. Ten were case reports related to adverse events; 66 were articles using a randomized, placebo-controlled, and ED treatment; and 46 were articles that dealt with the individual ingredients of EDs, such as caffeine effects on arginine metabolism ($n = 5$), vascular smooth muscle ($n = 2$), locomotor activity ($n = 7$), altered gene expression, stem cell growth and amino acid synthesis ($n = 7$), cardiovascular risk factors ($n = 4$), caffeine content in supplements and extraction from Yerba maté ($n = 2$), as well as taurine ($n = 10$), ginseng ($n = 3$), folic acid ($n = 3$), guaraná ($n = 1$), and Yerba maté ($n = 3$). Eight were articles that used surveys to characterize consumption patterns of EDs and the use of nutritional supplements, six were government reports, three were abstracts, and nine were non-peer-reviewed articles. This left 32 articles that were classified as interaction studies that examined the effects of the ingredients of EDs alone and/or in combination with caffeine on physical or cognitive performance. Of these studies, 20 involved human subjects, 11 utilized animal models, and 1 used cell cultures. The findings from these articles classified as interaction studies are discussed below for the various ingredients of the ED examined. A strength of recommendation taxonomy (SORT)[41] was used to document the quality of evidence for conclusions specific for each of these ED ingredients. The SORT used the following criteria: A, recommendation based on consistent and good-quality experimental evidence; B, recommendation based on inconsistent or limited-quality experimental evidence; or C, recommendation based on consensus, opinion, usual practice, case studies, or extrapolation from quasi-experimental research.

Taurine

Taurine is a non-essential amino acid found in high concentrations in the brain, heart, and skeletal muscle.[42] The potential benefits of taurine supplementation in humans before or during exercise have been attributed to its antioxidant effect in young men following a 6 g/day dosing regimen for 7 days[43] and increases in plasma concentrations in males following long-duration submaximal runs, implying a release from skeletal muscle.[44] Contrasting these reports, Galloway et al.[45] reported that following 7 days of 5 g/day supplementation, there was no change in resting skeletal muscle taurine content and no change in the muscle taurine response to 2 h of cycling exercise at 60% of maximal aerobic power. Furthermore, there were no effects on muscle metabolism during the exercise; this was despite the fact that plasma taurine increased fivefold for up to 4 h following the 1.66 g of the supplement that was taken three times daily with meals. Further, the acute ingestion of 1.66 g of taurine 1 h prior to 90 min of submaximal exercise had no effect on subsequent time-trial performance.[46]

Despite the fact that taurine levels in the brain are high, evidence for a mechanism that supports the benefits of supplementation on cognitive performance is scarce. Animal studies report that chronic taurine supplementation in old mice for 8 months prevents age-related declines in learning and memory[47] – changes that were attributed to the elevated levels of brain glutamate and gamma-aminobutyric acid neurotransmitters following supplementation.[48] However, supplementation for a shorter period of 4 weeks in young mice produced no change in learning and retention and no change in brain neurotransmitters.[48] Transport of plasma taurine across the blood-brain barrier is tightly controlled by Na^+- and Cl^--dependent transporter activity,[49] which is regulated at the transcriptional level by cell damage, osmolality, and taurine content in the brain.[50] Thus, it is unlikely that elevated plasma taurine levels that follow acute or chronic supplementation[45] would alter brain taurine levels and neurotransmitters in healthy young adults.

One of the first and most popular EDs, Red Bull®, contains 1 g of taurine in each 250 mL can. A number of studies have compared the effects of a placebo drink or one or more cans of Red Bull® on physical and cognitive performance.[14,51–64] Although the majority of the findings from these studies demonstrate the efficacy of Red Bull®, they do not identify which ingredient alone or in combination in this ED explains the positive effects observed.

Geiß et al.[65] were the first to examine the effects of some of the ingredients of Red Bull® on exercise performance. They performed a double-blind study that involved the following three experimental trials: 500 mL (2 cans) of Red Bull® (the test drink); Red Bull® without taurine, glucuronolactone, and caffeine (the placebo trial that contained glucose and sweetener); or Red Bull® without taurine and glucuronolactone (the control trial that contained 160 mg caffeine, glucose, and sweetener). The drinks were consumed after 30 min of exercise at 70% of maximal aerobic power. The submaximal exercise continued for a further 30 min, after which the power output was increased by 50 W every 3 min to exhaustion. Although the tests were administered in a double-blind manner, the published report did not mention that the order of the treatment trials was randomized and there was no familiarization session. In the placebo trial, the sugar content of the ED was retained and there was no measure of oxygen consumption during the exercise test. Interestingly, compared with the control condition, the time to exhaustion during the incremental exercise test was significantly greater in the other conditions, i.e., 2.8 min longer during the Red Bull® trial and 1.7 min longer during the placebo trial; the former improvement

represented the completion of an additional 50 W of exercise, requiring the equivalent of an additional 600 mL of oxygen consumption (or 7.5 mL/kg for those subjects who were described as endurance-trained athletes). There was no discussion by the authors that would account for this increased energy requirement or improved cycling efficiency in the absence of the measurement of oxygen consumption. Finally, the coefficient of variation for time-to-exhaustion during the incremental exercise test was twofold higher, at 25%, for the tests involving Red Bull® or placebo compared with the 13% coefficient of variation for the control trial with caffeine. This increased variability in the performance of this exercise test suggests the need to include one or more familiarization sessions in such experiments,[66] as well as the need to measure oxygen consumption to account for the additional energy requirement during the longer tests for some of the subjects.

A similar combination and dose of test, control, and placebo drinks was used to examine electroencephalographic (EEG) and cardiac parameters during and following an incremental exercise test that used blood lactate levels to gauge the intensity of effort.[67,68] These studies also did not include a familiarization session, a true placebo trial, or measurement of oxygen consumption. Artefact-free EEG measurements were used to determine the readiness potential associated with a self-paced kicking motion of the right leg at rest and at various stages of exercise,[68] and M-mode 2-dimensional echocardiography was used to measure fractional shortening and left ventricular end diastolic and systolic diameters at rest before and after consumption of the drink and following exercise.[67] During and following exercise, amplitude of the readiness potential was reduced during the Red Bull® trial; this was interpreted to imply that mental effort was reduced with taurine consumption. More than half of the 15 subjects in both the Red Bull® and the control trials indicated they could have continued exercising at a higher intensity. Following exercise, peak diastolic inflow velocity increased during both the Red Bull® and the control trials. The researchers also reported that fractional shortening of the left ventricle increased and left ventricular end-systolic diameter decreased only during the Red Bull® trial. However, inspection of the data revealed that similar or greater changes in the mean values also occurred during the placebo trial, but the changes did not attain statistical significance. Following exercise, the researchers also calculated a higher stroke volume during the Red Bull® trial; this would imply there was greater cardiac output, since heart rates were similar at 70 beats/min during this measurement. It is unclear what might account for the increased demand for cardiac output since, once again, oxygen consumption measurements were not included as a dependent measure in these studies.

The effects that 1 or 2 weeks of 4 mg/body weight (bw) caffeine or 15 mg/bw taurine supplementation, either alone or in combination, had on the treadmill running performance of mice was examined by Imagawa et al.[69] Treadmill exercise began 4 h after the final drug administration and included 90 min of running at 10 m/min followed by increases in treadmill speed of 5 m/min every 15 min, to the point where the mice stopped running despite electrostimulation. After 1 week, the group fed caffeine alone or in combination with taurine significantly increased their treadmill running distance, whereas no difference was observed in the control group or in those fed taurine alone. After 2 weeks of supplementation, there were no further improvements for the mice fed caffeine alone, but significant improvements were found for the group fed taurine alone and further additional increases in running performance were noted for the group fed both caffeine and taurine. Twenty-eight days of caffeine and taurine supplementation had no effect on the distribution or diameter of muscle fiber type in the gastrocnemius muscle of the mice. The findings from this study suggest there is an additive effect of taurine supplementation with caffeine that becomes evident after a period of 2 weeks in rodents. However, the translation of these data for their effect on human performance is not a straightforward undertaking. First, the authors suggest their findings might be explained by increased taurine concentrations in muscle due to the supplementation. Yet, taurine levels in muscle were not measured, and the only human study to assess changes in muscle concentrations related to taurine supplementation did not extend beyond 1 week of 5 g/day supplementation.[45] In addition, it is difficult to compare the dosing used in animal studies to equivalent consumption in humans. Supplementation with 4 mg/bw caffeine or 15 mg/bw taurine for mice weighing 20 g would equate to dosages in humans that are at least tenfold higher than what might be used for human experimentation.[45,66] Finally, if the same 4-h period between the last drug administration and the beginning of the exercise challenge, as used in the mice, were to be used in humans, it would negate the ergogenic effect for regular human caffeine users[66] and reduce plasma taurine levels by more than 50% versus the levels expected 1–2 h following acute dosing.[45]

The role of nitric oxide in the caffeine-induced locomotor hyperactivity in mice was studied by Kimura et al.[70] Locomotor activity counts were increased significantly following intraperitoneal injection of caffeine in a dose-dependent manner from 2 through 10 mg/kg. In a subsequent experiment, the effects of arginine (600 mg/kg) or taurine (400 mg/kg), either alone or in combination with the 2 mg/kg dose of caffeine, were examined. When either of these amino acids was administered in combination with the caffeine, activity counts were

significantly increased. Again, it was interesting to note that these activity counts were increased to levels that were comparable to those observed for the group of mice that received the 2 mg/kg dose of caffeine in the first study, and they were still far below the levels recorded following a 5 or 10 mg/kg caffeine dose. Additional experiments with a nitric oxide synthase inhibitor returned activity counts to control levels following the administration of taurine or arginine with caffeine, leading the authors to conclude that the interactive effect of these amino acids with caffeine involved an increased synthesis of nitric oxide. Again, it is difficult to translate the findings from this study to potential effects on human performance. First, the dose of taurine that was administered (400 mg/kg) would equate to the unrealistic consumption of over 25 cans of Red Bull® for a 70 kg individual. It is also difficult to understand the extent of the variability in activity counts recorded (from 450 to almost 1,500) for the different groups of mice receiving the same 2 mg/kg dose of caffeine and the fact that activity counts at close to 4,000 following 5 or 10 mg/kg doses of caffeine were two- to threefold greater than the counts recorded following the administration of caffeine together with either arginine or taurine.[70]

There is clearly a lack of definitive evidence-based support in humans to justify the addition of taurine to a caffeinated ED with the claim that the taurine will cause greater improvements in physical and cognitive performance than can be attributed to the effects of caffeine alone. The human studies that are often cited to support the addition of taurine to an ED[65,67,68] have been improperly designed and lacked the appropriate dependent measures to test the stated hypothesis. Extrapolation of findings from animal studies is difficult due to problems with dosing and biological differences between species. Appropriately designed studies to isolate the effects of taurine and caffeine in EDs have only been used to address the diuresis effect of the drinks.[71] In addition, the most conclusive studies, to date, have shown that acute or chronic taurine supplementation has no effect on muscle concentration or metabolism during submaximal endurance exercise.[45,46]

Evidence statement. There is inconsistent or limited-quality experimental evidence indicating that the addition of taurine to a caffeinated energy drink will cause greater improvements in physical and cognitive performance than can be attributed to the effects of caffeine alone. (Evidence Category B.)

Glucuronolactone

Glucuronolactone is a naturally occurring metabolite formed from glucose in the liver.[72] Ingested glucuronolactone is readily absorbed, and then hydrolyzed and excreted in the urine as glucuronic acid.[73] An early study, which involved the injection of 100 mg/kg of glucuronolactone or other sugar carbon complexes, such as glycogen, glucose, galactose, fructose, or pyruvate, three times daily in rats during rest periods that preceded swimming tests to exhaustion, revealed positive effects on swim performance, blood glucose, and liver glycogen during the second and third tests following glucuronolactone injection.[74] However, similar findings were also evident following the injection of glucose and galactose and were consistent with the known ergogenic effects of exogenous carbohydrate supplementation during prolonged exercise.[75,76] In addition, this 100 mg/kg dose of glucuronolactone three times daily would equate to the consumption of 35 cans of Red Bull® for a 70-kg individual, given the amount of glucuronolactone in each 245 mL serving (see Table 1).

Other than the reports discussed in the previous section for taurine,[65,67,68] no articles were found that compared the effects of glucuronolactone alone and in combination with caffeine on physical or cognitive performance. Certainly, this is one ingredient for which evidence-based studies are needed to justify its popularity in various EDs (see Table 1).

Evidence statement. There is no experimental evidence showing that the addition of glucuronolactone to a caffeinated energy drink will cause greater improvements in physical and cognitive performance than can be attributed to the effects of caffeine alone. (Evidence Category C.)

Glucose

It is well documented that endurance exercise performance can be extended if carbohydrates are included in the fluid consumed at regular intervals.[75,76] Optimal concentrations of 6–8% can provide an exogenous source of carbohydrate oxidation at rates approximating 60 g/h for each liter of fluid consumed.[77] Sport drinks, such as Gatorade®, are designed to provide these optimal concentrations of carbohydrate, whereas the sugar content of most EDs are closer to 11–12% by volume (see Table 1), which are levels at which gastric emptying would be slowed.[77]

Given the independent ergogenic effects of carbohydrate or caffeine ingestion, several investigators have studied the interactive effects of these substances when they are concomitantly ingested. Hulston and Jeukendrup[78] examined the impact of 0.7 g/min of carbohydrate ingested alone or in combination with 5.3 mg/kg of caffeine during 105 min of steady-state exercise at approximately 60% of maximal aerobic power, followed by a time trial lasting about 45 min. Rates of appearance and

disappearance of glucose were significantly higher with carbohydrate ingestion but were unaffected by the additional ingestion of caffeine. Time trial performance was improved significantly by almost 5% when caffeine was ingested with the carbohydrate, implying that this additional ergogenic effect was due to the independent effect of the caffeine. Unfortunately, these authors did not include an experimental condition that involved only the ingestion of the 5.3 mg/kg of caffeine. Similarly, a recent study revealed greater 15-min time trial performance following 2 h of submaximal exercise and attenuated declines in post-exercise leg maximal voluntary contraction forces with a carbohydrate-electrolyte beverage that contained caffeine and other ingredients common to EDs, when compared with a carbohydrate-electrolyte beverage alone.[79] This study also did not include an experimental condition involving the ingestion of the 5.8 mg/kg of caffeine alone, so attributing the ergogenic effect solely to the additional caffeine in the carbohydrate-electrolyte beverage could not be done conclusively. A recent meta-analysis revealed that effect sizes were almost twofold greater for caffeine versus placebo studies compared with studies that examined the combined effects of caffeine and carbohydrate ingestion in comparison with carbohydrate alone[80]; it also suggested the ergogenic effect of caffeine may be reduced when carbohydrate is added to the drink. Yet, the results of these studies could also be interpreted to suggest that an individual ceiling exists for any given ergogenic effect, whether it is achieved through the delivery of caffeine alone or in combination with carbohydrate. Following exhaustive exercise that leads to low levels of muscle glycogen, the consumption of 1 g/kg/h of carbohydrate, together with 8 mg/kg of caffeine over 4 h, creates greater rates of muscle glycogen resynthesis in trained endurance athletes compared with the ingestion of carbohydrate alone.[81] Thus, the ergogenic benefits of caffeine may be reduced when combined with carbohydrates during exercise, but the combination of carbohydrate and caffeine may be an important strategy following exhaustive long-duration exercise to assist with muscle glycogen repletion.

There is also substantive evidence supporting the independent effects of glucose and caffeine on cognitive performance. However, only three studies were identified that examined the individual and interactive effects of glucose and caffeine on cognitive and/or psychomotor performance. Following a night of restricted sleep totaling 5 h, a 2-h driving simulator test conducted the next afternoon from 14:00 to 16:00 h under three double-blind and randomized conditions was used to study the effect of a glucose (30 g of sugar) or glucose (65 g) and caffeine (46 mg) drink on performance.[82] Sleep-related incidents, defined from video recordings as due to eye closure or vacant staring ahead, were the lowest over the 2-h test with the glucose and caffeine drink, although differences among conditions were not significant. Similarly, EEG recordings were not different among conditions but suggested reduced levels of sleepiness with the sugar and caffeine drink. Subjective ratings of sleepiness, however, were significantly reduced during the 2nd hour of the driving test when the drink contained both sugar and caffeine. Based upon their own previous research that tested driver sleepiness following the consumption of one can of Red Bull®,[61] the authors concluded that the impact on driver performance was due to the caffeine rather than the glucose content of the drink. Clearly, the experimental design used by Horne and Anderson[82] would have provided stronger support for this conclusion if it had included a drink with only caffeine, as well as one with the same glucose content as in the drink containing both glucose and caffeine.

A tailored version of the Cognitive Drug Research assessment battery was used to assess the effects of an ED and its caffeine, glucose, and herbal fractions on memory and attention.[83] Following a familiarization session, subjects performed five double-blind and randomized tests in the morning that consisted of baseline testing, the consumption of a 250 mL drink, and additional testing with the cognitive battery that began 30-min postingestion. The drinks were placebo (water plus artificial sweeteners) provided alone or together with 75 mg caffeine, 37.5 g of glucose, 12.5 mg of ginseng, and 2 mg of *Ginkgo biloba* extract or the complete energy drink containing all of the ingredients. Performance on the tests administered to provide an outcome score for secondary memory (such as the delayed word and picture recognition and the immediate and delayed word recall tests) and on tests used to indicate speed of attention were significantly improved following ingestion of the entire ED. However, trends ($0.1 > P > 0.05$) towards improved outcome measures for quality of memory, secondary memory, and accuracy of attention were observed following ingestion of the drink containing caffeine alone. Interestingly, the authors measured blood glucose levels to confirm the amount of increase following ingestion of the drinks containing glucose, but they relied on heart rate, rather than direct measures of plasma concentrations, to indicate the influence of caffeine. It was concluded that the combination of glucose with caffeine in an ED, rather than either ingredient alone, was essential to produce a positive effect on cognitive performance. More recently, Adan and Serra-Grabulosa[84] used a double-blind randomized group design to compare the effects of 75 mg of caffeine or 75 g of glucose, either alone or in combination, on cognitive performance using a test battery that began 30 min following ingestion of 150 mL of the treatment drink and required an additional 30–45 min to complete. Saliva and blood samples were used to confirm the ability of the

drinks to alter caffeine and glucose levels, respectively. Simple reaction time was significantly slower for the placebo group compared with the groups ingesting any of the other drinks. The authors reported that the type of beverage had no effect on choice or sequential reaction time, but they then proceeded to perform post-hoc analyses to isolate differences among treatment means. In these analyses, glucose ingestion alone was found to improve performance on the Purdue Pegboard assembly task in comparison with placebo or caffeine. The ingestion of glucose and caffeine together improved scores on a verbal memory task during the latter portions of the test. Collectively, for these groups of rested college-aged men and women, the authors stated that the effects of 75 mg of caffeine or 75 g of glucose alone or in combination were modest compared with placebo. Interestingly, although salivary caffeine concentrations were elevated following ingestion of the caffeine and glucose beverage, the values were lower than those in the group that received the same dose of caffeine without glucose; this suggests either a slowing of caffeine absorption into the circulation or an acceleration of its removal from the circulation when combined with glucose. The findings from these studies suggest that the combined ingestion of glucose and caffeine may enhance cognitive performance in sleep-restricted individuals for about 30–60 minutes post-ingestion, but caffeine ingestion alone may provide benefits that last for longer periods.

Evidence statement. There is inconsistent or limited-quality experimental evidence to indicate that the addition of glucose to a caffeinated ED will cause greater improvements in physical and cognitive performance than can be attributed to the effects of caffeine alone. (Evidence Category B.)

Vitamins

Most EDs contain varying amounts of B vitamins and make unsubstantiated claims that these ingredients will increase the body's energy level. However, for most active adults, a balanced nutritious diet will provide sufficient quantities of the B complex vitamins and there is no need for further supplementation.[85,86] There are some exceptions for special populations; for example, folic acid supplementation (vitamin B_9) is recommended before and during pregnancy[87] and with advancing age.[88] No studies were found that compared the effects of vitamin supplementation alone and in combination with caffeine on physical or cognitive performance.

Evidence statement. There is no experimental evidence showing that the addition of multivitamins to a caffeinated energy drink will cause greater improvements in physical and cognitive performance than can be attributed to the effects of caffeine alone. (Evidence Category C.)

Guaraná

Guaraná (*Paullinia cupana*) is a plant native to Brazil, where it is grown and farmed.[89] Extracts of seeds from the fruit of guaraná contain caffeine at concentrations that vary from 2% to as high as 15% of the dry weight.[90,91] Guaraná extracts also contain saponins and tannins,[92] which exert antioxidant effects,[93] and the flavonoids catechin and epicatechin, which reduce platelet aggregation.[94]

Several studies with rodents have compared the behavioral effects of guaraná with caffeine in an attempt to clarify whether any observed effects were due to the caffeine content alone or to other active ingredients. Espinola et al.[92] compared the physical and cognitive effects of acute and chronic low and high doses of guaraná with those of caffeine in mice and rats. The authors stated that the guaraná powder contained approximately 2% caffeine, such that the higher dose of guaraná (3 mg/mL) should have provided about 60% of the caffeine administered to the rodents that received caffeine in pure form. To study the chronic effects, animals received their treatments through *ad libitum* fluid ingestion, whereas the acute effects involved intraperitoneal injections. Both the low and high doses of guaraná improved physical performance during a forced swimming test after 100 and 200 days of treatment, whereas there was no effect with caffeine. Following the acute injection of caffeine or both doses of guaraná, memory was improved during a passive avoidance test; in contrast, memory was improved only with the lower dose of guaraná after 12 months of chronic administration. Since caffeine treatment showed no effect on physical performance and little effect on cognitive tests, and since physical and cognitive performance were improved with the lower dose of guaraná, the authors concluded that these effects were most likely due to the saponins and tannins present in the seed of the plant, rather than to the caffeine. Unfortunately the volumes of *ad libitum* fluid consumed were not reported, so it is difficult to know the actual amounts of the active ingredients that were ingested. In addition, circulating concentrations of caffeine were not determined. Nevertheless, the concentration of guaraná in the fluids differed tenfold between the low and high doses, and the concentration of caffeine in the lowest dose of guaraná was only 6% of the concentration administered with the caffeine treatment. Thus, the caffeine consumed by the animals that received the lowest dose of guaraná was unlikely to account for the observed effects.

The effect of the caffeine content in guaraná on lipid metabolism in trained and sedentary rats was examined

by comparing normal and decaffeinated extracts of the plant powder.[91] Measures of lipid metabolism, which included muscle oleate incorporation, carnitine palmitoyltransferase activity, and mRNA expression and plasma lactate concentrations during exercise, were unchanged following consumption of the decaffeinated guaraná extract, but they were indicative of increased fatty acid oxidation with the consumption of the normal extract. The findings imply that these effects were due to the caffeine content of the intact extract. However, the two doses of guaraná extract used provided doses of caffeine that were five- to tenfold greater than the doses commonly used to study exercise metabolism in humans.[66]

The effects on immobility time during a forced swimming test and an open-field test of locomotion in mice were examined 1 h following the ingestion of 25, 50, and 100 mg/kg of guaraná or 10, 20, and 30 mg/kg of caffeine.[95] These tests are used, respectively, for animal models of depression and central nervous system activation. It should be noted that the authors did not disclose the caffeine content of the guaraná extract that was used. Both of the lower doses of guaraná and caffeine decreased immobility time during the swimming test, thereby demonstrating antidepressant-like properties, whereas only the highest dose of both treatments increased activity counts during the open-field test. Since caffeine acts primarily via adenosine receptors, animals were pretreated with the adenosine A_1 receptor agonist, cyclopentyladenosine, which increased immobility times during the forced swimming test. These effects were reduced with a 20 mg/kg dose of caffeine but were not significantly altered with a 50 mg/kg dose of guaraná. These findings imply guaraná acts through a different mechanism than adenosine receptor antagonism. However, it should be noted that caffeine in doses of 20 mg/kg, an order of magnitude greater than typical human doses, probably acts via mechanisms other than adenosine antagonism.[38] In addition, without verification of the caffeine content consumed with the 25, 50, or 100 mg/kg doses of guaraná used in this study, it is not possible to make valid comparisons with the effects of the 10, 20, or 30 mg/kg doses of caffeine.

Similarly, Otobone et al.[96] compared the effects in rats of acute or chronic ingestion of crude or semipurified extracts of guaraná with intraperitoneal injections of caffeine. A single dose of any of the guaraná extracts failed to influence activity during the behavioral tests that were used. In contrast, following 40 days of administration, the crude extract and semipurified form significantly reduced immobility time during the forced swimming test, again demonstrating antidepressant-like properties, but no effect was observed during the open-field test of locomotor activity. These effects were similar to those observed following injections of the antidepressant drug imipramine. In contrast, daily injections of 10 mg/kg caffeine reduced immobility time and increased locomotor activity, results that are consistent with the effects commonly observed for psychostimulant drugs in rodents. The authors concluded that the effects observed following the chronic administration of the guaraná extracts were not due to caffeine but more likely reflected the impact of the tannin component in the seeds. However, this study also lacked verification of the amount of caffeine consumed by the animals through the guaraná extracts, thereby limiting the validity of the authors' conclusions.

Earlier studies with human volunteers compared the effects on cognition after the daily ingestion of either 1 g of guaraná powder or the roughly equivalent dose of 25 mg of caffeine, for 3 days by younger adults[97] or for 5 months by adults over 60 years of age.[98] A randomized double-blind group design utilizing common tests to measure cognition revealed no effects following the administration of guaraná or caffeine in either the younger[97] or the older adults.[98] For both of these studies, the 25 mg dose of caffeine utilized would be at the low end of the effective dose-response relationship for the influence of caffeine on cognition in rested volunteers.[99] More recent studies have shown that guaraná extracts containing 200 mg of caffeine together with varying doses of epigallocatechin-3-gallate in green tea increased 24-h energy expenditure,[100] and a vitamin, mineral, and guaraná supplement containing approximately 40 mg of caffeine improved cognitive performance for 60 min postingestion compared with placebo.[101]

A randomized group design, which used a decaffeinated drink as the control, compared the effects of 100 mg of caffeine in a coffee, guaraná, or yerba maté beverage on mood, vigilance, logical reasoning, and cardiovascular measures of blood pressure and heart rate.[102] Testing was performed prior to consumption of each drink and then 60 min and 150 min postingestion. Guaraná was associated with increased systolic pressure, from 112 at baseline to 120 mmHg 150 min after ingestion. No other effects on blood pressure or heart rate were attributed to the drinks' ingredients. There was a trend for alertness to be more positively affected following consumption of guaraná, and both the caffeine and guaraná drinks were associated with improved accuracy during the vigilance task. Unfortunately, this study did not determine the concentrations of caffeine in plasma or even saliva following drink ingestion, nor did it measure the caffeine content of the drinks consumed. As a result, it is very difficult to interpret the different effects of guaraná and yerba maté, for example, without knowing the amount of caffeine consumed or the associated change in plasma concentrations following drink consumption.

Following an initial study that demonstrated psychoactive effects of a 75 mg dose of guaraná, which contained only 9 mg of caffeine, for up to 6 h following ingestion,[103] Haskell et al.[104] compared the effects of four doses of guaraná (37.5, 75, 150, or 300 mg) on cognitive performance at 1, 3, and 6 h postingestion. In both of these studies, the method by which guaraná was extracted from the seeds produced about a 12% methylxanthine concentration in the resultant extract.[103] Thus, the four doses of guaraná ingested should have provided approximately 4.5, 9, 18, and 36 mg, respectively, of caffeine. Interestingly, salivary samples were taken prior to ingestion of the guaraná capsules to verify abstinence from caffeinated drinks prior to testing, but no further salivary samples were collected to validate the dose of caffeine resulting from ingestion of the guaraná capsules. The authors' Cognitive Drug Research cognitive assessment battery revealed improved outcomes for secondary memory due to two lower doses of guaraná, but no other effects of guaraná were noted for the other outcome measures, such as speed of attention, speed of memory, accuracy of attention, or working memory, for these rested volunteers. Nonetheless, the authors concluded that the observed effects could not be attributed to caffeine given the very small dose of 5–10 mg that was in these capsules. In fact, these small doses of caffeine are comparable to the amounts typically found in decaffeinated coffee,[105] which is often used as the placebo control treatment.[102,105]

Findings from both animal and human studies seem to suggest that guaraná can influence behavior and cognitive performance through caffeine-independent mechanisms. However, the possible ergogenic effects of guaraná have not been documented in humans. Future human studies should include determinations of the subjects' plasma caffeine concentrations following the ingestion of guaraná extracts or supplements to help verify the actual amounts of caffeine ingested. In addition, measures of antioxidant effects, such as determination of malondialdehyde, which is formed with the degradation of polyunsaturated lipids with reactive oxygen species, should also be included as an index of the effect of the tannin component in the guaraná extract.

Evidence statement. There is inconsistent or limited-quality experimental evidence to indicate that improvements in cognitive performance following the ingestion of guaraná can be attributed to the effects of ingredients other than the caffeine content of the herbal supplement. (Evidence Category B.) There is no experimental evidence showing that improvements in physical performance following the ingestion of guaraná can be attributed to the effects of ingredients other than the caffeine content of the herbal supplement. (Evidence Category C.)

Yerba maté

Like guaraná, yerba maté (*Ilex paraguariensis*) is a plant native to South America, which is farmed and consumed primarily as a tea or cold drink (see Heck and Meji[106] for review). Yerba maté leaves contain the methylxanthines caffeine and theobromine, which total approximately 1.2 g/100 g dry weight or about 70 mg/100 mL as an aqueous extract.[107] Extracts from the yerba maté plant also contain phenolic compounds,[107–109] tannins,[109] and saponins,[110] which possess antioxidant and anti-inflammatory activity[109,110] and demonstrate an antiparkinsonian profile in animal models.[108]

In addition to the previous study by Meyer and Ball[102] that compared the cardiovascular effects of guaraná and yerba maté drinks with caffeinated coffee, one study was identified that compared the effects of varying doses of 62.5, 125, and 250 mg/kg of yerba maté tea extract to 1 or 10 mg/kg caffeine using an animal model to examine spontaneous locomotor activity, short-term memory, and learning.[111] Intraperitoneal injections of caffeine (10 mg/kg) and all doses of the tea extract did not affect spontaneous locomotor activity, but they significantly improved short-term memory during a social recognition task. Similar findings were observed following the oral dose of 125 mg/kg of yerba maté extract administered alone or when the oral dose of 62.5 mg/kg of extract was combined with the intraperitoneal injection of 1 mg/kg of caffeine. In a similar fashion, short-term memory evaluated with an inhibitory avoidance task was significantly improved with the 10 mg/kg dose of caffeine and the two lower doses of yerba maté extract, but the combination of the lowest doses of caffeine and tea extract failed to influence short-term memory during this avoidance task. Due to the similarities in effects between the doses of caffeine and yerba maté alone or in combination, the authors concluded that yerba maté influenced cognitive performance via the same mechanism of caffeine, i.e., antagonism at adenosine receptors.

Like with so many of the previous animal and human studies, the major criticism with these findings is the lack of measurement of the caffeine concentration for both the yerba maté tea extracts and plasma levels in the animals. Using 1% of dry weight for the caffeine in extracts of yerba maté leaves,[107] the amount of caffeine in the 62.5, 125, and 250 mg/kg extracts used by Prediger et al.[111] would correspond to 0.6, 1.3, and 2.5 mg/kg caffeine. If this is correct, it would appear that a threshold dose of slightly greater than 1 mg/kg caffeine is necessary to influence cognitive performance in the rat. This threshold value was estimated from the positive effects observed following 125 mg/kg of tea extract, or 1.3 mg/kg caffeine, following the combination of 1 mg/kg caffeine and 62.5 mg/kg tea extract, for a total caffeine

dose of 1.6 mg/kg, and the lack of effect observed following the dose of 1 mg/kg caffeine.

It is apparent that a need exists for well-designed human studies to examine the effects of yerba maté on physical and cognitive performance. Studies using extracts from this plant's leaves should include measures of caffeine in blood, or at the very least saliva, to verify the amount of caffeine provided to the volunteers. In addition, as suggested previously for studies involving guaraná, measures of the antioxidant and possibly anti-inflammatory effects related to ingestion of the tea extract should be included in an attempt to isolate the effects due to the methylxanthine and phenol components of the supplement.

Evidence statement. There is no experimental evidence showing that improvements in physical and cognitive performance following the ingestion of yerba maté can be attributed to the effects of ingredients other than the caffeine content of the herbal supplement. (Evidence Category C.)

Additional interactions

Carnitine is another common ingredient in many EDs (see Table 1) and it is known to play a critical role in assisting the entry of fatty acids into the mitochondria. Both animal[112] and human[113] studies have reported improved exercise performance and fat loss when carnitine and caffeine are ingested together; however, large doses of caffeine are typically used in animal studies,[112] which are considered non-physiological in humans. In addition, the benefits of carnitine ingestion on muscle metabolism during exercise are not supported[114] and a recent analysis of the findings from several studies demonstrated that caffeine has no effect on fat or carbohydrate metabolism during exercise.[115] Further, when coingested with a high-fat meal, caffeine has demonstrated no effect on exercise time to exhaustion at approximately 75% of maximal aerobic power and no effect on circulating tyrosine or tryptophan as peripheral markers representing the modulation of dopamine and serotonin, respectively, as indicators of central fatigue.[116] Thus, the inclusion of carnitine in EDs for the purpose of promoting increased rates of fatty acid oxidation is questionable.

Evidence statement. There is no experimental evidence showing that the addition of carnitine to a caffeinated energy drink will cause greater improvements in physical and cognitive performance than can be attributed to the effects of caffeine alone. (Evidence Category C.)

St. John's Wort (*Hypericum perforatum*) is an herbal supplement that is used to treat depression,[117] yet its effectiveness is unclear.[118] One study reported that *Hypericum perforatum* eliminated the augmented locomotor activity that followed the intraperitoneal injection of caffeine in mice.[119] Since pretreatment with arginine reversed the inhibitory effect of *Hypericum perforatum* on caffeine, the authors concluded that the effects of *Hypericum perforatum* were due to its inhibition of nitric oxide synthase. These findings suggest that the inclusion of *Hypericum perforatum* in the ED may counter the ergogenic effects that would be attributed to the caffeine content. It is worth noting that this was one of the few animal studies that used doses of caffeine from 4 to 16 mg/kg, which are comparable to those used to study the effects of caffeine on physical performance.[66]

Evidence statement. There is no experimental evidence showing that the addition of St. John's Wort to a caffeinated energy drink will cause greater improvements in physical and cognitive performance than can be attributed to the effects of caffeine alone. (Evidence Category C.)

Ginseng is another herbal supplement common to many EDs (see Table 1). There are several forms of ginseng, with the most popular being Chinese ginseng (*Panax ginseng*), but American (*Panax quiquefolium*) or Siberian (*Eleutherococcus* senticosus) ginseng are also often consumed.[120] One study was identified that compared the effects of 75 mg of guaraná, which contained only 9 mg of caffeine, 200 mg of *Panax ginseng*, or their combination on cognitive performance for up to 6 h following ingestion.[103] Both guaraná and ginseng alone were associated with positive effects on the different outcome measures from the Cognitive Drug Research assessment battery, yet there was little, if any, evidence of synergistic effects on cognitive performance when both guaraná and ginseng were ingested together. In contrast to these findings, systematic reviews have concluded there is little evidence to substantiate the proposed cognitive benefits of ginseng consumption.[121,122] Similarly, evidence-based support for the purported ergogenic effects that follow acute or long-term ingestion (up to 6 weeks) of ginseng is weak.[120,123,124] As a result, the addition of ginseng to an ED for the purpose of enhancing physical or cognitive performance is currently not tenable and there is no evidence to suggest it would interact with the known effects of caffeine.

Evidence statement. There is no experimental evidence showing that the addition of ginseng to a caffeinated energy drink will cause greater improvements in physical and cognitive performance than can be attributed to the effects of caffeine alone. (Evidence Category C.)

DISCUSSION

This review presents a systematic evaluation of the evidence-based findings purported to substantiate the efficacy of ingredients other than caffeine in EDs, which are promoted as beverages that enhance physical and cognitive performance or increase energy expenditure. The marketing and sale of these drinks, primarily to adolescents and young adults, represent a multibillion dollar industry globally, yet claims of their ability to increase energy appear to be unsubstantiated for the majority of their ingredients.

Marketing claims that taurine will increase physical and cognitive performance are not supported by the available evidence. Findings by Galloway et al.[45] conclusively showed that taurine supplementation for 7 days had no effect on muscle taurine levels and no effect on muscle metabolism during submaximal exercise. In addition, despite observed elevations in plasma levels following acute supplementation,[45] transport across the blood-brain barrier is tightly regulated, so taurine levels in the brain would likely be unaltered from normal levels.[50] Unfortunately, the studies often cited to substantiate the marketing claims for taurine[65,67,68] have lacked experimental trials that isolate the effects of the amino acid and, importantly, have lacked the critical dependent measures necessary to conclusively test the studies' hypotheses.

Evidence to support the addition of glucuronolactone to EDs is nonexistent. As stated above for taurine, no studies, to date, have appropriately tested the effects of glucuronolactone alone on physical and cognitive performance, and those that studied this ingredient with taurine[65,67,68] require additional dependent measures to validate their findings.

The glucose content in EDs is not designed to optimize absorption of fluid and carbohydrates during exercise, as is the case for sport drinks, such as Gatorade®.[77] As a result, if the ED is consumed as a source of fluid and carbohydrate during exercise, then better choices are available for this purpose. There is some evidence to support the beneficial effects of the glucose in EDs for improving cognitive performance for up to 60 min post-ingestion,[83] but the addition of caffeine enhanced and sustained the effects of glucose for up to 2 h post-ingestion.[82–84]

For young, healthy adults, a balanced nutritious diet will provided sufficient quantities of the vitamin B complex without the need to supplement intake through the consumption of EDs. In addition, there is no evidence to support the claims that additional supplementation with the vitamin B complex will enhance physical and cognitive performance.

There is some evidence from well-controlled, placebo and randomized double-blind studies that support a caffeine-independent mechanism for the beneficial effects of extracts from the guaraná plant (*Paullinia cupana*) on cognitive performance in humans.[103,104] In these studies, extracts from guaraná provided doses of caffeine that were purported to be less than 10 mg. Thus, the positive effects detected could be due to the saponins and tannins in the seed of the plant, rather than the caffeine, and these conclusions would be consistent with the effects observed in animal studies.[92,96] However, a major flaw with these studies was the absence of measurement of circulating caffeine concentrations following guaraná ingestion. Thus, these studies should be repeated in other laboratories to confirm the reported observations. Studies definitively demonstrating that saponins and tannins have such cognitive-enhancing properties were not found in the existing literature. One might expect similar conclusions to be evident with extracts from yerba maté (*Ilex paraguariensis*) but this was not the case for the single human[102] or animal[111] study that compared tea leaves or extracts from the plant to comparable doses of caffeine. Although some animal studies have documented ergogenic effects following guaraná ingestion during open-field locomotor tests[95] or treadmill runs to exhaustion,[92] the results were equivocal as to whether the effects were attributable to caffeine or to the polyphenols in the plant extract. The present literature search revealed no evidence-based studies in humans that examined the ergogenic effects of guaraná, let alone support the claim that the extract enhances physical performance via a non-caffeine-dependent mechanism. Similarly, no studies could be found that examined the ergogenic effects of yerba maté in humans.

The existing literature contains no evidence that addition of other supplements, such as ginseng, carnitine, or St. John's Wort, to EDs provides any benefit to physical or cognitive performance.

In contrast to the overwhelming lack of evidence-based findings to substantiate the ability of EDs to enhance physical and cognitive performance through non-caffeine-dependent mechanisms, the evidence to support a caffeine-dependent mechanism is substantial. The reader is referred to several excellent reviews that summarize caffeine's pharmacology, metabolism, mechanism of adenosine receptor antagonism, as well as the physical and cognitive performance effects with varying doses of the drug.[34–36,38,40,125,126] It is generally agreed that as little as 40–60 mg of caffeine can exert positive effects on cognitive function,[99,127,128] with larger doses, which typically exceed 200 mg or about 3 mg/kg, required to enhance physical performance when the dose is ingested about 1 h before exercise.[129] Interestingly, the dose of caffeine required for an ergogenic effect appears to be lower if the caffeine is administered after exercise has begun[130] or after an initial bout of exercise has been completed but

prior to a second bout of exercise several hours later.[131] Several factors, such as history of use, genetic variation in the expression of the cytochrome P450 enzyme or the adenosine A_{2a} receptor, and whether an individual is rested or fatigued, can influence the magnitude of the physical and cognitive effects to a given dose of caffeine (for a recent review see Lieberman et al.[38]).

Caffeine content for a single serving of the EDs listed in Table 1 ranges from a low of 47 mg to a high of 280 mg. Certainly one serving of any of these drinks would be sufficient to impact cognitive function[99,127,128]; one serving of Cocaine or two servings of Red Bull and most of the other EDs 1 h prior to exercise would also approach a dose of caffeine that could impact physical performance.[129] Similarly, the ingestion of two servings of Red Bull towards the latter stages of 2 h of submaximal exercise could increase time-trial cycling performance comparable to performance improvements that follow much larger doses of caffeine (equivalent to six cans of Red Bull) consumed prior to the start of exercise.[130]

RECOMMENDATIONS FOR FUTURE RESEARCH

It is apparent from this review that multiple well-designed, randomized, placebo-controlled studies are needed to support the claims that EDs enhance physical and cognitive performance via a caffeine-independent mechanism. Specifically, experimental designs similar to the one described by Riesenhuber et al.[71] should be used to examine the individual and interactive effects of the various ingredients in the EDs containing caffeine. If taurine is purported to affect human muscle function and exercise performance, it should be ingested separately as a treatment condition, at various doses, and compared against caffeine alone and in combination. The same studies should be conducted for glucuronolactone, since there is presently no human research that justifies its inclusion in these drinks. In addition, a need exists to conduct studies on exercise performance using appropriate doses of guaraná and additional human studies are necessary to verify the physical and cognitive performance effects of yerba maté ingestion. The effects of acute versus chronic ingestion of these ingredients should also be explored.[45]

It is equally important that future study designs include the appropriate dependent measures to test the hypotheses. For all studies, measurements of plasma, or at least salivary, caffeine levels would be necessary to verify the absence of a caffeine effect or the equality of caffeine intake via plant extract or anhydrous supplement provided in the ED.[132] For exercise studies, the measurement of oxygen consumption would be an absolute necessity to define the aerobic energy turnover during performance tests to exhaustion. For claims regarding cognitive function or mental energy, the appropriate mood questionnaires and cognitive performance tests are essential. For a comprehensive discussion of methods to assess mental energy, see Lieberman.[26] In addition, the measurement of blood antioxidants, reactive oxygen species, and nitric oxide levels would be valuable to help define the role of the saponins and tanins that are contained within the guaraná and yerba maté extracts. Finally, it is essential that studies be conducted and their results interpreted in an unbiased manner that ensures they are scientifically valid and can be replicated by other laboratories. Replication across laboratories is essential to ensure findings are accurate and reliable.

CONCLUSION

It is hoped that this review will provide stimulus for research that evaluates the claims made by the manufacturers of EDs and their critics. At this time, there is little, if any, solid evidence to support an increase in either physical or mental "energy" due to consumption of these drinks, except for the increases attributable to the caffeine in these products.

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