No Bull: Science, Manufacture, and Marketing of Red Bull and Other Energy Drinks

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(Photo by Yohan Moon)

The increasing prevalence of energy drinks over the past decade is a phenomenon that cannot simply be dismissed as a passing obsession. What began with the advent of Red Bull in 1984 has evolved into a colossus of different brands claiming anything from sharpened mental acuity to enhanced athletic performance. Austrian-born Red Bull founder and CEO Dietrich Mateschitz relies on the younger generation for his sales base, exploiting the teenage drive for risk-taking and adventure using dramatic product names, draconian logos, and sponsorship of extreme sporting events [1]. Predictably, a multitude of competitors have followed suit, introducing similar concoctions with dicey names such as Cocaine, Dare Devil, Pimp Juice, Venom, and Monster. However, none of the claims of enhanced performance have been qualified by the U.S. Food and Drug Administration, thereby conjuring substantial criticism from the media and a variety of third-party organizations [2]. Yet at this point in time, neither advocate nor critic speaks with certainty.

All things considered, the chronicles of Red Bull are more of tenacious entrepreneurship than of science. However, the rationale behind its chemical formula reveals the potentially medicinal properties of its components. While overseas as a traveling toothpaste salesman, Mateschitz discovered the revitalizing effect of a syrupy tonic sold at local pharmacies in Thailand. The mixture, composed of only water, sugar, caffeine, taurine, and the carbohydrate glucuronolactone, soon became a mainstay remedy for his chronic jet-lag. After reading a financial article listing the top ten taxpayers in Japan, he was surprised to learn that a certain Mr. Taisho, who manufactured a similar restorative beverage, was listed among the other entrepreneurs. The ingredients were explicitly listed on the can itself, and neither trademark nor patent existed to protect its formula; hence, Red Bull was born [3].

Careful observation of any university library will reveal the undeniable popularity of iPods and Red Bulls – the arsenal for the true titan of academic endeavor confronting a full night of intellectual tribulation. Nevertheless, some conjecture whether Red Bull's buzz serves only to distract the active mind in the same way that prolonged auditory stimulation seems to. The most immediate answer is given on the container itself, which specifically claims to improve performance in times of elevated stress or strain, increase endurance, increase reaction speed, and stimulate metabolism [4]. Surprisingly, the only active ingredients aside from water, sugar, and caffeine, are the amino acid taurine and the carbohydrate glucuronolactone [3]. A series of past Japanese studies on taurine had suggested cardiovascular benefits, further convincing Mateschitz of its revitalizing properties. However, taurine is not an entirely unfamiliar biochemical intermediate as some people might imagine. From a human physiological standpoint, taurine (2-aminoethanesulphonic acid, [NH2-CH2-CH2-SO4]) is a major constituent of bile found in the lower intestine [5]. Produced in the liver and brain, taurine plays an important role in the regulation of osmolarity, muscle contraction, and neuroprotection [6]. While technically not considered an amino acid (it conspicuously lacks a carboxyl group), taurine is a derivative of the sulfhydryl amino acid cysteine, and it constitutes the only naturally-occurring sulfonic acid [7]. Human taurine synthesis occurs in the liver, although it is also naturally produced in the testicles of numerous mammals, and urban legends suggest

that the commercial sources of taurine are derived from bull urine and semen. Although taurine is found in both of these sources, the pharmaceutical industry actually obtains taurine from isethionic acid, which in turn, is obtained from the reaction of ethylene oxide with aqueous sodium bisulfate. In 1993 alone, approximately 5,000-6,000 tons of taurine were produced [8].

However, it must be noted that taurine is not the only active ingredient among the host of energy drinks on the market today. Generally, a given energy drink will include an amalgamation of caffeine, B-vitamins, and herbal extract. Other common ingredients include guarana, ginseng, L-carnitine, glucuronolactone, and ginko biloba. Many contain high levels of sugar, but many brands also offer artificially-sweetened "low-carb" versions. Nevertheless, the primary ingredient in nearly all energy drinks is caffeine, of which the average 16-fluid ounce serving contains 150 mg [2]. Little is known about the health effects of taurine and glucuronolactone, other than the fact that the given quantities in stimulant drinks are several times higher than that of a normal diet [9].

Nevertheless, taurine plays a major regulatory role within the human body. Found in high concentrations in skeletal muscles, it functions in regulating myofibril contraction. It increases force generation by enhancing the accumulation and release of calcium ions within the sarcoplasmic reticulum. Increasing intracellular taurine levels also augments the mean rate of increase in the force response. It has been suggested that the balance of endogenous myofibril taurine concentrations is critical for maintaining the appropriate force output during muscle contraction. Muscle fibers possibly modulate their contractility by increasing the taurine levels in response to neuronal inputs. Considering taurine's role in muscle contraction, it may appear that increasing blood taurine concentration through dietary intake could enhance contractile force. However, considering that intracellular taurine concentration is tightly regulated [10], it remains unknown whether an increase in taurine plasma levels following consumption would have any noteworthy effect.

Since taurine exerts neuroprotective activity against excitotoxicity and oxidative stress, it is no surprise that massive amounts are released in the event of an ischemic episode. An in vivo analysis indicated that during ischemia, a seventeen-fold increase in taurine levels is typically observed in the brain. However, one must realize that there are two sources of taurine in the brain; direct synthesis from neurons and transport across the Blood-Brain Barrier (BBB). The Blood-Brain Barrier constitutes the membrane surrounding blood vessels leading to the brain, which regulates the exchange of molecules. The BBB is highly permeable to non-polar compounds but less permeable to polar ones. This regulation prevents harmful substances from entering the brain and only permits the passage of substances necessary for normal brain function. While caffeine can readily diffuse across the BBB, the entry of taurine seems to be regulated more rigidly [11].

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Taurine is present in high concentrations throughout the brain, and it has been hypothesized that ingesting taurine in conjunction with caffeine improves concentration and reaction speed while also enhancing emotional status. Seidl et al. performed a double-blinded, placebo-controlled study in which the experimental group ingested a capsule containing caffeine, taurine, and glucuronolactone whereas the control group received a placebo capsule. The authors reported that members of the experimental group had shorter motor reaction times and better overall psychological well-being when evaluated. Hence, they concluded that taurine in conjunction with caffeine and glucuronolactone had positive effects on cerebral function. They also conjectured that taurine might interact with GABAergic, glycinergic, cholinergic, and adrenergic neurotransmitter systems. Nevertheless, they also agreed upon the possibility that such findings on cognitive performance may have been attributable solely to caffeine [12]. Unfortunately, none of the above experiments examined the possibility that caffeine alone could have produced such results. It is widely known that caffeine competitively inhibits adenosine receptors and thereby increases cAMP concentration [13]. This blockade can free cholinergic neurons from inhibitory control, leading to pervasive excitatory responses and the suppression of fatigue. These properties of caffeine alone may explain the favorable cognitive and emotive influences as demonstrated by the experiments [14].

Further refutation of the study by Seidl et al. stems from the fact that sodium and chloride dependent taurine transporters exist in the BBB. The activity of these transporters is closely regulated by transcription of the genes encoding them [16]. Such transcription seems to be dependent on the degree of cell damage, osmolality, and level of taurine in the brain, thereby suggesting that active expression of this gene serves as an acute response to neuronal perturbance or crisis. Hence, it is intuitive that under normal non-ischemic conditions, taurine levels within the brain are maintained at a stable level [15]. Therefore, an increase in the taurine plasma level resulting from dietary supplementation is not likely to cause a sudden influx of taurine into the brain. Furthermore, considering the substantial amount of endogenous taurine already present in the brain, it is questionable whether any entry would make a significant difference to the overall concentration [16].

Taurine itself is naturally present in a variety of meat, seafood, and milk [17]. However, taurine from the consumption of energy drinks is several times higher than that from the intake of a normal diet [5]. Under normal physiological circumstances, taurine is highly-conserved in the adult human body and present in relatively large quantities [9]. It has been estimated that a 70 kg (155 lb.) human is likely to contain 70 g of taurine, and the mean daily intake has been estimated to be somewhere between 40 and 400 mg [5]. In contrast, many energy drinks may contain up

to 4,000 mg of taurine. Nevertheless, there is almost no data to suggest that consumption of taurine alone poses any substantial risk to human health. However, Simon, Michele, and Mosher's study examined the growing trend of mixing energy drinks with alcohol. It was determined that blending energy drinks with alcohol greatly increased the number of energy drinks consumed per session, particularly in males aged 19-24 years. In addition, the data suggests that taurine may somewhat ameliorate the unfavorable effects of alcohol consumption [18]. Conversely, alcohol is known to exercise an inhibitory effect on taurine homeostasis in humans. The implication is that the massive influx of taurine from energy drinks encourages binge drinking. The advent of the Jägerbomb aptly reflects the social understanding of the antagonistic effects of both compounds. To this effect, drinkers attest to more reckless behavior and to a greater overall capacity for consumption. A study conducted in early 2006 concluded that combining energy drinks with alcohol predisposes drinkers to alcohol abuse since the depressant effects of the alcohol are somewhat mitigated by the stimulant effects of the energy drink [19]. Additional concern exists for the havoc that the depressant-stimulant combination wreaks on the heart. Alcohol alone, if abused, has been shown to reduce brain activity, impair cardiac function, and potentially lead to myocardial infarction [20]. In combination with an energy drink, effects on the consumer may include shortness of breath and an irregular heartbeat. Moreover, the body's defenses are weakened by the dehydration from alcohol and caffeine, both of which are diuretics [21].

Caffeine Content in Popular Energy Drinks

Energy Drink	*Serving Size*	*Caffeine (mg)*
Spike Shooter	8.4 oz.	300
Cocaine	8.4 oz.	280
Monster Energy	16 oz.	160
Full Throttle	16 oz.	144
Rip It, all varieties	8 oz.	100
Enviga	12 oz.	100
Tab Energy	10.5 oz.	95
SoBe No Fear	8 oz.	83
Red Bull	8.3 oz.	80
Red Bull Sugarfree	8.3 oz.	80
Rockstar Energy Drink	8 oz.	80
SoBe Adrenaline Rush	8.3 oz.	79
Amp	8.4 oz.	74
Glaceau Vitamin Water	20 oz.	50
SoBe Essential Energy	8 oz.	48
Coffee, generic brewed	***8 oz.***	***133***
Starbucks Coffee (Grande)	***16 oz.***	***320***
Coca-Cola	***12 oz.***	***35***

(Table by Nicky Mehtani; information courtesy of www.energyfiend.com)

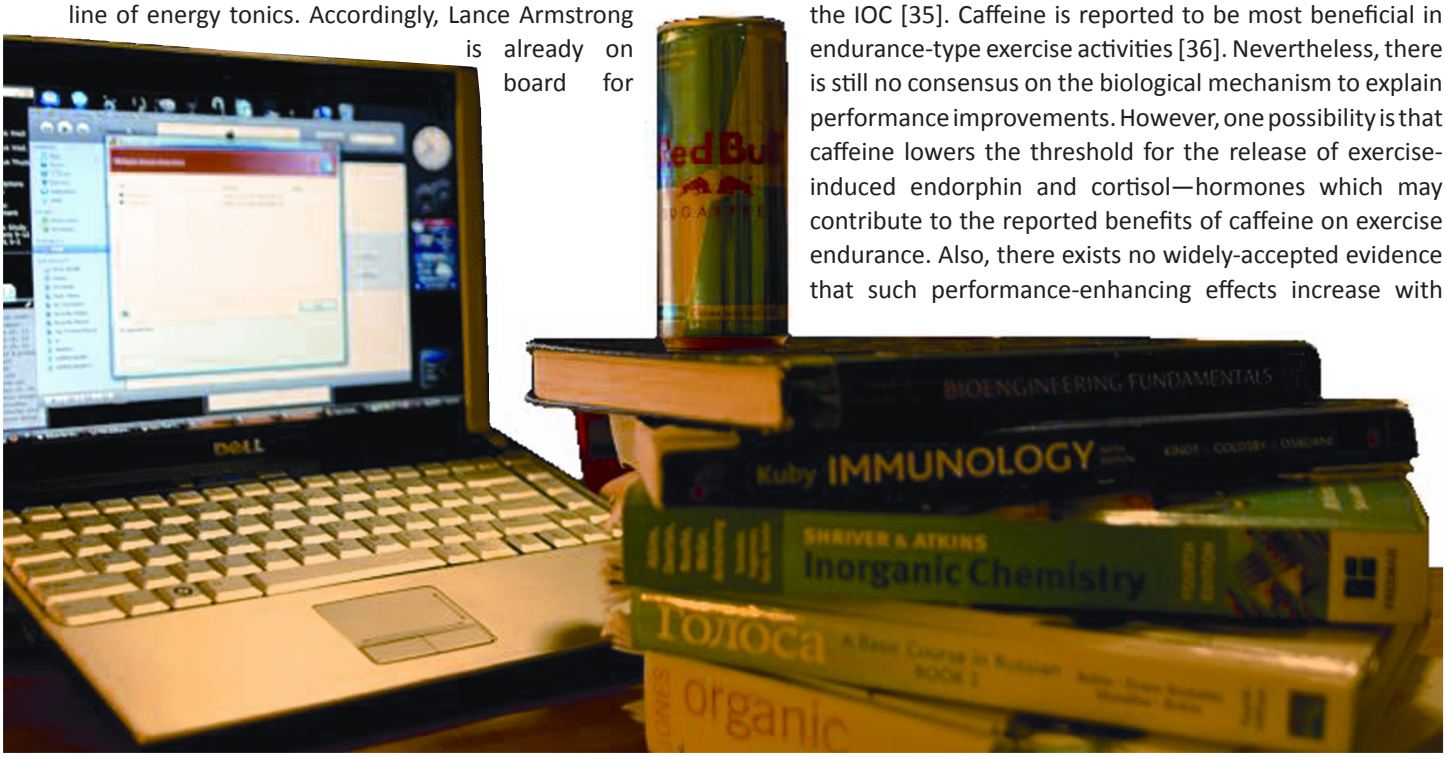
Yet despite the injurious social trends that have become associated with energy drinks, many studies have demonstrated the applicative efficacy of the products in their pure form. With regards to the psychological effects of Red Bull Energy Drink, two studies reported significant improvements in cognitive performance in addition to increased mental alertness [22]. Moreover, consumption of energy drinks may induce a mild to moderate euphoria primarily caused by the stimulant properties of caffeine and ginseng [16]. The restorative properties were attributed to a combination of caffeine and sugar in energy drinks, though a concerted effect between glucose and caffeine has also been suggested. Concerning generalized physiological effects, the consumption of Red Bull alone was shown to promote endurance during repeated cycling tests in young healthy adults [23].

The short term physiological effects of energy drinks were most thoroughly examined by Alford, Cox, and Wescott in a series of three studies conducted on a small population of students from the University of Bristol in England. The studies investigated psychomotor performance (reaction time, concentration, and memory), subjective alertness, and physical endurance. When compared with control drinks, containing neither taurine, caffeine, nor glucoronolactone, Red Bull significantly improved aerobic endurance in addition to anaerobic performance in stationary cycling tests. Significant improvements in mental performance were also noted, especially with respect to choice reaction time, concentration, and memory. These consistent improvements in both mental and physical performance were interpreted as reflecting the combined effects of the active ingredients [22]. The same study was conducted based on the fact that Red Bull contains several active components (taurine, glucuronolactone, caffeine, and several B-vitamins), which render a multiplicity of effects on human metabolism. Perhaps more fundamentally, Red Bull also contains glucose, which is metabolized to release energy during both aerobic and anaerobic metabolism and may improve cognitive performance [14].The fact that Red Bull is also endowed with a host of B-group vitamins must not be overlooked however. It is widely known that vitamin B-12 (cyanocobalamin) plays a critical role in human brain function and is intimately associated with energy production [24]. Nevertheless, the most important conclusion drawn from this study is that the anti-hypertensive actions of taurine may oppose increases in blood pressure from caffeine, reflecting that the ingredients act in concert and not independently to achieve the observed effects [14]. Although most improvements in mental acuity are attributed to the caffeine content, it should be noted that energy drinks contain several other biologically-active ingredients that possibly contribute to this effect [15].

Perhaps surprisingly, the biological effects and health consequences of caffeine, despite extensive research, remain the subject of ongoing debate. In the UK, the mean daily caffeine intake from tea, coffee, and carbonated beverages is estimated to be 278 mg/day for a typical 70 kg male [25]. In addition to coffee, tea, and carbonated beverages such as soft drinks, caffeine is present in many medications, headache treatments, and diet pills. In fact, caffeine is an active ingredient in more than 70% of the soft drinks consumed in the United States [12]. However, one must assess not only the quantity ingested but also the rate at which it is metabolized. All of the caffeine contained in a cup of coffee (115-175 mg) is cleared from the stomach within forty-five minutes of ingestion [26]. The caffeine is then absorbed from the small intestine, but does not accumulate in the body as it is rapidly metabolized by the liver, with a half-life of 4 hours for a normal adult [27]. Increased half-life values can be found in women using oral contraceptives (5-10 hrs) and in pregnant women (9-11 hrs) [28]. One review of caffeine dependence studies shows a wide variety of withdrawal symptoms including headache, irritability, drowsiness, mental confusion, insomnia, tremors, nausea, anxiety, restlessness, and increased blood pressure [29]. It is interesting to note that the symptoms of caffeine withdrawal also occur in the case of excess consumption [30]. On the other hand, lower doses of caffeine (20-200 mg per day) have been associated with positive effects on mood, such as perceived feelings of increased energy, imagination, efficiency, self-confidence, alertness, motivation, and concentration. While caffeine is reported to reduce reaction time during simple tasks, the effect is thought to be from enhancing coordination rather than from accelerating mental activity [16].

In contrast to the more detrimental pursuits practiced by consumers, the newest line of energy drinks is marketed with a health component, suggesting benefit to individuals partaking in athletic pursuits. The progeny of this innovation is Free Radical Scavenger Energy (a.k.a. FRS Energy), which constitutes the newest line of energy tonics. Accordingly, Lance Armstrong is already on board for endorsements. The legendary cyclist makes the supportive claim: "With all I have going on, I need a source of sustained energy. FRS fits in line with me wanting to be ninety, wanting to keep running marathons, riding my bike, being fit, and having fun." Apparently, the marketing angle on energy drinks has progressed from late-night fix to sheer invincibility. The basic premise of FRS energy is that it simultaneously fights fatigue and cancer. FRS differs from its competitors in that it is endowed with a different central component known as quercetin, which plays a dual role in the human body both as a stimulant and as a flavonoid [31]. Flavonoids are typically secondary plant metabolites known to sequester numerous mutagens and carcinogens [32]. But FRS also claims that this plant derivative also combats fatigue by inhibiting the enzyme Catechol-O-methyltransferase (COMT), which is responsible for the degradation of catecholamine neurotransmitters including dopamine, epinephrine, and norepinephrine. These neurotransmitters are largely responsible for the "fight or flight" response generated in times of duress [33]. Contrary to other energy drinks, FRS claims not to have the commonly associated withdrawal and crash effects [32]. This claim is based on the fact that quercetin has a physiological half-life of 16 hours, as compared to the 4-hour half-life of caffeine, thereby extending its window of physiological effects on the body. Quercetin also helps to fight cellular damage and fatigue caused by the oxidants that accumulate from daily activity, exercise, and stress [34].

The mass-manufacture of quercetin might present a temporary loophole in high-powered athletic drug screening. Currently, caffeine use in Olympic sports is a contentious issue, and the International Olympic Committee (IOC) considers a urinary concentration of caffeine of 12 mg/L to be a positive drug test. This is due to the fact that caffeine has been shown to have performance-enhancing effects at concentrations that would result in a urinary excretion below 12 mg/L as set by the IOC [35]. Caffeine is reported to be most beneficial in endurance-type exercise activities [36]. Nevertheless, there is still no consensus on the biological mechanism to explain performance improvements. However, one possibility is that caffeine lowers the threshold for the release of exercise-induced endorphin and cortisol—hormones which may contribute to the reported benefits of caffeine on exercise endurance. Also, there exists no widely-accepted evidence that such performance-enhancing effects increase with



(Graphic by Nicky Mehtani and Yohan Moon)

additional caffeine doses [26]. On the contrary, the dehydration effects of caffeine and the absorption inhibition effects of glucose pose a serious threat to an athlete training in warm weather conditions [14].

It seems as if the principle concerns regarding energy drinks stem from one of the two associated risks of ingesting something with a high caffeine content. One is the possibility of caffeine overdose that can result in tremors, seizures, or even death [37]. The LD50 for caffeine depends on body mass, but ranges from 13-19 g as the mean lethal dose for a 70 kg (155 lb) male, which equates to approximately 80 cups of coffee [38]. Many deaths have been linked to the excessive caffeine content in energy drinks, which is a consequence of the misleading display of nutrition facts on the container. Manufacturers often limit the serving size to half or even a third of the bottle and do not factor in the hidden caffeine content of the herbal additives such as guarana. Such commercial subterfuge allows for rapid ingestion of large quantities of caffeine under the assumption that you are consuming nothing more than the equivalent of two cups of coffee [21]. The second associated risk is that of dehydration, which also results from excessive caffeine intake [39]. Claims that energy drinks enhance athletic performance have led to consumption both before and after athletic activity. Coupling fluid loss from exercise with the diuretic properties of caffeine facilitates accelerated dehydration rates [26]. Reflecting on the recent proliferation of the energy drinks industry, the Stimulant Drinks Committee of the British Nutrition Committee issued a series of recommendations for the consumer. Primarily, the committee advises discretion in the consumption of stimulant drinks with alcohol. Likewise, it deems energy drinks unsuitable for children under the age of sixteen, for pregnant women, or for individuals sensitive to caffeine. Finally, it recommends that stimulant drinks not be consumed as a thirst quencher in association with sports and exercise [36]. Even so, the true test of the efficacy and safety of energy drinks will only come from decades of widespread consumption by the general populace.

Nevertheless, one must consider the societal ramifications of widespread consumption. Assuming that energy drinks do confer some sort of competitive advantage, whether it be in the athletic or intellectual realm, what are the consequences? This same question was posed by David Eagleman, assistant professor of neurobiology and anatomy at Baylor College of Medicine, during the Rice Scientia lecture last fall. He stressed one factor that must be taken into consideration is the relatively high cost of energy drinks, as most products sell for about $3 a can. Eagleman also made the very apt remark that many gateways to economic success are based on standardized tests mandating a specified degree of mental capability [40]. He went on to insinuate that socio-economic disparities might be exacerbated when the affluent have unrestricted access to such mind-enhancing products. Competition for high-stakes testing such as the SAT is enormous and reports abound of identity fraud and violation of test protocols that are in place to ensure the standardized nature of these monolithic rites of passage into the professional world [41]. Operating under the assumption that energy drinks do confer some real performance advantage, one can only speculate on how the retail of such a competitive edge will influence existing class disparities. In the same light, any student has heard of someone taking self-prescribed Adderall to jack their focus for the next big exam. When school becomes a sport, what will be the next regulatory countermeasure, retinal scans and blood testing before the MCAT? Nevertheless, despite the debatable efficacy of existing energy drinks, their development marks the realization of a concept that will likely be pursued in the future. That is, the idea of biological performance enhancement not for sport, but for academia will be manufactured, marketed, and sold in a diversity of ways.

(Graphic by Rodrigo Flores)

In sum, what began with the introduction of Red Bull twenty-five years ago has proliferated into an assortment of products that demonstrate short-term physiological benefits. However, the effects of regular long-term consumption have yet to be determined. Although energy drinks have traditionally associated themselves with risk-taking and subversive behaviors, the consolidation of various stimulant and focus-enhancing substances into one beverage represents an effort to maximize productivity. Not surprisingly, new product lines supported by world-class athletes claiming added health benefits constitute the newest progression for the energy drink enterprise. Finally, one must question the socio-economic ramifications of widespread use of legalized performance enhancers. Nevertheless, for now at least, the buying and selling of human energy remains caveat emptor, though there is no better remedy for the infamous all-nighter.

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