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The Potential Negative Effects of Energy Drinks

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Abstract:

Background: Energy drinks are non-alcoholic beverages formulated to enhance alertness, physical performance, and mental focus. They typically contain caffeine, sugar, amino acids (like taurine), vitamins (such as B-complex), and herbal extracts (like guarana or ginseng). Since their introduction in the 1980s and 1990s, energy drinks have gained popularity worldwide, especially among adolescents, young adults, athletes, and professionals seeking improved performance and reduced fatigue. The consumption of energy drinks, however, has been a subject of concern due to potential health risks such as cardiovascular effects, sleep disturbances, anxiety, and metabolic issues when consumed excessively. Their market continues to expand globally, driven by lifestyle demands, sports culture, and aggressive marketing strategies.

Keywords: Energy drinks, Caffeine, Physical performance, Mental focus, Health risks, Adolescents and young adults, Cardiovascular effects.

Introduction:

Energy drink is a product invaded the markets as well as the minds of the young generation. It resembled a new form of addiction and is believed to have a mystic influence on the performance of these people. It comes in various forms and tastes **(1)**.

The first energy drink appeared in the United States of America (U.S.A.) in 1949 and was marketed as "Dr. Enuf. In Europe, they were launched for the first time in 1987; then the market expanded throughout the world, becoming very popular after the launch of Red Bull in 1997 **(2)**. Manufacturers recently have shifted their consumer focus from athletes to young people. Energy drinks are aggressively marketed in places popular with teens and young adults. Red Bull, Monster, NOS, Rockstar, Lucozade, Eastroc Super Drink, Bang Energy, and 5 Hour Energy are Prominent examples of energy drinks **(3).**

The explosive increase in the consumption of EDs over the past years has led the scientific community to investigate the influence of such products on human health and to identify the reasons for their consumption. EDs sometimes referred to as"stimulant drinks" and are being marketed as enhancers of energy, concentration, and physical and cognitive performance. Also, being a good source of vitamin B increases health benefits of EDs **(4, 5).**

Because of the benefits of EDs mentioned before, many aspects in the society are encouraged to use EDs, of example, people engaged in various exercise regimes or in situations causing tiredness, fatigue are drived towards the consumption of energy drinks **(6).**

Whenever parents feel their children are getting week and incapable of performing well, especially during exams time, they immediately rush to the nearest supermarket and buy a pack of EDs for their children hoping it will affect their energy immediately and help them perform better **(7).**

Also, many players enter the functional energy drink space in the market because of seeking for rich sources of immunity-boosting foods and beverages that contain vitamins, minerals, and other essential ingredients that boost immunity (**8).**

Energy drinks mainly differ from other soft drinks regarding their high-level caffeine and taurine content. They belong to a class of products, non-alcoholic beverages in liquid form **(9).** They come in different types; energy shots, fruit-based, non-fruit-based, sugar-free, and plant-based. There are two kinds of energy drink products. One is sold in containers similar in size to those of ordinary soft drinks, such as a (473 ml) Bottle. The other kind, called "energy shots," is sold in small containers holding (60 ml) of concentrated liquid **(10)**.

Many of the EDs contain different ingredients such as caffeine, guarana, ginseng, yerba mate, acai berry, ginkgo biloba, methylxanthines, sugar, glucuronolactone, taurine, maltodextrin, B vitamins: B2 (riboflavin), B3 (niacin), B6 (pyridoxine, pyridoxal, and pyridoxamine), Inositol B8 and B12, vitamin C, vitamin D, calcium, iron, chromium, zinc, manganese, molybdenum, artificial sweeteners, aspartame, and sucralose **(4)**.

Red Bull is a type of energy drinks. Its components are carbonated water, sucrose, glucose, citric acid, taurine, sodium bicarbonate, magnesium carbonate, caffeine, niacinamide (vitamin B3), calcium pantothenate (vitamin B5), Pyridoxine HCI, vitamin B12, natural and artificial flavours. One 250-ml can of Red Bull Energy Drink contains 80 mg of caffeine **(11)**. Some energy drinks are labeled as "nutritional supplements," so they may present much more caffeine than similar products commonly regulated as beverages. Moreover, **Erdmann et al. (12)** stated that knowledge of potential interaction between caffeine and taurine and subsequent studies of ED ingredients would make side effects more predictable in case of inordinate usage**.**

The action and the mechanism of action of Red Bull ingredients:-

The mechanism of action of Red Bull depends on the mechanism of action of the ingredients present in this drink; cafiene and taurine. Caffeine is a methylxanthine which presents naturally in leaves and seeds of many plants. It is produced artificially and is present in major constitute of beverages like coffee and tea. EDs are used due to their CNS stimulating effect stemming from caffeine **(13).**

Caffeine also can easily cross the blood-brain barrier and produces a central nervous system stimulantion through preventing the inhibitory role of adenosine over the release of dopamine and other neurotransmitters like acetylecholine (Ach) and norepinephrine (NE) **(14)**. This occur because caffeine non-selectively and partially antagonizes adenosine-binding adenosine A1 receptors (A1Rs) and A2Rs **(15).**

Other biological effects of caffeine, as showen in figure (1), include intracellular calcium accumulation and phosphodiesterase inhibition. The latter two effects are unlikely to mediate the cognitive effects of caffeine, however, because the required doses are in the toxic range (≥ 400 mg) **(14)**.

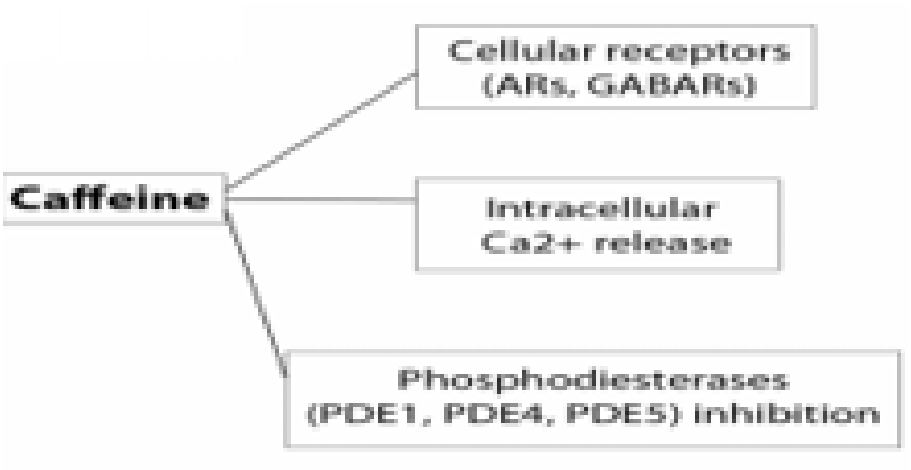

Figure (1): Mechanism of action of caffeine **(16)**

Regarding the second main ingredient in RB, taurine, it is an organic molecule named for the Latin taurus, which means ox or bull because it was originally extracted from bull semen and ox bile. Taurine enters the intracellular environment and exerts cytoprotective effects by scavenging reactive oxygen species, stabilizing mitochondrial membranes, and maintaining ion homeostasis **(17).**

Ramírez-Guerrero et al. (18) stated that taurine plays an important role in osmolarity regulation, and neuroprotection, maintaining glutathione stores and upregulation of anti-oxidant responses**.** It also aids athletic performance and endurance through helping muscle function and aids blood sugar regulation and cardiac health **(19)**.

Glucuronolactone is a potent detoxification compound naturally found in almost all connective tissues of the human body. It is produced from the breakdown of glucose in the liver and may be found in the natural food and drinks such as red wine. The quantities of glucuronolactone obtained from the natural sources are relatively low compared to that taken from synthetically form like EDs and dietary supplements **(20).**

Vitamin B complex, which includes vitamins such as B1 (thiamine), B2 (riboflavin), B3 (niacin), B6 (pyridoxine), B9 (folate), and B12 (cobalamin), plays a crucial role in energy metabolism. These vitamins are essential for converting carbohydrates, fats, and proteins into usable energy in the body **(21).** They also support enzymatic reactions that drive metabolic pathways, particularly in the production of adenosine triphosphate (ATP), the primary energy carrier in cells. Deficiency in these vitamins can lead to fatigue, weakness, and poor cognitive function **(22).**

Vitamins B3, B6, and B12 are added to enhance mental performance and support the metabolic processes involved in energy production. While moderate consumption may offer temporary benefits, excessive intake can lead to potential side effects such as nerve damage (with high doses of B6) or liver stress (with excessive niacin) **(23).**

The potential negative effects of caffeine and energy drinks:

The combination of these stimulants, like caffeine and sugar, with high doses of B vitamins may create a false sense of increased energy. Additionally, long-term overconsumption of fortified energy drinks can increase the risk of adverse health effects, particularly in individuals with underlying health conditions or those sensitive to caffeine and vitamin overload **(24).**

Considering the doses stated on the labels, no energy drink exceeded the safe upper limit of caffeine consumption for healthy adults (400 mg). However, energy drink users tend to consume these products in multiple serving doses per day, and they usually consume them in addition to, rather than replacing caffeine from other sources, so consuming these energy drinks can produce adverse effects if warn wasnot taken **(25).**

Regarding caffiene use, there are circumstances that must be taken in attention. Poor caffeine metabolizers, people who suffer from medical conditions (e.g., cardiac or liver conditions), children and adolescents (who are not habitual caffeine users) are more vulnerable to caffeine related disorders even after the consumption of ordinary levels of caffeine **(26).**

Also, long-term or over-consumption of caffeine can lead to caffeine physical dependence that potentiates the reinforcing effects of caffeine to avoid withdrawal symptoms. That effect was reported by **Bodur et al. (27)** who reported that chronic caffeine-containing beverage users had showed clinical evidence of caffeine-induced stress, tolerance on continued use, and withdrawal anxiety. Insomnia, migraine, and other side effects can occur with regular caffiene use **(28)**.

Multiple molecular effects of caffeine suggest that it may promote bone loss and becomming a risk factor for osteoporosis **(29)**. Caffeine intake can also cause electrolyte imbalance such as hypokalemia and hypophosphatemia **(30).**

As caffiene has controversal effects that were presented in different studies, so RB may also give bad effects insteed of the desired benefits. **Low et al. (31)** identified caffeine as one of 22 metabolites predictive of cognitive decline in population over a 13-year period, despite using caffeine to increase cognitive level. **Gloyer et al. (32)** also reported that excessive caffeine consumption could contribute to T-cell activation and inflammation in rheumatoid arthritis, despite the known anti-inflammatory action of caffiene reported by **Asoudeh et al. (33)**.

Although caffeine is the main active component, other ingredients, especially taurine, are present at high concentrations in energy drinks. The actual effects of the combination of these substances are not fully understood, so this combination may pose a substantial risk to users. The adverse effects of energy drink can be related to either the toxicity of ingredients or specific situations in which energy drinks are used such as ingestion in combination with alcohol (**34).**

Several studies reported many side effects of EDs of which; increasing the incidence of epileptic seizures, brain haemorrhage, acute kidney failure, rhabdomyolysis and metabolic acidosis **(35)**. Sugar added EDs cause hyperglycemia, hyperlipidemia and hyperinsulinemia leading to insulin resistance and predisposing to metabolic syndrome **(36).**

Energy drinks were also reported to cause disturbance in hemodynamics causing hypertension, all kinds of arrhythmias, heart failure and heart attacks. They have a detrimental effect on platelet and endothelial functions with resultant hypercoagulable state and consequently increased risk of thrombosis **(37).**

Other studies declared that Frequent energy-drink consumption is associated with allergy development including asthma, allergic rhinitis, and atopic dermatitis, in Korean adolescents. Also, RB could be considered as an aggravating factor for acute aortic dissection **(38)**.

Damaging effects of energy drinks on histology and ultrastructure of several organs were reported such as the cardiac muscle, gonads and liver **(39),** Glands like submandibular salivary gland, Thyroid gland and CNS organs like cerebellum and cerebral cortex **(40).** Also, **White et al. (41)** reported that energy drinks produce neurodegenerative changes in the hippocampus.

Energy drinks and cellular oxidative stress:

Oxidative stress refers to an imbalance between the production of reactive oxygen species (ROS) and the antioxidant defense mechanisms within the body. Under normal physiological conditions, a balance exists between oxidants and antioxidants, which is essential for maintaining cellular homeostasis. This equilibrium ensures that ROS participate in various signaling pathways without causing structural damage to biomolecules (**42)**.

When ROS levels exceed the capacity of antioxidant defenses, oxidative stress occurs, leading to damage of cellular components such as lipids, proteins, and nucleic acids. This oxidative damage has been implicated in the pathogenesis of numerous diseases, including cardiovascular disorders, neurodegenerative diseases, diabetes, and cancer. Persistent oxidative stress can also accelerate aging and impair tissue function **(43).**

Markers of oxidative stress can be assessed in both biological fluids and tissues. In tissues, common indicators include lipid peroxidation products such as malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE), which reflect oxidative damage to membrane lipids. Protein oxidation can be detected through protein carbonyl content, while nucleic acid oxidation is often measured by 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels (**44)**.

Antioxidant status within tissues can be evaluated by determining the glutathione ratio (GSH/GSSG) and the activity of key enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) (**45)**. Additionally, the expression of inducible nitric oxide synthase (iNOS) is considered an indirect marker of oxidative stress, as increased iNOS activity leads to higher nitric oxide production and subsequent formation of peroxynitrite, a potent oxidizing agent contributing to cellular damage **(46).**

The high caffeine content in energy drinks stimulates the central nervous system. This will increase metabolic activity, which can elevate the production of reactive oxygen species (ROS) **(45).** Additionally, the large amount of sugar promotes rapid glucose metabolism, further contributing to oxidative stress and energy imbalance **(47).**

Gaballa et al. (48) reported that oxidative stress was as a significant pathogenic mechanism underlying the organ damage due to long term energy drink consumption in a rat model. **El-Helbawy (49)** reported that EDs increased ROS production and tissue inflammation in the cerebral cortex. Also, **Valle et al. (50)** reported that energy drink consumption caused imbalance in the antioxidant defence system in the prefrontal cortex and in

the hippocampus. **Hanna et al. (51)** reported that the consumption of energy drinks led to a statistically significant rise in MDA levels in kidney and disrupted antioxidant activity of glutathione reductase (GSH) and superoxide dismutase,. Also, iNOS immuno expression , as an indirect marker for oxidative stress , was reported elevated in the endothelium of blood vessels due to energy drink consumption **(52).**

Energy drinks and cellular appoptosis:

Apoptosis, or programmed cell death, is a tightly regulated process essential for maintaining tissue homeostasis and eliminating damaged or unwanted cells. It involves intrinsic (mitochondrial) and extrinsic (death receptor) pathways **(53)**. The detection of apoptosis in tissues relies on specific molecular and biochemical markers that indicate the activation of apoptotic pathways. These markers can be classified based on their role in different stages of the apoptotic cascade, including initiation, execution, and DNA fragmentation **(54)**.

One of the key regulatory systems of apoptosis involves the Bcl-2 family proteins, which control mitochondrial membrane permeability. Pro-apoptotic proteins such as Bax and Bak promote mitochondrial outer membrane permeabilization and the release of cytochrome c, while anti-apoptotic proteins such as Bcl-2 and Bcl-xL inhibit this process. The Bax/Bcl-2 ratio is widely used as an indicator of apoptotic susceptibility in tissue samples **(55).**

Caspases are central mediators of apoptosis, and their activation is a hallmark of the process. Caspase-9 is associated with the intrinsic pathway, while caspase-8 is involved in the extrinsic pathway. The activation of caspase-3, an executioner caspase, represents the final step leading to the cleavage of cellular proteins and DNA fragmentation. Detection of cleaved caspase-3 by immunohistochemistry or Western blotting is commonly used to confirm apoptosis in tissue studies **(53).**

DNA fragmentation is a characteristic feature of late-stage apoptosis. The TUNEL assay (Terminal deoxynucleotidyl transferase dUTP nick end labeling) is one of the most widely applied methods to detect DNA strand breaks in tissue sections. Additionally, the presence of DNA laddering patterns upon electrophoresis further supports apoptotic cell death. These nuclear changes distinguish apoptosis from necrosis, where DNA degradation occurs in a more random pattern **(56).**

Other important markers include cytochrome c release from mitochondria, which signifies mitochondrial pathway activation, and Annexin V binding, which detects the externalization of phosphatidylserine on the cell membrane during early apoptosis. Furthermore, p53 activation and PARP cleavage (a caspase-3 substrate) are frequently analyzed to confirm apoptotic signaling in tissue studies. Together, these markers provide a comprehensive picture of apoptotic progression within tissues (**57).**

Gaballa et al. (48) reported that ED long term consumption for 12 weeks increased cellular appoptosis in renal tissue through induction of oxidative stress environment which was reported by **Surrallés and Doppler (58)** to impaire DNA repair. **Lu et al. (59)** previously stated that caffeine-induced apoptosis in osteoblasts via a mitochondria-dependent pathway. These conditions impair mitochondrial function, the primary source of cellular energy, creating a pro-apoptotic environment that favors cell death.

Kutia et al. (60) reported that excessive ED consumption caused mitochondrial dysfunction which could trigger the release of cytochrome c leading to cell death. Chronic exposure may also lead to autophagy dysregulation.

Conclusion:

Moderation is key when consuming energy drinks as avoiding excessive caffeine intake can reduce the risk of oxidative stress. Further studies are recommended to compare the effects of acute versus chronic exposure and to investigate dose-dependent responses.

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