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Review Article. The Impact of Caffeine and Energy Drinks on Health, Especially In High-Performance Athletes

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Abstract

According to Resolution 4150 of 2009 of the Ministry of Social Protection, an energy drink (stimulant) is a non-alcoholic beverage, generally carbonated, basically composed of caffeine, carbohydrates and various sugars of different absorption speed, plus other ingredients such as amino acids, vitamins, minerals and vegetable extracts, accompanied by acidulate additives, preservatives, flavorings and colorings.

These have been shown to generate detrimental effects on health after consumption, due to their components.

Side effects have been reported at the neurological and cardiovascular levels, in addition to being associated with withdrawal symptoms, such as headache, irritability, drowsiness, and alterations in mental state, insomnia, tremor, nausea, restlessness, palpitations, anxiety, gastrointestinal disorders and increased blood pressure. Other studies have shown possible clastogenic and cytotoxic effects of energy drinks.

Among the effects evidenced in multiple studies, an increase over the basal level of systolic blood pressure between 9-10 mmHg and diastolic of 3 mmHg has been observed after the consumption of Red Bull, likewise, an increase in heart rate of approximately 5 to 7 beats / min, an increase in cardiac output, respiratory rate, an increase in vascular resistance at brain level, a decrease in blood flow velocity of the brain, among others, has been evidenced. As time went by, this became more noticeable in the marking, and an increase in both systolic and diastolic blood pressure was observed after the consumption of energy drinks, as well as an increase in heart rate, serum noradrenaline values by 75%, and an increase in the QT interval by 5%. In one study, it was also evidenced that, after the consumption of large amounts, there was a prolongation of the QTc interval of up to 20 ms, which is significant when correlated with the risk of arrhythmias; it is important to consider that an increase of more than 10 ms is considered worrisome.

The use of caffeine at mild to moderate doses in order to generate a short-term ergogenic effect is safe and effective. It is important to take into consideration prior to supplementation the form of presentation, concentration, interactions, time of administration among other things to maximize the benefit and avoid adverse effects of these beverages.

Keywords: Energizers and cardiovascular effect; Cardiac condition due to energizers; energizers; Heart disease; Energizers in athletes; Energizers in high-performance athletes; Taurine; Caffeine

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Introduction

According to Resolution 4150 of 2009 of the Ministry of Social Protection, an energy drink is an an alcoholic beverage, generally carbonated, basically composed of caffeine, carbohydrates and various sugars of different absorption speed, plus other ingredients such as amino acids, vitamins, minerals and vegetable extracts, accompanied by acidulant additives, preservatives, flavorings and colorings [1].

Energy drinks, introduced in the market in the 1960s approximately [2]. They are mostly high in sugar and stimulants such as caffeine, taurine and, to a lesser extent, compounds such as L-carnitine, guarana, ginseng, B vitamins, among others. These beverages have gained importance in recent years, especially in young adults (between 18 and 35 years old), due to the belief that they improve performance by increasing energy, concentration, avoiding fatigue, among other effects, to perform better in the academic, work or sports environment, given the high competitiveness involved in these areas since some time ago; or at the same time, it is also used indiscriminately for recreational purposes to improve the taste and ingestion of larger quantities of alcoholic beverages, with the intention of diminishing the depressant effects and even maximizing the excitatory effects, in spite of the contradictory evidence that exists up to now, as described in a study carried out by Ballistreri et al [3].

Caffeine is believed to improve exercise capacity during prolonged submaximal exercise (> 90 minutes), sustained high intensity training (20 to 60 minutes) and even short duration, high intensity exercise (one to five minutes).

A single dose of 1 to 6 mg/kg (average 3mg/kg) of body weight one hour before exercise is believed to generate a significant ergogenic effect. Approximately 99% of caffeine is absorbed within 45 minutes after ingestion and peak concentrations are observed after 1 hour, maintaining plasma levels for up to 4 hours. It has been evidenced that the most rapid absorption occurs when chewing gum or using caffeine preparations that can be absorbed directly through the mucosa.

Among the effects generated, a greater stimulation of adrenaline, increase of cardiac in otropism, increase of skeletal muscle contractibility, decrease of perceived effort and fatigue, saving of glycogen and mobilization of fat are reported.

Methodology

The research was of bibliographic review type, of articles of scientific character, the method used was the Analytical one since by means of this method the information and knowledge will be dismembered from global concepts, in order to analyse this topic, by means of the search, choice, analysis and comparison of information, obtained from validated scientific articles, in the period of time from 2010 to 2020.

Inclusion and exclusion criteria

Inclusion criteria

- Scientific articles corresponding to bibliographic reviews, systematic reviews, retrospective reviews, meta-analysis, field research.
- Research conducted in Spanish or English, from 2010 onwards, free of charge or requested by the author, from scientific platforms.
- Articles with relevant information about didactic strategies for the impact of energy drinks on the cardiovascular system.
- Articles developed according to ACC (Average Count Citation) and SJR (Scimago Journal Raking) standards.

Exclusion criteria

- Articles not within the time period from 2010 to 2022.
- Articles without scientific basis
- Articles without focus to the stated objectives.

Search strategy

By means of the analysis and observation technique, the information required for the research was obtained, which was organized systematically in the present study.

The research was developed based on a bibliographic review of pages such as: Scopus, Scielo, EBSCO HOST, Dialnet, Redalyc, Elsevier, PubMed, among others, using articles published between 2010 - 2022. The articles were selected according to the inclusion and exclusion criteria, which have high reference quality and impact, in order to carry out a relevant research and meet the stated objectives, likewise the MeSH terms energizers and cardiovascular effect, cardiac condition due to energizers, energizers, cardiopathy, energizers in athletes, energizers in high-performance athletes, taurine, caffeine, caffeine and nervous system were used. We also used the bilean operators and or to obtain a result of more than 100 records, thus using 53 articles for this document.

Energy Drinks

The use of energizers before, during or after sports activity is probably not indicated. They contain not only caffeine, but multiple compounds that can interact with each other and even with medications consumed by the person who ingests them. On the other hand, they contain a high carbohydrate content that results in a slower absorption in the stomach and can cause nausea, bloating, cramps, diarrhoea or vomiting, which could eventually generate inconveniences during competitions.

The consumption of energy drinks, alone and in combination with alcohol or other drugs, is associated with an increase in emergency department visits.

The U.S. Food and Drug Administration (FDA) cite cases of acute myocardial infarction, seizures, cardiac arrest, anaphylaxis, miscarriage, arrhythmias, renal and hepatic failure, and psychiatric disorders associated with excessive consumption of energy drinks.

This, in a way, corroborates with the description by Higgins, who specifies it as an "awakened toxic drunk" who, despite being affected by alcohol, is connected thanks to the energy drink, which generates a feeling of confidence in his abilities and can lead him to take risks or potentially dangerous attitudes [4].

According to Higgins, risky behaviours that could be adopted are, for example, risky sexual activities, depression, aggressive behaviours, increased interactions and addictions both with cigarettes and alcohol, marijuana or other substances. And not only that, it is believed that the interaction with alcohol can generate greater dehydration and even greater arrhythmogenic effect, especially in people with underlying heart disease. It is

worth mentioning that, according to Higgins, energy drinks have caffeine concentrations that exceed the limits imposed by the FDA (between 71-316 mg of caffeine per 8 oz per serving). This is not the case with sodas (71 mg of caffeine per 12 or of liquid) [4, 5].

It is because of this, because of the amount of advertising campaigns, because of the impact on the economy that it generates as stated by Allied Market Research, referring that the global energy drinks market was valued at approximately $ 53.01 billion dollars in 2018 and estimating an increase of up to $ 86 billion by 2026 [6]. Because of their increasing association with adverse effects at the level of both the cardiovascular system (> 50% of reported cases correspond to this group according to a systemic review) and the nervous system, and finally because of the growing evidence of the synergy between caffeine, sugar, and taurine that has taken great interest from the scientific community [2, 3].

It is important to emphasize that an increase in complications, even fatal, has been observed associated with its consumption, especially when it is associated with alcoholic beverages, as well as in those persons who suffer from underlying cardiac pathologies. However, to date, the evidence remains contradictory and therefore controversial on the impact on health. This is probably due to the methodology of the studies carried out, the dose of each compound, the variability of the formulations, the frequency of consumption, as well as the age and comorbidities of the people participating in the studies, among others. It should be noted that in many countries these beverages have been banned. However, due to the scarce evidence in many of them, these bans have been revoked.

On the other hand, (Manrique, et al., 2018) have demonstrated detrimental effects on health before the consumption of energy drinks, given by the main components of these same. Side effects have been reported at the neurological and cardiovascular level, in addition to being associated with withdrawal symptoms, such as headache, irritability, drowsiness, mental state alterations, insomnia, tremor, nausea, restlessness, palpitations, anxiety, gastrointestinal disorders and increased blood pressure. Other studies have shown possible clastogenic and cytogenotoxic effects of energy drinks [4].

The Most Important Compounds in Energy Drink

Caffeine

The first study on the impact of caffeine on sports performance was conducted in 1907. However, despite this, the evidence has been contradictory or inconclusive in part due to small sample size studies. In order to counteract the methodological problems, we are currently looking for ways to perform meta-analyses with the aim of clarifying the panorama on the effect of caffeine.

A review by Grgic et al. of 21 meta-analyses on the impact of caffeine on sports performance from 2004 to 2019, which was published in the British Journal of Sports Medicine. It included 11 reviews of 21 meta-analyses, rated as moderate and high quality. These meta-analyses compared the effects of caffeine with a control group, mostly young men, taking into account various parameters such as aerobic endurance, muscular strength, muscular endurance, anaerobic power, jumping performance such as exercise speed. On analysis, a favourable ergogenic effect with moderate quality of evidence was evident in muscular endurance, muscular strength, anaerobic power and anaerobic endurance. The moderate and high quality meta-analyses provide moderate quality evidence on the ergogenic effect of caffeine on muscular endurance, muscular strength, anaerobic power and aerobic endurance.

For the moderate quality meta-analyses they provide low or very low quality evidence on jumping performance and exercise speed.

It should be noted that in most studies the use of anhydrous caffeine (concentrated powder) was evidenced, however, coffee was also used, also evidencing an ergogenic effect. It could be said that for a 70 kg person two cups of coffee can fulfil this objective or at a dose of 3mg/kg of weight.

In conclusion, the use of caffeine at light to moderate doses for the purpose of generating a short-term ergogenic effect is safe and effective. It is important to take into consideration prior to supplementation the form of presentation, concentration, interactions, time of administration among other things to maximize the benefit and avoid adverse effects [5].

It is known of its physiology that it is absorbed mainly at gastrointestinal level, generating maximum levels in blood 60 minutes after ingestion, with a half-life of 3 to 7 hours and with a bioavailability of 100%, elimination is mainly renal.

It is metabolized in the liver by the activity of cytochrome P450 enzymes, especially by cytochrome P4501A2 (CYP1A2), the main isoenzyme responsible for demethylating caffeine and its metabolites to give rise to monomethyl xanthines, a substrate of xanthine oxidase. The variability of CYP1A2 activity largely determines how caffeine will act in the body, as well as the response of the individual.

The CYP1A2 isoenzyme collaborates in the metabolism of several drugs, such as, for example, verapamil, diltiazem, theophylline, ciprofloxacin, fluoxetine, etc. This could eventually generate interactions with these drugs and thus increase the risk of adverse effects, counteract the activity of some of them and even, without generating a significant clinical impact, generate caffeine concentrations in urine higher than the limit established by the sports authorities (12mg/l) [6].

Caffeine is the most potent methyl xanthine and is present in many energy drinks. As it is both water and fat soluble [7], it crosses cell membranes, the blood-brain barrier and the placenta without difficulty, and is thus widely distributed throughout the organism [31].

It acts by competitively inhibiting adenosine receptors (mainly A1 and A2A) which increases the release of agonist agents of dopaminergic receptors, thus increasing the release of dopamine and its stimulant effect. This inhibition prevents the negative inotropic and vasodilator effect of adenosine, and also favors

platelet aggregation, an elevation of catecholamine, renin and fatty acids. On the other hand, the positive inotropic effect is potentiated thanks to the inhibition of phosphodiesterase and through the stimulation of calcium channels sensitive to ryanodine [19].

According to R Somers et al, studies suggest that caffeine "delays exercise fatigue at 80%-85% of VO2 max, increases endurance and performance in aerobic exercise sets lasting 30 minutes to an hour, and significantly increases athletic performance in 2,000 m rowing and 1,500 m swimming time trials. The cognitive performance enhancement of caffeine in states of low arousal and sleep deprivation is well documented" quoted verbatim from their article [7].

Something worth mentioning is that there is evidence suggesting that caffeine supplements can increase diuresis and contribute to dehydration, which would limit their use in athletes. The FDA recommends that athletes who consume caffeine should drink more fluids to avoid dehydration, especially when performing physical activity in places where temperatures are high. It is probable that caffeine has a diuretic effect by inhibiting phosphodiesterase in the renal proximal tubule, in addition to antagonizing adenosine receptors, which could contribute to the diuretic and natriuretic effect in people. In a meta-analysis that sought to demonstrate the impact of caffeine on diuresis during rest and exercise, especially at high temperatures, due to its possible repercussions on health and performance, it was found in 16 studies that caffeine has a positive effect on diuresis during exercise, especially at high temperatures. It was evidenced in 16 studies that provided about 28 investigations for the meta-analysis, where most studies had used 300mg of caffeine in various forms, showed a slight influence of caffeine on diuresis in an acute period. As the hours passed, this effect progressively diminished. In addition, it was shown that the impact of caffeine on diuresis is greater in women than in men (6 times greater), this may be largely due to a slower metabolism of caffeine probably due to a lower activity of CYP1A2 due to genetic, environmental and lifestyle factors. In addition, it was shown that the diuretic effect did not occur during exercise as other studies claim, probably due to an increase in serum catecholamine that would act at the level of the renal arterioles decreasing glomerular filtration. This suggests that the increase in serum catecholamine associated with exercise, especially at high temperatures, has an inversely proportional relationship with the diuresis generated by caffeine. On the other hand It was demonstrated that both the dose and the frequency of consumption did not have a significant impact on diuresis. Therefore, according to this meta-analysis, the consumption of caffeine in its various forms by healthy people who exercise did not generate a significant increase in diuresis, even demonstrating the opposite effect. It also highlights the ergogenic benefit generated by sports supplements at the recommended doses [32].

In another study conducted by Coso, 20,686 urine samples were taken for doping control between 2004 and 2008. 67.3% had a caffeine concentration of 5 µg. It was found that 3 out of 4 elite athletes consumed caffeine before and during sports competition. Endurance sports showed the highest urinary caffeine concentrations [33].

According to Rosen bloom, the concentration of caffeine that produces an ergogenic effect is 2 to 3 mg/kg body weight; figures between 5 to 9 mg/kg can increase epinephrine concentrations by 50% to 100%, which could increase heart rate. In the same study, it was mentioned that an American soccer player was dizzy and lightheaded during training, when he was evaluated they noticed that he had a decreased heart rate, for which reason they recommended hydration thinking that this was the cause of his problem, however, when he was referred to the dietician, he mentioned that the player used a "pre-training intensifier" evidencing an intake of approximately 10mg/kg of caffeine per day.

Caffeine has been widely used to generate an ergogenic effect. It is clear that, by antagonizing adenosine receptors, it generates a decrease in sleep and fatigue, this being one of the main mechanisms to generate this effect. It is known that adenosine and its analogues can generate an opposite effect. It is estimated that a caffeine dose of 2 to 3 mg/kg body weight is an effective dose to meet the objective. Regarding energy drinks, most studies mention that the main component that generates the ergogenic effect and side effects is given by caffeine and that there is not enough evidence to support a greater effect given by its other compounds. They emphasize the difficulties to have solid evidence given the methodological differences. The Academy of Nutrition and Dietetics suggests a moderate consumption of caffeine by athletes, this is defined as 200 to 300mg per day of caffeine. At these concentrations it is safe for athletes. Caffeine concentrations of 15 mg/ml or more in urine could generate a positive doping test. In general terms, it is suggested to avoid energy drinks in athletes [34].

It is important to point out that those who use this compound the most are athletes who compete in aerobic endurance events. Approximately since 1907, the possible ergogenic benefit it generates from the point of view of improving muscular work has been described, such an impact has generated that in the 70s and 80s in the Olympic Games, athletes were sanctioned when the presence of high concentrations in urine was confirmed. In 2004, the World Anti-Doping Agency (WADA) considered caffeine as a doping substance if it exceeded 12g/ml in urine (equivalent to the intake of 9mg/kg of caffeine) [31].

Now, based on some studies, we can say that the consumption of light to moderate doses of caffeine (4 to 6 mg/kg of caffeine) could be beneficial in high performance athletes, both for short and long duration activities, but not so in people who perform sporadically, in light intensity or who are not trained. The ergogenic benefit has been evidenced probably due to the increase of plasma catecholamine's, evidencing an increase in lipid metabolism with the consequent saving of glycogen, increase of fat oxidation at muscular level, increase of endorphin concentrations in blood which probably generates an analgesic effect increasing pain tolerance and reducing fatigue, increase of isometric strength of skeletal muscles, an increase of power during the Wingate test, increase of work production, improvement of performance, etc. It is worth mentioning that in other studies it has been evidenced that this positive ergogenic effect was achieved with the consumption of caffeine capsules, but not in other presentations such as coffee, decaffeinated coffee,

etc. This is probably because there are other compounds (e.g. chlorogenic acid - adenosine antagonist) in coffee that interfere with the action of caffeine. It is suggested not to exceed 9 mg due to an increased risk of toxicity and due to the nullification of ergogenic effects by an overstimulation of the CNS [31].

According to the Food and Drug Administration (FDA), in general terms, 400 mg of caffeine per day (4-5 cups of coffee) is safe for the body in healthy people. However, it suggests that the susceptibility of the organism to caffeine will depend not only on its concentration, but also on various factors such as the individual's metabolism. This is why there are people especially susceptible to its effects in which it is recommended to limit its consumption to the tolerated dose. In the same consumer update, they mention that the American Academy of Pediatrics recommends restricting its use in children and adolescents [35].

Another study suggests that caffeine supplementation in endurance exercise may have an impact on performance not only by an increase in maximal strength, muscular endurance, but also, suggests that it may be given by a reduction in perceived exertion rating. Furthermore, it suggests that the intake of 3 to 9mg /kg of caffeine 60 minutes before physical activity is safe as a supplement to generate an ergogenic effect. The evidence suggests that so far this action is only available in the form of capsules or powder, but not as energy drinks since there are not many studies that support it and there are several compounds in these that could interact with it and increase the risk of adverse effects [36].

Energy drinks have an average of 70 to 200 mg of caffeine per 16 or serving [37]. For reference, according to a note written in Medical News Today, an 8 of cup of decaffeinated coffee has approximately 2 mg, an 8 oz cup of filtered coffee contains 95 mg of caffeine, an 8 on cup of instant coffee has 62 mg of caffeine, a 1 oz dose of espresso generally contains 63 mg of caffeine and a 12 of cup of cold brewed coffee contains between 153 and 238 mg of caffeine [38].

According to R Somers, an energy drink can contain up to 32 fluid of, which would correspond to 6 doses of 1oz of espresso (400mg of caffeine) [8].

It is worth mentioning, as suggested by James, that 14% of deaths from coronary heart disease and 20% from stroke could be attributed to variations in blood pressure (systolic by 4mmHG and diastolic by 2mmHg) caused by caffeine consumption in the diet [9].

In addition, the FDA mentions that a rapid consumption of 1200 mg of caffeine could even generate convulsions [35].

It is worth mentioning that the wide contradictory evidence may be largely due to the fact that many studies have not taken into account some aspects that make caffeine metabolism very variable from person to person. Thus, they have not considered the history of habitual caffeine consumption, tolerance, polymorphisms associated with cytochrome P450 1 A 2, age, sex, the presence of comorbidities, as well as the presence of harmful habits and the use of drugs that may interact with it. In any case, so far it is known that moderate coffee consumption is safe and even beneficial for the body, with evidence of a lower risk of cardiovascular and all-cause death in regular consumers [19].

Taurine

Taurine is a derivative of the amino acid cysteine that is widely distributed in the cardiac and skeletal musculature. This is another important component that has been studied in recent years. Some studies suggest that it can generate multiple beneficial effects for the organism and that the harmful effects are generally reduced. Taurine intervenes in multiple processes such as improving the lipid profile, improving LDL uptake by the liver, decreasing the effect of angiotension 2, improving the kallikrein-kinin system and increasing vasodilation, among others. Several studies have shown that taurine is likely to improve physical performance by increasing blood flow at the muscular level due to the vasodilatation generated, and it is also suggested that taurine may attenuate many of the effects generated by caffeine [10].

In a randomized, double-blind, placebo-controlled trial conducted by Sun Q et al. in prehypertensive individuals, a mean reduction in systolic blood pressure (7.2 mmHg) and a reduction in diastolic blood pressure (4.7 mmHg) were evidenced with only a taurine dose of 1.6 g per day for 12 weeks. In addition, a reduction in systolic (3.8 mmHg) and diastolic (3.5 mmHg) blood pressure was evidenced on an ambulatory basis [11].

Caffeine and Taurine

It is known, that both caffeine and taurine generate both beneficial and detrimental health effects.

It is important to point out that cardiac inotropic activity was evidenced in an in vitro study carried out by R, Chaban et al. where 92 samples of cardiac muscle were extracted from the right atrium of 45 patients, which were treated with caffeine, taurine or with the association of both. The results of the study showed a significant increase in isometric contractile force for the use of caffeine alone or in combination with taurine (118 ± 03% and 124 ± 4% with a p value <0.01 for both), in contrast to that observed in the group of samples treated with taurine alone. In relation to the duration of contraction, a minimal but significant reduction in contraction was evident for the samples treated with caffeine alone or in combination with taurine (95 ± 1.6% and 92 ± 1.4% with a p value <0.01 for both), which was also not observed in the appendages treated with taurine alone [12].

This is important since it reinforces previous studies of the effect of caffeine and taurine alone or in combination on cardiac inotropism despite the limitations of the study. These samples were from elderly patients with cardiac disorders that required surgical intervention. In any case, it is worth clarifying that this study excluded patients with diseases that severely affect cardiac contraction, and also used appendages that showed adequate contraction in vivo and excluded samples that showed inadequate behavior during the control period [13].

In any case, there are several studies that suggest that taurine could generate adverse effects generally associated with caffeine, this is in contrast to what we have mentioned, since one of them suggests that the combination with caffeine can

abruptly raise blood pressure and, in addition, the consumption of taurine alone or in combination with caffeine has been seen to generate an increase in systolic volume. It is probable that the effects on the decrease in blood pressure are basically due to the consumption of taurine alone and in a chronic manner. For it would not be associated with higher doses than those available in energizers as mentioned in other studies, since they mostly contain 2 g on average. In summary, we could say that changes at the hemodynamic level have been evidenced with both compounds, but that the main impacts on it could be given either by caffeine alone, or associated with taurine at doses similar to those found in most energy drinks [14].

Caffeine has been reported to generate multiple benefits, among which we have an improvement of blood flow, increases energy utilization, improves mood, alertness, improves pain tolerance, improves sports performance. It has also been reported that taurine improves endurance performance and decreases the accumulation of lactic acid after exercise. According to Olatona et al, doses of 300 to 400 mg each day are safe for most individuals. It is believed that gradual consumption generates fewer adverse effects because very high concentrations in blood are not reached suddenly. Consumption of high amounts of caffeine before or during exercise increases the risk of developing myocardial ischemia.

Since many energy drinks are not classified as dietary supplements, they are not adequately regulated and are sold without major restrictions, which generates great concern.

A descriptive cross-sectional cohort study by Olatona et al. assessed the consumption of energy drinks among soccer players in Lagos, Nigeria. A random sample of 350 soccer players aged 21-30 years belonging to clubs in Laos was taken. It was observed that 76.3% of the players were consumers of energy drinks. Seventy-two percent of them drank at least two cans per week, 37% had mixed it with alcohol. Approximately 42% did so for leisure, 25.5% to increase energy and 25% consumed these drinks to improve sports performance.

It is estimated that moderate consumption, two 250ml cans (about 200mg of caffeine in total) are safe, and even have a Neuroprotective effect, generate a beneficial effect on mental illnesses, decreases depression. Mild to moderate consumption improves exercise endurance, cognition, reaction time and mood. Consumption at high doses of 600mg every day or more for 6 to 15 days can generate anxiety, headache, fatigue, and tremor. At these or even higher doses can generate intoxication, which generates insomnia, tremors, tachycardia, palpitations, stomach upset. If the dose exceeds 10g, cerebral edema, hypokalaemia, arrhythmias, alteration of consciousness, stroke, convulsions and even death may occur. Taurine interacts with caffeine and alcohol increasing the risk of renal failure.

It is believed that the interaction of alcohol with caffeine can generate, among other things, not only the sensation of a decrease in the effect of alcoholic beverages, but also increases the risk of consumption and addiction to other substances, increases the risk of risky behaviours, increases the probability of suffering hepatic and renal failure, psychotic conditions, convulsions, respiratory and cardiac disorders, and even death.

This study corroborates that there is little or no diuretic effect during exercise after consumption of energizers [42].

Sugars

Sugars contained in energy drinks could have an effect on heart rate, cardiac output and ventilator rate and even a vasodilator effect by themselves due to the thermo genic effect of the calories. According to a randomized crossover study by Conrad Grasser et al, the impact of fructose (60 - 30g), glucose (60g) or sucrose (60g) combined with 500ml of water on the cardiovascular system was demonstrated. They showed an increase in heart rate 60 minutes after ingestion, a reduction in peripheral resistance and an increase in cardiac output mediated by sucrose and glucose, in contrast to fructose which had the opposite effect on vascular resistance [43].

Caffeine and sugar

Caffeine and sugar, Interestingly, the research conducted by Conrad Grasser et al, where the differences in the impact of caffeine and sugar at concentrations similar to that of the Red Bull energy drink, on the hemodynamic of people, is evidenced. It became clear that a comparable concentration of caffeine exerts the same effect on blood pressure as the energy drink sweetened with sugar, but the difference lies basically in the pathways that are affected to generate this change. That is, the impact of caffeine alone was greater at the vascular level, while that of the energy drink with sugar was greater in the myocardium. It is worth mentioning that to date there are discrepancies such as those evidenced in the study by Konrad Grasser et al, with that of Rush et al, which demonstrated that the combined use did not show statistical significance compared to the consumption of caffeine or sugar individually [15]. However, one of the limitations to be emphasized in Rush's study was probably the time at which the heart rate was measured, since it was taken 30 minutes after consumption, and as seen in most of the studies previously described, the impact seems to be significant after 60 minutes. Nevertheless, this suggests the need for further studies to better understand the synergy of caffeine and sugar on cardiovascular adverse effects [16].

In a study by Coso et al, the aim was to evaluate the effect of energy drinks on performance and urinary caffeine concentration in soccer players. After the consumption of the sugar-free energy drink (630 ml approximately), with an approximate composition of 3mg/kg, the muscular power generated during the jump test, the average jump height, the average running speed during the speed test, a greater distance reached at a higher speed during a simulated soccer match and an increase in the number of sprints during the entire match were significantly increased, which would generate a certain advantage in official matches. The concentration of caffeine after exercise was higher than that compared to placebo. It should be noted that a dose of 1mg/kg of weight is insufficient to generate an ergogenic effect.

Interestingly, even sugar-free energy drinks appear to exert a significant ergogenic effect. In any case, both carbohydrate intake and the association of sugar compounds seem to interact

with caffeine to increase not only its absorption, but also by enhancing its effect during physical activity [17].

In a previous randomized double-blind study conducted by R Somers et al, they compared the Rockstar energy drink against placebo to demonstrate the impact on the cardiovascular system of this drink; both contained the same amount of sugar. The placebo group showed an increase in plasma glucose (50mg/dl), systolic blood pressure (3 mmHg), heart rate (7 beats/min) and plasma norepinephrine (30%). This suggests that the sugary drink alone can generate an important stimulus on the sympathetic nervous system. Guarana, specifically its seeds contain methylxanthines (caffeine, theophylline and the bromine), which could increase energy and decrease appetite [18].

This, associated with the caffeine in energy drinks, could increase the risk of adverse effects. However, more studies are needed to clarify the role it plays in the complications associated with these drinks.

Other compounds such as B vitamins (vitamin B complex), L-carnitine, ginseng and glucuronolactone have not been extensively studied. Their safety for the cardiovascular system is unknown and their effects on performance are uncertain. This is why, to date, their use or disuse cannot be recommended. In addition, it is likely that energy drinks do not contain sufficient amounts of these compounds, which is why it is believed that they do not play a significant role in the body.

Taking into account the above, we could say that the effect of caffeine depends on multiple factors associated both to the concentration and to modifiable and non-modifiable risk factors of the consumer. Also as we have evidenced, caffeine by itself can generate adverse cardiovascular effects and the impact of the interaction between caffeine, taurine and sugar in these beverages cannot be underestimated, probably increasing the risk of adverse effects. It is likely that the rest of the compounds do not generate a significant impact, mainly because of the concentration of these compounds in energy drinks. In any case, further studies are required to corroborate what is suggested in this review. Finally, it is recommended to restrict the sale of energy drinks to minors, since this is an important stage for the development of the nervous and cardiovascular systems, as the effect on them at this stage is unknown, and also because of the impact not only on health, but also on the social and economic aspects [19].

Benefits and Risks of the Consumption of Caffeinated Beverages

Approximately 90% of the world's adults consume caffeine every day. The average caffeine consumption in U.S. adults is two cups per day (280mg of caffeine per day). Response to it is thought to depend on genetics, age, gender, interactions with medications and other substances, as well as frequency and concentration of consumption. The safe dose for adults is generally believed to be around 400mg and in children and adolescents 2.5mg/kg per day.

Those who consume more than 4 cups of coffee per day are considered high consumers. It has been seen that coffee consumption is higher in men than in women, in smokers than in non-smokers, higher in Caucasians than in Afro-descendants, higher probability of consuming caffeine in healthy people than in unhealthy people, coffee is preferred to tea in Europe, Australia, America in comparison with the rest of the world.

There are drugs that may eventually interact with caffeine, especially acebrophylline, doxofylline and stiripendol. In case of consuming them, it is indispensable to suspend the consumption of caffeine. Other known but weak interactions are with linezolid, ciprofloxacin, lithium, atomoxetine, among others. Coffee can decrease the absorption of alendronate and iron.

Within the beneficial effects in general terms we can highlight

1. **Cognitive**: neuropsychiatric: Caffeine affects cognition and mood both acutely and chronically. In rested people it improves reaction time and vigilance. In people deprived of sleep it collaborates with learning, decision making and performance in activities such as operation of vehicles and machinery, among other things. Regular consumers obtain better results in cognitive performance tests, reaction time and visuospatial reasoning.

2. **Alertness:** Caffeine improves alertness, mental energy, and concentration, especially when individuals are fatigued. It is believed that caffeine mitigates the effects caused by sleep deprivation. It causes an improvement in the formation of concepts, reasoning, memory, orientation, attention and perception, especially in people who work shifts or have jet lag.

3. **Headache:** It is believed that it can alleviate or trigger headache. It has been evidenced that its association with paracetamol or ibuprofen maximizes the analgesic capacity especially when used for migraine attacks. In any case, the habitual consumption of caffeine can trigger chronic migraines, or headache due to a rebound effect in people who are not used to its consumption. The most common symptom of caffeine withdrawal is headache.

4. **Parkinson's disease**: A decrease in the risk of developing this disease has been observed in men who consume caffeine, but not in women who use hormone replacement therapy in postmenopausal women, in whom an increased risk of developing Parkinson's disease has even been observed.

5. **Alzheimer's disease:** The evidence is scarce for the moment, however, a slight protective effect of caffeine for the development of this disorder is suggested.

6. **Psychiatric:** Caffeine intake is associated with a wide variety of symptoms and psychiatric disorders, but so far the evidence is contradictory. Caffeine intake can generate some symptoms, such as insomnia, irritability, nervousness, nervousness, panic attacks, anxiety, among other symptoms, and it is believed that those who suffer from pre-existing anxiety disorder are especially susceptible. It is even known that it could decrease the risk of depressive episodes.

7. **Cardiovascular:** In mild to moderate doses it decreases the risk of myocardial infarction. In high doses it could be arrhythmogenic and could trigger coronary events especially in susceptible individuals.

8. **Endocrine:** It is associated with a decreased risk of developing diabetes either after caffeinated or decaffeinated coffee intake. It seems that there is an inversely proportional relationship between the development of diabetes and the dose of coffee consumed. A significant benefit has been evidenced in those who consume between 4 to 6 cups a day; however, at lower doses it is suggested that it can also generate a protective effect. The consumption of decaffeinated coffee seems to reduce the glycosylated hemoglobin (HbA1c). Insulin resistance: It is related to a lower insulin resistance and a better control of postprandial glycemia in patients with diabetes.

9. **Gastrointestinal:** A reduction of constipation has been evidenced after its consumption.

10. **Cirrhosis:** It seems to reduce the risk of developing cirrhosis and has even been associated with a lower rate of disease progression in those suffering from advanced stages of hepatitis C.

11. **Cancer:** So far the evidence is inconclusive. There seems to be no association between cancer and the consumption of coffee or other caffeinated beverages. It even seems to generate a reduction in the risk of developing some types of cancers such as prostate cancer. More evidence is needed, since in the cases that suggest that it increases the development of cancer in many of the studies, some variables such as concomitant cigarette consumption were not controlled.

12. **Musculoskeletal:** Osteoporosis: It is suggested that coffee consumption at high doses, especially in those who consume low amounts (less than 800mg/day), is associated with a reduction in bone density, especially in women of slim build. Gout: It has been seen that the consumption of both caffeinated and decaffeinated coffee was associated with lower levels of uric acid in the blood and hyperuricemia, in addition, a lower incidence in the development of gout was evidenced.

13. **Frequency and urinary incontinence:** Some studies suggest that caffeine intake may increase the frequency and volume of diuresis; however, so far the evidence is unclear. It also seems that it could increase the incidence of urgency incontinence, but not that caused by stress or mixed incontinence.

14. **Mortality:** Several studies suggest that coffee consumption may reduce all-cause mortality.

15. **Caffeine withdrawal:** Headache, tiredness, fatigue, decreased energy, decreased activity, decreased alertness, decreased attention, drowsiness, depressed mood, irritability, among others. Symptoms similar to a cold, nausea, myalgia and especially headache may also occur, the latter being one of the most frequent. The incidence and severity is dose-dependent and withdrawal syndrome can occur even with doses as low as 100mg/day. Symptoms generally occur after 12 to 24 hours of caffeine discontinuation. They peak in one or two days and may persist for up to nine days. The minimum duration of caffeine maintenance leading to withdrawal symptoms is three days. Re-administration of caffeine has been shown to rapidly reverse withdrawal symptoms within 30 to 60 minutes [46].

Negative Effects on the Cardiovascular System Generated By Caffeine Consumption

1. **Arrhythmias:** Generally up to 400 mg per day (5 cups of coffee) seems not to cause arrhythmias in most cases. It is suggested to avoid high doses of caffeine especially in people with cardiac diseases. Moderate doses seem safe even for people susceptible to develop arrhythmias.

It has been shown that moderate doses of caffeine do not produce arrhythmias, and it has even been suggested that it could be a protective factor for the development of arrhythmias.

Variability of the cardiac frequency: It is believed that 400mg of caffeine in healthy adults does not generate significant alteration of the same.

2. **Blood pressure:** It is believed that blood pressure can be acutely elevated up to 10mmHg in sporadic drinkers; however, this has not been evidenced with regular consumers. It is also believed that, in those patients who are rapid metabolizers of caffeine, they are more prone to elevate blood pressure after consumption. It is believed that the elevation of blood pressure after caffeine consumption in hypertensive patients may be considerably higher than in those who normally have an optimal blood pressure. It is worth mentioning that the effects of chronic caffeine consumption on blood pressure are not clear at this time.

3. **Diuretic effect:** In people who do not perform physical activity, and who are not habitual consumers of caffeine, it has been seen that after the consumption of approximately 300mg of coffee (2 to 3 cups of coffee) an increase in diuresis can be generated in those who have been deprived of caffeine for days or weeks.

4. **Aortic rigidity:** It is believed that, after the consumption of caffeine, at doses of 200mg (2 cups of coffee), and to a greater extent associated with cigarettes, an increase in the speed of the pulse wave is generated. It is believed that caffeine generates an acute increase in aortic stiffness. The latter is an important determinant of cardiovascular performance and cardiovascular risk prognosis.

5. **Lipids:** It seems that caffeine intake in the form of filtered coffee does not generate alterations in total cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL) unlike that observed with unfiltered coffee, which generates alterations in these parameters except HDL.

Evidence suggests that caffeine intake in mild to moderate amounts is not associated with worse outcomes of cardiovascular disease, stroke, need for coronary revascularization or sudden cardiac arrest.

It is even suggested to be associated with a lower incidence of ischemic and hemorrhagic stroke, independent of cardiovascular risk factors.

Mortality: Most evidence suggests that the more coffee consumption, the lower the cardiovascular and all-cause mortality, however, this is not entirely proven.

Sudden cardiac arrest: It has been shown that the consumption

of 10 cups of coffee per day was a risk factor for sudden cardiac arrest (46).

Caffeine and arrhythmias

There are several factors that can increase the risk of developing arrhythmias, within them obesity and alcohol are well identified.

Caffeine pharmacology: Caffeine increases the sinus rate by generating a sympathomimetic effect generated by the inhibition of phosphodiesterase and by an increase in intracellular calcium produced by a blockade of calcium reception by the sarcoplasmic reticulum. This increase could generate atrial arrhythmias by enhancing the automaticity of atrial pacemaker cells and after triggering activity induced by depolarization. It is believed that at doses of 15mg/kg per minute it is capable of generating sympathetic overactivation, sinus tachycardia and ventricular ectopy culminating in ventricular fibrillation in rats.

Antiarrhythmic effect: Probably generated by the non-selective inhibition of adenosine A1 and A2A receptors, which would generate an increase in atrial refractoriness and thus prevent the development of atrial fibrillation.

Antioxidant effect of coffee: Probably generated by polyphenols and caffeine itself. These, when interacting with reactive oxygen species, prevent atrial remodeling and atrial fibrillation.

Coffee and atrial arrhythmia: So far, most studies have failed to demonstrate a detrimental effect of caffeine on atrial and ventricular electrophysiological properties. An inversely proportional relationship between caffeine consumption and the development of atrial fibrillation has even been demonstrated in several meta-analyses. It is believed that the incidence is reduced by 6% for each increase of 300mg/day of caffeine. In any case, this depends on the previous state of health, tolerance and other factors. For 25% of patients in such studies suggest that coffee is a trigger. In cases in which it is not well tolerated, especially in those who are not accustomed to its consumption or in those who have associated the development of arrhythmias after its consumption, they should refrain from ingesting caffeinated products.

It is also probable that the different response after caffeine consumption is due to the differences between individuals in terms of susceptibility to the effects on the electrophysiological and autonomic factors that trigger arrhythmias.

Coffee and ventricular arrhythmias: Several studies including a meta-analysis found no association between caffeine consumption and the development of ventricular ectopy.

Energy drinks: In general, the caffeine content of these beverages is higher than that of coffee. This, together with the interaction of other compounds in energy drinks including sugar, could generate a significant proarrhythmic effect. It is worth mentioning that these effects could be increased even more when associated with other substances such as alcohol or illicit drugs. It has been observed that even in healthy individuals without underlying cardiac pathology, atrial fibrillation, sustained ventricular tachycardia, ventricular tachycardia and ventricular fibrillation have developed after the consumption of energy drinks. Especially after consumption of two or more energy drinks within 24 hours. An increase in the QTc interval and the unmasking of long QT and Brugada syndrome has been seen in some cases.

Interestingly, it has been revealed that the consumption of energy drinks could lead to a prothrombotic state in patients with structural heart disease or pre-existing AF [45].

In 2008, German, Hong Kong and Tawain authorities found small amounts of cocaine in the energy drink Red Bull Cola [46].

Cardiac arrest and sudden death

In 2006, the American College of Cardiology / American Heart Association / Heart Rhythm Society (ACC / AHA / HRS) defined sudden cardiac arrest and sudden death as follows:

Sudden cardiac arrest is the sudden cessation of cardiac activity leading to the victim becoming unresponsive, with no normal breathing and no signs of circulation. If corrective action is not taken promptly, this condition progresses to sudden death. The cardiac arrest to indicate an event as described above, which is reversed, usually by CPR and/or defibrillation or cardio version, or cardiac pacing. Sudden cardiac death should not be used to describe events that are not fatal.

The most common cause of sudden cardiac arrest is ventricular fibrillation in people with underlying structural heart disease. Most present with altered consciousness within seconds or minutes. However, it is worth clarifying that most of them do not present premonitory symptoms. If they do present symptoms, they usually occur between 1 hour and 4 weeks before the event. Among the symptoms that are usually evidenced are palpitations, weakness, and among the most common are dyspnea and chest pain. Dyspnea was more common in women than chest pain.

In general terms, 70% of sudden cardiac arrests occur in the course of coronary artery disease. It can be triggered either by an acute coronary syndrome or by chronic coronary disease.

It is worth mentioning that 50% of the people who suffer a sudden cardiac arrest are the first manifestation of an unknown cardiac alteration.

The remaining 10% of sudden cardiac arrests are caused by heart failure and cardiomyopathy, left ventricular hypertrophy, myocarditis, hypertrophic cardiomyopathy, arrhythmogenic cardiomyopathy of the right ventricle, congenital anomalies of the coronary artery and mitral valve prolapse.

Between 10 to 12% of people less than 45 years of age suffer sudden cardiac arrest without presenting structural cardiac pathology. The most common are Brugada syndrome, idiopathic ventricular fibrillation, congenital or acquired long QT syndrome, familial polymorphic ventricular tachycardia, Wolff-Parkinson-White syndrome, among others.

Among the triggers, to name a few, we have ischemia, electrolyte disorders, some medications, activation of the autonomic nervous system, psychosocial factors, etc. It can also be caused by direct trauma to the precordial region, which could trigger ventricular fibrillation and lead to sudden cardiac arrest.

Among the most common risk factors in the absence of previously recognized cardiac pathology are dyslipidaemia, hypertension, smoking, excessive alcohol consumption, physical inactivity, obesity, diabetes mellitus and family history of premature coronary heart disease or myocardial infarction.

For practical purposes, we will touch on two aspects

Exercise: There is a very low risk of sudden cardiac arrest after strenuous exercise. If it occurs, it usually happens within 30 minutes after exercise, especially in those who perform physical activity sporadically, in those who generally lead a sedentary life. This risk is outweighed by the decreased risk of sudden cardiac arrest at other times of life. At the moment it is not known whether strenuous or non-strenuous physical activity is more beneficial.

It is worth mentioning that athletes usually have a lower basal heart rate and greater variability, which reduces the risk of sudden death.

However, if there are unknown underlying cardiac pathologies and they are associated with strenuous exercise; the risk of suffering these complications is higher. The most common disorders are hypertrophic cardiomyopathy, anomalous coronary artery of incorrect sinus origin, myocarditis and arrhythmogenic right ventricular cardiomyopathy.

Caffeine: According to Podrid, caffeine has not been shown to increase the risk of sudden cardiac arrest (50).

Athletes: summary of the risk of sudden cardiac death and sports participation

Sudden death in athletes is a rare phenomenon, which can occur in young athletes and in many cases the origin is unknown. It is well known that it generally occurs in athletes who have an undiagnosed underlying cardiac pathology. Most of the causes of sudden cardiac arrest are malignant arrhythmias such as sustained ventricular tachycardia or ventricular fibrillation.

It is well known that in athletes with some underlying cardiac pathology such as hypertrophic cardiomyopathy or arrhythmogenic cardiomyopathy and who perform prolonged physical activity can generate structural changes at the cardiac level that favor the development of malignant arrhythmias. In addition, the physiological demands of these individuals can also trigger these types of arrhythmias especially in those with known structural disorders.

It is important to note that regardless of whether they are elite or recreational athletes, both can trigger sudden death in individuals who are especially susceptible due to underlying cardiac pathology, either of structural or arrhythmic characteristics and who are subjected to great exertion.

The incidence of sudden death in young athletes is 1 in 50,000 and 1 in 100,000 per year. Interestingly, the evidence shows a higher risk for men, especially those of African descent.

In young athletes, under 35 years of age, the presence of underlying structural heart disease has generally been evidenced. The most common of these are hypertrophic cardiomyopathy, anomalous origin of a coronary artery, arrhythmogenic right ventricular/left ventricular cardiomyopathy (ARVC), myocarditis and coronary atherosclerosis. In those older than 35 years, coronary artery disease is the predominant cause of sudden death during exercise.

It is worth mentioning that primary electrical disease is an important cause of sudden death in patients who do not have a structural disorder at the cardiac level. Among the hereditary arrhythmia syndromes that could trigger it are long QT syndrome, short QT syndrome, Brugada syndrome, catecholaminergic polymorphic ventricular tachycardia, and early repolarization syndrome.

In other conditions, in the same way, without presenting underlying structural pathology, arrhythmic events can be triggered by direct trauma or idiopathic phenomena such as commotio cordis, and the presence of structural abnormalities such as hypertrophic cardiomyopathy can also be evidenced.

Effects of Energy Drinks on the Body

Among the effects evidenced in multiple studies, an increase over the basal level of systolic blood pressure between 9-10 mmHg and diastolic of 3 mmHg has been observed after consumption of Red Bull (the main drink studied), similarly, an increase in heart rate by approximately 5 to 7 beats / min, an increase in cardiac output, respiratory rate, an increase in vascular resistance at the cerebral level, a decrease in blood flow velocity of the same, among others, was evidenced. This became notably more marked with the passage of time [19].

It is worth mentioning that the differences or discrepancies between most studies regarding the acute response after the consumption of energizers, especially in the cardiovascular system, are basically due to the presence of sugar, caffeine and taurine, as well as the concentration of these in each beverage. Other factors that have had an influence are the volume ingested, the frequency, the method used to measure blood pressure, such as continuous hemodynamic measurements beat by beat (the most precise method), sporadic measurements with an automatic sphygmomanometer, mercury or cuff, the position of the blood pressure measurement and the heart rate, among others [2].

In any case, it is clear in most studies that the values of mean arterial pressure and heart rate were significantly higher against placebo after the consumption of 1 can of 355ml of Red Bull or other energy drinks with a similar concentration of caffeine and sugar from 60 minutes after its consumption, reaching the highest values between 80 and 100 minutes. On the other hand, it has been shown that there is no significant impact on the endothelium of the microvasculature, which suggests that the elevations in blood pressure are probably not due to alterations at this level [20].

Interestingly, a double-blind study conducted by Ragsdale et al. in students at Winona State University demonstrated that blood pressure elevations were probably not due to alterations at this level [2]. In this study, by means of a cold pressor test,

the effect at neuronal level was demonstrated after consumption of the Red Bull drink, where an increase in pain tolerance was evidenced which was significant (p\0.001, n = 21) (20).

According to several randomized studies described by Somers et al, an increase in blood pressure, both systolic and diastolic, was observed after the consumption of energy drinks, as well as an increase in heart rate, serum noradrenaline values by 75% and QT interval by 5%. In one study, it was also evidenced that, after the consumption of large amounts, there was a prolongation of the QTc interval of up to 20 ms, which is significant when correlated with the risk of arrhythmias; it is important to consider that an increase of more than 10 ms is considered worrisome [7].

Interesting is the case report by Dufendach et al. of a 13-year-old female patient who presented unmasked congenital long QT syndrome type 1 after consuming 16 ounces of an energy drink containing (160mg of caffeine) [21].

One of the complications that have been of most concern for some years, especially in young athletes, is sudden cardiac death following the consumption of energy drinks. In a study conducted by Keyvan et al, 13 cases of sudden death were identified, a large proportion of which were found in men less than 21 years of age, with underlying cardiac problems. Sudden death occurred during or after the consumption of energy drinks in addition to moderate to severe physical activity [22].

In a description by Higgins, a case was reported of a 17-year-old male patient who suffered coronary vasospasm with acute ST-segment elevation myocardial infarction associated with marked elevation of cardiac troponins after consumption of an energy drink. We also reported the death of a 14-year-old female patient associated with cardiac arrhythmia after the consumption of two energy drinks and the triggering of a coronary artery dissection in a 13-year-old male patient after the consumption of energy drink [4].

In a prospective study by Kozik et al, it was found that after consumption of an energy drink there was an increase in blood pressure both systolic and diastolic at rest (10mmhg and 5mmhg respectively) and during exercise (17mmhg and 10mmhg respectively). There was also evidence of a decrease in serum potassium of approximately 3 mmol/l with respect to baseline, and even mild asymptomatic hypokalaemia (3.2 mmol/l) was observed in 26% of the patients. The electrocardiogram also showed an increase in heart rate of 8 beats per minute at rest and 7 beats per minute during exercise, and a prolongation of the QTc interval at rest of approximately 23 ms and during exercise of 50 ms. Interestingly, one of the individuals after consumption developed a QTc of 497 ms and two individuals after exercise developed a QTc interval greater than 500 ms. The latter is interesting because there is evidence showing that with values higher than 500ms the risk of developing cardiac arrhythmias, mainly ventricular, increases. Another interesting finding was that 44% of the subjects developed changes in the T wave, either inversion or flattening, even showing in one of them an ST segment under level. It is worth mentioning that there were some limitations in the study, including the fact that it was not a randomized clinical trial, the amount of caffeine was not quantified like other compounds, as well as the presence of inconveniences at the time of choosing the formula to measure the QT interval in the participants, among other things [23].

Finally, it must be said that cases have been reported of young patients who, after the consumption of energy drinks alone or enhanced with other stimulants, have unmasked a Brugada syndrome, triggering acute myocardial infarctions with ST elevation (STEACS), coronary vasospasm, atrial fibrillation and even in other patients with underlying disorders such as, for example, in a repaired tetralogy of Fallot presented a non-sustained ventricular tachycardia culminating in ventricular fibrillation after consumption of Red Bull [24].

In a study by Nowak et al, 707 students attending secondary sports schools in Poland were surveyed. Most of them consumed 250 ml of energy drinks per day, and a small number consumed more than 750 ml each day. Consumption was more frequent in males than in females, and most of the students were more likely to play soccer, basketball, or volleyball. Sixty-nine percent of them practiced sports every day, the rest practiced less frequently. It was found that about 69% consumed energy drinks, 17% consumed them every day or at least 1 or 3 times a week. Most of them chose the energy drink because of its taste (47%) or price (21%). Most of them were aware of their composition and potential risks and claimed to have consumed them because of fatigue, thirst or drowsiness. Most of them remained asymptomatic after consumption (71%); however, some students presented insomnia, anxiety, tachycardia, nervousness, and irritability. In addition, it was reported that 1 out of 10 respondents used to mix energizers with alcohol with some frequency. Those who did, mentioned having presented at some time after consumption, abdominal pain, amnesia, headache, nausea, vomiting. It is interesting to note that the association of energizers with alcohol increases the likelihood of risky behavior, such as drinking and driving, sexual abuse, violence, use of other drugs that could even increase the risk of adverse cardiovascular and nervous effects. It has been seen that the use of energizers associated with alcohol masks its symptoms (56%) and this increases the risk of addiction by an increase in the frequency and intensity of the same and other substances. An interesting aspect of the study was that the associations between the consumption of energy drinks and alcoholic beverages were observed more in some disciplines than in others. Thus, they were more frequent in combat sports (19.5%), volleyball (17.7%) and soccer (15.7%). Among the symptoms that may occur are hallucinations, headache, tachycardia, anxiety, insomnia, hallucinations, chest pain, and gastrointestinal symptoms. It can also generate pontine myelinolysis, rhabdomyolysis, metabolic acidosis, migraines, and arrhythmias, among others [25].

It has also been shown that high caffeine consumption (more than 1g) increases the risk of depression, panic attacks and stress. Caffeine at doses of 5 to 10 g could be lethal. Another drawback is the high sugar content of these beverages (in many of them up to 60g of sugar), which not only, as mentioned above, enhances the activity of caffeine and taurine and increases the risk of side effects, but also increases the risk of developing obesity, caries, among other problems [26].

In a double-blind, placebo-controlled experimental design, the objective was to evaluate the perceived ergogenicity and adverse effects 60 minutes after consuming the energy drink. The study was conducted on 90 athletes with low regular caffeine consumption, of which 53 were men and 36 women at a caffeine dose of 3mg/kg versus placebo 0mg/kg. It was evidenced after analysing the questionnaires, that caffeine increased self-perceived muscle power during exercise and reduced overall fatigue the next morning after ingestion of the energy drink. However, no significant difference was evidenced in terms of perceived endurance and effort during high intensity exercise with respect to placebo. It is worth mentioning that an increase in adverse effects was identified, mainly insomnia, nervousness, and alteration of the activity of the individuals, however, there were no significant differences between both sexes. Interestingly, adverse events are already reported at doses of 3mg/kg, in contrast to what is described in other studies [27].

In a study by Nowak et al, it was observed that the most commonly reported acute symptoms after ingestion of an energy drink were excitement, headache, xerostomia, irritability and general malaise. After ingestion of a second dose of energizer, erectile dysfunction, increased drowsiness, irritability, stupor and decreased arousal were observed. After the third dose, increased arousal, abdominal pain, hand tremor, chest pain, palpitations and weakness were observed. Other studies also reported anxiety, nervousness, vomiting, paresthesia and increased diuresis [28] **(Table 1)**.

According to Higgins, caffeine contained in energy drinks could have an ergogenic activity with doses of 3-6 mg/kg body weight associated with an increase in power and aerobic activity by 4%. However, he mentions that the evidence is actually controversial and even suggests possible undesirable effects totally opposite to the wishes of athletes, such as muscle fatigue and decreased cerebral blood flow.

In a study carried out by the same author, it was shown that several hours after the consumption of an energy drink there was alteration at endothelial level, which suggests that it could generate alteration of blood flow in several vital organs such as the heart [29].

Table 1. The following table shows the most frequent acute and chronic adverse effects.

Efectos Adversos Agudos	Efectos Adversos Cronicos
Elevated blood pressure	Hypertensive heart disease
Elevated heart rate	Coronary artery disease
Increase in QTc interval	Atherosclerosis
Supraventricular arrhythmias	Cerebrovascular disease
Ventricular arrhythmias	Peripheral arterial disease
Coronary vasospasm	-
Coronary artery thrombosis	-
Takotsubo cardiomyopathy	-
Acute ST-elevation myocardial infarction	-
Aortic dissection	-
Orthostatic postural tachycardia syndrome	-
Sudden death	-

A possible mechanism for the development of sudden death in athletes after the consumption of energy drinks may be due to alterations in supply and demand [30] **(Figure 1)**.

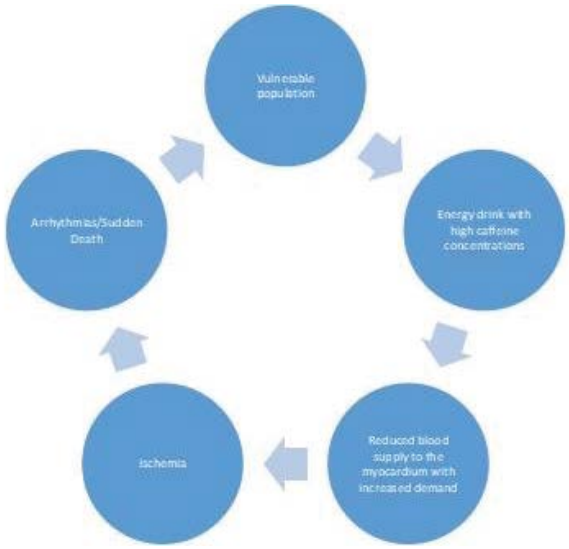

Figure 1 Possible Mechanism of Sudden Death Associated With the Consumption of Higgins Energy Drinks.

Results

Having said this, it is important to mention that the Substance Abuse and Mental Health Services Administration made clear the impact that these drinks have on the body. They mention that approximately 20,783 people went to the emergency department with symptoms related to their consumption in 2011, while the United States Poison Control Centers reported 4,854 calls associated with unwanted effects of energy drinks in the same way in 2011 [31].

According to Wassef et al, the most common adverse effects encountered probably attributed to caffeine and taurine for their psychoactive effect on the nervous system were seizures, psychomotor agitation, aggressive behavior, and suicidal ideation. While the most common cardiac disorders included arrhythmias such as atrial fibrillation, supraventricular and ventricular ectopy, coronary vasospasm, ST-segment elevation acute coronary syndrome, acute cardiomyopathies, repolarization disorders such as prolongation of the QT interval, unmasking of the genetic syndrome of long QT type 1, and, consequently, the appearance of complications associated with them. It is probable that some of these disorders, such as atrial fibrillation, are generated even in young people without underlying cardiac disorders, and in general terms, that they are due to hemodynamic, autonomic and electrocardiographic alterations after the consumption of these beverages, as suggested by Somers et al [32].

The problem of what has been described lies basically in the fact that most of these disorders were associated with the sporadic consumption of energy drinks, as well as in combination with alcoholic beverages. These probably still raises questions about the impact of these beverages on health.

Interestingly, in the United States more than 50% of college students consume at least one energy drink per month. In

addition, 44.8% of US military personnel deployed in Afghanistan consumed one energy drink per day, and 13.9% drank three or more energy drinks per day [33].

According to Froiland et al, a large proportion of athletes seek supplements to improve physical performance. Among these supplements, the most used in this study were energizers. It is estimated that approximately 73% of college athletes in the United States consume them [34].

It has been shown that the consumption of energizers is inversely proportional to age. In other words, the younger the age, the higher the intake of these products [35].

Nowak et al. document that more than 50% of adults and more than 40% of adolescents consume energy drinks (1-5 or more cans in relation to a single sports session) before, during and after physical activity. Interestingly, many of them are unaware of the composition and risks of their consumption and, even more interestingly, many athletes do so at the suggestion of their coaches [36].

For a long time, athletes, with the purpose of improving their performance, have consumed various supplements to improve ergogenicity, which is defined as "any mechanism to improve the production, utilization, control, efficiency in the use and recovery of energy, with the purpose of generating a competitive advantage against their adversaries". In recent times, caffeine has become the main component of multiple foods and beverages, including energy drinks. It has been used in the world of sports either alone or in combination with other psych stimulants [37, 38].

In a randomized, double-blind, placebo-controlled, counterbalanced crossover trial conducted by Chtourou et al, the intake of an energy drink "Red Bull" was compared against placebo in 19 physical education students who regularly performed physical activity, in order to determine the effect of the former after consumption on short-term performance, reaction times, psychological impact and physiological parameters. The results in favor of Red Bull showed an improvement in maximum power, average power, hand grip strength and a reduction in reaction time. There was also evidence of an increase in blood glucose and blood pressure before and after exercise, as well as an apparent reduction in anxiety, depression, anger, fatigue, confusion, reduced perception of effort, among others. Interestingly, there was an association between the gain in mean and peak power with a reduction in anger, fatigue and anxiety, as well as a reduction in reaction times associated with a decrease in anger and confusion and an increase in vigor, and also grip strength and reaction times were significantly correlated with blood pressure levels, suggesting that Red Bull intake has a positive effect on physical performance and reaction times. This effect on athletes may be largely related to changes not only at the physiological level, but also at the psychological level of the individuals. It is worth clarifying that the consumers did not drink caffeine on a regular basis, patients with comorbidities including cardiac pathologies were excluded and the study did not evaluate the ingredients individually [39].

In another study by Coso et al, where the use of an energy drink was compared against placebo during an international rugby competition, an increase in muscle power during the jumping series, the running rhythm during the games, as well as the speed of the athletes was demonstrated (14). In another study carried out by Fukuda et al, where a significant improvement in anaerobic performance of about 11% was evidenced after the consumption of a supplement with caffeine, creatine and amino acids [40].

In a study carried out by Gwacham et al, it was evidenced in contrast to what was described in the previous paragraph, observing in American soccer players that there was no significant influence on speed or anaerobic power after the consumption of an energy drink containing caffeine and taurine. However, it is worth mentioning that there were some drawbacks to the study. Many of the athletes were sporadic consumers and others were frequent consumers of caffeine and among the consumers the daily doses could be very variable. The interaction of the caffeine consumed with the energy drink, as well as tolerance, could have significantly influenced the results obtained in this study, which is why it was inconclusive [41].

In a systematic review and meta-analysis conducted by Souza et al, 34 studies were analyzed between 1998 and 2015. It was shown that the intake of energy drinks significantly improved sports performance. This was evidenced in part after improving strength and muscular endurance, in physical endurance tests, jumps and sport-specific actions, however, the same impact was not evidenced in terms of speed. Something interesting to highlight from the study is that a significant association was demonstrated between taurine dose (mg) and performance (slope = 0.0001; p = 0.04), which was not the case with caffeine (slope = 0.0009; p = 0.21) [42].

One observation is worth making. This difference between trained and untrained individuals is probably due either to the effect of the physiological adaptation of the athletes in combination with caffeine supplementation or due to the difference in endurance between athletes and non-athletes [43, 44].

In these studies, it is likely that the main motivation for its consumption was sleep-related problems and the intention of acquiring more energy to better meet their objectives. However, as the days went by, the effects were contrary to those expected **(Table 2).**

Energy Drinks In Athletes

According to E. Kaşıkçıoğlu, Energy drinks contain a wide variety of stimulants, many of them in unclear concentrations. These drinks are widely consumed by young people today including athletes, the latter with the intention of increasing performance in the

Table 2. Population at risk.

Under 18 years old	Breastfeeding mothers
New caffeine consumer	Caffeine consumption associated with other stimulants
Person particularly sensitive to caffeine	Comorbidities including cardiovascular disorders
Pregnant women	-

activity they perform and however, to date their effectiveness for that purpose has not been proven. It should be noted that in recent years it has become evident that the stimulants in these beverages, alone or associated with other compounds, can generate serious problems in the population, especially in those people with underlying silent cardiovascular pathology. More and more cases of sudden death are being reported in young people and athletes after consuming these beverages, probably due to the arrhythmogenic effect generated by their compounds [45, 46].

Despite the negative report on the use of energy drinks in athletes, caffeine by itself could generate beneficial effects depending on several factors.

As previously described, caffeine could generate interactions that would elevate the concentrations of caffeine in the urine and could be a problem in sports competitions.

There are several factors that affect caffeine clearance, such as the Asian or African population (they metabolize slowly compared to other populations), gender, age, genetics, and frequency of consumption, among others. It is worth mentioning that obesity modifies the pharmacokinetics of caffeine, increasing its half-life in blood. This, added to the interactions with multiple substances, the dose, frequency and speed of consumption, could increase the risk of adverse effects, especially in susceptible individuals.

Among the effects evidenced, there is a slight increase in diuresis, which does not seem to have a significant impact on the hydration status of athletes. In addition, despite the evidence against it, little, by the way, multiple benefits have been observed after its consumption, such as, for example, delaying the onset of fatigue, better tolerance to pain, generating a lower perception of effort and a greater feeling of having a lot of energy, an increase in lipolytic activity, glycogen saving, increased concentration and alertness, an increase in the production of average power, stimulates the loco motor system, among others.

According to studies, a consumption of less than 450mg of caffeine does not trigger or worsen cardiac disorders.

As for caffeine tolerance, defined as the need to progressively increase the dose to generate the desired effect, it is variable from one consumer to another, and is generally achieved at doses of 300 to 400mg three times a day for 7 to 15 days, and tolerance has only been evidenced for some of its effects. In people who do not consume regularly, nervousness, anxiety, restlessness and increased energy have been evidenced, which does not happen with regular consumers.

Similarly, in those who consume on a regular basis, a greater sense of well-being, improved attention, alertness have been observed, which also does not happen with those who consume sporadically.

In those who consume on a regular basis, a 90% reduction in blood pressure and heart rate has been observed after the consumption of moderate to high doses of caffeine (300 to 1000mg). This tolerance is lost after a short period of time following discontinuation of caffeine intake.

Symptoms attributed to withdrawal have been evidenced, such as drowsiness, irritability, headaches, colic, arthralgias, difficulty to concentrate, among others after 12 to 24 hours of caffeine suspension, with a peak at 48 hours that lasts between 1 to 5 days in habitual consumers. This is probably due to the recovery of the number of adenosine receptors.

Adverse reactions will depend on each person, and the symptomatology associated with caffeinism is variable. Among the most common symptoms are nervousness, muscle spasms, hyperreflexia, insomnia, headache, respiratory alkalosis, palpitations, among others. In some people it could precipitate panic attacks and worsen anxiety disorders.

Caffeine intoxication occurs after the consumption of 1 g or more of caffeine, and a dose of 3 to 10 g (12 energy drinks at least) are considered potentially lethal especially when consumed in a short period of time. The symptoms associated with intoxication are similar to those described in the previous paragraph. Among the most common symptoms, in order of frequency, are arterial hypertension, nausea and vomiting, restlessness, agitation or tremors, tachycardia, dizziness, among others. The main cause of death evidenced after its consumption is arrhythmias [18, 31].

The evidence supports the use of caffeine supplements for athletes engaged in aerobic rather than anaerobic activities because the evidence on the latter is controversial. What is certain is that caffeine by itself is an ergogenic substance that generates benefits especially in long duration sports of low to medium intensity or medium to high intensity interspersed. It is also important to rule out underlying problems before administration due to the growing evidence of even fatal disorders in young people and athletes. The average recommended dose is 6 mg/kg of caffeine 1 hour before the competition in the form of anhydrous caffeine capsules and taking special caution with what is ingested during 24 hours before the consumption of the same due to the possibility that other substances or foods contain caffeine increasing the risks of toxicity or due to its possible interaction with other drugs that could reduce to suboptimal doses or increase the potency of the same caffeine or drugs causing adverse effects that could become fatal [18, 31].

Individual sports in elite athletes

Improved activity at varying doses was evidenced in several studies

Two studies of similar characteristics showed that after the consumption of 3 mg/kg and 5 mg/kg of weight, 60 minutes before running 8 and 5 km on a track respectively, an improvement in performance was statistically significant compared to placebo.

Another study in professional swimmers showed that after consumption of 100mg of caffeine, 75 minutes before training or competition, especially in the afternoon hours significantly improved performance.

Another study conducted in elite junior tennis players, after the consumption of an energy drink at a dose of 3mg/kg of caffeine, 60 minutes before, showed a better grip strength, higher speed, intensity and number of sprints performed compared to placebo.

There was also an increase in the number of points won during a match.

In another study conducted on 6 judo fighters, after the intake of a 6 mg/kg capsule of caffeine, which was ingested 30 minutes before the activity, they faced 3 fights of the Senior Judo Fitness Test, after which a higher blood lactate level and a lower sensation of perceived effort compared to placebo were evidenced [26].

Collective sports

In two similar studies conducted with male and female volleyball players, it was evidenced that after ingestion of 3 mg/kg of an energy drink 60 minutes before the tests, improvements were observed both in ball speed in the serve, height of jumps, greater agility during the match compared against placebo.

In other studies carried out on well-trained soccer players in simulated 90-minute matches after the ingestion of an energy drink containing 3.7 mg/kg of caffeine 60 minutes before the test and every 15 minutes during the activity and in another that consumed a capsule of 6 mg/kg of caffeine in the same way 60 minutes before the test. In the first one, a higher jumping capacity than the control group and a higher average running speed were evidenced. In the other study, a greater jumping capacity was also evidenced, but also a greater passing accuracy [27].

According to Garcia, the dose of caffeine to generate a significant improvement in neuromuscular performance depends largely on the weight of the load used, as demonstrated in a study where the impact of caffeine on the neuromuscular tests of bench press and full squat was evaluated. In summary, it could be said that a dose of 3 mg/kg of caffeine is adequate to improve high-velocity muscular activity at low loads and that of 9 mg/kg is necessary for high loads. In any case, as we have said, doses of 9 mg/kg are not safe because of the increased risk of adverse effects.

The timing of caffeine administration to generate an ergogenic effect depends on the concentration of caffeine, the route of administration and the form of consumption. To date, it is suggested that for energy drinks or caffeinated capsules (which have the most evidence so far), 60 minutes before the bout is adequate to generate an ergogenic effect, while consumption of a caffeinated gum 5 minutes before exercise also showed a significant benefit.

Several studies have sought to demonstrate the effect of caffeine on cognitive function and on the individual's perception during sports performance. There has been evidence of an improvement after caffeine consumption in cognitive capacity, alertness levels and even a better mood, which can be beneficial for decision making and motivation during sporting events.

The adverse effects evidenced in athletes after caffeine consumption are arrhythmias, hand tremor, nervousness, hyperactivity and insomnia. It has even been demonstrated that these effects do not affect the sports activity during the performance in the different activities. However, this will depend on the discipline, since in shooting sports, if the participants present hand tremor, headache and anxiety, it will probably limit their performance in the competitions.

It is likely that on the other hand, as some studies have shown, that consumption on consecutive days continues to generate benefits. It has also been shown that consuming caffeine before training, especially maximal strength training, reduces pain levels 48 to 72 hours after exercise, and it has been shown that caffeine consumption, even during the following days after physical activity, reduces muscle pain of late onset [27].

In a randomized, double-blind, placebo-controlled study by Mora et al, it was shown that caffeine consumption counteracts the morning reduction in neuromuscular performance caused by circadian rhythm. It was shown that, after caffeine consumption, a direct effect on the musculature is the increase in muscle strength and power as long as the contractions are dynamic and not isometric. This increases muscular performance to the levels found in the afternoon.

Another observation to note is that, by consuming in the morning, it can minimize the adverse effects of caffeine, which would be of greater impact in the evening hours [28].

The National Collegiate Athletic Association of the United States (NCAA) released a report in 2012 of a survey conducted on substance use in approximately 21,000 college athletes. It showed that about 45% of them consumed energy drinks.

In the following table extracted from this article, we can see the percentage of men and women who practice different disciplines and report the use of energizers [34] **(Table 3)**.

Discussion

As we have evidenced, the important variability in terms of the methodology of the studies, I have generated many difficulties to draw objective conclusions and that can be easily extrapolated to the population. In any case, a few things are clear. First, the most important element in energy drinks is caffeine; second, the consumption of energy drinks with alcoholic beverages increases the risk of developing life-threatening complications; third, mild to moderate caffeine consumption seems to generate health benefits both in patients who do not engage in physical

Table 3. Percentage of men and women who practice different disciplines and report the use of energizers.

Use of energy drinks in college athletes		
Sport	**Men**	**Women**
Struggle	61.3%	-
Lacrosse	55.2%	46.2%
Ice hockey	53.7%	-
Baseball	52.9%	-
Golf	52.6%	49.4%
Tennis	52.5%	38.5%
Swimming	51.7%	41.2%
football	48%	43.3%
American football	44.3%	-
Athletics	38.2%	30.5%
Basketball	36.6%	-
Field hockey	-	40.5%
Softball	-	46.1%
Voleivol	-	48.9%

activity and in those who do, fourth, special care should be taken if there is cardiovascular, neurological or psychiatric pathology before recommending its use, and fifth, it would be interesting to carry out further studies to determine the ideal form of caffeine presentation to generate better benefits and less harm. It should be noted that our study covered a wide variety of topics, which made its organization and synthesis very difficult. We suggest for future studies to better define their objectives and develop them in a clear and more concise manner.

Conclusions

To date, the use of caffeine powder, gum or capsules with caffeine (which have greater evidence so far) is suggested, since it is found to be related to an adequate ergogenic effect and a reduction of muscle soreness of late onset after activity; approximately 48 to 72 hours. The recommendation is to ingest a single dose of 1 to 6 mg/kg (preferably between 3 and 5 mg/kg) of body weight 5 minutes before exercise for caffeinated chewing gums and 60 minutes before exercise for all other presentations. The consumption of light to moderate doses of caffeine could be beneficial in high performance athletes, both for short and long duration activities, but not so in people who perform sporadically, in light intensity or who are not trained.

The use of energizers is not recommended due to the large amount of substances or elements they contain that could interact and reduce or enhance the effect of caffeine, which is the key element in these beverages.

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