UNIVERSITY OF
SS. CYRIL AND METHODIUS
IN TRNAVA

Nova Biotechnol Chim (2023) 22(1): e1344
DOI: 10.34135/nbc.1344

Nova Biotechnologica *et* Chimica

Review

Health risks associated with the chronic consumption of energy drinks in children and adolescents

Katlego Sharon Mphahlele[1], Nosiphiwe Patience Ngqwala[1], Oscar Agbor Ambang[1], C. Sunitha Srinivas[1] and Roman Tandlich[1,2,✉]

[1] *Faculty of Pharmacy, Rhodes University, Grahamstown 6140, South Africa*
[2] *Faculty of Health Sciences, Technical University of Liberec, Studentská 2, Liberec 46117, Czech Republic*

✉ *Corresponding author: r.tandlich@ru.ac.za*

Article info

Article history:
Received: 2nd January 2022
Accepted: 30th September 2022

Keywords:
Adverse effects
Advertising
Alcohol
Caffeine
Regulations
Taurine

Abstract

Energy drinks (EDs) have been available at the global market for almost 100 years and today, they are advertised as 'tools' boost energy, enhance physical performance and mental alertness. Some of the main chemical components in EDs include caffeine, ginseng, and taurine. The market and consumption of these beverages is growing exponentially, and this is becoming a public health problem due to the adverse effects associated with these drinks. The main objective of this article is to review important ingredients in popular EDs in South Africa and look at their molecular mechanisms of action and interaction with other compounds within the body. At the same time, the authors aim to review the global consumption pattern of EDs among children and adolescents. Finally, this review article will provide an overview the health risks associated with EDs consumption. A literature review was conducted using scholarly databases. Keywords such as energy drinks, adverse effects, advertising, alcohol, caffeine, taurine, and regulations were used. Despite the claims of having significant benefits to mental and physical stamina, long-term consumption of EDs could have detrimental public health implications; and could result in increasing rates of the central nervous system disorders and the cardiovascular complications. A knowledge gap exists on how the lack of education impacts the decision of consumers of EDs and the parental guidance provided to children and adolescents in relation to the consumption of these beverages in South Africa. To address the issue of excessive ED consumption, communities need to be made aware of the harmful effects of these beverages through health education and implementing strict regulatory measures through policy.

Introduction

Energy drinks (EDs) have been available at the global market for almost 100 years and today, they are advertised as 'tools' boost energy, enhance physical performance and mental alertness. According to several reports, EDs are one of the most popular supplement commodities in the United States second only multivitamins (Froiland *et al.* 2004; Hoffman 2010; Campbell *et al.* 2013). EDs have not only appealed to the adult population but to children and adolescents too, as we have seen an increase in the consumption rate within these population groups. In 2015 and focusing on

the patterns of the ED consumption, the European Food Safety Authority commissioned survey-based research in 16 of the EU countries (European Food Safety Authority 2015). Among the adult population and the adolescent age groups (10 – 18 years old), as well as in the below-ten-year-old children, the results indicated that (< 10 years old) demographic 30 % of adults, 68 % of adolescents and 18 % of children were consuming EDs (European Food Safety Authority 2015). Correlating results were observed in a survey study conducted in 43 high schools in Ontario, which revealed that in a student population of 23,610; 73.6 % were reported to be consumers of EDs (Reid *et al.* 2015). In the recent years, novel findings have been published in scientific literature on the ED consumption and the related health effects. Some of the most concerning, and potentially damaging public health ones, include the increased probability and risks from childhood obesity, the increased probability in the rise of early onset cardiovascular pathophysiological conditions, suicidal ideation, and tendency, as well as impaired cognitive function in children (Usman and Jawaid 2012; Kammerer *et al.* 2014; Park *et al.* 2016). In addition to these health risks, aggressive behaviour and mood disorders were reported in a study and linked to caffeine consumption in 15 – 16 years olds (Soós *et al.* 2021).

Due to their potential effect of enhancing physical performance, EDs have become increasingly appealing and popular to sport athletes. The distinction between EDs and sports drinks (SD) must be noted and clearly defined. EDs and SDs are two different types of supplement beverages with their own specific performance enhancement claims and nutritional compositions. SDs are targeted at individuals who play sports (athletes) or engage in high-performance activities. Their aim is to provide hydration and electrolyte replenishment to the body with the intent to support it during a high-performance activity (Campbell *et al.* 2013). Carbohydrates are one of the molecules found in both EDs and SDs in different estimated quantities of around 12 g and 3 g respectively, this compound is the body's primary source of energy. EDs commonly contain caffeine as the main active ingredient, along with other ingredients such as ginseng, B vitamins, taurine, sugar, guarana, carnitine, green tea extracts and ginkgo biloba, which all have significant physiological effects on the body (Heckman *et al.* 2010). The observed exponential growth of ED consumption has become a great health concern towards nutrition and dietary inadequacies; some of the factors promoting this growth is the rise of the food processing industry, targeted advertising, and the absence of independent regulatory bodies (Higgins *et al.* 2010).

EDs entered the mainstream beverage industry first in the early 1960s and since then have grown exponentially into a multi-billion-dollar industry. Bailey *et al.* (2014) carried out a study, using data from 160 countries, which showed that the annual consumption of EDs was greater than 5.8 billion litres. In the United States alone, sales in 2015 were reported to be $13.4 billion, with the major ED companies at the helm of the market in terms of sales and advertising (Richter 2014). The aggressive growth of the EDs market is fuelled by advertising. One of the marketing strategies used to gain massive exposure is through providing financial support to well-known sports teams and sponsoring major events, such as sports competitions and music festivals as (MacKnight 2020; Erdmann *et al.* 2021).

The regulation of EDs, including health information and content labelling is different across countries and the absence of strict and consistent regulatory principles fuels the aggressive marketing of these beverages (Higgins *et al.* 2010). A knowledge gap exists on how the lack of education impacts the decision of consumers of EDs and the parental guidance provided to children and adolescents in relation to the consumption of these beverages in South Africa. This review article seeks to highlight the health risks associated with the chronic consumption of EDs in children and adolescents. Furthermore, interventions that can address and reduce the excessive consumption of these beverages will be discussed.

Experimental

A systematic literature review was conducted using the following databases: Cochrane Library, EBSCO host, Google Scholar, PubMed, Scopus, and ScienceDirect to search for relevant literature

published from 1980 to 2022. Only 9 publications were selected before the year 2005, 6 publications were selected between the year 2005 and 2009, the rest of the publications are from 2010 to 2022. We did not exclude articles based upon a date of publication due to lack of scientific research and literature in this area. Keywords such as adverse effects, advertising, alcohol, caffeine, taurine, and regulations were used. Furthermore, five different EDs were bought, together with Cola drink 1 and Cola drink 2. The ingredients of these beverages as shown on the packaging labels were analysed and compared, particularly looking at the amounts of caffeine, taurine, and sucrose in each of them. Using Google search, we looked at the quantity of caffeine found in brewed coffee, expresso, decaf coffee, ice tea, and green tea.

Results and Discussion

EDs are a rapidly growing market globally. They are popular among children, adolescents, and young adults. Various drinks were analysed based on their labelled content; the emphasis was particularly placed on the amount of caffeine, taurine, and sugar in each of them.

Table 1. A list of popular energy drinks in South Africa with the main ingredients (based on label analysis).

Energy Drinks & Soft Drinks	Caffeine content [mg.100 mL^{-1}]	Taurine concentration [%]	Sugar content [g.100 mL^{-1}]
ED brand 1	32	Not stated	6.0
ED brand 2	26	Not stated	3.5
ED brand 3	32	0.4	11 (sucrose)
ED brand 4	30	0.4	3.7
ED brand 5	32	0.4	Sugar free (contains sucralose)
Cola drink 1	34	0	10.6
Cola drink 2	37.6	0	40

Table 1. above shows some of the popular EDs consumed in South Africa which are namely ED brand 1, ED brand 2, ED brand 3, ED brand 4, and ED brand 5. ED brands 1 and 2 are locally produced and owned. The average caffeine content of the listed EDs is 32 mg.100 mL^{-1}. An interesting observation made from the table is that the quantity of caffeine in Cola drinks 1 and 2 which are 34 mg.100 mL^{-1}and 37.6 mg.100 mL^{-1} respectively. This is greater than that of the EDs. The sugar content varies between the EDs and Colas, with Cola drink 2 containing more sugar (40 g.100.mL^{-1}) than any one of the beverages. Perhaps more research is needed to investigate the impacts of cola in comparison with those of EDs, particularly looking at their caffeine content and the composition with other included ingredients. All the listed EDs have taurine concentration of 0.4 %, except of ED brand 1 having zero taurine content. Recently, ED brand 1 launched a new ED flavour which includes wormwood extracts as one of the ingredients. Wormwood, scientifically called *Artemisia absinthium* L., is known to have "anti-bacterial, anti-oxidant, anti-malarial, anti-inflammatory, anti-depressant and hepatoprotective pharmacological activities amongst others" (Ahamad *et al.* 2019; Batiha *et al.* 2020). The long-term use of wormwood has been reported to cause neurotoxic effects and mental disorder called "absinthism". These psychoactive and neurotoxic effects are due to the high concentrations of thujone which is a chemical substance found in *A. absinthium* and is known to be an antagonist of gamma-aminobutyric acid-a ($GABA_A$) receptor (Lachenmeier 2010; Batiha *et al.* 2020). The impacts of *A. absinthium*, particularly thujone in combination with caffeine and other chemical substances found in EDs still needs to be investigated.

Table 2. A list of different coffee and tea with their caffeine content.

Coffee and Tea (4-ounce)	Caffeine [mg]
1. Brewed coffee	45.4
2. Expresso	240.4
3. Decaf - coffee	0.0 – 3.0
4. Iced Tea	12.5
5. Green Tea	9.0

Table 2. A list of different coffee and tea with their caffeine contentabove shows the different caffeine quantities that were measured in coffee and tea that have been reported in literature. The concentrations of caffeine in brewed coffee and expresso are higher in values vs. the concentrations in EDs listed in Table 1.

Brewed coffee and expresso are made from coffee beans which contain caffeine, tannin, proteins, lipids, and carbohydrates (Sharma 2020). Although EDs and coffee/expresso contain a similar compound "caffeine" as the main ingredient, what sets them apart are the added ingredients, which exhibit different mechanisms and effects in the body. Tea contains four substances known to have a stimulating effect on the brain, which are caffeine, theophylline, theobromine, and L-theanine. Like caffeine, theophylline and theobromine belong to a class of xanthines, and they both have physiological effects. However, the amounts found in a cup of tea are so small that the impact on the body can be considered negligible (Gunnars 2022). According to the 2012 guidelines issued by the UK's Children Food Trust, it was recommended that children should avoid the consumption of food or drinks that contain caffeine, such as tea, coffee, cola, and other drinks (Children's Food Trust 2012).

Review of biochemical mechanism of action of the main ED ingredients

Caffeine

Caffeine is an alkaloid compound of the methylxanthine class, with its pharmacological mechanism of action including stimulation of the central nervous system (CNS) (Petre 2020). This class of drug is used clinically as a CNS stimulant, diuretic, bronchodilator, and cardiotonic. There is some evidence in biochemical and pharmacological literature that xanthines block or antagonize adenosine receptors in the human body (Bruns *et al.* 1980). Adenosine is a neurotransmitter that causes the brain to relax which decreases the nerve cell activity and leads to drowsiness and tiredness (Petre 2020). The formation of adenosine depends on the rate of ATP synthesis and breakdown (Bruns *et al.* 1980). Caffeine and adenosine have a similar molecular structure (Fig. 1), and therefore, the nerve cell recognizes caffeine as adenosine. The resulting binding causes the caffeine molecule to serve as an antagonist to the pharmacological activity of adenosine, which in turn leads to speeding up the nerve cell activity. The intracellular concentration of adenosine molecules rises as a consequence of the blockade of the receptors, thus activates noradrenaline neurons. The pituitary gland detects the cell activity and releases hormones that will activate the adrenal gland and therefore produce catecholamines (Brain *et al.* 2007). Caffeine blocks the activity of adenosine to open the brain's blood vessels, which leads to constriction and decrease in cerebral blood flow (Nehlig *et al.* 1992). Therefore, some headache medicines contain a combination of aspirin and caffeine. (Brain *et al.* 2007). An experimental study conducted by Conlay *et al.* (1997) showed how caffeine can change the adenosine plasma level in rats that were exposed to 0.1 % caffeine. Their adenosine plasma concentration increased from 0.32 ± 0.5 μM to 3.17 ± 0.30 μM when compared to the control group.

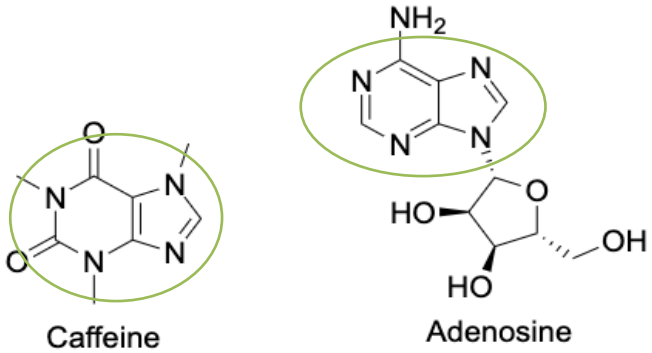

Fig. 1. Chemical structures of caffeine and adenosine illustrating the similarity of their molecular structure. Generated using Chemdraw software application.

Experimental studies have demonstrated that caffeine consumption influences the cardiovascular system in that it acutely increases blood pressure, circulating concentrations of noradrenaline, inhibits ischemic preconditioning and impairs endothelium dependent vasodilation (Nawrot *et al.* 2003; Riksen *et al.* 2009; Turnbull *et al.* 2017). A high intake of EDs can make the veins firm which will contribute to heart disease. The commonly reported conditions are heart palpitations, increased heart rate,

hypertension, chest pain, and dysrhythmias (Turnbull *et al.* 2017). An experimental research study found an association between myocardial infarction and ED consumption in healthy 17- and 19-year-old boys (Rath 2012).

Molecules of caffeine function as inhibitors of the adenosine receptors, which results in the enhancement of angiotensin II, epinephrine, and catecholamines. The increased production of angiotensin causes the rise in systolic blood pressure, whilst the increased level of catecholamines, particularly epinephrine elevates the heart rate. The study conducted by Alsunni (2015) showed that there is generally an increase in the heart rate and the blood pressure in human arteries once a patient has consumed a caffeinated drink. This is linked to the above mechanisms. Moreover, caffeine acts as a weak non-selective phosphodiesterase (PDE) inhibitor, whereas the cyclic-AMP (cAMP) is catalysed by the cAMP-dependent phosphodiesterase (PDE3) and this process leads to the change in concentration of cAMP inside the cell. The inhibition of this enzyme leads to the increase of cAMP concentration inside the cell, and this results in the increase of cardiac inotropy, chronotropy, and dromotropy (Klabunde *et al.* 2020).

Caffeine is rapidly absorbed in the gut, reaching nearly 100 % bioavailability in the body and peak plasma concentration within 30 – 120 min. It is metabolized largely by cytochrome P-450 and specifically by the CYP 1A2 isozyme (Babu *et al.* 2008). The major metabolites of caffeine are 3,7-dimethylxanthine (systematic name), which is trivially known as theobromine, and 1,3-dimethylxanthine (systematic name), which is trivially known as theophylline. Both compounds/metabolites complement the pharmacological effect of caffeine, while also being biologically active in the human body in their own right (Chen *et al.* 2017). Caffeine elimination follows non-linear pharmacokinetics that is based on the Michaelis-Menten kinetics equation. The caffeine half-life falls inside the interval from 3 to 6 h (Babu *et al.* 2008).

Taurine

Taurine has the systematic chemical name of 2-aminoethane-sulphonic acid ($C_2H_7NO_3S$). It is a *β*-amino acid, and its concentration is high in the heart and the skeletal muscles, as well as in other tissues, with the normal plasma concentration of 44 ± 8 $\mu mol.L^{-1}$. Although it falls under the group of amino acids, it does not take part in the formation of proteins (Schaffer *et al.* 2010). Taurine is a by-product of cysteine and methionine. It contains a sulfonate group and not a carboxyl group. This is how it differs from other amino acids hence it is considered as an amino sulfonic acid. The main route of taurine biosynthesis is illustrated below in Fig. 2 (Vitvitsky *et al*. 2011). In that figure, the molecule of the amino acid cysteine is converted into cysteinesulfinate by the action of cysteine dioxygenase. The next step in the pathway is catalysed by the cysteinesulfinic acid decarboxylase, with the reactant being cysteine sulfonate and the product being hypotaurine (Vitvitsky *et al*. 2011). As a result of this enzymatic reaction sequence, the final step occurs when hypotaurine undergoes oxidation to form taurine (Vitvitsky *et al*. 2011).

When it comes to additional biochemical effects in the human body, taurine is an organic osmolyte that regulates cell volume and is involved in modulating free calcium concentration inside the cell. This amino sulfonic acid is found throughout the body but does not form components of proteins. It is found mostly in the pupil, heart, brain, retina, muscle tissue, and the heart (Ripps *et al.* 2012). Taurine has an influence on the homeostasis of calcium within the cell through the pathway of Na^+/Ca^{2+} exchanger. It decreases glutamate-induced $[Ca^{2+}]_i$ accumulation in the cells by preventing the intracellular uptake of Ca^{2+} and the molecular mechanism of this is the reverse mode of the Na^+/Ca^{2+} exchanger (Wu and Prentice 2010). Literature suggests that taurine also influences the metabolism of energy in cardiac tissue and its deficiency leads to an impairment of the respiratory chain (Schaffer *et al.* 2016).

Fig. 2 above outlines the main steps of how taurine is formed: 1) Cysteine is catalyzed by the enzyme cysteine dioxygenase and oxidized into cysteine sulfinate; 2) Cysteinesulfinate decarboxylase

catalyzes cysteine sulfinate to form hypotaurine; 3) Hypotaurine is oxidized to taurine, catalyzed by hypotaurine dehydrogenase. There can be another branch of hypotaurine synthesis, in which cysteamine is converted to hypotaurine by the ADO enzyme activity (Vitvitsky *et al.* 2011).

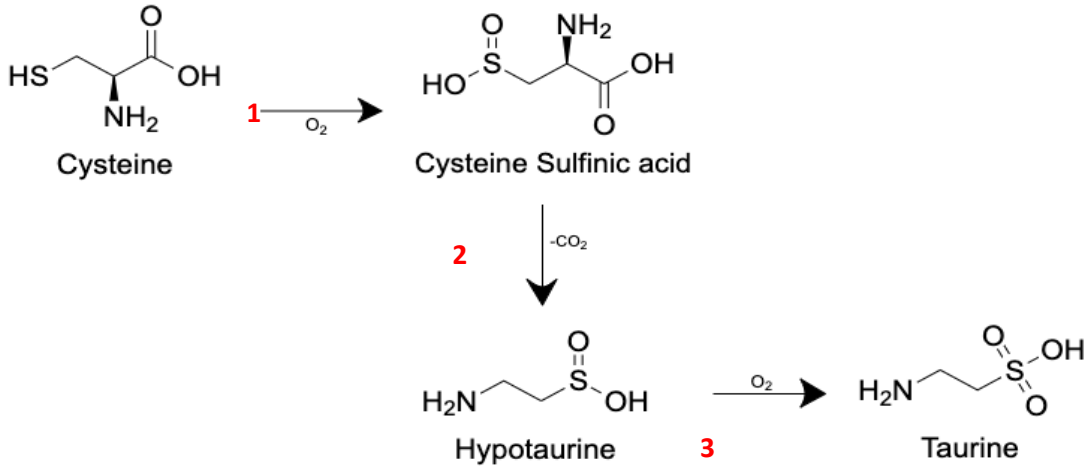

Fig. 2. A diagram illustrating the biosynthesis of Taurine. Generated using Chemdraw software application (based on the article by Vitvitsky et al., 2011).

In addition, taurine has a molecular structure similar to gamma-aminobutyric acid (GABA) illustrated in Fig. 3, and binds to GABA receptors where it potentiates GABA-ergic effects in the body (Reyes-Haro *et al.* 2014). Usually, when drugs interact with the GABA receptor, they potentiate an anxiolytic effect, therefore it is possible that taurine may have the same effect as well. Dombovy-Johnson (2010) suggests that when taurine is combined with caffeine it may increase caffeine stimulant activity by interacting synergistically. This finding is supported by research done on the sleep-wake activity of the combination of taurine and caffeine on *Drosophila melanogaster*, a species of fruit fly. The results have shown that caffeine increases locomotive activity and decreases sleep duration, whereas taurine decreases locomotive activity and increases sleep time. When taurine was added to caffeine it resulted in an inhibition of sleep with a greater effect than when caffeine was administered alone (Lin 2010). This could be a result of the fact that taurine is known to influence the metabolism of energy. Literature suggests that taurine deficiency-mediated defects lead to a reduction in ATP generation by impairing energy metabolism (Schaffer *et al.* 2016). Therefore, when the ratio of $NADH(+H^+)/NAD^+$ is elevated, the resulting action leads to the inhibition of key dehydrogenases such as those in the Kreb's cycle and they include "α-ketoglutarate dehydrogenase, isocitrate dehydrogenase and citrate synthase" (Schaffer and Kim 2018).

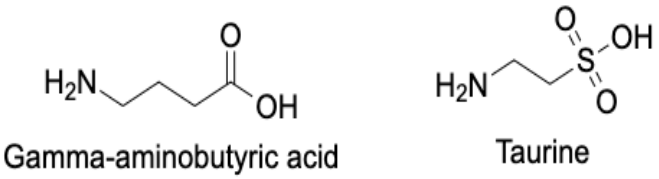

Fig. 3. Chemical structures of GABA and Taurine illustrating similar molecular structure. Generated using Chemdraw software application.

Cuttitta *et al.* (2013) investigated the role of taurine in the cardiovascular system. In the study, GABA was identified as the major inhibitory neurotransmitter responsible for the regulation of the heart. This neurotransmitter is found in the peripheral tissues as well as the CNS. The study was conducted on rabbits, and it was reported that GABA can suppress the release of noradrenaline which may lead to the regulation of vascular tone (Schaffer and Kim 2018). The selective permeability of the blood brain barrier restricts this inhibitory neurotransmitter from penetrating.

Alternatively, taurine has more permeability than GABA, therefore there is no concentration change in the brain following IV administration of GABA. The study also indicated that IV administration of taurine exhibited a significant decrease in systolic blood pressure in an experiment that was performed on conscious adult rats. Furthermore, it has been proven using an aortic ring preparation that taurine can act as a vasodilator. Taurine as a neuromodulator protects the CNS and reduces seizure episodes by agonizing the $GABA_A$ receptors which are found on the muscularis of the cerebral blood vessels and the aorta (Cuttitta *et al.* 2013). There are similar reports that have been published by Chan *et al.* (2013) and L'Amoreaux *et al.* (2010) in recent years.

In Japan, taurine has been approved to treat congestive heart failure. The chronic administration of taurine reduces the action of noradrenaline and angiotensin II, which decreases myocardial performance. Taurine can decrease catecholamine overflow through the alteration in Ca^{2+} transport, thus leading to the reduction of noradrenaline activity (Schaffer and Kim 2018). The therapeutic window period of taurine is at least 8 hours. This was proven in a study conducted by Sun *et al.* (2012) on experimental stroke in rats however, data is still lacking on the oral administration of taurine in humans. The NH_2 group in the covalent structure of taurine can undergo the Maillard-type reactions (Elzoghby *et al.* 2015). Carbonyl groups are found in many primary metabolites in the human body and examples of those molecules include glucopyranose and CH_3COH. Furthermore, it has been illustrated that taurine-glucose reaction results in an antioxidant effect and there is a likelihood of hindering taurine effect against protein modification when it reacts with acetaldehyde (Ogasawara *et al.* 1994).

Carbohydrates

Carbohydrates or sugars $[C_n(H_2O)_n]$ are molecular compounds that are the major source of metabolic energy in humans and mammals. The carbohydrate content of the human diet is usually derived from fructose corn syrup, glucose, and sucrose (Alsunni 2015). Lactose can also play a role here. As listed on the packaging labels, most EDs contain sugar in the form of sucrose. The World Health Organization (WHO) has decreased the suggested amount of sugar that should be taken daily from 10 % to 5%, this is about 25 g of sugar per day. The sugar content in the EDs falls within the recommended amount. The consumption of high sugar content for a long period is a risk factor for obesity which subsequently leads to diabetes. There is a strong link between the Body Mass Index (BMI), diabetes and insulin resistance. In obese individuals, the building-up of insulin resistance is influenced by the increase in quantity of free fatty acids, cytokines, hormones, and other substances involved in the development of insulin resistance (Al-Goblan *et al.* 2014).

An *in vivo* study that was performed on rodents showed that a high chronic consumption of fructose will result in obesity, high blood pressure, type 2 diabetes, hepatic and extrahepatic insulin resistance. In addition, the high intake of fructose can cause dyslipidemia and impair hepatic insulin sensitivity (Tappy and Lê 2010). Therefore, the high usage of EDs is an attribute that elevates the chances of developing type 2 diabetes and obesity (Alsunni 2015). Although the summary molecular formulas of fructose and glucose are the same ($C_6H_{12}O_6$), their metabolism and absorption pathways have some differences. Fructose absorption takes place in the gut via the GLUT-5 transporter facilitated diffusion (Goran *et al.* 2013), whereas glucose absorption is mediated by the SGLT1 co-transport mechanism. Scientific reports in the literature have indicated that molecules of fructofuranose, does not trigger the secretion of insulin and leptin hormones (Bray *et al.* 2004) instead, it is believed that it directly adds to weight gain and increases energy intake (Goran *et al.* 2013). Ragsdale *et al.* (2010) conducted a study which reported that there is an increase in blood sugar level after the consumption of EDs; and this can be explained by the study performed by Lee *et al.* (2005) which demonstrated that caffeine consumption leads to decrease in insulin sensitivity.

Alcohol and energy drinks

The trend of mixing EDs with alcohol is no longer seen as an abnormality, but more of a common

practice. Both alcohol and EDs have a diuretic and dehydrating effect therefore, they may decrease the body's capability to metabolize alcohol (Ferré and O'Brien 2011).

Caffeine and alcohol combinations

The underlying molecular mechanism of the interaction between alcohol and caffeine is unknown however, it is known that both can alter the neurotransmission of adenosine. In a review carried out by Ferré and O'Brien (2011) it is suggested that during alcohol consumption, caffeine blocks the adenosine Al receptors and thus opposes the undesirable effects of alcohol. In addition, the interaction of dopamine D_2 and adenosine A_{2A} receptors can increase the effect of alcohol-induced dopamine release, and this can occur through the blockade of adenosine A_{2A} receptors by caffeine.

Li *et al.* (2014) demonstrated that some EDs can increase or decrease the activity of alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH). The degradation happens when alcohol is ingested and broken down into acetaldehyde (toxic compound) by alcohol dehydrogenase and further metabolized to acetate (less active by-product) by aldehyde dehydrogenase (U.S. Department of Health & Human Services 2007). An increase in the activity of these enzymes results in rapid metabolization of ethanol or acetaldehyde (Li *et al.* 2014). Another study by Wang *et al.* (2016) selected 20 ED beverages to assess their effect on ethanol and acetaldehyde levels in the blood; literature supporting this study suggests that EDs increase the activity of alcohol dehydrogenase, leading to the increased toxic effects of alcohol in the body. Similar findings were reported by Rutledge *et al.* (2012). These cases highlight the dangers of mixing alcohol with EDs.

The effects of carbon dioxide on alcohol absorption

There is evidence suggesting that carbonation, or addition of CO_2 to EDs, may increase the alcohol absorption rate, which will overall lead to toxicity (Attila and Çakir 2011; Velazquez *et al.* 2012). It has been hypothesized that the gas released into the gastric lumen by carbonated beverages causes distension of the stomach, which ultimately elevates the rates of gastric emptying. This is believed to have effects on alcohol absorption rates (Roberts and Robinson 2007). There have been many speculations on carbonation and its effect on alcohol absorption rate therefore, further research needs to be conducted in this aspect of study.

The effects of carbon dioxide on the mucosal blood flow were looked at in a study conducted by Siński *et al.* (2003) whereby the research was investigating if the gastric mucosal blood flow (GMBF) can be influenced by the stimulation of the central chemoreceptors in rats. The experiment was conducted in a hypercapnic-hyperoxic atmosphere with the following chemical components in it and with the following volume fractions present (%, v/v): CO_2 (10 %), N_2 (40 %), and O_2 (50 %). The application of this gas mixture resulted in the activation of the central chemoreceptors which in turn resulted in the decrease of the GMBF. Findings from another research study by Sherwood *et al.* (2015) supported Dean's theory of gastric CO_2 ventilation and proved the hypothesis that, hypercapnia stimulates gastric CO_2 production and ventilation, thus rendering the "gastroesophageal dysfunction".

Health risks associated with chronic consumption of energy drinks among youth

Central nervous system effects

Despite having significant benefits for mental and physical stamina of some or all the above-mentioned ED components, chronic consumption can be potentially dangerous to the CNS. Caffeinism is a pathophysiological condition which results from consuming excessive amount of caffeine of extended periods for time i.e., it is a medical condition which results from chronic abuse of caffeine by an individual. The condition presents itself in the CNS and periphery in the form of anxiety, psychomotor alterations, sleep disturbances, mood disturbances, and the like. Research has shown that abstaining from caffeine causes withdrawal syndrome as a result of prior over-consumption and dependence on the

substance. The withdrawal symptoms include headaches, nausea, vomiting, diarrhea, facial flushes, muscle twitching, restlessness, and cardiac arrhythmias. At the same time, caffeinism can only be clinically diagnosed with blood tests. These symptoms can present themselves as quickly as 24 h from prior ingestion however, it has been reported that reintroducing caffeine into the body alleviates these symptoms within an hour of consumption (Doering *et al.* 2017). A long-term solution may be to gradually wear off caffeine until the individual is no longer dependent on it, or alternatively switch to a caffeine-free product.

If an individual consumes a caffeine dose equal to or above 200 mg, they may develop the symptoms of caffeine toxicity (Alsunni 2015). The most common CNS side effects reported include anxiety, tremors, confusion, irritability, psychosis, agitation, seizures, and altered mental status (Rath 2012; Alsunni 2015). In addition, excessive chronic consumption of caffeine stimulates a "pro-nociceptive state of cortical hyperexcitability that can trigger or intensify headaches" (Espinosa *et al.* 2017). Caffeine induces four psychiatric disorders that are recognized by the Diagnostic and Statistical Manual of Mental Disorders (DSM). This is a diagnostic guideline used by psychiatrists and clinicians to diagnose psychiatric illnesses, namely "caffeine intoxication, caffeine-induced sleep disorder, caffeine-related disorder, and caffeine-induced anxiety disorder" (Bedi *et al.* 2014).

Park *et al.* (2016) sought out to study the association between ED consumption and mood disorders in Korean adolescents. Their findings revealed that ED consumption was statistically significantly linked to sleep problems, extreme stress, "suicidal ideation and a higher risk of suicide attempt" (Park *et al.* 2016). Depending on subjective sensitivity, ED consumption has been linked to events of memory loss, anxiety, and certain types of sleep disorder (Daly *et al.* 1983; Nehlig *et al.* 1992). This has consequentially translated to fatigue during class hours, resulting in behavioural problems and lower academic performance (Dikici *et al.* 2013). The study by Park *et al.* (2016) also suggested a positive association between the consumption of EDs, soft drinks, and fast-food products. Adolescents who consumed EDs and fast-food products for 5 or more days a week were shown to be more susceptible to mental health risks and mood disorders. However, the study results did not indicate that there was a directional causality between ED consumption and mental illness. Further to this point, it can be inferred that stress, anxiety, and sleep disorders could be seen as pathophysiological states that would encourage an adolescent to consume EDs to resume a level of 'functionality'. Thus, a reverse causality is equally plausible. A cross-sectional study was conducted at a primary school in Iceland, whereby a population-based survey was carried out with 11,267 boys and girls aged between 10 – 12 years participating (Visram *et al.* 2016). In this study, the percentage of boys and girls who reported to have consumed EDs daily were 7 % and 3 %, respectively. Some of the symptoms that were experienced and communicated were headaches, stomach-aches, and insomnia. There is currently not enough scientific information on the risks associated with the chronic consumption of EDs by children aged under 12 years, thus more research needs to be done in this age group. Dikici *et al.* (2013) described a case report of a healthy adult male who was rushed to the emergency ward with epileptic seizure and ischemic stroke. This incident occurred following the consumption of three 250 mL EDs with alcohol by the patient. There was no history of epilepsy in the patient or his family. Another case report of an 18-year-old male patient was described by Hernandez-Huerta *et al.* (2017) where the patient on admission presented with a psychotic episode after consuming 6 cans of EDs per day for 7 days. He did not have a history of any psychotic disorders, although his paternal family had a history of undefined mental disease. These case reports suggest that excessive consumption of caffeinated drinks may induce seizures and psychotic disorders.

Cardiovascular system effects

According to WHO, cardio-vascular diseases (CVDs) are the leading cause of global deaths with an estimation of 31 % deaths claimed globally in 2016. The chronic consumption of high-caffeinated beverages is a major concern due to effects they have on the cerebrovascular system. Caffeine is

a sympathomimetic, thus its ingestion causes vasoconstriction and elevates blood pressure, the extent to which is dependent on the dose of caffeine, dosage form (capsule or liquid), and subjective sensitivity (Grasser *et al.* 2016). Doerner *et al.* (2015) studied the effect of ED consumption on myocardial contractility and their investigations found that there was an increased contractility of the left ventricle an hour after ingestion of caffeine and taurine mixture. In addition, observed an increase in diastolic pressure when caffeine was consumed alone. Other such studies have confirmed the blood pressure elevating effect of caffeinated drinks, and all account conclude that ED consumption is directly associated with, at the very least, acute increases in blood pressure (Cavka *et al.* 2015). Nowak *et al.* (2018) on the other hand, reported a statistically significant increase in the diastolic blood pressure based on the results of a study on 68 young adolescents. With dependence being a very possible outcome of consistent use of and tolerance to caffeinated EDs, it is possible for EDs to become a dangerous dietary addition that in the long term, may potentiate events such as early onset hypertension and other cardiovascular illnesses such as tachycardia.

Cannon *et al.* (2001) wrote up and published a case report on the health outcomes of a 25-year-old Australian woman, who developed intractable ventricular fibrillation, a condition where the heart quivers in beat rather than in rhythm, caused by a combination of their consumption of a "natural energy" guarana health drink and the underlying pre-existing mitral valve prolapse. The case was already studied by other authors, but it is mentioned here against due to its clinical significance (Doering *et al.* 2017). The patient was discovered to have consumed a 55 mL squirt bottle of an ED with guarana and ginseng, and it was confirmed that she had no other sources of dietary caffeine apart from tea. During her autopsy, toxicologists detected caffeine in her aortic blood at a concentration of 19 $mg.L^{-1}$, the equivalent of 15 – 20 cups of coffee and the link had been made to the natural ED consumed as it contained 10 $g.L^{-1}$of caffeine. Despite the patient having a pre-existing cardiac condition, the levels of caffeine in her blood including the post-mortem results, indicated the extremely high concentrations of caffeine from the consumed ED which potentiated a fatal cardiac arrhythmia (Cannon *et al.* 2001). Another case report of a 13-year-old female who was consuming EDs every day for two consecutive weeks was described by Mangi *et al.* (2017). The patient was presented to the hospital with chest pains, palpitations and her QT interval was prolonged. A genetic test was performed which confirmed that she had a long QT syndrome (LQTS). This is a condition where the heart's electronic system is disordered and takes a long to recharge after each heartbeat, resulting in a QT interval longer than normal. This disorder occurs when there is a defect in the ion channels and can lead to a potentially life-threatening cardiac arrhythmia.

Regulations and advertising legislation for caffeinated beverages in South Africa

The market for EDs in South Africa has been rising rapidly, with an estimated increase of 2 to 3 L per capita between the years 2009 and 2014 (Stacey *et al.* 2017). Advertising is one of the driving factors that influences consumption and spikes the volume of sales. Stacey *et al.* (2017) studied the consumption of EDs and the influence of marketing in South Africa. Their findings revealed that there is minimal scientific research on the advertisement and the consumption of caffeinated beverages in South Africa. The government introduced a sugar tax on soft drinks with the aim to reduce their consumption. This proposal was published in 2016 and came into effect on the 1st of April 2018; where some manufacturers replaced the sugar with artificial sweeteners (Zero sugar drinks), some reduced the sugar whilst others remained the same.

The Minister of Health has amended the regulations of soft drinks, and the legislation that has been put into place requires manufacturers to display the following messages on the label of the container with capital letters of a height not less than 3.0 mm (South Africa. Department of Health 2018): i) "High caffeine content"; ii) "Not recommended for children under 12 years of age, pregnant women, persons sensitive to caffeine and not to be consumed as a mixture with alcohol beverages". The manufacturers are also required to state the amount of caffeine in mg/serving size and mg/100 mL. The executive director of the BevSA

declared that all their members have signed a marketing code that prevents the marketing to children younger than 12 years as regulated (South Africa, Department of Health 2018). Although a marketing code has been signed, there still seems to be an aggressive marketing that attracts diverse children who are particularly below 12 years of age, tom. For example, one of the most popular EDs is highly marketed to events such as the X-games, wrestling (WWE) and other extreme sports which attract a large adolescent demographic.

Suggested proposals for the public health management of ED consumption by children and adolescents in South Africa

According to Curran and Marczinski (2017) seventy percent of children, as well as around 40 % of teenagers, consumed caffeine doses in excess of the 3 $mg.kg^{-1}$.day. Such consumption levels can result in adverse caffeine effects just by consuming one ED together with other food sources. The results were calculated from an experiment where the following population groups; "5 – 12 years old (children), 13 – 19 years old (adolescents) and 20 – 24 years old (young men) had consumed a single retail unit of ED" (Curran and Marczinski 2017). These experimental results, along with the EDs-related scientific information mentioned in this article, show the seriousness of this (potential) health-related issues from the consumption of EDs. As a result, policy interventions are needed to protect the health of children and adolescents against EDs. Given that caffeine is a psychostimulant drug with proven adverse effects upon high consumption, its inclusion in soft drinks should be treated the same way as other drugs, such as alcohol. The fact that the packaging label states that ED is "Not recommended for children under 12" (Curran and Marczinski 2017), should propel the banning of its sales to children, and places such as schools and events organised for children should not allow EDs to be sold there.

Stacey *et al.* (2017) studied the consumption of EDs and the influence of marketing in South Africa, their findings revealed that there is minimal scientific research on the advertisement and the consumption of caffeinated beverages in South Africa. They further concluded that viewers, who are exposed to TV channels that advertise EDs are likely to be consumers. How the viewers comprehend the message of the advertisement differs, especially when it comes to their (health) literacy levels. A child/South African citizen, who is proficient in English, will understand an advert about EDs very differently when compared to their counterparts, whose mother tongue or major medium of communication is not English. The same applies to parents or guardians; most of these adverts, including the packaging labels are written in English and the comprehension may differ in accordance with the English-proficiency level or mother tongue of the speaker. Therefore parents/guardians and their approach to their children ED consumption might differ.

More focus should be placed on regulatory measures to update the ED packaging labels. Specifically speaking about EDs, the label should be designed and populated with information so that "all" children, who are 12 years or younger, including adolescents and parents/guardians, are able to understand the packaging label and avoid the negative side-effects of ED consumption. Considering the education disparities that some parts of the population in South Africa are subjected to, raises the potential challenge of the general and universal application of English as the language of the labels and medium to disseminate information about the ED health effects. This calls for more regulatory measures to be implemented to overcome such challenges. To address the challenges related to of the EDs consumption by children and adolescents, educational health programmes and campaigns targeted at children, adolescents, adults (particularly parents and guardians) need to be initiated and rolled out at school and community levels (especially the low-income parts of South Africa). Pamphlets and posters showing images of the harm caused by the chronic usage of EDs can be distributed near and around social places. Social media is one of the platforms that could be used to mostly reach adolescents with the ED-related public health campaigns.

Conclusion

In the current article, the authors sought to place a focus on some of the health risks associated with the chronic consumption of EDs in children and adolescents. Additionally, they propose interventions that can be implemented to address this issue. The exponential growth of the sales and consumption of EDs needs to be matched with strict regulatory measures to protect vulnerable population groups from the associated health risks. EDs are dangerous to the health of children and adolescents, therefore consumption of EDs by this age group should be targeted for urgent public health interventions. South Africa has one of the most unequal societies in the world and the country is still draped with inequalities inherited from the colonial times. Socio-economic factors therefore play an important in public health. Any intervention must be targeted for the local education and literacy levels have, as well as the links to the decision-making of consumers in relation to EDs. The parental guidance provided to children and adolescents in relation to the consumption of these beverages in South Africa.

Conflict of Interest

The authors declare that there is no conflict of interest.

References

Ahamad J, Mir SR, Amin S (2019) A pharmacognostic review on *Artemisia absinthium*. Int. Res. J. Pharm. 10: 25-31.

Al-Goblan AS, Al-Alfi MA, Khan MZ (2014) Mechanism linking diabetes mellitus and obesity. Diabetes Metab. Syndr. Ob. 7: 587-591.

Alsunni AA (2015) Energy drink consumption: Beneficial and adverse health effects. Int. J. Health Sci. (Qassim) 9: 468-474.

Attila S, Çakir B (2011). Energy-drink consumption in college students and associated factors. Nutrition. 27: 316-322.

Babu KM, Church RJ, Lewander W (2008) Energy drinks: The new eye-opener for adolescents. Clin. Pediatr. Emerg. Med. 9: 35-42.

Bailey RL, Saldanha LG, Dwyer JT (2014) Estimating caffeine intake from energy drinks and dietary supplements in the United States. Nutr. Rev. 72 (Suppl 1): 9-13.

Batiha GES, Olatunde A, El-Mleeh A, Hetta HF, Al-Rejaie S, Alghamdi S, Zahoor M, Beshbishy AM, Murata T, Zaragoza-Bastida A, Rivero-Perez N (2020) Bioactive compounds, pharmacological actions, and pharmacokinetics of wormwood (*Artemisia absinthium*). Antibiotics 9: 353.

Bedi N, Dewan P, Gupta P (2014) Energy drinks: potions of illusion. Indian Pediatr. 51: 529-533.

Brain M, Bryant CW, Cunningham M (2007) How caffeine works. https://science.howstuffworks.com/caffeine4.htm (accessible on Sept 16, 2022).

Bray GA, Nielsen SJ, Popkin BM (2004) Consumption of high-fructose corn syrup in beverages may play a role in the epidemic of obesity. Am. J. Clin. Nutr. 79: 537-543.

Bruns RF, Daly JW, Snyder SH (1980) Adenosine receptors in brain membranes: binding of N6-cyclohexyl[^{3}H]adenosine and 1,3-diethyl-8-[^{3}H]phenylxanthine. Proc. Natl. Acad. Sci. USA 77: 5547-5551.

Campbell B, Wilborn C, la Bounty P, Taylor L, Nelson MT, Greenwood M, Ziegenfuss TN, Lopez HL, Hoffman JR, Stout JR, Schmitz S, Collins R, Kalman DS, Antonio J, Kreider RB (2013) International society of sports nutrition position stand: energy drinks. J. Int. Soc. Sports Nutr. 10: 1.

Cannon ME, Cooke CT, McCarthy JS (2001) Caffeine-induced cardiac arrhythmia: An unrecognised danger of healthfood products. Med. J. Aust. 174: 520-521.

Cavka A, Stupin M, Panduric A, Plazibat A, Cosic A, Rasic L, Debeljak Z, Martinovic G, Drenjancevic I (2015) Adrenergic system activation mediates changes in cardiovascular and psychomotoric reactions in young individuals after RedBull© energy drink consumption. Int. J. Endocrinol. 2015: 751530.

Chan CY, Sun HS, Shah SM, Agovic MS, Ho I, Friedman E, Banerjee SP (2013) Direct interaction of taurine with the NMDA glutamate receptor subtype via multiple mechanisms. *In* El Idrissi A, L'Amoreaux W (eds), Taurine 8. Advances in Experimental Medicine and Biology, Springer, New York, NY, USA, pp. 42-52.

Chen F, Hu ZY, Parker RB, Laizure SC (2017) Measurement of caffeine and its three primary metabolites in human plasma by HPLC-ESI-MS/MS and clinical application. Biomed. Chromatogr. 31: e3900.

Children's Food Trust (2012) Voluntary food and drink guidelines for early years settings in England – A practical guide. http://cft-staging-cdn.core-clients.co.uk.s3-eu-west 1.amazonaws.com/2015/06/CFT_Early_Years_Guide_Interactive_Sept-12.pdf (accessible on Sept 16, 2022).

Conlay LA, Conant JA, deBros F, Wurtman R (1997) Caffeine alters plasma adenosine levels. Nature 389: 136.

Curran CP, Marczinski CA (2017) Taurine, caffeine, and energy drinks: Reviewing the risks to the adolescent brain. Birth Defects Res. 109: 1640-1648.

Cuttitta CM, Guariglia SR, El Idrissi A, L'Amoreaux WJ (2013) Taurine's effects on the neuroendocrine functions of pancreatic β cells. *In* El Idrissi A, L'Amoreaux W (Eds.), Taurine 8. Advances in Experimental Medicine and Biology, Springer, New York, NY, USA, pp. 299-310.

Daly JW, Butts-Lamb P, Padgett W (1983) Subclasses of adenosine receptors in the central nervous system:

Interaction with caffeine and related methylxanthines. Cell. Mol. Neurobiol. 3: 69-80.

Dikici S, Saritas A, Besir FH, Tasci AH, Kandis H (2013) Do energy drinks cause epileptic seizure and ischemic stroke? Am. J. Emerg. Med. 31: P274.E1-274.E4.

Doering PL, Moorman Li R (2017) Substance-Related Disorders II: Alcohol, Nicotine, and Caffeine. *In* DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG Posey LM (Eds.), Pharmacotherapy: A Pathophysiologic Approach, McGraw-Hill Education, USA, chapter 66.

Doerner JM, Kuetting DL, Luetkens JA, Naehle CP, Dabir D, Homsi R, Nadal J, Schild HH, Thomas DK (2015) Caffeine and taurine containing energy drink increases left ventricular contractility in healthy volunteers. Int. J. Cardiovasc. Imaging 31: 595-601.

Dombovy-Johnson M (2010) The effects of taurine and caffeine alone and in combination on locomotor activity in the rat. Col. Acad. Rev. 7: 10 (170-188).

Elzoghby AO, Elgohary MM, Kamel NM (2015) Implications of protein- and peptide-based nanoparticles as potential vehicles for anticancer drugs. Adv. Protein Chem. Struct. Biol. 98: 169-221.

Erdmann J, Wiciński M, Wódkiewicz E, Nowaczewska M, Słupski M, Otto SW, Kubiak K, Huk-Wieliczuk E, Malinowski B (2021) Effects of energy drink consumption on physical performance and potential danger of inordinate usage. Nutrients 13: 2506.

Espinosa Jovel CA, Sobrino Mejía FE (2017) Cafeína y Cefalea: Consideraciones Especiales. Neurología 32: 394-98.

European Food Safety Authority (2015) EFSA Explains Risk Assessment: Caffeine. EFSA.

Ferré S, O'Brien MC (2011) Alcohol and caffeine: The perfect storm. J. Caffeine Res. 1: 153-62.

Froiland K, Koszewski W, Hingst J, Kopecky L (2004) Nutritional supplement use among college athletes and their sources of information. Int. J. Sport. Nutr. Exerc. Metab. 14:104-120.

Goran MI, Ulijaszek SJ, Ventura EE (2013) High fructose corn syrup and diabetes prevalence: A global perspective. Glob. Public Health 8: 55-64.

Grasser EK, Miles-Chan JL, Charrière N, Loonam CR, Dulloo AG, Montani JP (2016) Energy drinks and their impact on the cardiovascular system: Potential mechanisms. Adv. Nutr. 7: 950-960.

Gunnars K (2022) 4 Stimulants in tea - More than just caffeine. https://www.healthline.com/nutrition/stimulants-in-tea (accessible on Sep 18, 2022).

Heckman MA, Sherry K, Gonzalez de Mejia E (2010) Energy drinks: An assessment of their market size, consumer demographics, ingredient profile, functionality, and regulations in the United States. Compr. Rev. Food. Sci. Food. Saf. 9: 303-317.

Hernandez-Huerta D, Martin-Larregola M, Gomez-Arnau J, Correas-Lauffer J, Dolengevich-Segal H (2017) Psychopathology related to energy drinks: a psychosis case report. Case Rep. Psychiatry 2017: 5094608.

Higgins JP, Tuttle TD, Higgins CL (2010) Energy beverages: content and safety. Mayo Clin. Proc. 85: 1033-1041.

Hoffman JR (2010) Caffeine and Energy Drinks. J. Strength Cond. Res. 32: 15-20.

Kammerer M, Jaramillo JA, García A, Calderón JC, Valbuena LH (2014) Effects of energy drink major bioactive compounds on the performance of young adults in fitness and cognitive tests: A randomized controlled trial. J. Int. Soc. Sport. Nutr. 11: 44.

Klabunde RE (2020) Phosphodiesterase inhibitors. https://www.cvpharmacology.com/vasodilator/PDEI (accessible on Oct 21, 2022).

L'Amoreaux WJ, Marsillo A, El Idrissi A (2010) Pharmacological characterization of GABAA receptors in taurine-fed mice. J. Biomed. Sci. 17 (Suppl 1): S14.

Lachenmeier DW (2010) Letter to the editor: Wormwood (*Artemisia absinthium* L.) - A curious plant with both neurotoxic and neuroprotective properties? J. Ethnopharmacol. 131: 224-227.

Lee S, Hudson R, Kilpatrick K, Graham TE, Ross R (2005) Caffeine ingestion is associated with reductions in glucose uptake independent of obesity and type 2 diabetes before and after exercise training. Diabetes Care 28: 566-572.

Li S, Gan LQ, Li SK, Zheng JC, Xu DP, Li HB (2014) Effects of herbal infusions, tea and carbonated beverages on alcohol dehydrogenase and aldehyde dehydrogenase activity. Food Funct. 5: 42-49.

Lin FJ, Pierce MM, Sehgal A, Wu T, Skipper DC, Chabba R (2010) Effect of taurine and caffeine on sleep - wake activity in *Drosophila melanogaster*. Nature Sci. Sleep 2010: 221-231.

MacKnight JM (2020) Energy drink use in sport. Cur. Sports Med. Report. 19: 102-103.

Mangi MA, Rehman H, Rafique M, Illovsky M (2017) Energy drinks and the risk of cardiovascular disease: a review of current literature. Cureus 9: e1322.

Nawrot P, Jordan S, Eastwood J, Rotstein J, Hugenholtz A, Feeley M (2003) Effects of caffeine on human health. Food Addit. Contam. 20: 1-30.

Nehlig A, Daval JL, Debry G (1992) Caffeine and the central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects. Brain Res. Rev. 17: 139-170.

Nowak D, Gośliński M, Nowatkowska K (2018) The effect of acute consumption of energy drinks on blood pressure, heart rate and blood glucose in the group of young adults. Int. J. Environ. Res. Public Health. 15: 544.

Ogasawara M, Nakamura T, Koyama I, Nemoto M, Yoshida T (1994). Reactivity of taurine with aldehydes and its physiological role. *In* Huxtable RJ, Michalk D (eds), Taurine in health and disease, Advances in Experimental Medicine and Biology, Springer, Boston, MA, USA, pp. 71-78.

Park S, Lee Y, Lee JH (2016) Association between energy drink intake, sleep, stress, and suicidality in Korean adolescents: Energy drink use in isolation or in combination with junk food consumption. Nutr. J. 15: 87.

Petre A (2020) What is caffeine, and is it good or bad for health? https://www.healthline.com/nutrition/what-is-caffeine (accessible on Sept 16, 2022).

Ragsdale FR, Gronli TD, Batool N, Haight N, Mehaffey A, McMahon EC, Nalli TW, Mannello CM, Sell CJ, McCann PJ, Kastello GM, Hooks T, Wilson T (2010) Effect of Red Bull energy drink on cardiovascular and renal function. Amino Acids 38: 1193-1200.

Rath M (2012) Energy drinks: what is all the hype? The dangers of energy drink consumption. J. American Acad. Nurse Practitioners 24: 70-76.

Reid JL, Hammond D, McCrory C, Dubin JA, Leatherdale ST (2015) Use of caffeinated energy drinks among secondary school students in Ontario: Prevalence and correlates of using energy drinks and mixing with alcohol. Can. J. Public Health 106: e101-e108.

Reyes-Haro D, Cabrera-Ruíz E, Estrada-Mondragón A, Miledi R, Martínez-Torres A (2014) Modulation of GABA-A receptors of astrocytes and STC-1 cells by taurine structural analogs. Amino Acids 46: 2587-2593.

Richter F (2014) Energy drinks. https://www.statista.com/chart/1935/statistics-on-energy-drinks/ (accessible on Sept 16, 2022).

Riksen NP, Rongen GA, Smits P (2009) Acute and long-term cardiovascular effects of coffee: Implications for coronary heart disease. Pharmacol. Ther. 121: 185-191.

Ripps H, Shen W (2012) Review: Taurine a 'very essential' amino acid. Mol. Vis. 18: 2673-2686.

Roberts C, Robinson SP (2007) Alcohol concentration and carbonation of drinks: The effect on blood alcohol levels. J. Forensic Leg. Med. 14: 398-405.

Rutledge M, Witthed A, Khouzam RN (2012) It took a Redbull to unmask brugada syndrome. Int. J. Cardiol. 161: e14-e15.

Schaffer S, Kim HW (2018) Effects and mechanisms of taurine as a therapeutic agent. Biomol. Ther (Seoul). 26: 225-241.

Schaffer SW, Shimada-Takaura K, Jong CJ, Ito T, Takahashi K (2016) Impaired energy metabolism of the taurine-deficient heart. Amino Acids 48: 549-558.

Schaffer SW, Jong CJ, Ramila KC, Azuma J (2010) Physiological roles of taurine in heart and muscle. J. Biomed. Sci. 17: S2.

Sharma H (2020) A detail chemistry of coffee and its analysis. *In* Castanheira, ED (eds), Coffee - production and research, IntechOpen, Rijeka, Croatia, pp. 79.

Sherwood J, Landon C, Dean J (2015) Chronic CO_2 retention stimulates gastric acid secretion and induces gastric mucosal hyperplasia in rats. The FASEB Journal 29 (S1): 849.8.

Siński, M, Kowalczyk P, Stolarczyk A, Sawionek Ł, Przybylski J (2003) Influence of the stimulation of central chemoreceptors on the gastric mucosal blood flow in artificially ventilated and spontaneously breathing rats. J. Physiol. Pharmacol 54: 553-559.

Soós R, Gyebrovszki Á, Tóth Á, Jeges S, Wilhelm M (2021) Effects of caffeine and caffeinated beverages in children, adolescents and young adults: short review. Int. J. Environ. Res. Public Health 18: 12389.

South African National Department of Health (2018) Regulations no. 638 governing general hygiene requirements for food premises, the transport of food and related matters. https://www.cgcsa.co.za/wp-content/uploads/2019/04/Hygiene-Regulations-R.638.pdf. (accessible on Sep 16, 2022).

Stacey N, van Walbeek C, Maboshe M, Tugendhaft A, Hofman K (2017) Energy drink consumption and marketing in South Africa. Prev. Med. 105: S32-S36.

Sun M, Zhao YM, Gu Y, Xu C (2012) Therapeutic window of taurine against experimental stroke in rats. Transl. Res. 160: 223-229.

Tappy L, Lê KA (2010) Metabolic effects of fructose and the worldwide increase in obesity. Physiol. Rev. 90: 23-46.

Turnbull D, Rodricks JV, Mariano GF, Chowdhury F (2017) Caffeine and cardiovascular health. Regul. Toxicol. Pharmacol. 89: 165-185.

U.S Department of Health & Human Services (2007) Alcohol Alert 72. https://pubs.niaaa.nih.gov/publications/aa72/AA72.pdf (accessible on Sep 17, 2022).

Usman A, Jawaid A (2012) Hypertension in a young boy: An energy drink effect. BMC Res. Notes 5: 591.

Velazquez CE, Poulos NS, Latimer LA, Pasch KE (2012) Associations between energy drink consumption and alcohol use behaviors among college students. Drug Alcohol Depend. 123: 167-172.

Visram S, Cheetham M, Riby DM, Crossley SJ, Lake AA (2016) Consumption of energy drinks by children and young people: A rapid review examining evidence of physical effects and consumer attitudes. BMJ Open 6: e010380.

Vitvitsky V, Garg SK, Banerjee R (2011) Taurine biosynthesis by neurons and astrocytes. J. Biol. Chem. 286: 32002-32010.

Wang F, Zhang YJ, Zhou Y, Li Y, Zhou T, Zheng J, Zhang JJ, Li S, Xu DP, Li HB (2016) Effects of beverages on alcohol metabolism: potential health benefits and harmful impacts. Int. J. Mol. Sci. 17: 354.

Wu JY, Prentice H (2010) Role of taurine in the central nervous system. J. Biomed. Sci. 17 (Suppl 1): S1.