beverages

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Review

Caffeinated Beverages—Unveiling Their Impact on Human Health

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Abstract: Caffeine is among the most commonly used and consumed stimulants worldwide. It is a naturally occurring stimulant mainly found in coffee and tea. It is also present in sweetened beverages, which are very popular among young people. Recently, the consumption of energy drinks has been increasing, which are other examples of drinks containing caffeine. Is caffeine beneficial or harmful to human health? Due to its antioxidative properties, it has become attractive for many scientific studies. Caffeine consumption can have both positive and negative effects on the human body; it affects the activity of the digestive and respiratory systems, the function of the urinary tract, and the function of the central nervous system. Caffeine is a psychostimulant. It increases brain activity and alertness, reducing the perception of fatigue. Many people consume beverages containing caffeine to experience these effects, which can help them stay awake and focused. However, high consumption may not be beneficial to health; it is also associated with increased headaches and insomnia. The effects of caffeine on the body depend on its dosage, the type of drink consumed, and individual variability. It is also essential to know its effect on the body during pregnancy. This review discusses the latest knowledge about caffeine's positive and negative impacts on the human body, as nowadays, more and more people, especially younger people, reach for energy drinks.

Keywords: caffeine; caffeinated beverages; coffee; energy drinks; tea

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1. Introduction

Caffeine is one of the most commonly consumed substances. Besides the social aspects, its effects, such as taste, improved concentration, and increased physical energy, are attributed to its consumption [1]. Caffeine is present in many plants; its primary source is the coffee plant (leaves and beans). However, it may also be present in other plants, such as tea leaves, yerba mate, guarana berries, and cacao beans [2]. Caffeine may also be found in energy drinks, soft drinks, gums, and medications [1,3]. In 2020–2021, coffee consumption was nearly 176 million bags with a weight of 60 kg worldwide [4]. South America, specifically Brazil, is considered the leading coffee producer worldwide, followed by Vietnam and Colombia. Coffee plants are grown in more than 70 tropical countries, and coffee is the second most exported commodity in the world after oil [5].

More and more people worldwide enjoy drinking coffee because of its distinctive aroma and taste, and it is slowly becoming a habit and a part of the culture in many countries. Therefore, caffeine intake is part of people's daily routines worldwide. Caffeine is the subject of increasing scientific interest because it is a bioactive molecule with both

positive and negative effects on various systems. It has been shown to affect the urinary tract, as well as the central nervous, digestive, and respiratory systems [6–8].

Many studies focus on caffeine's effect on exercise performance [9,10]. Caffeine is used in ergogenic supplement formulations during exercise. Its ergogenic effects may be due to factors such as increased substrate utilization, delayed fatigue, and alertness [9]. A moderate dose of caffeine before exercise can effectively increase fat utilization during aerobic exercise performed after a period of fasting. Of course, the participant's fitness level is also important, which may modulate the magnitude of the effect of caffeine on fat oxidation during exercise [10]. It was also observed that caffeine affects bone mineral density [11,12].

Table 1 summarizes the most important beneficial and adverse effects of caffeine. The effect depends on the quantity and individual differences. Children, adolescents, people with hypertension, and older people may be more susceptible to the adverse effects of caffeine consumption [6].

Table 1. Beneficial and adverse effects of caffeine.

	Beneficial Effects of Caffeine	**Adverse Effects of Caffeine**
Nervous system	psychostimulant [6,13,14], boosts alertness, concentration, mood, overall well-being [13], reduces risks of cognitive decline [13], stroke [13], Alzheimer's disease [6,13], and Parkinson's disease [6,13], increases mental performance and vigilance, reduces the risk of depression [7]	addiction [15], insomnia [6,7,11,15], anxiety, restlessness [6,7], nervousness, facial flushing, irritability, muscle twitching, disorientation, hallucinations, psychosis, seizures [16] insomnia and induces anxiety [7]
Cardiovascular system	increases blood pressure in the short term (partial tolerance develops with regular intake) [7]	tachycardia or irregular heartbeat, arrhythmias, ischemia, and rhabdomyolysis [16]
Urinary tract	decrease kidney stone formation, decrease renal fibrosis [6]	diuretic effect [6,11,16,17], hypercalciuria [11]
Musculoskeletal system		increases risk of osteoporosis and hip fracture [11], inhibits vitamin D receptor activity, increases the urinary excretion of calcium [12],
Gastrointestinal tract	stimulate hydrochloric acid secretion, increase gastric acid secretion, increase gastric acid concentration [6], reduce the risk of liver fibrosis, cirrhosis, and cancer [7], anti-inflammatory activity, reduce cancer risk [8]	gastrointestinal irritation [16], interference with absorption of iron [11], higher risk of inflammation of the intestinal mucosa and stomach [6]
Endocrine system	reduces skeletal muscle insulin sensitivity in the short term (tolerance develops with habitual intake) [7]	
Reproductive system		reduces fetal growth, increases the risk of pregnancy loss [7,17], stillbirth, and neonatal death [17]
Lungs	benefit premature infants with apnea by reducing lethargy and helping with orthostatic hypotension [7,18]	

This review overviews the caffeine molecule, its properties, and its metabolism. It focuses on caffeine-containing beverages, which are among the most popular beverages (after water) among adults and older people worldwide. Other popular caffeine-containing beverages, like energy and sweetened drinks, are particularly favored by young peo-

ple, adolescents, and even children. This article also describes the composition of these beverages and their potential effects on the human body.

2. Methods

This review aimed to collect currently available data on scientific publications describing the structure and metabolism of caffeine, the effects of caffeine and caffeinated beverages (coffee, tea, energy drinks, and sweetened beverages containing caffeine) on human health, and the mechanisms of action of caffeine. Both research articles and review articles were included in the manuscript. Articles written in a language other than English were excluded. Keywords and permutations of phrases and their combination used in the search were: caffeine, dosage of caffeine, dosage of caffeine according to age, health benefits of caffeine, adverse effects of caffeine, caffeine metabolism, caffeinated drinks, coffee, tea, energy drinks, caffeinated sweetened beverages, and their combinations. The primary sources used for literature searches during the preparation of this manuscript were Google Scholar, PubMed, ScienceDirect, and Scopus databases. In addition, information from additional scientific databases and websites such as the National Institutes of Health, World Population Review, Pubchem, Food Drug Administration, European Food Safety Authority, and WHO was also included. Due to missing data, the original time range of articles in the last 10 years was extended to include papers from 1990.

3. Caffeine

Caffeine (1,3,7-trimethylxanthine, also known as guaranine or methyltheobromine) (Figure 1) is an odorless, white powder with a bitter taste [19,20]. Caffeine is water soluble and fat soluble and is distributed throughout the body. Caffeine can cross the blood–brain barrier [20]. Caffeine is freely soluble in pyrrole, soluble in pyridine, acetone, chloroform, ether, and benzene, slightly soluble in petroleum ether, freely soluble in tetrahydrofuran containing 4% water [21].

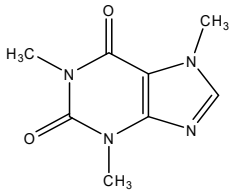

Figure 1. Structure of caffeine.

Caffeine is a naturally occurring plant-derived compound that belongs to the purine alkaloids, with the molecular formula $C_8H_{10}N_4O_2$ and a molecular weight of 194.19 g/mol [20]. Caffeine was first isolated from coffee seeds in 1820 by German scientists Runge and Von Giese [22,23]. It can also be produced synthetically through the methylation of xanthines and theophylline [3,6].

Regarding plant composition, caffeine comprises approximately 2–5% of the dry matter of tea and 1–2% of the dry matter of coffee [22]. Its biosynthesis occurs via a four-step reaction pathway (Figure 2), including three methylation reactions and one nucleosidase reaction, with xanthine as the precursor. The enzyme N-methyltransferase catalyzes the first, third, and fourth steps and requires S-adenosyl-L-methionine (SAM) as the methyl group donor [22,24].

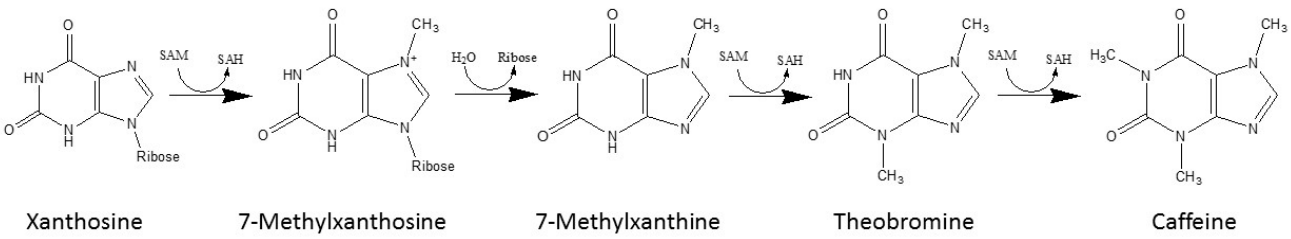

Figure 2. Biosynthetic pathway of caffeine from xanthosine (adapted from [25]).

Caffeine can be consumed in various forms: through drinks, in pills or capsules, in stick formats, or even as chewing gum [26].

The average daily caffeine dose for adults is estimated at 2.4 mg/kg of body weight (bw) [27], with up to 400 mg considered safe for most adults [27,28]. Individual sensitivity to caffeine varies widely, as does the rate of caffeine metabolism, influenced by factors such as fatigue, smoking status, age, and time of day [26,28]. The European Food Safety Authority (EFSA) published a document recommending a safe single dose of caffeine according to age (Table 2). For toddlers (12–36 months), there is no available information about a safe single dose of caffeine intake; for children aged 3–10 years, it is 3 mg/kg bw; for adolescents (10–18 years) it is 3 mg/kg bw, and for adults, elderly and very elderly it is 200 mg or 3 mg/kg bw. Caffeine daily intake was also estimated; a daily dose of caffeine varies between individual age groups. It was estimated to be 0–2.1 mg/kg/bw in toddlers. It is slightly higher in children's age, specifically 0.2–2.0 mg/kg bw; in adolescents, it is 0.4–1.4 mg/kg bw. In adults, the elderly, and the very elderly, the daily caffeine dose was estimated at 37–319 mg, 23–362 mg, and 22–417 mg, respectively [29]. However, caffeine intake in childhood can interfere with normal development, affecting skills acquisition, emotional health, and social well-being. Children with existing health conditions like high blood pressure, chronic kidney disease, or anxiety disorders may experience more pronounced side effects [30].

Table 2. The average caffeine daily intake and safe single dose of caffeine according to age (adapted from [29]) among the Member States of the European Union.

Age		Caffeine Dosage (Range)	Safe Single Dose of Caffeine
12–36 months	Toddlers	0–2.1 mg/kg bw	N/A
3–10 years	Children	0.2–2.0 mg/kg bw	3 mg/kg bw
10–18 years	Adolescent	0.4–1.4 mg/kg bw	3 mg/kg bw
18–65 years	Adults	37–319 mg	200 mg (3 mg/kg bw)
65–75 years	Elderly	23–362 mg	200 mg (3 mg/kg bw)
75 years and above	Very elderly	22–417 mg	200 mg (3 mg/kg bw)

N/A—not available; mg = milligrams; kg = kilograms; bw = body weight.

During pregnancy, a maximum daily intake of 200 mg is recommended, as excess caffeine may increase the risks of complications such as low birth weight, premature birth, stillbirth, and miscarriage [31,32].

In the food industry, caffeine is used as an additive to enhance flavor and alleviate fatigue. It is a key ingredient in many foods and beverages (e.g., tea, coffee, chocolate, mate, guarana, energy drinks, and sports supplements) [19,22]. In the cosmetic industry, caffeine is incorporated into topical weight loss and skin care products due to its antioxidative properties, ability to prevent fat accumulation, and support for skin microcirculation. Moreover, caffeine is also used in the treatment of cellulite [22,33]. Caffeine is a component

of both prescription and over-the-counter medications for headaches and colds, where it enhances the analgesic effects of these drugs [33].

3.1. Metabolism of Caffeine in the Human Body

It has demonstrated protective properties against oxidative stress, acting as a potent antioxidant and stimulant for the nervous system [34]. Caffeine can improve attention and memory at low doses and may even have anti-cancer and diuretic effects. It is also common in performance-enhancing supplements for athletes [33]. Specific populations are more susceptible to caffeine's adverse effects, including pregnant and breastfeeding women, children, adolescents, young adults, individuals with heart or mental health conditions, and those with other health concerns. Due to new caffeine-containing products and evolving consumption patterns, health and regulatory authorities are increasing oversight of total caffeine intake and its potential cumulative effects on behavior and physiology [35]. Caffeine is typically consumed through drinks and food. This molecule is soluble in both water and lipids, allowing it to easily cross the blood–brain barrier and be present in all body fluids, including cerebrospinal fluid and saliva. In pregnant and breastfeeding women, caffeine is also found in the umbilical cord and breast milk, thus reaching both the fetus and breastfed infants [6,35]. When ingested orally, caffeine is rapidly and completely absorbed through the stomach and small intestine, entering the bloodstream within an hour and diffusing into tissues. Due to its hydrophobic nature, caffeine can cross all biological membranes. In humans, the peak plasma concentration of caffeine typically reaches 15–20 min after oral ingestion [36]. Its stimulating effects may begin within 15–30 min and last for several hours [29].

No significant differences have been noted in caffeine absorption by the small intestine across gender, environmental factors, genetic background, or other variables [35]. Caffeine is metabolized in the liver through phase I enzymes specifically the cytochrome P450 oxidase system. The enzyme CYP1A2 is responsible for about 80% of its metabolism, converting caffeine into three primary metabolites: paraxanthine (84%), theobromine (12%), and theophylline (4%) [36]. Paraxanthine, the main metabolite from caffeine's 3-demethylation, is formed alongside theobromine (3,7-dimethylxanthine) and theophylline (1,3-dimethylxanthine) through the actions of CYP1A2 [6,37].

These metabolites may undergo further demethylation by CYP1A2, acetylation by N-acetyltransferase 2, and oxidation by xanthine oxidase or CYP3A4. Most caffeine metabolites are excreted in the urine, including 1-methyluric acid, 5-acetylamino-6-formylamino-3-methyluracil, 1-methylxanthine, 1,7-dimethyluric acid, and paraxanthine [38]. Only a tiny percentage (0.5–4%) of caffeine is excreted unchanged in bile and urine [39]. Paraxanthine is the primary metabolite in plasma, while methylated xanthines and methyluric acids are the main metabolites excreted in the urine [37].

Caffeine's half-life varies significantly between individuals and depends on factors like age, body weight, pregnancy status, medication use, liver health, and enzyme levels. In healthy adults, caffeine's half-life averages about 3–4 h; for women taking oral contraceptives, it extends to 5–10 h, while in pregnant women, it ranges from 9 to 11 h [6,29,40]. In infants and young children, caffeine's half-life is much longer, at approximately 65–130 h, due to the immaturity of their kidneys and liver [35].

Caffeine consumed by the mother readily crosses the placental barrier, reaching the fetus. However, neither the placenta nor the fetus can metabolize caffeine effectively. This is because the placenta contains CYP1A1 isoenzymes but lacks CYP1A2, and the fetus does not produce the liver enzymes to metabolize caffeine [41,42]. Caffeine can impact fetal development, potentially leading to chromosomal anomalies, growth restrictions, and low

birth weight [33]. High caffeine consumption during pregnancy is also associated with an increased risk of miscarriage [43].

3.2. The Mechanism of Action of Caffeine in the Human Body

Caffeine operates through several mechanisms in the human body. Its actions include (A) acting as an antagonist of adenosine receptors, (B) acting as an antagonist of glycine receptors, (C) inhibiting phosphodiesterase enzymes, (D) releasing calcium from intracellular stores, and (E) serving as a $GABA_A$ receptor antagonist [14,40,44,45]. The most significant effect of caffeine is its antagonism of adenosine receptors, specifically through the non-selective blockade of A1 and A2A receptors. Adenosine receptors, widely expressed throughout the body, are typically activated by adenosine. A1 receptors have a high affinity for adenosine, while A2A receptors exhibit a lower affinity [44].

Adenosine regulates several physiological functions through G protein-coupled receptors by altering the cellular concentration of cyclic adenosine monophosphate (cAMP). The binding of adenosine to A1 receptors inhibits adenylyl cyclase via the Gi protein, reducing intracellular cAMP levels. Conversely, adenosine binding to A2A receptors stimulates adenylyl cyclase via the Gs protein, increasing cAMP concentration [33,40]. Adenosine receptors are involved in various physiological and pathological processes, including cardiac rhythm and circulation, ischemia–reperfusion, renal blood flow, lipolysis, immune response, inflammation, sleep regulation, and angiogenesis, as well as neurodegenerative disorders.

Caffeine's molecular structure resembles that of adenosine, allowing it to competitively bind to adenosine receptors and block the effects of adenosine on A1 and A2A receptors. This antagonistic effect can be achieved even at low caffeine concentrations, such as those in a single coffee cup [33,40,46]. Caffeine-blocking adenosine receptors influence brain functions, particularly sleep, memory, learning, and cognition. It is believed to have potential therapeutic effects on conditions like migraine, depression, schizophrenia, epilepsy, Alzheimer's disease, Parkinson's disease, and Huntington's disease [47].

Caffeine has also been shown to promote the excitation of the sympathetic nervous system. Peripheral vasoconstriction is thought to be the dominant mechanism. Caffeine stimulates the release of catecholamines (adrenaline) and renin, which can, in turn, lead to increased blood pressure, heart rate, total energy expenditure, and thermogenesis in interscapular brown adipose tissue. This effect of caffeine ultimately contributes to significantly increased physical performance and alertness [48–50].

In addition to antagonizing adenosine receptors, caffeine at low doses can also competitively bind to and antagonize the glycine receptor. When activated, this receptor exerts an inhibitory effect on neurons, synergistically enhancing caffeine-related excitation [45].

The effect of caffeine as a phosphodiesterase inhibitor is observed at higher doses [33,40]. Caffeine and its metabolites act as weak competitive phosphodiesterase inhibitors, leading to cAMP accumulation as the enzyme is inhibited at elevated caffeine concentrations [33]. cAMP, an intracellular second messenger, can then activate hormone-sensitive lipase in adipose tissue, promoting lipolysis in this way [51]. This effect of caffeine is used in obesity management. It is supposed that caffeine can affect weight loss by increasing energy expenditure, suppressing appetite, altering lipid metabolism, and influencing gut microbiota [52,53]. The specific mechanism of action in this area is still largely unknown. It is mainly attributed to its effects on the downregulation of key regulators of adipogenesis [52]. Caffeine can increase fat oxidation through phosphodiesterase inhibition and suppress the negative effects of adenosine on increased noradrenaline release [54]. Caffeine can cause a decrease in adipocyte lipid droplet size and adipocyte size by increasing the secretion of catecholamines and subsequent activation of hormone-sensitive lipase; another mechanism is the blockade of adrenergic receptors and increased levels of cAMP levels. Caffeine accelerates beta-oxidation by suppressing fatty

acid synthases and upregulating peroxisome proliferator-activated receptor alpha. Caffeine also stimulates brown adipose tissue by increasing peroxisome proliferator-activated receptor gamma coactivator 1-alpha, promoting thermogenesis [53,54]. Tabrizi R. et al. (2019) prepared a systematic review regarding the effects of caffeine intake on obesity, which also included studies that did not show any beneficial effect of caffeine on body weight and weight loss. Therefore, the effect of caffeine consumption on improving diet for weight loss and reducing body fat percentage remains controversial [54].

Caffeine-induced calcium release occurs only at very high, non-physiological concentrations, at which point caffeine can readily diffuse into cells and activate calcium channels in the endoplasmic and sarcoplasmic reticulum. This triggers calcium release, affecting neurotransmission and other calcium-sensitive processes [33].

Finally, extremely high and toxic levels of caffeine are required to block $GABA_A$ receptors, as caffeine has a weak binding affinity for benzodiazepine receptors and only a weak antagonistic effect on $GABA_A$ receptors [33,40].

Caffeine offers several health benefits for the human body, but these depend on the amount of caffeine consumed (Figure 3). Moderate caffeine intake can help prevent or manage various health conditions, while excessive intake can lead to addiction, insomnia, and other side effects [15].

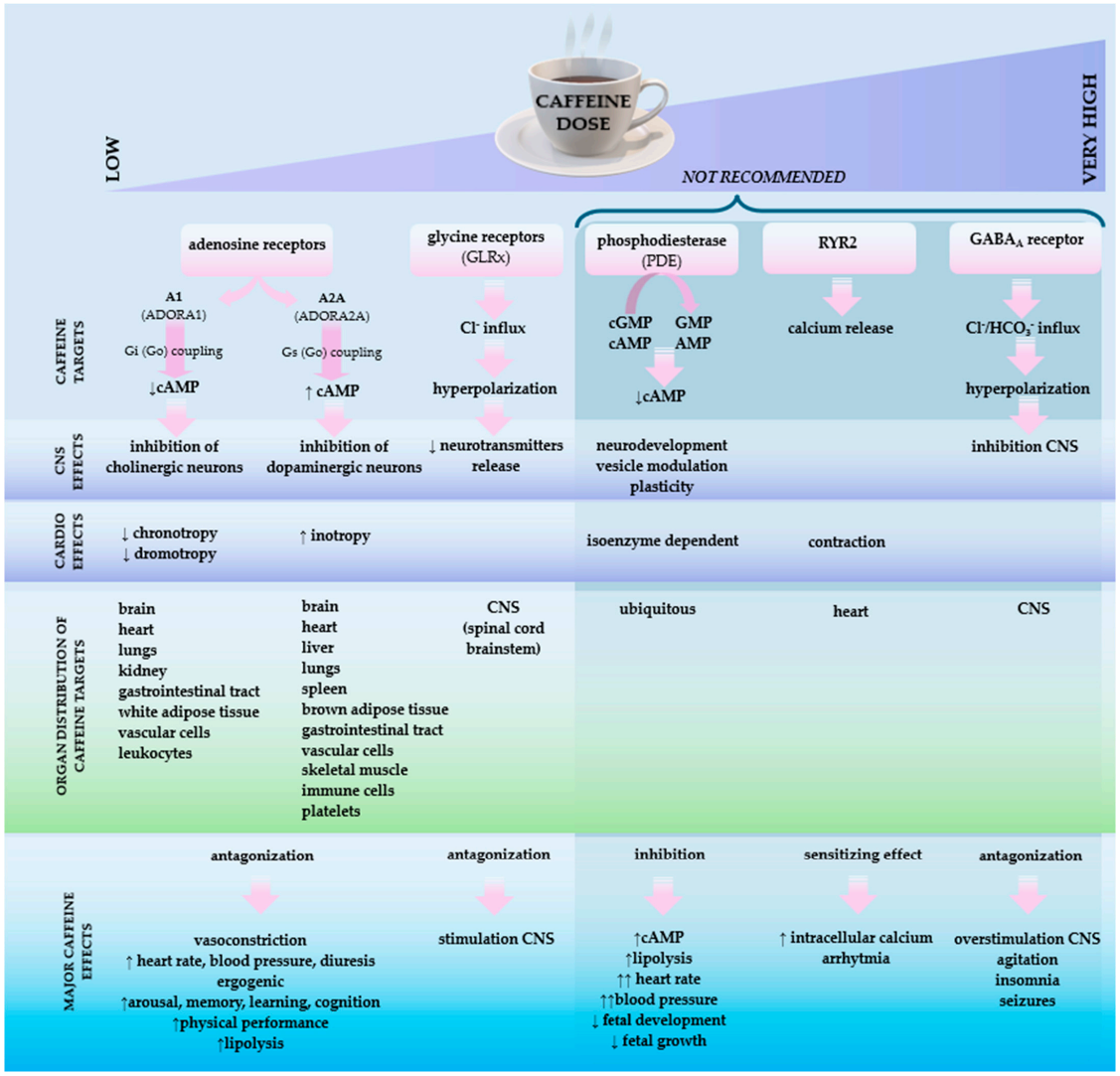

Figure 3. The major effects of caffeine on the human body. The mechanism of action of caffeine is mediated through interaction with multiple proteins. This interaction depends on the caffeine dose

or its affinity for the given proteins. Caffeine targets include adenosine, glycine and $GABA_A$ receptors, phosphodiesterase, and the intracellular calcium channel RYR2 (pink rectangles). The figure highlights the physiological effects in the CNS and myocardium after activating these proteins (violet rectangles) and the organ distribution of these caffeine targets (green rectangle). The effects of caffeine include antagonism of A1, A2A, glycine, and GABAA receptors, inhibition of PDE, and sensitization of the RYR2 calcium channel with associated manifestations (turquoise rectangle), based on references [45,55–69].

4. Caffeinated Beverages

Caffeinated beverages are among the most widely consumed drinks worldwide, although consumption levels vary significantly across regions. Reports indicate that coffee is adults' primary source of caffeine, whereas adolescents prefer tea and sweetened soda drinks [33]. Coffee, tea, cocoa, sweetened drinks, and energy drinks are globally popular and socially accepted. This is due to the stimulant effects of caffeine [70].

It is estimated that approximately 90% of all adults worldwide consume caffeine daily [71]. Caffeine concentrations differ across various products, including within different caffeinated beverages (Table 3). Among these drinks, coffee typically contains one of the highest levels of caffeine.

Additionally, caffeine supplementation to enhance both mental and physical performance is increasingly popular among young, active individuals [72,73]. In a study by Mitchell et al. (2014), which examined data from Kantar Worldpanel, researchers concluded that approximately 98% of daily caffeine intake comes from coffee, carbonated sweetened drinks, tea, and energy drinks [74].

Table 3. Caffeine content in common caffeinated beverages.

Type of Beverage	Volume of Beverage (mL)	Amount of Caffeine (mg)	Amount of Caffeine (mg in 100 mL)	Ref.
Decaffeinated coffee	150	2–5	1.3–3.33	[75]
Coffee instant	150	66	44	[76]
Espresso	200	388	194	[77]
Espresso shot	25	106	424	[78]
Coffee with milk	250	158	63.2	[77]
Cappuccino/Cafe Latte	200	126	63	[77]
Black tea (leaves)	250	43	17.2	[76]
Black tea (bags)	250	31	18.6	[76]
Green tea (leaves)	250	41	16.4	[76]
Green tea (bags)	250	34	13.6	[76]
Energy drink	250	80	32	[77]
Caffeinated sweetened drink	375	32	8.5	[78]
Cocoa	150	2–7	1.3–4.6	[75]

In addition to caffeine, tea, and coffee contain other compounds that can have both beneficial and adverse effects on human health. These include antioxidants—specifically polyphenols, catechins, and flavonoids. While tea, coffee, caffeinated sodas, and energy drinks contribute caffeine to the diet, each offers unique nutritional properties [71].

4.1. Coffee

It is reported that coffee is one of the three most consumed beverages in many cultures worldwide, probably thanks to its stimulating effect but also thanks to its unique taste and aroma [40,79]. Coffee is the second most consumed drink among adults, the first place belongs to water [80]. In 2020, 9.997 billion kilograms of coffee were consumed, slightly more than the previous year [4]. The history of coffee consumption is quite long, and its beginning dates back to the discovery of coffee beans in Africa or the Middle East. However, coffee cultivation began in Ethiopia and soon moved to Yemen. Coffee cultivation reached such proportions in Yemen that it overshadowed Ethiopia [80].

Nowadays, coffee is considered a brewed beverage, which is prepared from the roasted seeds of the Coffee bush (genus *Coffea*). The berries of this bush contain coffee beans, so the berries are processed and dried after ripening. The two main species of coffee are Arabica (*Coffea Arabica*) and Robusta (*Coffea Canephora*) [81]. Currently, due to the large-scale production of Arabica and Robusta coffee, coffee beans and the beverages derived from them are considered commodities of enormous economic importance. They have an excellent production history and an important role in the global market but also in research [73,81]. It is estimated that around 2 billion cups of coffee are consumed daily [82].

Currently, coffee is considered a functional drink because it contains bioactive compounds, namely alkaloids (caffeine and trigonelline) and phenolic compounds (chlorogenic acids), and other secondary metabolites that demonstrate health benefits for the human body, but with appropriate daily consumption [83]. Alkaloids and polyphenols show high levels in coffee beverages and/or increased bioavailability after coffee consumption [40,51,84]. Chlorogenic acids can be metabolized into phenolic acids (caffeic, ferulic, and isoferulic acid) and then into metabolites in the large intestine (dihydrocaffeic acid, dihydroferulic acid). Extensive conjugation occurs at the intestine and liver level, which is why it is possible to identify many metabolites, such as aglycone, sulfate, glucuronide, and methyl, after drinking coffee [40]. Coffee also contains lactones, diterpenes (cafestol and kahweol), vitamin B3, magnesium, and potassium [40,80,85].

There are differences regarding the chemical composition of coffee beverages, including differences in the presence and levels of bioactive compounds. These differences are related to various factors, such as the variety of coffee, growing conditions, processing conditions (fermentation, decaffeination, or roasting), and, of course, storage, conditions and types of preparation of the coffee brew [40,84,86].

If talking about decaffeinated coffee, it does not mean caffeine-free coffee. Different methods and extraction agents are used for the decaffeination process. However, even after decaffeination, coffee beans contain residual amounts of caffeine. Certain national and international rules determine that the decaffeinated process should reduce methylxanthine concentration by 97–99.9% in ground roasted coffee and by 97% in instant coffee without significantly impacting other natural compounds. A much stricter standard is in the countries of the European Community, where decaffeinated coffee must be 99.9% alkaloid-free [37]. As for the amount of caffeine, 0.3–0.5 mg of caffeine/100 g is found in decaffeinated ground roasted coffee [87], while 0.7–0.9 mg/100 g of caffeine is in instant decaffeinated coffee [88].

Effect of Coffee Consumption on Human Health

It is widely known that regular coffee and/or espresso coffee consumption is a relatively common and popular habit, especially among adults. Regular coffee consumption is associated with a healthy profile of coffee drinkers and a reduced risk of some chronic and degenerative diseases. Individual responses to coffee vary; some people are more sensitive to

its effects than others. However, most people can enjoy up to 4 cups of coffee daily as part of their eating habits and active life [84]. This represents approximately 400 mg of caffeine.

Various epidemiological, in vitro, and in vivo studies have investigated the protective effects of coffee beverages and their most common and biologically available compounds in the development of gastrointestinal and liver cancer. It has been shown that caffeine, chlorogenic acid, and trigonelline when administered individually, modulate common molecular targets directly involved in key cancer hallmarks [84]. The meta-analysis by He et al. (2020) focused on the association between coffee consumption and the risk of oral cavity cancer; they summarized case–control studies and cohort studies, concluding that high or intermediate coffee intake may reduce the risk of oral cavity cancer [89]. An updated meta-analysis involving 22 studies (cohort and case–control) performed by Xie et al. (2016) reported that an increase in coffee consumption was associated with a decreased risk of gastric cancer [90]. Li et al. (2019) concluded that there is an association between pancreatic cancer risk and coffee consumption and that coffee consumption is associated with an increasing risk of pancreatic cancer in a dose-dependent manner [91]. A meta-analysis by Brave et al. (2017) observed a 34% reduction in the risk of primary hepatocellular carcinoma and a 38% reduction in the risk of chronic liver disease among regular coffee drinkers compared with no or occasional drinkers. The risk reduction was proportional to the amount of coffee consumed and was present in all reviewed studies [92].

Coffee drinks have a diuretic effect and a transient hypertensive effect due to the presence of caffeine. Caffeine also increases stomach acid secretion and stimulates the activity of the heart and kidneys. Theobromine, also present in the seed, has a diuretic and antispasmodic effect similar to theophylline [81]. Seal et al. (2017) conducted a study on ten healthy adults (eight men and two women; age: 27 $\pm$ 5 years) to investigate the diuretic effect of caffeine. Their results suggest that a caffeine intake of 6 mg/kg in coffee can induce an acute diuretic effect. In contrast, 3 mg/kg does not disrupt fluid balance in healthy adults who drink coffee occasionally at rest [93]. Zhang et al. (2015) conducted a meta-analysis (including sixteen studies) that assessed caffeine-induced diuresis in adults during rest and exercise. They concluded that caffeine had a slight diuretic effect that was negated by exercise. Concerns about unwanted fluid loss associated with caffeine consumption are unfounded, especially if ingestion precedes exercise [94].

Existing studies indicate that regular coffee consumption can reduce the probability of type 2 diabetes mellitus by 60% for both caffeinated and decaffeinated drinks. However, caffeine did not contribute to this effect, and the specific substances responsible for this benefit are still unknown. The mechanism of action for diabetes prevention is also not yet clear. There is evidence of increased insulin secretion and sensitivity (compared to the caffeine effect in skeletal muscle). Coffee acts primarily (if not exclusively) via postprandial glucose homeostasis [40,81,95]. It is well known that coffee has a stimulating effect on the central nervous system. It can increase the effect of painkillers, reduce fatigue, and be used in the treatment of migraines [81].

Regular coffee consumption also seems to protect against some neurodegenerative diseases. Existing epidemiological studies have shown that regular coffee consumption can reduce the risk of Alzheimer's disease [95], Parkinson's disease [95,96], and dementia [96]. Existing studies in a rat/mice study have shown that moderate caffeine intake can inhibit memory impairment and confirmed that caffeine could protect against Alzheimer's disease by promoting the survival of cerebral striatum and cortex cells and inhibiting the apoptosis pathway [95]. On the other hand, it is believed that the effects of coffee on neurodegenerative diseases may result from the synergistic action of many active compounds present in coffee [96].

Regarding the association between drinking coffee and the occurrence of cardiovascular diseases, meta-analyses have yielded controversial results. An association between

coffee consumption and a higher risk of cardiovascular diseases, such as stroke, heart failure, and total cardiovascular disease mortality, was not supported. It was concluded that there is no clinical basis for the association of moderate coffee intake with an increased risk of cardiovascular disease [40]. Regular coffee consumption is even reported to be associated with a lower risk of cardiovascular death and various adverse cardiovascular outcomes, including coronary heart disease, congestive heart failure, and stroke. The effects of coffee on arrhythmias and hypertension are neutral [97].

4.2. Tea

Tea is a very popular drink worldwide. More than two billion cups of tea are consumed daily [98]. It is said that tea is consumed by more than two-thirds of the world's population and drinking tea has become part of our social culture [99–101]. Tea is prepared from the young leaves of the *Camellia sinensis* L. plant [99,101]. The process of growing tea plants and the habit of drinking this beverage dates back to ancient times in China [100]. Immediately after harvesting, the tea leaves are brought to the factory for processing. The processing of tea leaves requires several steps, namely withering, rolling, fermentation, post-fermentation, and roasting (drying). This makes it possible to obtain several types of tea [102]. Based on the fermentation degree, the tea is classified into six types: black, dark, green, oolong, yellow, and white (Figure 4). Caffeine is the most abundant alkaloid present in all six types of tea [102,103].

Horzic et al. (2009) determined caffeine content in different teas extracted in household conditions (the water temperature ranges from 80 °C to 100 °C). They evaluated the highest caffeine content in all teas (black tea, oolong tea, green tea, white tea) extracted at 100 °C and decreased in order white tea > oolong tea > green tea > BT. The lowest caffeine content at 80 °C was observed in Oolong tea (156 mg/L), followed by black tea (184 mg/L), white tea (198 mg/L), and green tea (297 mg/L) [104].

The processes for making each type of tea differ in the degree of enzymatic oxidation or "fermentation". In this case, fermentation is called natural browning catalyzed by enzymes endogenous to the plant [100]. Tea contains polyphenol compounds, theaflavins, caffeine, theobromine, theanine, and volatile organic compounds. These bioactive compounds are responsible for the taste of tea, its aroma, and its effects on the human body. Polyphenols comprise about 30% of the dry weight of tea, including flavanols, flavonols, flavonol glycosides, and polyphenolic acids. Epigallocatechin (EGC) and epigallocatechin gallate (EGCG) are the predominant flavanols or catechins in tea leaves [101,105].

The tea prepared from *Clitoria ternatea* L. has attracted considerable interest based on its various applications in agriculture and medicine. *Clitoria ternatea* L. is a plant, also known as butterfly pea, which produces flowers with a characteristic blue color [106]. *C. ternatea* is used in traditional medicine to improve cognitive function and relieve fever, inflammation, and pain [107]. It is used as an antioxidant and natural food colorant. Blue tea is an aqueous extract prepared from the blue petals of *Clitoria ternatea*; it is rich in anthocyanins [106].

Figure 4. The six main types of tea according to the manufacture processing (adapted from [102,108]).

Effect of Tea Consumption on Human Health

Drinking tea is associated with many health benefits due to its high content of polyphenolic compounds, caffeine, and catechins, which exhibit antioxidative, regulatory, and anti-inflammatory effects, respectively. Accumulating evidence attributes tea consumption with various health benefits, including reduced risk of cardiovascular diseases, heart diseases, liver diseases, malignancy, chronic inflammation, diabetes mellitus, neurological diseases, and skin aging [99,109]. The reduced risk of cardiovascular diseases is attributed to the synergic effects of tea catechins, which increase antioxidant activity, alleviate metabolic syndrome, inhibit angiotensin-converting enzymes, improve endothelial dysfunction, prevent cardiac hypertrophy, and protect mitochondria from damage [110]. Yang et al. (2004) investigated the effect of tea drinking on the risk of hypertension in 1507 subjects. This study showed that 600 habitual tea drinkers (39.8%) who consumed 120 mL/day or more for at least 1 year had a significantly lower risk of developing hypertension than non-habitual tea drinkers [111].

Tea consumption is also considered a natural adjunctive therapy for neurodegenerative diseases. For instance, Alzheimer's disease affects a growing population of elderly patients [112]. A meta-analysis by Jiang et al. (2023) that included seven prospective cohort studies involving almost 411 thousand individuals demonstrated that tea intake or consumption (green or black tea) is associated with a significant reduction in the risk of dementia, Alzheimer's disease, and vascular dementia among populations with less physical activity, older age, and smokers [113].

Tea drinking has also been associated with beneficial effects on various types of cancer (e.g., stomach, lung, ovarian, oral cavity, and thyroid). This effect is mainly attributed to the high content of catechins in tea and their antioxidative activity. Interestingly, in most cohort and case–control studies, a reduction in cancer risk was more often observed and associated with green tea consumption [109]. In summary, tea has significant antioxidative, anti-inflammatory, antihypertensive, anticarcinogenic, antimicrobial, neuroprotective, cholesterol-lowering, and even thermogenic properties for the human body. These properties far outweigh the few reported toxic effects [114]. For instance, excessive tea consumption may cause nutritional and other problems due to the binding activity of tea polyphenols, and caffeine content [115].

4.3. Energy Drinks

Energy drinks are considered the fastest-growing product in the beverage industry. The first energy drink, sold under the name Dr. Enuf, was introduced in the USA in 1949 [116]. This marked the beginning of the energy drink industry. Energy drinks were first introduced to the European market in 1987. Subsequently, the market for these beverages spread worldwide, with a significant surge in popularity after the introduction of novel products in 1997. In the past two decades, there has been a dramatic increase in the consumption of energy drinks, particularly among teenagers and young adults [117]. The average annual growth rate of energy drink sales was 55% from 2002 to 2006 [116]. The Food and Drug Administration (FDA) defines energy drinks as "a class of products in liquid form that typically contain caffeine, with or without other added ingredients" [118]. Energy drinks are primarily sold in places popular with young people. Two-thirds of energy drink consumers are between 13 and 35 years old. In the US, energy drinks are currently the second most common dietary supplement young people use [117]. Authors Nadeem et al. (2021) report the most frequently used energy drinks [119]. The caffeine content in these drinks varies but is around 150 mg per 500 mL. The sugar content is around 55 g per 500 mL [118]. The other ingredients found in energy drinks are listed in Table 4.

Table 4. Other ingredients of the most frequently used energy drinks (adapted from [118]; the order of the most frequently used drinks is according to [119]).

Energy Drink	Volume (mL)	Other Ingredients
1	500	taurine (2000 mg), gluconolactone (1200 mg), inositol (NS), vitamins B3, B5, B6, B12 (NS)
2	500	taurine (NS), gluconolactone (NS), carnitine (NS), inositol and guarana (NS), ginseng (400 mg), vitamins B2, B3, B6, B12 (NS)
3	500	taurine (NS), guarana, vitamins B3, B6, inositol (NS), carnitine (NS)

NS—not specified.

Effect of Energy Drinks Consumption on Human Health

Energy drinks are formulated to improve physical and mental stimulation through a combination of stimulants and energy boosters. Consuming energy drinks can increase alertness, attention, and energy, improve memory, and elevate mood [117,119], but on the other hand, they can also increase blood pressure, heart rate, and breathing [119]. Many studies have investigated the influence of energy drinks on sports performance. These studies have shown that energy drinks can significantly increase reaction power during exercise (without affecting anaerobic performance) and improve endurance performance without increasing perceived exertion [117]. They also promote alertness during high-intensity physical exercise and have become one of the most commonly consumed substances among athletes and other people engaged in physical activity [120].

However, some studies have shown no significant effects or harmful health consequences of energy drinks on exercise performance. This may be due to methodological differences, such as gender, caffeine dose, energy drink composition, and placebo type [117]. The effects of energy drinks on cognitive function and mood have also been evaluated. Cognitive functions were assessed using automated tests, while mood was assessed using questionnaires. The results showed that both cognitive functions and mood significantly improved in partially sleep-deprived individuals who consumed energy drinks [121]. The increased consumption of energy drinks is associated with certain health risks [122]. Due to the significant increase in energy drink consumption among young adults and athletes, concerns have arisen about potential health risks associated with excessive consumption [118]. One potential risk is caffeine overdose, as over 75% of children (aged > 5 years) and adolescents (aged 12–17 years) consume caffeine regularly, with an average daily consumption of 25 mg/d among children aged 6 to 11 years and 50 mg/day among adolescents aged 12 to 17 years [35]. The risk of acute caffeine toxicity from energy drinks is linked to inadequate labeling, aggressive advertising that may induce higher consumption, and the lack of restrictions on sales, allowing children and adolescents to purchase them [116].

In children and adolescents for whom caffeine consumption is not every day, caffeine intoxication may occur due to a lack of pharmacological tolerance. Genetic factors may also contribute to individual susceptibility to caffeine-related disorders, caffeine intoxication, dependence, and withdrawal. Compounds that are part of energy drinks (guarana, yerba mate, kola nut) can potentially enhance caffeine's biological effects. Guarana with caffeine alone or together with taurine may induce neurotoxicological effects but also interfere with redox homeostasis [123]. Caffeine intoxication caused by drinking energy drinks leads to tachycardia, vomiting, cardiac arrhythmias, seizures, and even death. Caffeine can increase blood pressure, disrupt sleep patterns in adolescents, worsen psychiatric illness, cause physiological dependence, and increase the risk of subsequent addiction [124]. When

consuming energy drinks together with alcohol, the incidence of adverse effects is higher; these consumers often even use drugs or become heavy drinkers later in life [125].

Energy drinks are primarily associated with cardiovascular risks [122]. Consumption of energy drinks has been linked to myocardial infarctions, cardiomyopathies, and sudden cardiac death. This is attributed to the ergogenic effects of high caffeine content, as well as large amounts of taurine, sugars, and B vitamins in energy drinks [122,126].

Additionally, significant cardiac manifestations, such as ventricular arrhythmias, increased heart rate, elevated blood pressure, ST-segment elevation, and QT interval prolongation, have been observed after consuming energy drinks [122,126]. Of course, as with other beverages and energy drinks, the mechanisms by which they may negatively affect the cardiovascular system vary depending on the ingredient. In the case of caffeine, it acts mainly as an antagonist of adenosine receptors, thus blocking its vasodilatory effect. It causes an increase in plasma adenosine levels, which in turn increases sympathetic tone, catecholamine levels, peripheral vascular resistance, and renin secretion. This may be a possible mechanism by which energy drinks increase heart rate and blood pressure [122]. Another mechanism of caffeine is the inhibition of phosphodiesterase, which leads to an increase in myocardial cyclic adenosine monophosphate and a positive inotropic effect on the myocardium [127].

High doses of caffeine in energy drinks increase diuresis [128], which can lead to increased urine production and dehydration. The consumption of energy drinks can also cause increased diuresis and electrolyte imbalance. A study by Riesenhuert et al. (2006) investigated the possible diuretic effects of caffeine and taurine in 12 healthy male volunteers. They showed that the diuretic and natriuretic effects of the tested energy drink were primarily mediated by caffeine. Taurine did not play a significant role in fluid balance in moderately dehydrated, healthy young drinkers. They concluded that the diuretic potential of energy drinks would not differ significantly from other caffeinated beverages [128].

A strong correlation has been demonstrated between energy drink consumption and dental erosion [129]. Silva et al. (2021) studied the effects of energy drinks on dental erosion. Dental erosion is associated with increased consumption of acidic beverages; energy drinks have pH values ranging from 2.36 to 3.41. Based on the study model, all energy drinks examined were erosive to tooth enamel [130].

The combination of energy drinks and alcohol is hazardous. Consumers who mix alcohol with energy drinks tend to consume significantly more alcohol than those who drink alcohol alone. Because this combination may mask symptoms of alcohol intoxication, the risk of alcohol-related injuries may increase [119,128].

4.4. Caffeinated Sweetened Beverages

Sweetened drinks, like sweet teas and colas are popular, especially among children. In addition to added sugar, these drinks contain caffeine, making them a significant source of caffeine intake in childhood. These drinks are readily available and popular worldwide [131,132]. Despite their energy content, they lack micronutrients. Manufacturers of sweetened drinks claim that caffeine is added as a flavor enhancer. However, there is limited evidence to support this claim. A 500 mL serving of cola typically contains 53–65 mg of caffeine. This relatively high amount can contribute to caffeine addiction and affect behavior, such as increasing attention, mood, and motor activity [132]. Children are particularly vulnerable to excessive caffeine intake from sweetened beverages, as these are their primary source of caffeine [133]. Children aged 8–14 consume caffeine-sweetened beverages due to their palatability, particularly their sweet taste. Children have a greater preference for sweets compared to adults [131].

Effect of Caffeinated Sweetened Beverages Consumption on Human Health

High caffeine consumption from these types of beverages can disrupt sleep patterns. It is generally accepted that individuals who consume large amounts of caffeine may have more disrupted sleep [133]. Because of the potential adverse effects of caffeine on neurological and other physiological systems (including caffeine intake from sweetened beverages), the American Academy of Pediatrics recommends that all children avoid caffeinated beverages [134]. Consumption of caffeinated sweetened beverages has been associated with neurobehavioral risk factors for substance abuse, such as increased impulsivity and lower working memory performance [135]. Pregnant women are also at risk of consuming caffeinated soft drinks, and these women should reduce their caffeine intake, especially if it exceeds the WHO recommended limit of 300 mg/day. Increased caffeine consumption during pregnancy is associated with an increased risk of early pregnancy loss, stillbirth, and neonatal death [17].

Regular consumption of sugary drinks is also harmful due to their high sugar content, which has negative effects on human health. Excessive consumption of sugary drinks is associated with higher energy intake, overweight and obesity [131,132], high rates of dental caries [136], and even a higher risk of early menarche [134].

4.5. Cocoa-Based Beverages

Cocoa-based beverages are also very popular. They have been used for centuries [137] and have a better safety profile than coffee. The caffeine content in cocoa beans is low; the main alkaloid present is theobromine, which is also a degradation product of caffeine [36]. Theobromine has effects similar to caffeine, mainly adenosine receptor antagonism [138] and phosphodiesterase inhibition [139]; however, even though theobromine has around 10 times higher concentration than caffeine in cocoa-based beverages [140], it produces minor subjective effects compared with caffeine. Therefore, chocolate drinks are expected to present the least psychostimulant activity, considering only caffeine concentrations [141].

To enhance clarity, Table 5 concisely summarizes the key effects of the caffeinated beverages under discussion.

Table 5. Summarized beneficial and adverse effects of caffeinated beverages.

Beverage	Beneficial Effects	Adverse Effects
Coffee	stimulates central nervous system [81] reduces the probability of type 2 diabetes mellitus, increases insulin secretion and insulin sensitivity [40,81,95] protects against some neurodegenerative diseases, reduces the risk of Alzheimer's disease [95]	increases stomach acid secretion, stimulates the activity of the heart and kidneys, diuretic and antispasmodic effect [81] controversial results regarding cardiovascular diseases [40]
Tea	reduces risk of heart diseases, liver diseases, malignancy, chronic inflammation, diabetes mellitus, neurological diseases, and skin aging [99,109] protect against neurodegenerative diseases [112]	nutritional problems [115]

Table 5. *Cont.*

Beverage	Beneficial Effects	Adverse Effects
Energy drinks	increase alertness, attention, improves memory, and elevate mood [117,119]	increase blood pressure, heart rate, and breathing [119] caffeine intoxication, dependence, and withdrawal [123] cardiovascular risks [122], tachycardia, vomiting, cardiac arrhythmias, seizures, and even death [124] increase blood pressure, disrupt sleep patterns in adolescents, worsen psychiatric illness, cause physiological dependence, and increase the risk of subsequent addiction [124] increase diuresis [128] dental erosion [129]
Caffeinated sweetened drinks	increase attention, mood, and motor activity [132]	overweight and obesity [132] childhood obesity, development of cardiometabolic disease [131] interrupted sleep [133] tooth decay [136] higher risk of earlier menarche [134] higher impulsivity and lower working memory performance [135]

5. Conclusions

This overview article delves into caffeine, a widely consumed psychoactive stimulant. Caffeine is present in many foods (chocolates, candies, frozen desserts) [142], beverages (coffee, tea, energy drinks, soft drinks) [142], cosmetics (skin care, sun protection) [143], and pharmaceutical products [142]. Caffeine is often added to common analgesics (e.g., paracetamol, ibuprofen, acetylsalicylic acid) to increase their pain-relieving ability [144]. It is known for its ability to increase attention, alertness, mood, and well-being. Most people, if not all, have encountered or will encounter caffeine at some point. Popular drinks such as coffee and tea contain caffeine. Drinking caffeinated beverages is a traditional and cultural custom, and these are among adults' most popular drinks. The production and consumption of energy drinks, which are high in caffeine, are increasing worldwide, gaining significant popularity among adolescents, children, and athletes. Caffeine is also a flavor enhancer in sweetened beverages, which are popular, especially among children. Caffeine has been the subject of extensive scientific research due to its bioactive properties. While caffeine in reasonable amounts has positive effects, excessive consumption can lead to serious health complications, especially in children and adolescents. Caffeine intake in children and adolescents is problematic due to its availability. This age group can gradually develop a caffeine addiction, and it can even lead to other addictions in older age. Excessive caffeine intake in childhood can cause intoxication. Moreover, sweetened caffeinated beverages can lead to additional health risks, such as overweight and obesity, disrupted sleep, and tooth decay, which can ultimately lead to socio-psychological problems. Therefore, knowing the possible risks of consuming caffeinated beverages among children is important. It may be appropriate to limit or completely exclude the serving of these beverages to children [125,145].

Since caffeine has also been shown to positively affect the human body, the results of many studies could be beneficial for developing functional foods or complementary medicines.

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