

Caffeine in Soft Drinks and Beverages: Sources, Pharmacology and Toxicology

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Abstract

Caffeine is consumed globally. Caffeine occurs frequently in plants and has been included for millennia into common beverages like tea, coffee and more recently in sodas. Lately caffeine has been included in energy drinks and medications. Caffeine is a neural stimulant and although addiction to caffeine is rare, many are unaware of its potentially addictive, destructive or lethal properties. This appraisal focuses on the natural sources of caffeine, its medicinal pharmacology, its inclusion in common recreational beverages, and deconstructs and cautions about many of its side effects.

Keywords: Addiction, beverages, cola, caffeine, coffee, drugs, energy, guarana, tea, soda, toxicity.

Background and Introduction: Excluding biological molecules necessary for human metabolism, (like water, essential amino and fatty acids, carbohydrates, vitamins, minerals and trace elements) few iatrogenic, yet naturally derived, molecules promote global fellowship, comfort and harmony more than alcohol and caffeine. Alcohol consumption is constrained by complexity of manufacture, distribution and cost, while caffeine is easily accessible from nature, is globally available in moderate climates and relative to alcohol, is more simply prepared and much cheaper. Consequently caffeine is the most frequent and common recreational drug, consumed worldwide. It is imbibed daily, mainly in beverage form as tea, coffee, pop-sodas and energy-drinks. (1)This imbibing frequency attests to the safety of caffeine, but like with most substances, the dose makes the poison. Micro-dosing of caffeine for its beneficial effects has allowed widespread consumption as a stimulating beverage. (2-6)There is a global assumption that there are few, if any, disadvantages, and most ignore problems which arise from overdosing on caffeine. Caffeine poisoning is rare, but overdosing does occur, is ubiquitous, and although the symptoms are well-understood, tolerated and well-managed, caffeine abuse, for various reasons is increasing. (1-6, 21)

Aim: This report appraises the sources and properties of caffeine, focuses on its prevalence in common recreational beverages, and assesses its pharmacology and use in medicine, including cautions about undesirable properties, and some side effects from caffeine overdosing.

Sources of caffeine. Caffeine is a vegetable white alkaloid, which forms into silky white needle- shaped crystals. Caffeine is synthesized in the in the leaves of, and found in, the bean-

seeds of *coffee* (*Coffea Arabica*, a bush native to Abyssinia and Africa), the leaves of *tea* plants (*Camellia* and *Gordonia*, mainly *C. sinensis*, a shrub native to South Eastern Asia, and China, family Thea) and the leaves and seeds of *guarana* (*Paullinia cupana* or *sorbilis*, family Sapindaceae, a vine native to Brazil). Tea and coffee are cultivated globally where weather, soil and climatic conditions are favorable. Guarana is mainly cultivated in Brazil and some other South American countries. (5, 6).

The main active substance in these plants, among many other ingredients derived from the plants, is caffeine. Caffeine is derived from coffee, *thein* from tea and guaranin from guarana; these terms are all synonyms for caffeine. Tea plants contain variable amounts of caffeine between 1% and 4%. All these substances mentioned are used in medicines, often in combination with other drugs, for the relief of headaches. (5, 6)

There are over two thousand volatile compounds found in coffee, including pheobromine and theophylline, but the main psycho- active ingredient in coffee, as well as in tea and guarana, remains caffeine. Caffeine in combination with theophylline, acts agonistically as a diuretic, a bronchodilator and a respiratory stimulant. Guarantin contains caffeine, saponin, a volatile oil and paullinitannic acid. Other health effects of tea are discussed elsewhere. (6)

Caffeine is laced into many energy “Soft-Drinks”. See Table 2. . There is a large variation of volumes and caffeine concentrations in these soda drinks, from as low as 34 mg caffeine per drink, to over 500mg in selected energy drinks. Some drinks are offered in small volumes (50mls/2.5ozs to over 20 ounces/ 350 mls). Young people may consume two or three drinks in the belief that “more is better,” with easy consequent overdosing and signs of caffeine toxicity. There is no restriction of access to these energy drinks and all may be purchased by anyone ‘over the counter.’ These energy drinks are not only associated with caffeine overdose but with dental damage (erosion, sensitivity) and gastro-intestinal pathologies (epithelial dysplasia and weight gain) too. (7)

Pure caffeine has a slight lemon taste, is naturally synthesized molecule and besides being found in plants, it is added in controlled amounts to medicines, energy drinks and pop-sodas.

Pharmacology of Caffeine in Medicine: Caffeine acts on the central nervous system with consequential brain and psychological excitation; it is also a cardiac and respiratory stimulant, assists in dilating bronchioles, and is a diuretic. (8, 9)

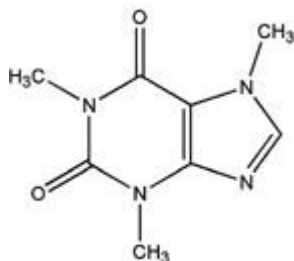


Figure 1: The chemical structure of Caffeine. The molecule combines easily with benzoate, citrate and other bioactive molecules like adenosine. (8, 28)

Caffeine acts as an agonist potentiater for many other drugs. As caffeine citrate, in combination with anti-inflammatories like acetylsalicylic acid (ASA) and acetaminophen (paracetamol), caffeine acts agonistically, and consequently it is used to relieve headaches. Caffeine is also used in combination with opioids like codeine or aconite, to counter the suppressive effects of these drugs on nerves and target organs. For example, when codeine causes constipation, caffeine is used to counter that effect in compounded medications. Caffeine gives some relief to asthma attacks, but is not always potent enough on its own. Accordingly caffeine is used in combination with other broncho-dilators like epinephrine (the Cathecholamines). (17) Caffeine also counters the neural effects of alcohol. (22)

Disadvantages of Caffeine Consumption and Toxicity:

That caffeine counteracts the effects of alcohol is known and drinkers will naively consume energy drinks to moderate the effects of alcohol; this encourages increased consumption of alcohol with its concomitant chronic effects of alcoholism, and this does not auger well for the long-term health of those drinkers (20, 32).

Caffeine has a stimulatory effect on neurons in the central nervous system. Consequently caffeine is reported as increasing wakefulness, attention, focus, alertness and concentration spans. (27, 29-31)

Over-dosing on caffeine may cause irritability, raised blood pressure, tachycardia, dyspnoea, sweating and jitteriness; one or all symptoms may manifest with caffeine overload. The changes in vital signs and symptoms become apparent when excess caffeine is consumed over a short period of time. (25,33-38) Caffeine toxicity can cause overstimulation of the heart with resultant arrhythmia and death.(36) *In vitro* fertilization (IVF) results decrease because of reduced sperm counts from men who consume large quantities of coffee. When caffeine intake exceeds 265mg/day, this renders the lowest chance of IVF success. (36)

Posology, safety and dosages of Caffeine.

A daily dose of no more than 400mg for average 70Kg male is considered safe. Less than 300mg caffeine per day is deemed 'safe' for pregnant mothers. Daily doses below 250mg consumed by the mother, is considered acceptable for healthy viability of an intra-uterine foetus. Chronic caffeine poisoning is characterized by nausea and vomiting, hyperactivity, excitement, agitation, inability to concentrate; overdosing, affects work performance, increases anxiety, insomnia, frequency of headaches, cardiac rhythm disturbances and palpitations. Large doses of (over 500mg) caffeine imbibed in a short period may induce signs of overdosing, precipitate cardiac arrhythmias and result in death. (14, 22, 23)

Pop sodas have become a major source of caffeine intake. Teens often regularly consume 4 to 6 cans of pop-soda daily. Besides posing problems relating to teeth and weight, other negative side effects of caffeine poisoning may manifest too. While the acid and sugar content of pop-and energy drinks cause pathological dental, weight and epithelial changes, it is the caffeine content of those beverages which act as a neural stimulant. Caffeine containing beverages, like guarana-pop and most cola-sodas, are frequently combined with organic acids and sugars, dissolved into a CO₂ gaseous soft-drink mix. Their chronic frequent consumption causes erosion of teeth, increased dental sensitivity and decay. These effects are not from the action of caffeine, but from stagnant microbial biofilm metabolizing fermentable sugars and added acids together in the polysaccharide matrix, derived from the contents of the drinks. (18-22, 32)

Amount of Caffeine for Addiction:

Caffeine habituation may happen with regular doses, as low as 100mgs per day. There is 80-160mgs caffeine in energy drinks, while 237 mls coffee can contain 100-150mg caffeine. Many people are habituated to starting their day with more than one cup of coffee, and teenagers are progressively drinking more energy drinks. Up to 400mg per day for most adults (weight ~70 kg) is deemed safe; that is equivalent to multiple drinks daily to reach this dose.

Caffeine in common beverages:

Caffeine in varying amounts is found in coffee, energy drinks, colas, guarana sodas, and tea. Amounts may vary within the natural sources (from tea-leaves and coffee beans) but manufacturers of caffeine containing drinks, usually vary slightly and maintain consistent stable levels of caffeine through quality controls, and these have been reported. See Table 1, 2 and Table3.

Caffeine in Beverages: ED = Energy Drink

	Tall StarbucksCoffee	RegularDrip coffee	MonsterED	RedBullED	NoFearED	RegularTea	Can of CocaCola
Caffeine:mg/ml	0.55	0.45	0.36	0.32	0.20	0.13	0.10
Mg caffeine/beverage	195	107	170	80	94.6	30	36
Size of beverage in ml	355	237	473	250	473	237	355

Table 1: The caffeine contents of commonly consumed beverages. Note the amount of caffeine in a cup- of-tea (~237ml) compared to a regular cup-of-coffee (~237ml) has been known for decades. The amount of caffeine is over three times the dose in a cup of coffee compared to a cup of tea. (107mg versus 30 mg caffeine). The range of caffeine intake among the drinks imbibed, is between 30mg and 195 mg per beverage, depending on quantities and qualities consumed. **ED = Energy Drink (8,9) .**

Caffeine Energy Drinks Legal from 2008 in Canada

- Wired X505 (24ozs) 505mg
- Fixx 20ozs 500mg
- BooKoo Energy 24 ozs 360mg
- Redline Power Rush 2.5 ozs 350mg
- Redline RTD 8ozs 250mg
- No Fear 16ozs 174mg
- Monster 16 ozs 60mg
- Rockstar 16 ozs 160mg
- Short Espresso 100mg
- Typical pop-drinks:-

- Classic Coca-Cola 12ozs 34.5mg
- Pepsi-Cola 12 ozs 38mg
- Dr Pepper 12 ozs 41mg
- Mountain dew 12 ozs 54mg

Table2: Amounts of Caffeine in Energy Drinks and ‘Classic’ Sodas in Canada vary. The range is wide with doses between 34 mg Caffeine in Sodas, to over 500mg in Energy Drinks. **(10) Jnl Drug & Alcohol Dependence 2013.**

Table 3 shows the dose of caffeine in a (250ml) cup of black coffee, latte, energy drink, black tea, green tea and cola drinks. The caffeine range is large, and all these drinks are freely available to consumers.

Type of drink	Amount of Caffein per 250ml.
Latte: coffee made with milk	113-280mg
Instant coffee with one teaspoon:	60-70mg
Black Camelia sinensis tea:	30-50mg
Green tea:	30-50mg
Energy drink:	80mg
Cola:	36-48mg

Table 3: Caffeine in common drinks. Teas, coffees and energy drinks contain caffeine in 250mls. (8-12)

Additives to Energy Drinks

Caffeine alone has a slight acidic taste, but other substances are also added to energy drinks. These chemicals are used as preservatives or to enhance, dominate or mask the taste of caffeine. *These are some of the known additives to energy drinks:* - Mono- and disaccharide carbohydrates: Glucose, fructose and sucrose; *artificial sweeteners* like *sucralose, asulfame and cyclamates*. *Taurine; Glucuronolactone; Guarantin* (The Brazilian herb that contains caffeine), *Inositol* ... a sugar alcohol, *D-Ribose*, a monosaccharide, and *phthalates*, from plastic containers. *Bisphenol A (BPA)*; a 60 kg person will have to drink 7, 400 to 355ml cans daily, for over seven decades, to approach Health Canada's acceptable daily limit. BPA is an epoxy liner and "Canadian consumers can rest assured that soft drinks and their packaging are safe and meet or exceed all Canadian regulatory requirements. *Dimethylpolysiloxane* is used as an anti-foaming agent for manufacture. *Carnitine, arginine, creatine...* all may be present, and ginseng from Asia may be added as an antioxidant. (22, 41) Teas are a natural source of *fluorides* (6) Fluoride and these other contents mentioned above do not have a moderating effect on the caffeine activity in these beverages.

Taste, smell and organoleptics used to deliver Caffeine:

The typical coffee taste, aroma and organoleptic sensations of coffee derives from *Caffeol*, also known as Caffeone; this is a mixture of furfural (50% v/v), small quantities of valeric acid,

phenol, pyridine, and a nitrogenous substance, comes from this. (16) The characteristic aroma of most teas derive from *theaflavin*, which is a mixed combination of phenyl-ethyl alcohol, citronellol, hexenol, beta-phenyl acetic aldehyde, terpenes, terpene alcohols, lactones, ketones, esters, spiro compounds, monoterpenes and 2-phenyl-2-butenal, all of which may co-exist in varying proportions in tea brews. Some specific molecules can pleasantly dominate the tea fragrance, such as oil of bergamot in Earl Grey tea. (16) *Guaranin* is added to a mixture of acid and CO₂ gaseous sweetened drink, and these products are globally widely consumed as guarana – pop, especially in Brazil. (18) The flavorings mentioned here all mask the taste of caffeine and add to the organoleptic properties of caffeine containing drinks. (17-19)

Discussion: Some religions, (like Muslims and Jews) tolerate caffeine consumption in tea, coffee and soft drinks. Others, like The Mormons, traditionally disallow imbibing these drinks, but recently exceptions are made. (42) Because caffeine drinks are easily available and targeted at young drinkers, abuse from overdosing is now more frequently being encountered in young athletes among children and teens. (44, 45) Brewed coffee has a wide range of active chemicals that affects changes on body metabolism. Unfiltered coffee is a significant source of diterpenes like cafestol which moderate cholesterol increase of blood. Epidemiology indicates caffeine intake from coffee drinking assists in preventing some chronic diseases, like Parkinson's disease, type 2 diabetes mellitus, and hepatic cirrhosis and hepato-cellular cancer. There is sparse evidence that coffee consumption is *causatively* related with significant increases of cardiovascular disease. Yet there is an *association* between coffee consumption and cardiovascular disease risk factors, such as hypertension and plasma homocysteine levels. Associative causes between coffee drinking and cancer is exiguous. With adults imbibing quite large amounts of coffee (300–400 mg/d of caffeine, equivalent to 3-4 cups per day), there are minimal health risks with some indications for enhancing health. Yet many sufferers of hypertension including children, adolescents, and seniors, are susceptible to the negative effects of caffeine. Pregnant women should restrict caffeine intake to no more than 300 mg/d of caffeine to prevent an increased risk of impaired fetal growth and/or spontaneous abortion. (23- 27)

Concluding remarks:

The terms *caffine*, *thein* and *guaranin* are all synonyms for *caffeine*, and bottlers of drinks may use these terms to imply the caffeine added to the drink is a “natural” derivative.(34) The body can withstand moderately high doses (300-450mg/day Caffeine) of caffeine. Young adults consume large doses of caffeine in energy drinks, to counter the effects of alcohol, and this may lead to liver toxicity and alcohol abuse. (21) Some nations consume regular high doses of caffeine; for example the Scandinavians (Finland, Norway, Swedes and Iceland) consume most caffeine daily, the equivalent of 388mg caffeine in coffee per day, which is very close to 5 Red

Bull drinks per day.(40) Coca-Cola has a slightly more caffeine than tea (34-38 mg in colas and 30mg in tea respectively), but Energy Drinks range of caffeine, depending on doses and volumes of each drink varies between 60mg and 500mg per beverage. Drinking infusions of *Camellia sinensis* tea, allows a person to drink at least *three cups of tea* (about 90mgms caffeine) equal to a similar intake of caffeine from *one cup of coffee* (about 90mgm caffeine)! TLV's (Threshold Limit Values) or MAC's (Maximal Allowable Concentrations) for Caffeine are obscure, as caffeine is rarely prescribed on its own, and TLV's and MAC's vary from source to source. (42, 43) The combination of alcohol and caffeine can increase the rate of alcohol-abuse and damage. Excess abusive imbibing of caffeine laced energy drinks may lead to more serious drug addiction. (3, 24)

Conclusion: *All these drinks (coffees, teas, guarana-pop, colas and energy drinks) are glorified commercialized tasty beverages for caffeine delivery systems.* Caffeine toxicity may be rare but fatal cases from cardiac arrhythmias or suicide are not unknown and are reported from excess intakes of caffeine over a short period of time. (35-43) With marketing of energy drinks containing caffeine, especially to children and adolescents, clear warnings about toxicity and maximum allowable doses, should be on the containers; manufacturers should provide caution about overdosing.

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