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Review Article

Coffee is a Medical Advice

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ABSTRACT

Caffeine is methylxanthine naturally occurring in some beverages and also used as a pharmacological agent. Caffeine's most notable pharmacological effect is as a central nervous system stimulant, increasing alertness and producing agitation. It also relaxes smooth muscle, stimulates cardiac muscle, stimulates diuresis, and appears to be useful in the treatment of some types of headache. Several cellular actions of caffeine have been observed, but it is not entirely clear how each contributes to its pharmacological profile. Among the most important are inhibition of cyclic nucleotide phosphodiesterases, antagonism of adenosine receptors, and modulation of intracellular calcium handling Coffee contains antioxidants that may offer some cardiovascular protection, and research is showing that it reduces the likelihood of developing diabetes, which is itself a major heart disease risk factor. But it also increases homocysteine levels and may have negative effects on the aorta. However, it also contains thousands of different chemicals, including carbohydrates, lipids, nitrogenous compounds, vitamins, minerals, alkaloids, and phenolic compounds. Caffeine is the most widely consumed psychoactive drug worldwide and appears to exert most of its biological effects through the antagonism of the adenosine receptor. Adenosine is an endogenous inhibitory neuromodulator that prompts feelings of drowsiness, and thus caffeine induces generally stimulatory effects in the central nervous system. In addition, the physiological effects of caffeine intake include acute elevation of blood pressure, increasing metabolic rate, and diuresis. By suppressing the actions of adenosine, caffeine increases neural activity in the brain, which leads to a temporary increase in mental alertness and thought processing, while reducing drowsiness and fatigue. Contrary to popular belief, caffeine does not directly increase energy metabolism in the body; in fact, long-term consumption actually suppresses it, which can lead to adrenal fatigue. Further, by counteracting adenosine, caffeine also significantly reduces blood flow to the brain, which leads to headaches, dizziness and reduced fine motor coordination.

Keywords: caffeine; chlorogenic acid; coffee drinking; type 2 diabetes; hypertension.

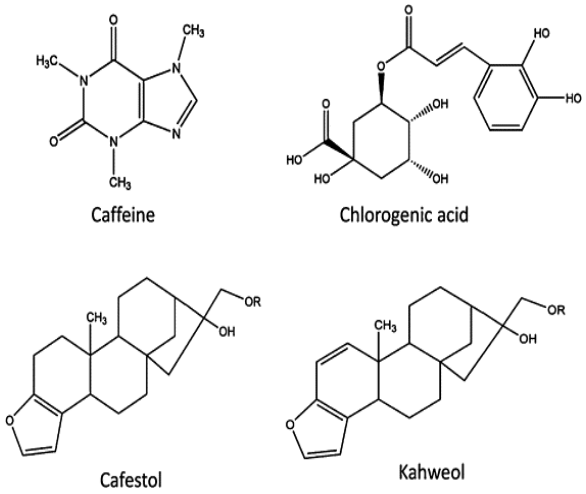
INTRODUCTION & REVIEW

As such, coffee drinking is an important part of modern daily life. Caffeine is probably the most frequently ingested pharmacologically active substance in the world. It is found in common beverages (coffee, tea, soft drinks), in products containing cocoa or chocolate, and in medications. [8] Because of its wide consumption at different levels by most segments of the population, the public and the scientific community have expressed interest in the potential for caffeine to produce adverse effects on human health. It has been told that coffee is a driving force for humans to develop science, because it has an alerting effect on the human brain. However, some people report experiencing

irregular heartbeat or headaches and are thus reluctant to drink coffee, which suggests individual variation to coffee intolerance. [2] The aim of this review is to briefly summarize the effects of coffee on human health. The possibility that caffeine ingestion adversely affects human health was investigated based on reviews of (primarily) published human studies obtained through a comprehensive literature search. Based on the data reviewed, it is concluded that for the healthy adult population, moderate daily caffeine intake at a dose level up to 400 mg day^{-1} (equivalent to 6 mg kg^{-1} body weight day^{-1} in a 65-kg person) is not associated with adverse effects such as general toxicity, cardiovascular effects, effects on bone status and calcium balance (with consumption of adequate calcium), changes in adult behavior, increased incidence of cancer and effects on male fertility. The data also show that reproductive-aged women and children are 'at risk' subgroups who may require specific advice on moderating their caffeine intake. Based on available evidence, it is suggested that reproductive-aged women should consume $\leqslant$ 300 mg caffeine per day (equivalent to 4.6 mg kg^{-1} bw day^{-1} for a 65-kg person) while children should consume $\leqslant$ 2.5 mg kg^{-1} bw day^{-1}.Coffee has taken an important place in human society for at least 1200 years. Its consumption, which probably originated in northeast Africa, spread out to the Middle East in the 15^{th} century and thence to Europe. After oil, coffee has become the second most valuable commodity around the world. [3] Today, coffee is among the most widely consumed pharmacologically active beverages, and its consumption has become a regular part of daily life worldwide. It is estimated that more than half of Americans drink coffee every day. The average consumption for a person in the European Community is 5.1 kg/year, which is similar to that in the United States. [1] Caffeine is the most commonly consumed psychoactive drug in the world, and some of its behavioral effects (such as arousal) may resemble those produced by cocaine, amphetamines, and other stimulants. [4] Coffee consumption accounts for about 75% of the adult intake of caffeine in the United States, although that might be changing among younger adults with the growing popularity of energy drinks. The caffeine content of coffee varies greatly, depending on the beans, how they're roasted and other factors, but the average for an 8-ounce cup is about 100 milligrams (mg). [3] Tea has about half as much caffeine as coffee. Decaffeinated coffee has some caffeine, but the 2 to 4 mg in an 8-ounce cup is a smidgen compared with the caffeinated version. The lethal dose of caffeine is about 10 grams, which is equivalent to the amount of caffeine in 100 cups of coffee.

Caffeine gets absorbed in the stomach and small intestine and then distributed throughout the body, including the brain. [21] The amount circulating in the blood peaks 30 to 45 minutes after it's ingested and only small amounts are around eight to 10 hours later. In between, the amount circulating declines as caffeine gets metabolized in the liver. Tobacco and marijuana accelerate caffeine metabolism, which reduces the time caffeine circulates in the body. [20] Oral contraceptives slow it down, so they have the opposite effect. Researchers have identified genes that influence a person's natural risk of caffeine metabolism, which might explain why some people are exquisitely sensitive to caffeine while others are not. Caffeine probably has multiple targets in the brain, but the main one seems to be adenosine receptors. [7] Adenosine is a brain chemical that dampens brain activity. By hogging adenosine's receptors, caffeine sets off a chain of events that affects the activity of dopamine, another important brain chemical, and the areas of the brain involved in arousal, pleasure, and thinking. A part of the brain affected by Parkinson's disease, called the striatum, has many adenosine receptors; by docking on them, caffeine seems to have some protective effects. [19] Outside the brain, caffeine can be a performance

enhancer, boosting the strength of muscle contraction and offsetting some of the physiological and psychological effects of physical exertion. But, especially in the short term, it also has negative effects, which include raising blood pressure, making arteries stiffer, and increasing levels of homocysteine, insulin, and possibly cholesterol. [16] Habitual use may cause some of these effects to wear off. For some conditions, though, coffee may have some benefit despite, rather than because of, caffeine. [6]



Chemical structures of major biologically active compounds in coffee

Figure options

Observation

Although caffeine is a major component of coffee, the content is highly variable- ranging between 30 mg and 175 mg in a cup (150 mL) of home-prepared coffee. Based on the data reviewed, it can be concluded that moderate caffeine intake (2–3 cups or 300 mg/day) is not associated with adverse effects, such as cardiovascular stimulatory effects and behavioral changes, at least in healthy adults. [4] However, caffeine is not completely harmless. In fact, caffeine crosses the human placenta, rapidly reaching a similar concentration in the fetus and mother. The excessive intake of caffeine has been implicated as a cause of spontaneous abortion or impaired fetal growth. [3] Caffeine intake for women who plan to become pregnant and for women during gestation should not exceed 300 mg/day. In a variety of studies for caffeine ingestion, children can be defined as another risk group because altered behavior including nervousness or anxiety is found. [3] It is judged that an intake of 2.5 mg/kg body weight/day is an upper limit of caffeine consumption in children (Federal Department of Health, Ottawa, Ontario, Canada). [18] Coffee is the number one diet source of antioxidants in many countries including the United States, Italy, Spain, and Norway. [17] Coffee beans contain phenolic antioxidant compounds. The major polyphenol in coffee is chlorogenic acid. Chlorogenic acid is one of the major strong antioxidant compounds in coffee. [5] The antioxidant activity of coffee depends on the chemical composition. In addition, it was observed that the antioxidant activity of coffee varies according to the degree of roasting. Maximum antioxidant activity was measured for the medium-roasted coffee. [6] Coffee consumption has been associated with higher concentrations of serum total cholesterol and low density lipoprotein cholesterol. Cafestol and kahwoel are two diterpenes found in coffee oil. Diterpenes are the main cholesterol-raising compounds in coffee, but they are mostly removed by paper filters. Therefore, unfiltered coffee is a significant source of diterpenes, whereas the consumption of filtered coffee results in very little increase in serum cholesterol. [7] However, in many cases, conflicting findings and concerns have arisen, making it difficult for health professionals and the public to interpret the data. Coffee consumption tends to attract tobacco smoking, but many studies did not account for this potential confounding the data analysis. [8,18] some measurement errors seem to be inevitable in the assessment of coffee consumption, because people consume a wide variety of coffee from day to day. Coffee intake is determined by the size of the coffee cup and the strength of the brew as well as frequency of consumption. Despite 20 years of reassuring research, many people still avoid caffeinated coffee

because they worry about the biological effects of caffeine. What is the conclusion of so much attention? We have thought that coffee is good for your health when consumed in moderation. Harvard Women's Health Watch (2004) reported that current research reveals that in moderation coffee is a safe beverage that may even offer some health benefits. [9] However, it is also emphasized that difficulties and challenges in designing a solid experiment or clinical trials to elucidate the effects of coffee on human health are present. Many studies show that coffee consumption may help prevent several chronic diseases. In particular, long-term coffee consumption is associated with significant dose-dependent reductions in the risk of developing type 2 diabetes. [4] Furthermore, coffee intake reduces the risk of liver damage in people at high risk for liver disease including hepatic injury, cirrhosis, and hepatocellular carcinoma. [10] Its consumption is also inversely associated with the risk of Parkinson's disease in men and women who have never used postmenopausal estrogen. [11] The risk of Alzheimer's disease is lower in those who regularly consume caffeine-containing coffee than in those who do not drink it. [12] Coffee has also been shown to improve endurance performance in long-duration physical activities. It is very interesting that the relative risk of suicide was decreased by 13% for every cup of coffee consumed daily. [13] In general, coffee consumption has been inversely associated with the risk of cancer at various sites including liver and colorectum, but there is no clear explanation of how coffee protects against cancer. [14]

DISCUSSION

It should be considered that coffee does have modest cardiovascular effects such as tachycardia, high blood pressure, and occasional arrhythmia. [1] The acute effects of coffee on the cardiovascular system might arise in the time immediate to coffee intake or in more susceptible individuals. [10] Recent analyses have concluded that a weak inverse association may exist between coffee consumption and the risk of stroke, but further research is needed to clarify this. [14] Although there is no definite clinical relationship between coffee intake and the risk of cardiac arrhythmia, many doctors would not recommend coffee for the patients. Any contribution of coffee ingestion to the development of hypertension is likely to be small, but it is considerable particularly in infrequent coffee drinkers. [4] Caffeine leads to a slight decrease in the efficiency of calcium absorption in gastrointestinal tract. Thus, an adequate intake of calcium and vitamin D and a limitation of coffee intake to 2–3 cups/day may help reduce the risk of osteoporosis and its related fracture particularly in elderly adults. [3] Coffee consumption is used for social activity, leisure, improvement of work performance, and well-being. Coffee is not only a medicinal alternative but also a beverage containing numerous potential health benefits. The results from many types of research suggest the positive effects of coffee consumption on various aspects of health, as mentioned above briefly. Despite the general good outcomes, it should be emphasized that individual sensitivity to coffee and the biological effects of coffee among humans may vary because of personal single nucleotide polymorphic variants, as shown in an investigation on genetic polymorphisms in apolipoprotein E (*APOE*). [15] And some negative effects of coffee tend to emerge in excessive drinking, so it is the best to avoid heavy coffee intake. This minireview covers just a few of the health benefits and adverse effects associated with drinking coffee. Further studies on the functionally significant polymorphisms are needed for a better understanding of the effects of coffee on personal health. In excess, coffee, and more particularly, caffeine, can cause problems. But the fretting about two or three cups a day, or even more, is fading as study results suggestive of health benefits from coffee keep on coming in. In 2011, researchers

reported findings that coffee drinking is associated with a lower risk of depression among women, a lower risk of lethal prostate cancer among men, and a lower risk of stroke among men and women. Go back a little further, and you'll come across reports of *possible* (it's not a done deal) protective effects against everything from Parkinson's disease to diabetes to some types of cancer (see sidebar below).Caffeine has been studied more than any other ingredient in coffee, and it tends to get credit if the body part benefited is the brain. [16] But coffee contains literally a thousand different substances, and some of the lesser lights are thought to be responsible for healthful effects in other parts of the body. Some studies show caffeinated and decaffeinated coffee as having the same effect, which suggests that something else in coffee is involved. It gets complicated, though. Caffeine and some of these other substances in coffee seem to have their good and bad sides, and coffee's overall effect may depend on how much they cancel each other out.

Alzheimer's disease	Human and animal studies show hints of protection. Some preliminary evidence suggests activity against beta-amyloid plaque that may have a causative role in Alzheimer's.
Cancer	Studies suggest a lower risk for some cancers (endometrial, aggressive prostate, estrogen-negative breast), but not others (esophageal). Antioxidant and anti-inflammatory substances could be responsible for possible anticancer activity.
Diabetes	Effects on insulin and blood sugar levels that would promote diabetes seem to be temporary. Regular use is associated with lower risk, and high intake (3–6 cups a day) seems to have a greater effect. Protection may come from increases in the hormone adiponectin and other factors that affect insulin and blood sugar levels.
Heart attack	Coffee drinking increases some factors (homocysteine) associated with higher risk. But moderate consumption (1–3 cups a day) has been linked to a small decrease in risk. The evidence for a possible protective effect is stronger for women.
Liver disease	Coffee drinking is associated with lower levels of enzymes that indicate liver damage and inflammation. Coffee may improve response to some treatments for hepatitis C. Findings suggest some protection against liver cancer. Cafestol and kahweol, substances found in unfiltered coffee, may be responsible for liver benefits.
Parkinson's disease	Studies show a moderate (25%) decrease in risk for coffee drinkers. The effect is less in women. Research has found evidence of activity in the part of the brain affected by Parkinson's.
Stroke	Moderate consumption (3–4 cups a day) is associated with lower risk. But chance of a stroke may increase immediately after intake, particularly among infrequent consumers.

SUMMARY & CONCLUSION

Coffee drinkers concerned about cholesterol weren't happy about some early study results showing that coffee seems to increase cholesterol levels, and "bad" LDL cholesterol levels in particular. [15] But upon closer inspection, the bad news turned out to be not so bad, because the cholesterol-raising effect seems to be limited to coffee that hasn't been filtered, which includes Turkish coffee, coffee brewed in a French press, and the boiled coffee consumed in Scandinavia. [14] The cholesterol-raising ingredients in coffee are oily substances called diterpenes, and the two main types in coffee are cafestol (pronounced CAF-estol) and kahweol (pronounced KAH-we-awl). They are present either as oily droplets or in the grounds floating in the coffee. But a paper filter traps most of the cafestol and kahweol, so coffee that's been filtered probably has little, if any, effect on cholesterol levels. [13] The best evidence is for paper filters, but an interesting study published in 2011 showed that filtering methods used in Singapore (the so-called sock method, which uses a cotton-nylon cloth) and India (metal mesh) were also effective at trapping cafestol. Espresso contains more cafestol and kahweol than paper-filtered coffee, but because it is consumed in smaller amounts, it may not have much of an effect on people's LDL level. [11] There is a twist to this aspect of the coffee story, because cafestol and kahweol may also have some health benefits that are lost when they're filtered out. The research is in the preliminary stages, but cafestol and kahweol could have some anticancer effects and be good for the liver. Blood pressure. . [12] Results from long-term studies are showing that coffee may not increase the risk for high blood pressure over time, as previously thought. It's possible that people develop a tolerance to coffee's hypertensive effects after a while. Coffee might have anti-cancer properties. Last year, researchers found that

coffee drinkers were 50% less likely to get liver cancer than nondrinkers. A few studies have found ties to lower rates of colon, breast, and rectal cancers. Several studies have shown that caffeinated and decaffeinated coffees have different health effects. Cholesterol. Two substances in coffee - kahweol and cafestol - raise cholesterol levels. [10] Paper filters capture these substances, but that doesn't help the many people who now drink non-filtered coffee drinks, such as lattes. Researchers have also found a link between cholesterol increases and decaffeinated coffee, possibly because of the type of bean used to make certain decaffeinated coffees. Heavy coffee drinkers may be half as likely to get diabetes as light drinkers or nondrinkers. Coffee may contain ingredients that lower blood sugar. A coffee habit may also increase your resting metabolism rate, which could help keep diabetes at bay. Coffee drinkers are less likely to suffer symptomatic gallstone disease, possibly because coffee alters the cholesterol content of the bile produced by the liver. Coffee seems to protect men but not women against Parkinson's disease. One possible explanation for the sex difference may be that estrogen and caffeine need the same enzymes to be metabolized, and estrogen captures those enzymes.

Explanations for the association between coffee consumption and lower rates of heart disease and diabetes often point to chlorogenic acid and other obscure antioxidant substances as the responsible parties. Antioxidants are substances that sop up reactive molecules before they have a chance to harm sensitive tissue like the lining of blood vessels. [9] Chlorogenic acid was probably the main antioxidant in your cup of coffee this morning. Some experiments have shown that it may also inhibit absorption of glucose in the digestive system and even out insulin levels. [8] Chlorogenic acid might be another coffee ingredient with a split personality. Along with caffeine, it seems to push up levels of homocysteine, an amino acid that has been associated with artery-clogging atherosclerosis.

A health drink? Not quite.

It is one thing to say that coffee may be good for you; it's another to say it's *so* good for you that drinking it should be recommended. And we're not there yet. All of the favorable studies and all of the seemingly healthful ingredients in coffee are good news for coffee drinkers. They can relax and enjoy their habit. And people who don't drink coffee can find plenty of other things to do to help keep themselves healthy.

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