INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

The Effects of Caffeine on The Human Body: A Comprehensive Review

Kushagra Chaturvedi*, Rupal Mahure, Aditya Kawade, Dr. Vaibhav Uplanchiwar

Nagpur College of Pharmacy.

ARTICLE INFO

Published: 04 May 2025
Keywords:
Caffeine, Performance enhancement, Mental awareness, Physical endurance, Metabolic syndrome, Adverse effects, Pregnancy complications, Epigenetic effects, Adenosine receptor blockade, Cognitive enhancement.
DOI:
10.5281/zenodo.15336451

ABSTRACT

Caffeine, 1,3,7-trimethylxanthine chemically, is one of the most used dietary compounds globally, found in tea, coffee, and soft drinks. Tea and coffee constitute the main sources of caffeine, with energy drinks also being a source. Moderate caffeine intake is safe and supported by regulatory authorities. Caffeine offers performance-enhancing effects like heightened mental awareness and physical endurance. Recent studies associate caffeine with weight loss and lowering the risk of metabolic syndrome. Adverse effects of excessive caffeine consumption, particularly in pregnant women and children, should be taken into account. Recent patterns of caffeine consumption have generated the concern of health authorities about its behavioral and physiological cumulative effect. Susceptible groups, such as children and pregnant women, can be harmed by caffeine consumption. Caffeine is extremely safe in healthy adults but can be detrimental to cardiovascular function and sleep in certain susceptible populations. New evidence unveils the impact of caffeine on embryonic development and pregnancy complications. Individual differences in caffeine's effects indicate the possibility of epigenetic control. Epigenetic alterations in the fetus can result from caffeine exposure, influencing subsequent generations. The paper discusses how caffeine affects the capacity .

INTRODUCTION

Caffeine is one of the most used used substance having centrally excitatory effect .Nowadays its is used from childrens to the elderly people.It is derived from products based on coffee, coffee beans and tea leaves.When the caffeine is administered orally it shows the rapid absorption with the bioavailability of 99% (Ősz et al., 2022).Caffeine is one of the most widely used psychoactive substances across the globe, having a stimulating action on the central nervous system. Caffeine is chiefly present in coffee, tea, and energy drinks, and also in certain drugs.The drug is appreciated owing to its action to increase vigilance and foster physical performance. The

***Corresponding Author:** Kushagra Chaturvedi
Address: Nagpur College of Pharmacy.
Email ✉: chaturvedikushagra23@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

chemical composition of caffeine and its significance in general is what this review will deal with.

❖ Chemical Structure of Caffeine

Molecular Composition

It is 1,3,7-trimethylxanthine in chemical terms, a purine base of class methylxanthine, to which class belong theobromine and theophylline too. It possesses a molecular formula of C8H10N4O2 and a molecular weight of 194.19 g/mol (Atemni et al., 2022).

Physical Properties :- It is odorless and is colorless at room temperature with a distinctive bitter taste. It is extremely soluble in boiling water, and this can be further amplified by acids or complexing with compounds such as benzoate, citrate, and salicylate. Its melting point ranges from 234 to 239°C, and at a temperature of approximately 178 to 180°C, it sublimes under normal pressure (Atemni et al., 2022)

❖ Natural Sources of Caffeine: -

Coffee beans

Coffee beans are one of nature's richest sources of caffeine, and one serving of brewed coffee can range from 70 to 280 mg of caffeine depending upon brand and preparation method. Coffee plants belonging to Rubiaceae are cultivated primarily due to their coffee beans produced from them(Atemni et al., 2022).

Tea leaves

Commelia tea leaves are also a significant source of caffeine. Tea varies in amount of caffeine with black tea containing more than white or green tea (Atemni et al., 2022; Eteng et al., 1997).

Cocoa beans

Cocoa beans include theobromine, a metabolite of caffeine, among others. They are used for making chocolate and chocolate drinks. Though theobromine is the predominant alkaloid in cocoa, caffeine is present in small quantities (Eteng et al., 1997).

Others Plants

Some plants such as Cola acuminata (cola nuts), Paullinia cupana (guarana), and Ilex paraguayensis (maté) have caffeine content that is utilised in regional traditional beverages (Eteng et al., 1997).

Synthetic and Processed Source :-

Energy Drinks

Energy drinks are a popular synthetic source of caffeine, typically containing 80-150 mg of caffeine per 236 mL serving. These drinks are often consumed for their stimulating effects (Bakaloudi et al., 2022).

Medications and Supplements

Caffeine is also found in various over-the-counter medications and dietary supplements, where it is used for its stimulant properties (Atemni et al., 2022; Eteng et al., 1997).

❖ Global consumption :-

Regional and cultural patterns vary with respect to consumption of caffeinated products,with coffee leading in Western countries overall and tea leading in most countries of Asia. It is due to local traditions that this consumption trend exists. During the COVID-19 pandemic, there were reported changes in patterns of caffeine use, with some reporting reduced use from lockdown-related restrictions that prevented visits to

coffeehouses and social interactions.A systematic review of existing use of caffeine under lockdowns showed that most people cut their coffee and energy drink consumption, but there were subgroups, such as menopausal women, whose coffee consumption increased, showing varying effects of changes in behavior in subgroups of people.Overall, the global image of consumption of caffeine is complicated by cultural practices, health fads, and unrelated factors such as pandemics, so that there is an ongoing need to disentangle its effects upon way of life and health (Bakaloudi et al., 2022).

❖ **Importance of studying caffeine's effects :-**

1. Neuroprotective and Cognitive Effects :

Parkinson's and Alzheimer's Diseases

Regular use of caffeine is connected to a lowered risk of having diseases of the brain, including Parkinson's and Alzheimer's (Atemni et al., 2022).

A met-analysis reported a risk of Parkinson's disease that was 25% lower in coffee consumption, and increased caffeine consumption being associated with enhanced risk decrease (Atemni et al., 2022).

Cognitive Function and Mood

Caffeine stimulates brain activity, mood, and body performance, which underpin its popularity (Atemni et al., 2022).

It can also increase attention and vigilance, which can be especially useful under conditions of stress, like during the COVID-19 stay-at-homeorders (Bakaloudi et al., 2022).

2. Metabolic and Cardiovascular Health :

Metabolic Benefits

Caffeine intake was associated with a lower risk of type 2 diabetes, especially in those who have certain genetic polymorphisms (Abalo, 2021). It also influences lipid metabolism, potentially affecting cholesterol levels and cardiovascular health (Bakaloudi et al., 2022).

Cardiovascular Effects

Whereas caffeine acutely elevates blood and heart rate, its effects on cardiovascular health in the longer term are both complicated and possibly dependent on a person's genes (Atemni et al., 2022).

3. Reproductive and Developmental Concerns:

Pregnancy and Fetal Development

Caffeine passes across the placenta, and excessive consumption during pregnancy can have a developmental effect during fetal life, potentially resulting in negative consequences including low birth weight and developmental delay. Pregnant women should limit their consumption of caffeine in order to reduce risks to the foetus (Eteng et al., 1997).

4. Antioxidant and Anti-inflammatory Properties:-

a) Antioxidant Actions:

Components Contributing to Antioxidant Effects

Coffee, one of the richest dietary sources of caffeine, also includes many compounds that have antioxidant activity, including chlorogenic acids and polyphenols, and potentially contributes to its health effects.The antioxidant properties of caffeine itself are not the major drivers of the health effects of coffee, and other coffee

compounds are thought to contribute more to its health effects (Abalo, 2021).

Molecular Mechanisms-

The interaction of caffeine with the adenosine receptors, especially the A2A, can indirectly affect the pathways of oxidative stresses, although the mechanisms are not fully explicated yet (Fisone et al., 2004)Research using animal studies indicates caffeine modulates the functioning of proteins responsible for antioxidant protection, but the effects tend to be credited to the general content of coffee, not caffeine alone (Abalo, 2021).

b) **Anti-inflammatory Actions :**

Caffeine and Inflammatory Biomarkers The consumption of caffeine has also been examined in the context of inflammatory markers, including c-reactive protein (CRP). The evidence remains contradictory due to differences in study populations as well as methodology. Regular low levels of caffeine intake were not seen to exhibit strong anti-inflammatory effects in a group of healthy subjects, indicating that caffeine's potential to exert anti-inflammatory effects might either exist in limited or context-specific ways (Abalo, 2021).

Mechanisms of Action-

The anti-inflammatory effects of caffeine have also been proposed to result from the blockage of adenosine receptors, specifically the A2A receptors, which are involved in regulating inflammatory processes. The inhibition of A2A receptors by caffeine will have neuroprotective effects under conditions of excitotoxicity and cerebral ischemia, which are characterized by inflammatory processes (Fisone et al., 2004).

❖ **Pharmacokinetics of Caffeine :-**

1) Absorption and Distribution :

Rapid Absorption

Caffeine is rapidly absorbed in the gastrointestinal tract and reaches peak absorption within a period of 45 minutes after its ingestion(Alsabri et al., 2017; Atemni et al., 2022). Peak plasma levels are reached approximately one hour after consumption, reflecting effective absorption 3 Traverses the blood-brain barrier and the maternal-fetal barrier, which points to its extensive distribution in the body (Atemni et al., 2022).

Factors Affecting Absorption-

Differences in the absorption of caffeine can also depend on the method of administration, the type of caffeine, and the presence of other dietary components like fiber. Smoking and the consumer's age also contribute to the variation in absorption (Michałowska et al., 2014).

2) Volume of Distribution

The volume of distribution of caffeine varies from 0.5 to 0.75 L/kg, reflecting its distribution in body fluids and tissues (Alsabri et al., 2017).

Metabolism of Caffeine:-

i. Primary Metabolic Pathways

Caffeine is metabolized mainly in the liver by N-methylation, acetylation, and oxidation by the hepatic microsomal enzyme systems. The primary enzyme catalyst of caffeine N-methylation is the isozyme CYP450-1A2, resulting in the production of the prevailing metabolite, paraxanthine, in humans (Michałowska et al., 2014).

ii. Metabolite Formation and Excretion

Paraxanthine is the major metabolite, achieving ten-fold concentrations compared to other

metabolites, including theophylline and theobromine. Caffeine is eliminated in the urine in less than 48 hours, in only 1 percent of its original form, indicating extensive biotransformation. (Michałowska et al., 2014).

iii. Genetic and Environmental Influences

Caffeine acetylation is under genetic control, and it varies the clearance rate, affecting blood levels.

Oral contraception can double the half-life of caffeine, indicating the role of hormonal and genetic variables in affecting the rate of metabolism (Michałowska et al., 2014).

Factors Affecting Metabolism-

Genetic polymorphisms, lifestyle habits like smoking, and oral contraceptives use can have a strong effect on caffeine's metabolism (Atemni et al., 2022; Grzegorzewski et al., 2022). Smoking causes the caffeine to be metabolized faster, whereas oral contraceptives delay its metabolism, increasing the half-life of caffeine in users (Davide Verotta et al., 2005; Grzegorzewski et al., 2022).

3) Excretion :

i. Clearance and Half-Life

Individuals have quite different caffeine clearance rates, generally in the order of 1 to 3 mg/kg/min (Alsabri et al., 2017). The half-life of caffeine is around 4 hours but can last longer in some populations, including pregnant women and those with liver disease (Alsabri et al., 2017; Atemni et al., 2022).

ii. Renal Excretion

Most of the caffeine is metabolized prior to excretion, and a fraction of it is directly passed in the urine (Alsabri et al., 2017).

❖ Mechanisms of Action :-

1) Adenosine Receptor Antagonism :

Caffeine is a primary adenosine receptor antagonist. Through the inhibition of adenosine receptors, caffeine blocks the inhibitory action of adenosine on neuronal activity, and there is a resulting increase in alertness and a decrease in effort perceived at exercise. Adenosine receptors are present in many tissues, including the brain, heart, and skeletal muscle, and it is this that accounts for the far-reaching effects of caffeine in the body (Graham, n.d.).

Excitation-Contraction Coupling

Caffeine can increase muscle contractility by modulating excitation-contraction coupling processes. This can occur by increased calcium release through the sarcoplasmic reticulum, which is important in the contraction of muscles. Research indicates that caffeine augments force development during low-frequency muscle stimulation, indicating a direct action of the muscle fibers (Graham, n.d.).

Sympathetic Nervous System Activation

Caffeine triggers the release of catecholamines, including adrenaline, which can increase fat oxidation and the availability of energy during exercise. Its metabolic role in this increase is, however, questioned, as it might not play a crucial role in the effects of caffeine as an ergogenic substance (Graham, n.d.).

Impact on Fat and Carbohydrate Metabolism

Although caffeine is supposed to raise fat oxidation and spare muscle glycogen, the evidence to support this effect is not consistent. Respiratory exchange ratio or free fatty acid levels did not change noticeably upon caffeine consumption, according to some research. Caffeine also can have

effects on blood sugar levels by suppressing the uptake of glucose in contracting muscles, though this action is not always observed(Graham, n.d.).

2) Dopamine System:

Caffeine and Dopamine Receptors

Caffeine also shows antagonist activity at the receptors of adenosine, specifically A1 and the A2A receptors, that are also implicated in their interaction with receptors of dopamine. This interaction is responsible for caffeine's psychostimulatory effects. Caffeine blockade of adenosine A2 receptors is able to increase dopaminergic activity by inhibiting the inhibitory effect of adenosine on dopamine D2 receptors, causing enhanced release of the dopamine and increased receptor sensitivity (Ferré, 2008; Fisone et al., 2004).

Behavioral Effects and Dopamine

The potential of caffeine to intensify the action of dopamine receptor agonists indicates a crucial role in the modulation of dopaminergic neurotransmission. This is obvious in animal models whereby motor activity is increased and the actions of dopamine agonists are replicated by caffeine. The adenosine and dopamine receptor interaction is a complicated one, including receptor heteromers that affect neurotransmission and account for the stimulatory effects of caffeine (Ferré, 2008).

3) Norepinephrine System :

Caffeine and Norepinephrine Release

Caffeine's excitation of the sympathetic nervous system can result in increased catecholamine release, including norepinephrine. This is one of its wider effects of increasing alertness and arousal. The inhibitory activity of caffeine at adenosine receptors indirectly modulates the release of norepinephrine and hence its stimulating effects on mood and behavior (Atemni et al., 2022).

Impact on Mood and Behavior

The rise in release of norepinephrine caused by the consumption of caffeine accompanies increased alertness and mood enhancement, though it can also cause jitteriness and anxiety at excess dosages.The effects of caffeine on norepinephrine are a part of its more general effect on the central nervous system, affecting multiple systems of neurotransmitters to cause its typical psychostimulatory effects (Atemni et al., 2022).

❖ **Pharmacological Implications :-**

Caffeine's Stimulant Properties

The stimulatory effects of caffeine onpsychomotor processes are mainly achieved by its action as an antagonist of the A2A receptors, which regulate the activity of the striatal projection neurons responsible for motor control (Alsabri et al., 2017; Fisone et al., 2004). Caffeine's increase in the response of the dopamine receptors also helps contribute to its stimulating effects, boosting mood, vigilance, and attention (Alsabri et al., 2017).

***Role in Lipolysis and Metabolism* :**

Caffeine influences metabolic processes by inhibiting phosphodiesterases, leading to increased cyclic AMP levels, which play a role in lipolysis and energy metabolism (Herman & Herman, 2012).

❖ **Physiological Effects :-**

1) Central Nervous System Effects :

i. Stimulation and Alertness

Caffeine is a central nervous system stimulant that acts by blocking the receptors for adenosine, specifically the A1 and A2A receptors, and results in enhanced vigilance and decrease in the perception of tiredness(Atemni et al., 2022; Kalmar & Cafarelli, 1999). Boosts the release of neurotransmitters, including dopamine, which helps in the enhancement of mood and cognitive functioning (Alsabri et al., 2017).

ii. Fatigue Delay

Caffeine postpones the onset of fatigue during exercise by inhibiting the receptors of adenosine in the central nervous system, possibly increasing endurance performance (Mark Davis et al., 2003). It prolongs the time to exhaustion in exercise, implying a central mechanism of action (Kalmar & Cafarelli, 1999; Mark Davis et al., 2003).

2) Cardiovascular Effects :

i. Blood Pressure and Heart Rate

The acute intake of caffeine will produce transient elevations in blood pressure and heart rate as a result of its sympathetic nervous system stimulatory activity (Atemni et al., 2022; Turnbull et al., 2017). Caffeine's inimical action upon adenosine receptors has the potential to stimulate sympathetic nervous system activity and thereby cause these cardiovascular consequences (Atemni et al., 2022)

ii. *Cardiac Arrhythmias*

Excessive caffeine consumption may lead to cardiac arrhythmias, particularly in individuals with pre-existing disease; however, in the general population, moderate consumption is considered sufficiently safe (Atemni et al., 2022; Turnbull et al., 2017).

3) Metabolic Effects :-

Increased Metabolic Rate

Caffeine increases metabolic rate and energy expenditure, promoting lipid oxidation and thermogenesis, which can be beneficial for weight management. It mobilizes calcium in the endoplasmic reticulum, impacting muscle contraction and the metabolic processes (Atemni et al., 2022).

4) Diuretic Effects :-

Caffeine is a diuretic, causing the production of more urine by promoting renal blood flow and suppressing sodium reabsorption (Alsabri et al., 2017).

5) Potential Adverse Effects :-

i. *Vigilance and Arousal*

Caffeine boosts vigilance and arousal and will increase the quality of repetitive task performance and delay the onset of sleep. This is due to its effect on the adenosine receptors and the effect it has on neurotransmitter systems (Nehlig et al., 1992).

ii. Anxiety and Sleep Disturbances

Too much caffeine can cause anxiety, nervousness, and disturbed sleep, especially in people who are not regular users (Alsabri et al., 2017). Caffeine, though it can cause increased alertness, also tends to increase levels of anxiety and disturb sleep, especially in susceptible individuals. This is due to its stimulating action on the CNS and its property of suppressing thalamic activity, which is implicated in sleep disturbance (Nehlig et al., 1992).

iii. *Gastrointestinal Disturbances*

Caffeine can cause increased secretion of gastric acid, thereby contributing to gastrointestinal distress in certain individuals (Alsabri et al., 2017).

6) Neurological and Psychological Effects :-

i. *Cognitive Performance:* Alertness, Attention, Reaction Time

Caffeine improves attention and alertness, especially at low to moderate levels, and this can enhance cognitive functioning and reaction time (Bolton & Null, n.d.; Uddin et al., 2017). Research indicated that caffeine use can result in enhanced attention and quicker reaction time, and it is useful in the context of tasks that need sustained attention (Fiani et al., 2021).

ii. *Mood and Mental Health:* Anxiety, Depression, Euphoria

While it is true that caffeine causes a mild euphoria, as a result of increased levels of dopamine, it also worsens depression and anxiety symptoms, particularly at high levels of dosages (Bolton & Null, n.d.; Uddin et al., 2017). A moderate consumption of caffeine is correlated with a decrease in depression risk, mainly in women, but excessive use causes increased agitation and anxiety (Abalo, 2021; Jee et al., 2020).

iii. *Sleep Patterns* : Sleep Latency, Duration, Quality

Evening consumption of caffeine can increase the time it takes to fall asleep, decrease the total time slept, and change the quality of sleep by influencing the stages of sleep like REM sleep (Bolton & Null, n.d.; Uddin et al., 2017). The effects on sleep are dependent on the dose, and increased dosing results in greater disturbance, and chronic users exhibit some tolerance to the effects (Jee et al., 2020).

iv. *Addiction and Dependence :* Tolerance, Withdrawal Symptoms

Regular use of caffeine can result in tolerance, and one needs more and more of it to get the same stimulating effects. When consumption of caffeine is stopped or lowered, symptoms of withdrawal like headaches, tiredness, and irritability are experienced (Bolton & Null, n.d.; Uddin et al., 2017). The enhancement of dependence is associated with the antagonistic actions of caffeine at adenosine receptors, which can result in increased density of the receptors and the development of withdrawal when one stops using caffeine (Fiani et al., 2021).

❖ **Caffeine in Specific Populations :-**

i. Children and Adolescents :

Blood Pressure Effects

Adolescents 12 to 19 years of age have been proven to increase systolic and diastolic blood pressures (SBP and DBP) in a dose-response manner. Absorption of caffeine prior to exercise in children (7-9 years) caused augmented DBP during rest and exercise, and variable effects in the case of SBP (Turnbull et al., 2017).

Sleep and Behavioral Effects

Caffeine also negatively impacts the quality and duration of sleep in adolescents, and excessive consumption is associated with more disturbed sleep. The effect of caffeine on depression and anxiety in adolescents varies by gender, as boys have more anxiety and girls have more depression at high consumption levels (Jee et al., 2020).

ii. Pregnant and Lactating Women :

Fetal Development Concerns

Caffeine passes the placenta and will have effects on fetal development, eventually causing delayed closure of the neural tube and other types of developmental problems in animal research. Pregnancy complications include spontaneous abortion and fetal distress in cases of high caffeine consumption (Eteng et al., 1997).

Intrauterine Growth Retardation and Low Birth Weight

Epidemiological research has associated consumption of caffeine during pregnancy with both low birth weight and intrauterine growth retardation (IUGR). Even moderate daily consumption of caffeine (100-200 mg) has been shown to lead to increased risks of miscarriage and fetal growth restriction (Qian et al., 2020).

Spontaneous Abortion and Subfertility**: -**Caffeine use has also been linked to a greater risk of spontaneous abortion and subfertility (Qian et al., 2020).

Endocrine and Neurological Effects **:-** Caffeine intake while pregnant can modify maternal endocrine reactions and influence fetal brain development, which might result in developmental problems in the long term (Eteng et al., 1997).

iii. Elderly :-

Cognitive and Neurological Effects

Caffeine intake in the elderly is also related to a decrease in the risk of dementia, especially in women, indicating a cognitive protective effect. Regular consumption of caffeine can support cognitive functioning and avert cognitive decline in the elderly (Jee et al., 2020).

iv. Athletes :-

Ergogenic Effects **:**

Athletes utilize caffeine during sporting events due to its ergogenic properties of prolonging endurance and boosting exercise time to fatigue by a period of 20-50%. The effects of caffeine on the central nervous system (CNS), including the blockage of adenosine receptors, account for its potential to delay fatigue and enhance the quality of performances (Mark Davis et al., 2003).

Metabolic and Performance Impacts **:** While caffeine can increase fat oxidation and spare muscle glycogen, its primary performance-enhancing effects are likely due to CNS stimulation rather than metabolic changes (Mark Davis et al., 2003).

Individual Differences and Dosage :-

1. ***Variability in Response***

Individual variation in caffeine sensitivity can strongly impact its ergogenic efficacy, and some will even suffer anxiety or gastrointestinal upset. The ideal dosage to promote both cognitive and physical functioning is approximately 300 mg, though it can fluctuate depending on the specific conditions of the individual (McLellan et al., 2016).

2. ***Arousal and Performance***

The effects of caffeine are moderated by the arousal of individuals, the Yerkes-Dodson law indicating that moderate levels of arousal will increase performance, and high levels of it could deteriorate it. The interaction between caffeine-induced excitement and performance is complicated and potentially task difficulty and personality dependent (McLellan et al., 2016).

Health Benefits of Caffeine :-

1) Neuroprotection :

Parkinson's and Alzheimer's Disease

The consumption of caffeine has also been associated with a lower risk of neurodegenerative conditions like Parkinson's and Alzheimer's disease. Evidence indicates that caffeine could prevent oxidative damage and AD-like pathology, delay the loss of dopaminergic neurons, and promote mitochondrial activity (Uddin et al., 2017). Regular consumption of coffee has in epidemiological studies been found to be associated with a decrease in the development of these diseases, possibly due to the caffeine preventing amyloid-beta peptide buildup and diminishing neuroinflammatory reactions (Uddin et al., 2017).

Inverse Relationship with Disease Development
Epidemiological studies have repeatedly found a negative, dose-response correlation of coffee/caffeine use and risk of Parkinson's disease development**.** Increased consumption of caffeine is correlated with a decrease in risk of Parkinson's disease, and up to an 80% decrease in risk in those who use more than four caffeinated coffees per day (Nehlig, 2016).

2) Antioxidant Properties :-

Antioxidant Activity in Coffee

A primary caffeine-containing beverage, coffee, contains antioxidants including chlorogenic, ferulic, and caffeic acids. These are the substances responsible for coffee's high antioxidant activity, which is useful in preventing lipid peroxidation and oxidative stress.The antioxidant activity of caffeine, albeit weaker than that found in other components of coffee, contributes to the overall antioxidant activity of coffee beverages (Yashin et al., 2013).

3) Microbiome Modulation :-

Caffeine also impacts the gut microbiota, possibly causing health benefits. Aided by the alterations in the microbial composition and metabolites caused by caffeine, its protective effects in diseases might result (Safe et al., 2023).

4) Possible Protective Effects Against Certain Cancers :-

Cancer Prevention and Treatment

Caffeine was found to exhibit anticancer activity by suppressing a variety of pathways that play a role in cancer development, including the MAPK/ERK and PI3K/Akt pathways. It might reinforce the cytotoxic action of some anticancer medications and has also been seen to prevent tumor initiation and progression, implying a potential role in cancer therapy and chemoprevention (David Osarieme, et al., 2019).

5) Enhanced Physical Performance

Caffeine is also found to increase performance in endurance activities like running, cycling, and cross-country skiing. Moderate levels of caffeine (2-3 mg per kilogram body mass) have actually increased endurance by lowering fatigue and enhancing alertness. In racquet sports, including tennis, there is evidence that caffeine benefits specific skills, including forehand strokes, but not others, including backhand strokes. This implies the effects of caffeine might be both skill-specific and dependent on the (Burke, 2008). Caffeine also helps in enhancing the physical performance of a person, especially in endurance events. It boosts muscle contractility, fat oxidation, and endurance, which benefits the performance of athletes (Kalmar & Cafarelli, 1999; Szerej et al., 2024).

The ergogenic effects are due to the action of caffeine in the central nervous system, whereby it inhibits the adenosine receptors, resulting in the enhanced release of neurotransmitters and enhanced motor unit activation (Kalmar & Cafarelli, 1999).

Adverse Effects and Toxicity :-

i. **Caffeine-Induced Anxiety and Insomnia:**

Anxiety Symptoms

Too high a dosage of caffeine will produce symptoms of anxiety neurosis, which include irritability, nervousness, and restlessness.The stimulating effect of caffeine on catecholamine release can worsen symptoms of anxiety, especially in people suffering from pre-existing anxiety disorders (Bolton & Null, n.d.; Uddin et al., 2017).

Insomnia

Caffeine also causes disturbance in the sleep pattern, and it results in insomnia. It is a dose-related effect and more so in the case of people who don't use caffeine habitually (Bolton & Null, n.d.; Uddin et al., 2017). The substance can delay sleep onset and reduce total sleep time, affecting both the quality and quantity of sleep (Uddin et al., 2017).

ii. Cardiac Arrhythmias:

Increased Heart Rate

Caffeine induces tachycardia, a condition of abnormally fast heartbeat, and it is a typical symptom of caffeine overdose (Szerej et al., 2024). The impact of the drug on the cardiovascular system includes an increase in heart rate and a risk of arrhythmias, particularly at excessive dosing levels (Alsabri et al., 2017; Szerej et al., 2024).

Mechanisms of Cardiac Effects :
Antagonism of adenosine receptors by caffeine and its action on catecholamine levels can result in a rise in cardiac output and arrhythmias (Alsabri et al., 2017; Willson, 2018). The risk of cardiac arrhythmias is elevated in the presence of pre-existing cardiovascular conditions (Willson, 2018).

iii. Osteoporosis and Calcium Loss

Bone Health Concerns

The high intake of caffeine might disrupt calcium absorption and metabolism, hence causing bone loss and a high risk of osteoporosis. Caffeine mobilizes calcium in the cells, a factor that could lead to bone density loss in the long term (Uddin et al., 2017).

Potential Mechanisms

Caffeine's diuretic effect can lead to calcium loss, which can have a detrimental effect on bone health. Chronic high caffeine use is related to low bone mineral density, especially in those populations that have other risk factors for osteoporosis (Alsabri et al., 2017).

iv. Interaction with Other Substances

Synergistic Effects with Smoking and Alcohol
The effects of caffeine can also become intensified when it is combined with other drugs like alcohol and smoking, possibly accentuating its negative health effects (Reyes & Cornelis, 2018).

Impact on Nutrient Absorption
Caffeinated drinks like coffee and tea can disrupt the absorption of nutrients like calcium and iron, which is of special concern in the case of people having dietary requirements or augmented nutritional needs (Reyes & Cornelis, 2018).

❖ **Caffeine Substitutes and their health benefits:-**

Caffeine-Free Options

Most coffee substitutes contain no caffeine and are, therefore, safe for use by people who are caffeine-sensitive or who want to cut down on caffeine consumptionSubstances like chicory, dandelion, and barley provide the coffee-like sensation but without the stimulating properties of caffeine, which in certain people can cause problems like insomnia or anxiety (Tahmouzi et al., 2024).

Potential Health Benefits

Coffee substitutes can present a number of health benefits, including anti-inflammatory activity and enhanced hepatic function. For instance, chicory root has been found to have anti-inflammatory effects, whereas roasted roots of dandelion have the ability to promote liver health. The inulin content in chicory and in dandelion makes these alternatives useful for the purpose of diabetics, hypercholesterolemia, or obesity, as inulin serves as a prebiotic in the support of gut health (Tahmouzi et al., 2024).

❖ **Recommended Intake and Regulatory Guidelines :-**

Caffeine usage is regulated by guidelines in order to guarantee safety, specifically regarding daily intake levels and labeling of products. This answer considers the recommended levels of daily intake and the guidelines of different health bodies, including the WHO, FDA, and EFSA, as well as labeling and regulation of products containing caffeine.

Recommended Intake Limits :

1) ***General Population***

The Food and Drug Administration (FDA), Health Canada, and the European Food Safety Authority (EFSA) have agreed that the general adult population as a whole will not be at risk of significant harm when the daily intake of caffeine is not in excess of 400 mg (Willson, 2018). Furthermore, Health Canada considers safe the daily consumption of 450 mg of caffeine in healthy adults (Heckman et al., 2010). Health Canada recommends that children aged 10 to 12 years old restrict their caffeine intake to no more than 85 mg per day (Heckman et al., 2010).

2) ***Children and Adolescents***

Health Canada advises children in the age group of 10 to 12 years to limit caffeine consumption to 85 mg per day (Heckman et al., 2010). The safe limit of caffeine intake is proposed by the EFSA at 3 mg/kg body weight per day in children and adolescents (Temple et al., 2017).

3) ***Pregnant Women***

Health Canada and the EFSA suggest limiting caffeine consumption by pregnant women to a maximum of 300 mg per day(Heckman et al., 2010; Willson, 2018). The American College of Obstetricians and Gynecologists recommends that pregnant women limit caffeine consumption to below 200 milligrams a day (Temple et al., 2017).

Regulatory Guidelines :

Caffeine Labeling I

n the EU, products with more than 150mg/L caffeine are obliged to carry the label "High Caffeine Content" and the caffeine content expressed in milligrams per 100 mL In Canada, products containing 320 mg/L of caffeine are Natural Health Products, and their labeling must indicate so (Heckman et al., 2010)**.**

Product Regulation

The U.S. FDA considers caffeine Generally Recognized as Safe (GRAS) in cola-type soft drinks, up to a concentration of 200 ppm or a content of 71 mg in a 12 oz soft drink. In Australia and New Zealand, caffeine in cola-type soft drinks is permitted up to a content of 145 mg/L, and 320 mg/L in the case of energy drinks (Heckman et al., 2010).

❖ **Future research :-**

Interdisciplinary Approaches

The effects of caffeine can be better studied by incorporating genetics, physiology, and behavioral science into one interdisciplinary approach. Such multifaceted studies could lead to more personalized recommendations for caffeine consumption based on genetic profiles. Exploring the interaction between genetic factors and environmental influences, such as smoking and habitual caffeine use, could provide deeper insights into individual differences in caffeine metabolism and effects (Fulton et al., 2018). The topic of future research is crucial in advancing our understanding and management of various issues, including health disorders and environmental challenges. The provided papers offer insights into potential research directions in the areas of Caffeine Use Disorder and caffeine remediation from environmental systems. These areas highlight the need for further investigation to improve diagnostic tools, understand genetic factors, and develop effective environmental technologies.

Caffeine Use Disorders :

1. *Epidemiological Studies*

Since the most recent data is more than 15 years old, there is an urgent need for updated epidemiological studies to look at caffeine consumption among adults and children in the US. To comprehend differences in caffeine consumption rates, comparative studies between the US and other nations are required (Meredith et al., 2013).

2. *Genetic Research*

As heritability studies have not yet concentrated on caffeine use disorder, further study is required to look into the role of genetic determinants in the development of this particular disorder. The possible contribution of certain genetic polymorphisms, like those in the ADORA2A gene, to caffeine use disorder should be investigated (Meredith et al., 2013).

3. *Comorbidity with Psychiatric Disorders*

Researching the relationship between non-drug psychiatric diseases and caffeine use disorder may shed light on the wider effects of caffeine use on mental health (Meredith et al., 2013).

Environmental Remediation of Caffeine :-

1. *Technological Challenges*

Photocatalysis, while successful, is not cost-efficient, and current technologies for removing caffeine, like photolysis and biodegradation, have limitations by their sluggish processes. Although phytoremediation is gaining popularity as a green technique, it may negatively impact aquatic plants and animals, thus balanced approaches are required (Korekar et al., 2020).

2. *Molecular Imprinting Techniques*

The method of molecular imprinting (MIP) has demonstrated promise in lab settings for the removal of caffeine, a larger-scale evaluation of this technology is urgently needed for wastewater

treatment. Successful use of MIP in environmental systems requires an understanding of the variables influencing polymer-ligand recognition (Korekar et al., 2020).

3. ***Environmental Impact***

The fact that caffeine is present in water sources on a global scale, there's a need for effective approaches of removing it to guarantee the supply of clean water (Korekar et al., 2020).

CONCLUSION: -

The therapeutic properties of tea, particularly Camellia sinensis, are noted for their health-promoting potential and safety. Caffeine is a naturally occurring alkaloid found in 60 plant species, categorized as a pharmaceutical and personal care product (PPCP) due to environmental concerns. The extensive use of PPCPs leads to bioaccumulation, necessitating discussions on caffeine's fate, consumption, and toxicology. Global average caffeine consumption is 177.69 mg/person/day, below EFSA's recommendation of 400 mg/day. Caffeine is widely consumed and has been extensively researched for its health effects and pharmacology. Individual genetics and consumption patterns significantly influence caffeine's physiological and psychological effects. The Research primarily focuses on acute caffeine administration, which may not reflect typical consumption patterns. Moderate caffeine consumption is associated with potential health benefits, despite ongoing debates about its drawbacks. The review highlights caffeine's complex role in health, emphasizing the need for balanced consumption. The paper discusses caffeine's environmental impact and its effects on various organisms, emphasizing the need for monitoring and removal strategies.

REFERENCES

1. Gramza-michałowska, A. (2013). Caffeine in tea camellia sinensis – content, absorption, benefits and risks of consumption. Journal of Nutrition, Health & Aging (No. 2; Vol. 18). https://doi.org/10.1007/s12603-013-0404-1
2. Abalo, R. (2021). Coffee and caffeine consumption for human health. In Nutrients (Vol. 13, Issue 9). MDPI AG. https://doi.org/10.3390/nu13092918
3. Alsabri, S. G., Mari, W. O., Younes, S., Alsadawi, M. A., & Oroszi, T. L. (2017). Kinetic and Dynamic Description of Caffeine. Journal of Caffeine Research. https://doi.org/10.1089/jcr.2017.0011
4. Atemni, I., Tounsadi, H., & Rais, Z. (2022). Caffeine: Sources, pharmacology, health benefits and adverse. Journal of Applied Science and Environmental Studies JASES, 5(1), 59–74. https://doi.org/10.48393/IMIST.PRSM/jases-v5i1.43795
5. Bakaloudi, D. R., Evripidou, K., Jayawardena, R., Breda, J., Dardavessis, T., Poulia, K. A., & Chourdakis, M. (2022). The Impact of Lockdowns on Caffeine Consumption: A Systematic Review of the Evidence. In International Journal of Environmental Research and Public Health (Vol. 19, Issue 9). MDPI. https://doi.org/10.3390/ijerph19095255
6. Bolton, S., & Null, G. (1981). Caffeine: Psychological effects, use and abuse. Journal of Orthomolecular Psychiatry, 10(3), 202–211. https://psycnet.apa.org/record/1982-20636-001
7. Burke, L. M. (2008). Caffeine and sports performance. Applied Physiology, Nutrition and Metabolism, 33(6), 1319–1324. https://doi.org/10.1139/H08-130
8. David Osarieme, E., Modupe, D. T., & Oluchukwu, O. P. (2019). The Anticancer Activity of Caffeine - A Review. Archives of

Clinical and Biomedical Research, 03(05). https://doi.org/10.26502/acbr.50170077

9. Davide Verotta, C., Csajka, C., Haller, C. A., Benowitz, N. L., & Verotta, D. (2005). British Journal of Clinical Pharmacology Mechanistic pharmacokinetic modelling of ephedrine, norephedrine and caffeine in healthy subjects. Br J Clin Pharmacol, 59, 3–335. https://doi.org/10.1111/j.1365-2125.2005.2254.x
10. Eteng, M. U., Eyong, E. U., Akpanyung, E. O., Agiang, M. A., & Aremu, C. Y. (1997). Recent advances in caffeine and theobromine toxicities: a review. In Plant Foods for Human Nutrition (Vol. 51). Kluwer Academic Publishers. https://doi.org/10.1023/A:1007976831684
11. Ferré, S. (2008). An update on the mechanisms of the psychostimulant effects of caffeine. In Journal of Neurochemistry (Vol. 105, Issue 4, pp. 1067–1079). https://doi.org/10.1111/j.1471-4159.2007.05196.x
12. Fiani, B., Zhu, L., Musch, B. L., Briceno, S., Andel, R., Sadeq, N., & Ansari, A. Z. (2021). The Neurophysiology of Caffeine as a Central Nervous System Stimulant and the Resultant Effects on Cognitive Function. Cureus. https://doi.org/10.7759/cureus.15032
13. Fisone, G., Borgkvist, A., & Usiello, A. (2004). Caffeine as a psychomotor stimulant: Mechanism of action. In Cellular and Molecular Life Sciences (Vol. 61, Issues 7–8, pp. 857–872). https://doi.org/10.1007/s00018-003-3269-3
14. Fulton, J. L., Dinas, P. C., Carrillo, A. E., Edsall, J. R., Ryan, E. J., & Ryan, E. J. (2018). Impact of genetic variability on physiological responses to caffeine in humans: A systematic review. In Nutrients (Vol. 10, Issue 10). MDPI AG. https://doi.org/10.3390/nu10101373
15. Graham, T. E. (1994). Caffeine and Exercise Metabolism, Endurance and Performance. Canadian Journal of Applied Physiology. (Vol 19, Issue 2, pp. 111-138). https://doi.org/10.1139/h94-010
16. Grzegorzewski, J., Bartsch, F., Köller, A., & König, M. (2022). Pharmacokinetics of Caffeine: A Systematic Analysis of Reported Data for Application in Metabolic Phenotyping and Liver Function Testing. In Frontiers in Pharmacology (Vol. 12). Frontiers Media S.A. https://doi.org/10.3389/fphar.2021.752826
17. Heckman, M. A., Weil, J., & de Mejia, E. G. (2010). Caffeine (1, 3, 7-trimethylxanthine) in foods: A comprehensive review on consumption, functionality, safety, and regulatory matters. Journal of Food Science, 75(3). https://doi.org/10.1111/j.1750-3841.2010.01561.x
18. Herman, A., & Herman, A. P. (2012). Caffeine's mechanisms of action and its cosmetic use. In Skin Pharmacology and Physiology (Vol. 26, Issue 1, pp. 8–14). https://doi.org/10.1159/000343174
19. Jee, H. J., Lee, S. G., Bormate, K. J., & Jung, Y. S. (2020). Effect of caffeine consumption on the risk for neurological and psychiatric disorders: Sex differences in human. In Nutrients (Vol. 12, Issue 10, pp. 1–20). MDPI AG. https://doi.org/10.3390/nu12103080
20. Kalmar, J. M., & Cafarelli, E. (1999). Effects of caffeine on neuromuscular function. Journal of applied physiology (Vol. 87, Issue 2, pp. 801-808) https://doi.org/10.1152/jappl.1999.87.2.801
21. Korekar, G., Kumar, A., & Ugale, C. (2020). Occurrence, fate, persistence and remediation of caffeine: a review. Environmental Science and Pollution Research, 27(28), 34715–34733. https://doi.org/10.1007/s11356-019-06998-8

22. Mark Davis, J., Zhao, Z., Stock, H. S., Mehl, K. A., Buggy, J., Hand, G. A., Mark, J., & Mehl, K. A. (2003). Central nervous system effects of caffeine and adenosine on fatigue. Am J Physiol Regul Integr Comp Physiol, 284, 399–404. https://doi.org/10.1152/ajpregu.00386.2002.-Caffeine
23. McLellan, T. M., Caldwell, J. A., & Lieberman, H. R. (2016). A review of caffeine's effects on cognitive, physical and occupational performance. In Neuroscience and Biobehavioral Reviews (Vol. 71, pp. 294–312). Elsevier Ltd. https://doi.org/10.1016/j.neubiorev.2016.09.001
24. Meredith, S. E., Juliano, L. M., Hughes, J. R., & Griffiths, R. R. (2013). Caffeine Use Disorder: A Comprehensive Review and Research Agenda. Journal of Caffeine Research, 3(3), 114–130. https://doi.org/10.1089/jcr.2013.0016
25. Nehlig, A. (2016). Effects of coffee/caffeine on brain health and disease: What should i tell my patients? In Practical Neurology (Vol. 16, Issue 2, pp. 89–95). BMJ Publishing Group. https://doi.org/10.1136/practneurol-2015-001162
26. Nehlig, A., Daval, J.-L., & Debry, G. (1992). Caffeine and the central nervous system: mechanisms of action, biochemical, metabolic and psychostimulant effects. In Brain Research Reuiews (Vol. 17). https://doi.org/10.1016/0165-0173(92)90012-B
27. Ősz, B. E., Jîtcă, G., Ștefănescu, R. E., Pușcaș, A., Tero-Vescan, A., & Vari, C. E. (2022). Caffeine and Its Antioxidant Properties—It Is All about Dose and Source. In International Journal of Molecular Sciences (Vol. 23, Issue 21). MDPI. https://doi.org/10.3390/ijms232113074
28. Qian, J., Chen, Q., Ward, S. M., Duan, E., & Zhang, Y. (2020). Impacts of Caffeine during Pregnancy. In Trends in Endocrinology and Metabolism (Vol. 31, Issue 3, pp. 218–227). Elsevier Inc. https://doi.org/10.1016/j.tem.2019.11.004
29. Reyes, C. M., & Cornelis, M. C. (2018). Caffeine in the diet: Country-level consumption and guidelines. In Nutrients (Vol. 10, Issue 11). MDPI AG. https://doi.org/10.3390/nu10111772
30. Safe, S., Kothari, J., Hailemariam, A., Upadhyay, S., Davidson, L. A., & Chapkin, R. S. (2023). Health Benefits of Coffee Consumption for Cancer and Other Diseases and Mechanisms of Action. In International Journal of Molecular Sciences (Vol. 24, Issue 3). MDPI. https://doi.org/10.3390/ijms24032706
31. Szerej, K., Dorobek, W., Stankiewicz, K., & Świeczkowski-Feiz, J. (2024). The Role of Caffeine in Enhancing Physical Performance: From Metabolism to Muscle Function. Journal of Education, Health and Sport, 59, 158–165. https://doi.org/10.12775/jehs.2024.59.010
32. Tahmouzi, S., Nasab, S. S., Alizadeh-Salmani, B., Zare, L., Mollakhalili-Meybodi, N., & Nematollahi, A. (2024). Coffee substitutes: A review of the technology, characteristics, application, and future perspective. In Comprehensive reviews in food science and food safety (Vol. 23, Issue 6, p. e70041). https://doi.org/10.1111/1541-4337.70041
33. Temple, J. L., Bernard, C., Lipshultz, S. E., Czachor, J. D., Westphal, J. A., & Mestre, M. A. (2017). The Safety of Ingested Caffeine: A Comprehensive Review. In Frontiers in Psychiatry (Vol. 8). Frontiers Media S.A. https://doi.org/10.3389/fpsyt.2017.00080
34. Turnbull, D., Rodricks, J. V., Mariano, G. F., & Chowdhury, F. (2017). Caffeine and cardiovascular health. Regulatory Toxicology

and Pharmacology, 89, 165–185. https://doi.org/10.1016/j.yrtph.2017.07.025

35. Uddin, M. S., Abu Sufian, M., Hossain, M. F., Kabir, M. T., Islam, M. T., Rahman, M. M., & Rafe, M. R. (2017). Neuropsychological Effects of Caffeine: Is Caffeine Addictive? Journal of Psychology & Psychotherapy, 07(02). https://doi.org/10.4172/2161-0487.1000295
36. Willson, C. (2018). The clinical toxicology of caffeine: A review and case study. In Toxicology Reports (Vol. 5, pp. 1140–1152). Elsevier Inc. https://doi.org/10.1016/j.toxrep.2018.11.002
37. Yashin, A., Yashin, Y., Wang, J. Y., & Nemzer, B. (2013). Antioxidant and antiradical activity of coffee. In Antioxidants (Vol. 2, Issue 4, pp. 230–245). MDPI. https://doi.org/10.3390/antiox2040230.

HOW TO CITE: Kushagra Chaturvedi*, Rupal Mahure, Aditya Kawade, Dr. Vaibhav Uplanchiwar, The Effects of Caffeine on The Human Body: A Comprehensive Review, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 5, 617-633 https://doi.org/10.5281/zenodo.15336451