

Would “Low Caffeine Intake” rather than “No caffeine intake” assure healthy human body?

Tabinda Sattar*

Institute of Chemical Sciences, Bahaudin Zakaraya University Multan, Pakistan

Abstract

Background: Caffeine consumption is now common worldwide, due to its wide benefits. Caffeine intakes would affect the three major systems like mental, cardiovascular and reproductive ones.

Aims: This review focuses on the point that caffeine prohibition will make you unable from enjoying the unlimited caffeine benefits.

Methods: When the caffeine intake amounts exceed about 300 mg/day, then some adverse effects may be resulted.

Results: Although stamina to consume caffeine vary from person to person and is gender specific also. But low to moderate caffeine intakes ((~40 mg to ~300 mg/day) have been reported for the positive effect on overall human body resulting in alertness, vigilance, complex decision making, cognition, attention improve, muscle strength, endurance, improved cardiac and sexual health.

Conclusions: So in order to fully benefit from it you need to be vigilant about the caffeine amounts of the caffeinated products you are taking and also your body capacity of caffeine consumption.

Keywords: Caffeine consumption, Caffeine benefits, Caffeine intakes, Caffeine doses, Caffeine sources.

Introduction

The widely used central nervous system stimulant and psychoactive drug is not other than the caffeine. Different parts of world differ in the usage of caffeine although it is legal and unregulated [1]. Chemically related to adenine and guanine bases, it is very bitter in taste. Seeds, nuts and leaves of some plants found in Africa, East Asia and South America are the main sources of caffeine. Although many artificial sources of caffeine are present which are widely used worldwide? [2]

The main function of caffeine is the improved body performance by relief from conditions of drowsiness and sleepiness. The chemistry behind the mechanism of action of caffeine lies in the fact that the caffeine can reversibly blocks the adenosine receptors that creates the drowsiness conditions after long wakeful hours [3]. Caffeine can affect the overall human health. Caffeine intakes in moderate and low amounts can cause increase in alertness, energy and cognitive functions. But excessive amounts of caffeine have been reported not only creating some psychological effects (e.g., changes in motivation, determination, belief, mood states, etc.) but cardiovascular and sexual effects as well.

For most healthy adults, the safe amount of caffeine for most healthy adults is up to 400 milligrams (mg) per day. Although the same amount of caffeine may be too much for children. So there are no hard and fast rules for the standard bearable amounts of caffeine although all the humans using caffeinated

products should be aware of the amounts of caffeine present in that specific caffeinated products under their regular use. On the whole all persons may use caffeinated food products and fully enjoy its benefits but should avoid too much use of these on regular basis [4].

As the amount of caffeine varies widely among different food products of the same type for instance the coffee variety of different kinds may contain different caffeine amounts [5]. So a person should be well aware off the amounts of caffeine present in the caffeinated products under regular use. (Table 1) describes the highest and lowest amounts of caffeine present in coffee, energy drinks and other caffeinated food products. If a person wants to avoid any unpleasant side effects of caffeine then he or she should choose the coffee or energy drink having less caffeine rather than having highest caffeine as too much of caffeine is harmful for all age groups and genders as well [6].

Despite of the empirical facts that high levels of caffeine are harmful in children and adolescents too, many parents still remain unconscious with the caffeine intakes of their children and themselves as well. Nevertheless the caffeine intakes are safe in adults but adults should also be well aware off the caffeine contents of the caffeine present in the caffeinated food products [7]. In developed countries like United States America, caffeine consumption in children and adults should be according to the recommendations of the American Academy of Pediatrics. As mostly parents are not aware off the caffeine intakes of their children and there is no record of

*Correspondence to: Tabinda Sattar, PhD Scholar, Institute of Chemical Sciences, Bahaudin Zakaraya University Multan, Pakistan, E-mail id: pamsariam22@gmail.com

Received: 05-Feb-2023, Manuscript No. AAJNHH-23-89395; Editor assigned: 08-Feb-2023, Pre QC No. AAJNHH-23-89395(PQ); Reviewed: 22-Feb-2023, QC No. AAJNHH-23-89395; Revised: 24-Feb-2023, Manuscript No. AAJNHH-23-89395(R); Published: 28-Feb-2023, DOI: 10.35841/aaajnhh-7.1.135

Table 1. Major Food Items having Relevant Caffeine Amounts.

	Coffee	All	8Oz	2-200
1	Highest Caffeinated Coffe	Starbucks Blonde, Roasted Coffee	Vent, 20Oz	475
	Lowest Caffeinated Coffee			
2	Tea	Brewed, Decaf	8Oz	02-May
	Highest caffeinated Tea	All	8Oz	0-95
3	Lowest Caffeinated Tea	Starbuck Latte Chai	8Oz	47
	Soft Drink	Herbal Tea	8Oz	0
4	Highest Caffeinated Soft Drink	All	8Oz	0-60
	Lowest Caffeinated Soft Drink	Pepsi Zero Sugar	20Oz	115
5	Energy Drinks	7Up, Fanta, Sprite	20Oz	0
	Highest Caffeinated Energy Drink	All	8Oz	50-200
6	Lowest Caffeinated Energy Drink	Bang Energy	16Oz	351
	Caffeinated Snack Food	Starbuck Refresher Can	12Oz	50
7	Highest Caffeinated Snack Food	All	36g	20-150
	Lowest Caffeinated Snack Food	Steam Caffeinated Peanut Butter	36g	150
8	Ice Cream & Yougurt	GU Energy Chews(Strawberry/Black berry)	4Chews	20
	Highest Caffeinated Snack Food	Bang (Caffeinated Icecream)	40Oz	1-125
9	Lowest Caffeinated Snack Food	Haagen Dazs Chocholate Icecream	40Oz	Less than 1
	Chocolate Candy & Chocolate Drink	All	1 Box	2-600
10	Highest caffeinated Snack Food	Crackheads Gourmet Chocholate-Coffee	1 Box	600
	Lowest Caffeinated Snack Food	Hershey's Chocholate Low Fate Milk	12Oz	2
11	Over the Counter Pills	All	2 Tablets	65-300
	Highest Caffeinated Snack Food	Zantex-3-Weight Loss Supplement	2 Capsules	300
12	Lowest Caffeinated Snack Food	Anacin	2 Tablets	83
	Pure Caffeine	All	1 tsp	70-200
13	Highest Caffeinated	Caffeine Powder	1/16 or 1/32 tsp	200
	Lowest Caffeinated	Liquid Caffeine (Brand)	1tsp	83

the routine address at the pediatric appointments so caffeine consumption in USA is producing irrelevant records about highest caffeine damages [8].

Caffeine use is different at different country levels. (Table 2) describes the highest caffeine users throughout this world. Although Finland is considered as the highest coffee consumer but overall caffeine is most highly used in Sweden [9]. In spite of the beneficial effects of caffeine, the severe kinds of harmful effects of caffeine usage also reported from the highest caffeine consumer in the world that is none other than Sweden. From these preliminary reports, it can be well considered that caffeine remains a friend for human body until and unless it is used in moderate amounts, but it may be proved as foe if high doses used on regular basis [10].

What would caffeine do with human body

Blood- brain barrier that separates the blood stream from brain is rapidly crossed by the caffeine that is both water and lipid soluble. When inside the brain, caffeine rapidly reduces the effects of adenosine. Caffeine will act as non selective and competitive antagonist of adenosine receptors as its structure is quite similar to that of adenosine receptors [11]. Caffeine is also an antagonist of inositol triphosphate receptor 1 and ionotropic glycine receptors (. It can also act as a voltage dependent activator of the cyanodine receptors (RYR1, RYR2, and RYR3).

No direct binding of caffeine and dopamine receptors is still reported. But it can subsequently affect the binding activity

of dopamine at its receptors specifically A1-D1 receptors (heterodimine) and A2A-D2 receptors (heterotetramine). Caffeine can mediate the psychostimulant effects and pharmacodynamic interactions of A2A-D2 to the point dopaminergic psycho stimulant. The release of dopamine in the dorsal striatum and nucleus accumbens core is the main responsibility of caffeine use. Caffeine plays a role in the raising intracellular CAMP, activates proteins kinase A TNF-alpha and leukotriene synthesis [12].

Caffeine can inhibit TNF-alpha, leukotriene synthesis that will reduce the inflammation and innate immunity [13]. It also affects the cholinergic system where it inhibits the enzymes. The main wakefulness prompting effects of caffeine are resulted by disinhibition of tuberomammily nucleus. In the ventrolateral preoptic area (VLPO) adenosine A2A receptors are antagonized by caffeine. Only 45 minutes are sufficient for caffeine to get absorbed by small intestine and thus instantly distributed to the bodily tissues [14].

The half life of caffeine is different among different individuals according to pregnancy, other drugs, liver enzyme function and age [15]. Among healthy individuals the total time required for body to eliminate one-half of caffeine doze is 3-7 hours. In pregnant women during third trimester it will be 15 hours, while oral contraceptives it may be 14 hours and decrease to 30-50% due to smoking. In new born this time would be 80 hours [16]. After using fluroxamine-antidepressant (4.9 hours increase to 56 hours). Cytochrome P450 oxidase can metabolize the caffeine in liver. Parazanthine (84%), theobromine (12%),

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Table 2. List of Top 10 Highest Caffeine Consuming Countries.

Number /Country	Highest Coffee Consumers (Kg)	Highest Tea Consumers (lbs)	Highest Soft Drink Consumers	Highest Chocolate Drink Consumers(Pounds)	Highest Total Caffeine Consumers (mg/Day)
1	Finland (12)	Turkey(3.16)	Argentina(155)	Switzerland(18.1)	Sweden(388)
2	Norway(9.9)	Ireland(2.19)	United States America(154)	Germany(16.3)	Norway(379)
	Iceland(9.0)	United Kingdom(1.94)	Chile(141)	Austria(15.7)	Netherland(369)
4	Denmark(8.7)	Iran(1.50)	Mexico(137)	Ireland(14.6)	Denmark(354)
5	Netherland(8.4)	Russia(1.38)	Uruguay(113)	United Kingdom(15.1)	Finland(322)
6	Sweden(8.2)	Morocco(1.22)	Belgium(109)	Norway(13)	Germany(292)
7	Switzerland(7.9)	Newzealand(1.19)	Germany(98)	Estonia(12)	Switzerland (275)
8	Belgium(6.8)	Egypt(1.01)	Norway(98)	Sweden(11)	Austria (276)
9	Luxembuy(6.5)	Poland(1.00)	Saudi Arabia(89)	Kazhaghstan(10.9)	Nicerogue (219)
10	Canada(6.2)	Japan(0.99)	Bolavia(89)	Slovakia(10.7)	France(215)

theophylline (4%) and 1,3,7-trimethyl acid (minor quantity). These will increase free fatty acid level, urine volume, relaxes smooth muscles and dilates blood vessels collectively [17,18].

The caffeine intakes will be proved very much beneficial if taken in moderate amounts. When inside human body, caffeine affects three major systems like mental, cardiovascular and sexual ones. The main effect of caffeine can be recognized as the central nervous system stimulant. It can give temporarily relieve from drowsiness and fatigue. Also its stimulating effect can produce alertness in right way. A research report has revealed that a 45 percent low risk of suicide has been detected in those participants who were taking caffeine in regular and moderate amounts. Caffeine intake in high amounts may cause confusion and headaches [19].

Gender differences are related with effects of the caffeine intakes. Male cardiac and reproductive systems are not much affected by high caffeine intakes. Whereas the high caffeine intake may create some issues with pregnancy in case of females. Heartburn, nausea and vomiting are some symptoms of high caffeine intakes. Irritability and muscle aches may be some symptoms of caffeine withdrawal. The present study is related to the effects of caffeine intakes on human body [20].

Mental effects of caffeine

Mental effects of caffeine are nevertheless much important. Different doses of caffeine have different mental effects. Although low to moderate values can improve cognitive function and high doses may lead towards cognitive failures. Neuromodulating and homeostatic effects of caffeine acts on two receptors with contrasting actions. The A1 and A2A receptor antagonism of caffeine will influence the optimal levels of adenosinergic activity [20]. The authors reported that different doses of caffeine impact differently upon mental conditions.

Anxiety, jitters and nervousness are the main results of high caffeine intakes. While low caffeine intakes will surely give soothing effects to mental health of humans. Daytime sleepiness in adolescents may be caused by high doses of caffeine [21]. So high caffeine intakes on regular basis would have negative impact upon the human health. As caffeine has become the most used psychoactive drug worldwide during the last decade [22]. The dopaminergic activity including mood, attention, executive functioning, and regulation of behavioral traits are greatly affected by the caffeine [23-25].

According to some research reports, the caffeine consumption has great impact upon the depression. Low to moderate values of caffeine intake may decrease the depressive symptoms. Although high amounts caffeine intake can have negative effects. Several studies have reported that caffeine consumption is significantly associated with depressive symptoms and that it decreases the risk of depression [26]. Physical resistance performance is also made better by the moderate intakes of caffeine [27]. Increase in alertness and decrease in both the reduced sleepiness as well as fatigue are the common effects of moderate and low intakes of caffeine [28]. Insomnia is the main adverse effect of high caffeine intakes [29, 30].

The prevalence of caffeine dependence has been reported which indicate that the habitual caffeine users will show a rate of endorsement of clinically meaningful indicators of distress and functional impairment [31]. A condition for further study included is the Diagnostic and Statistical Manual of Mental Disorders (5th ed.) which has been discussed in the diagnostic criteria for Caffeine Use Disorder [32]. The year wise work of different researchers upon the mental and cognitive effects of caffeine has been described in (Table 3).

Low to moderate intakes of caffeine either in the form of a coffee or other caffeine sources is very beneficial in increasing the alertness and cognitive functions of body. It has been reported that the cognitive function in hemodialysis patients was improved by the coffee drinking which is the main source of caffeine intake. The higher mean scores on all tested cognitive domains were achieved by the regular coffee drinkers [33]. The beneficial impact on cognitive function in hemodialysis patients was noted by low to moderate caffeine intake due to selective enhancement of attention and vigilance on alertness and cognitive functions. Moderate amounts of caffeine intakes can impair the cognitive ability in regular caffeine users.

Patients with headache can be treated by the use of caffeinated headache medications, either alone or in combination with other treatments. The over-the-counter treatment of headache has demonstrated the role of caffeine in migraine and headache. Caffeine was found involved as the analgesic adjuvant in the acute treatment of primary headache. Efficacy of analgesics along with caffeine was found more effective rather than analgesics alone. But the nervousness (6.5%), nausea (4.3%), abdominal pain/discomfort (4.1%), and dizziness (3.2%) were noted in patients taking heavy doses of caffeine based medications.

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Table 3. Mental Effects of Different Doses of Caffeine Intake.

Mental Properties/ Year wise Work	Dose	Lara et al., 2010	James et al., 2011	Ishak et al., 2012	Steven et al., 2013	Petar et al., 2014	Richard et al., 2015	Cappelletti et al., 2016	Temple et al., 2017	Callogen at al., 2018	Cornelis at al., 2019
Increased Alertness/Attention	L	D	D	D	D	D	D	D	D	D	D
	M	D	D	D	D	D	D	D	D	D	D
	H	D	D	D	D	D	D	D	D	D	D
Cognitive Function	L	D	D	D	D	D	D	D	D	D	D
	M	D	D	D	D	D	D	D	D	D	D
	H	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Elevating Mood	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	D	D	D	D	D	D	D	D	D	D
	H	D	D	D	D	D	D	D	D	D	D
Cognitive Failure	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Depressive Symptoms	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	D	D	D	D	D	D	D	D	D	D
Psychiatric Disorders	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	D	D	D	D	D	D	D	D	D	D
	H	D	D	D	D	D	D	D	D	D	D
Psychotic/Mannic Disorders	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	D	D	D	ND	ND	ND	D
	H	ND	ND	ND	ND	D	D	D	ND	D	ND
Obsessive Compulsive Disorders	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	D	D	D	D	D	D	ND	ND	ND	ND
	H	D	D	ND	D	D	D	D	D	D	D
Polymorphism of A ₂ Receptors	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	D	D	D	D	D	ND	D	D	D
Anxiety	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	D	D	D	D	D	D	D	D	ND	ND

The mainly concentration, memory enhancement and physical performance are the main tasks of caffeine usage. The locomotors activity stimulation and anxiogenic-like effects of caffeine are mainly due to coffee and caffeine-containing products which may affect the central nervous system [34]. But more and more dependence upon caffeine has become significant leading towards individuals at risk for premature and unnatural death due to caffeine intoxication. Hence right caffeine doses are necessary for attaining its beneficial effects. Otherwise its lethal effects can destroy the mental health if taken in high dosage for longer time periods [35].

Coffee, tea, and chocolate are natural and main sources of caffeine and due to its common availability it has become the top most used psychoactive drug worldwide. Arousal, alertness, energy, and elevated mood are the main consequences of caffeine usage [33]. With the passage of time other caffeine sources has been introduced. Due to change in consumption patterns of the more traditional sources of caffeine there may be a need of increased scrutiny by health authorities and regulatory bodies about the overall consumption of caffeine [36,37].

But the rate of caffeine intake may vary accordingly as in pregnant and lactating women, children and adolescents, young adults, and people with underlying heart or other health conditions, such as mental illness [38]. An amount of caffeine may be potentially vulnerable to the negative effects; on the other hand the same dosage of caffeine may result in alertness, energy and cognitive function of a healthy adult.

Along with high caffeine dosage, the point of concern is also related to the body conditions of caffeine using persons. So the healthy adults can safely consume caffeine as compared to the vulnerable populations [39,40].

Due to its reported ergogenic properties like enhanced muscular force development and central nervous stimulation, the use of caffeine across sports and exercise is very common. All explore CAF expectancies, in conjunction with/without CAF pharmacology. Several studies have revealed the fact that the endurance capacity, weightlifting performance, simple reaction time and better memory were noted in persons by regular caffeine consumption [41]. But the fact remains in place that the caffeine consumption in regular users and non-regular users will imply different effects. Also the caffeine impact will vary person to person depending upon body capacity and body conditions.

Cardiovascular effects of caffeine

Caffeine affects the cardiovascular system, both in positive and negative ways depending upon the caffeine consumption. When taken in moderate amounts it can help with the proper blood flow, pressure and rate. No adverse effects can strike the cardiac system until the caffeine dose crosses the low to moderate intake values. Higher caffeine intakes can result in mild increase in blood pressure in hypertensive patients. So while taking caffeine you should be well familiar about your body capacity of caffeine consumption, only then you can fully enjoy caffeine benefits [42].

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The relative risks of total cardiovascular disease (CVD), coronary heart disease (CHD) and acute myocardial infarction (AMI) has been reported by the excessive and generous intakes of caffeine on regular basis [43-45]. The effects on arrhythmia, heart failure, sudden cardiac arrest, stroke, blood pressure, hypertension by the regular and excessive users of caffeine beverages have evaluated the fact that excessive amounts of caffeine intakes will surely result in biomarkers of effect, including heart rate, cerebral blood flow, cardiac output, plasma homocysteine levels, serum cholesterol levels, electrocardiogram (EKG) parameters, heart rate variability, endothelial/platelet function and plasma/urine catecholamine levels [46].

While studying about cardiovascular effects of caffeine, it is still difficult to decide that what amounts of caffeine intakes can be counted as the excessive amounts. As the literature describes caffeine levels up to 600 mg/day in most cases may be mild, transient or reversible. A range of reversible and transient physiological effects are associated with the caffeine intake so these can result in the specific cardiovascular effects [47]. As data on taking caffeine above 600 mg/day is not up to the mark, so the identifiable daily greater uptakes of caffeine is so difficult. The decreased risks of total cardiovascular disease; arrhythmia; heart failure; blood pressure can be resulted from mild caffeine intakes.

The guidelines listed on caffeine consumption can never be strict to adhere as it is consumed both from natural and artificial sources (coffee and tea) as well. The proposed beneficial role in alertness, performance and energy expenditure along with its side effects has lead to the concerns regarding the safety of caffeine in the cardiovascular system. The question remains “Which dose is safe?, as the population. The population, type and dose of caffeine are the things that must be considered while taking the safe dose of caffeine that does not appear to adhere to the strict [48].

Potential concerns regarding, adverse cardiovascular sequel of a stimulant like caffeine are well observed. Reports on the excessive use of caffeinated beverages have revealed the conditions of hypertension, coronary artery disease, rhythmic disorders and heart failure in billions of patients worldwide. On the other hand, moderate amounts of caffeinated beverages may be proved beneficial for the coronary heart disease, heart failures and arrhythmia [49]. The year wise work of different researchers upon the cardiovascular effects of caffeine has been described in (Table 4).

Several research reports have revealed that positive effects of caffeine on the cardiovascular health are obtained. Many positive inotropic and chronotropic effects of caffeine on the cardiovascular effects of caffeine -like effects have been reported. The locomotor activity stimulation and angiogenic

Table 4. Cardiovascular Effects of Different Doses of Caffeine Intake.

Cardiovascular Properties/Year wise Work	Dose	Eumann et al., 2010	Pelli et al., 2011	Sonsalla et al., 2012	Salvemini et al., 2013	Dinget al., 2014	Cappelletti et al., 2015	Wilson et al., 2016	Turnbull et al., 2017	Sharaet al., 2018	Zhouet al., 2019
Cardiovascular Disease(CVD)	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	D	ND	ND	ND	ND	ND	ND	ND
	H	D	D	D	D	D	D	D	D	D	D
Coronary Heart Disease (CHD)	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	D	D	ND	D	D	D	D	D	D	D
Arrythmia	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	D	D	D	D	D	D	D	D	D	D
	H	D	ND	D	ND	ND	D	ND	D	ND	ND
Increased Heart Rate	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	ND	D	D	D	D	ND	D	D	D
High Blood Pressure	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	D	ND	D	D	ND	D	D	D	D	D
Heart Stroke	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	D	ND	ND	D	ND	ND	D	ND
	H	D	D	D	D	D	D	D	D	D	D
Endothelial/Platelets Dysfunction	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	D	D	D	ND	ND	ND	D
	H	ND	ND	ND	ND	ND	ND	ND	ND	D	ND
Sudden Cardiac Arrest	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Increased Cholesterol Levels	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	ND	ND	D	D	D	ND	D	D	ND
Hypertension	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	D	ND	ND	D	ND	D	ND	D	D	D

effects of caffeine based products are due to their underlying motivations which result in concentration, memory enhancement and physical performance. The individuals' preexisting metabolism alterations or diseases along with caffeine's interaction with other substances are the factors that may lead towards the lethal or toxic effects of caffeine, when caffeine intake is beyond the safe limits [50].

Generally speaking the coffee consumption has been reported as safe for human heart as evidenced by prospective cohorts, meta-analyses and clinical investigations. While talking about the CVD risk factors, the chronic coffee intake consumption may result in little increase in blood pressure. As atherogenic lipid levels are raised due to the boiled coffee brewing so you should aware off the caffeine amounts and brewing methods of the coffee you are taking. Very little risk for atrial or ventricular arrhythmias due to coffee intakes has been reported in our society [51]. More critical research is required for the effects of newer caffeinated beverages with high caffeine and calories amounts per serving.

In most cases, only mild, transient, and reversible cardiovascular effects of caffeine without any long lasting adverse effects have been recorded for the caffeine consumption at levels up to 600 mg/day. As significant amounts of research reports on the effects of daily intakes greater than 600 mg are not available so the levels at which caffeine intake may cause harm to the cardiovascular system have not yet been established. But one thing is clear that no biomarkers of cardiac effect (heart failure; blood pressure, hypertension, CHD, CVD, arrhythmia) have been reported with moderate caffeine intakes even in regular coffee drinkers [52-55].

According to some research reports the cardiovascular activity in humans is highly affected when the widely used drug-caffeine is used without having any information about the caffeine amounts present in caffeinated and decaffeinated coffee. The mechanism of action of caffeine is related to increase in intracellular calcium concentration along with sensitization of dopamine receptors and the release of norepinephrine [56]. Very high doses of caffeine are involved with supraventricular and ventricular tachyarrhythmias, that may lead to the blockade of adenosine receptors. Although more research is required in order to fully understand the extended psychophysiological effects of caffeine as acute stimulant. Future progress in caffeine-related investigations involving research in psychophysiology and behavioral medicine will open more gateways to understand the upper intake levels of caffeine consumption. Until then the only way to avoid any bad cardiac events related with caffeine intakes is to be aware off the caffeine amounts of your caffeine based product intakes so that you may fix your caffeine to moderate level. Prohibition of caffeine intakes is not the very much good solution because it will snatch the joy of a friendly drink along with all its beneficiaries [57-60].

Sexual effects of caffeine

Caffeine has different effect upon male and female body. Greater positive subjective effects have been noted in case of male's reproductive system as compared to that of female.

Caffeine would also have different effects on blood pressure of normal and hypertensive patients. The same amounts of caffeine may be adverse for a normal individual that may be suitable for lowering the blood pressure of a hypertensive male or female thus improving the phenomenon of reproduction as well [49].

Very little or no subjective responses to caffeine were involved with higher levels of estradiol. As the cardiac activity affected by caffeine was more prominent in females related to greater increase in diastolic blood pressure after caffeine intakes [61]. It was found interconnected with that of reproduction because the sexual life is highly dependent over the whole body conditions in spite of the reproductive organs only. The change in steroid hormone concentrations was also noted after caffeine intakes relevant with the gender differences. The estradiol level was found high with low blood pressure after caffeine consumption but in females it was totally opposite response with high blood pressure with high estradiol levels [62, 63].

Although no adverse effects of caffeine consumption has been reported for the modest level of caffeine consumption. Still caffeine consumption is considered as an unhealthy habit especially during pregnancy. As caffeine has an ability to accumulate in fetal tissues so consumption of caffeinated beverages during pregnancy may lead towards the fetal growth restriction, congenital malformations, stillbirth and long-term behavioral effects in offspring. The diverse pharmacological effects of caffeine may result in the fertility problems along with fetal growth and development [64].

It has been reported that the sperm concentration is highly affected by the long-term caffeine consumption although no effects on sperm motility, hepatic, cardiac, or renal functions has been reported yet. The cytoarchitecture of the testes and serum testosterone level of male offspring of Wistar rats has been reported after the maternal exposure to caffeine which would have adverse effects on the birth weight. According to some recent research, in some female hypertensive patients, the caffeinated beverages have been found to impose very positively related effects with sexual orgasm and sexual satisfaction (Gaskin et al). So the sexual activity in such patients would be improved by the long-term usage of caffeinated beverages in low to moderate amounts [65-69].

It has been reported that the greater risk of caffeine effects on the male and female reproductive systems would be possible in the individuals of subpopulations including unhealthy populations, individuals with preexisting conditions like co exposures and with a risk-taking behavior outcomes in comparison to that of healthy adults males and healthy pregnant women [70].

Caffeine intakes have been found very useful in cases of Erectile Dysfunction (ED). It was reported that a caffeine intakes of approximately 2-3 cups daily cups of coffee (170-375 mg/day) may reduce the odds of prevalent ED. Even the overweight, obese and hypertensive men were observed with this reduction in ED after caffeine consumption. More factors involved in this phenomenon are remained to study yet [55].

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According to some research reports there was found 42% less risk of ED in those men that were taking 1-2 cups of coffee on regular basis. A low risk of infertility was also reported in some hypertensive women having 1-2 cups of coffee regularly as it would sooth their muscles thus making the body more suitable for the ones that wish to conceive [71].

Higher caffeine intakes may negatively affect the male reproductive system because too much caffeine can damage the perm DNA. However low-caffeine intakes are involved in increasing fertility by improving the semen quality. So caffeine does not have a negative effect upon the male reproductive systems until it is taken in low to moderate amounts. In cases, where any crucial results related to reproduction are produced after caffeine consumption, there may be some involvement of the other factors like life style, weight and other physical activities [72].

Several studies have reported the positive effects of caffeine including a good effect on sex hormones including the reduction in clearance during the luteal phase. While regarding the caffeine effects on the male and female reproductive systems, no adverse effects would be resulted if moderate amounts of caffeine intakes. Even low to moderate caffeine intakes would help with the reproduction in both males and females by many means. In male and female atheletes, ergogenic effects from caffeine intakes were observed and caffeine was found to have

the more positive effects on delayed-onset muscle soreness (DOMS) in case of male athletes [73].

On the other hand as caffeine is a psycho stimulant so during pregnancy and lactating period, it should be critically used within limits having full knowledge about the caffeine amounts present in the caffeinated products used by the women. Sometimes the person taking caffeine is not well aware of the caffeine amounts of the caffeinated beverages that he or she is taking so caffeine consumption may be out of the restricted amounts that may cause some issues especially during very sensitive time period (pregnancy, lactation) of women [73]. (Table 5) describes the year wise work about the caffeine effects on sexual health of both the males and females.

Conclusion

In conclusion, the current study is about the caffeine consumption and its effects upon major human systems. Year wise work of different researchers about caffeine benefits have been discussed in order to get a current knowledge about the caffeine’s positive or negative effects over the body. As we are unaware of the caffeine amounts of the caffeinated products that we are taking so we don’t even have a idea about how much caffeine amounts we are using on daily basis. So in order to avoid any inconveniences created from the caffeine, we should be vigilant about the amounts of caffeine intakes.

Table 5. Sexual Effects of Different Doses of Caffeine Intake.

Sexual Properties/ Year wise Work	Dose	Faraget al., 2010	Brent et al, 2011	Hatch et al., 2012	Chenet al., 2013	Rudolph et al., 2014	Lopiz et al., 2015	Doepkar et al., 2016	Ricci et al., 2017	Callogen et al., 2018	Nisenblat et al., 2019
Male Fertility	L	D	D	D	D	D	D	D	D	D	D
	M	D	D	D	D	D	D	D	D	D	D
	H	D	D	D	D	D	D	D	D	D	D
Low Sperm Quality	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Sperm Anuploidy	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	ND	D	ND	D	ND	ND	ND	D	ND
Low Sperm Motility	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Fecundability	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Low Serum Volumes	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	D	D	D	D	D	D	D	D	D	D
Low Female Fertility	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	D	D	D	ND	ND	ND	D
	H	ND	ND	ND	ND	ND	ND	ND	ND	D	ND
Genital Arousal Disorder	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Early Miscarriage	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	D	D	ND	D	D	ND	D	D	D
	H	D	D	D	D	D	D	D	D	D	D
Ovulation Disorders	L	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	M	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	H	ND	D	ND	ND	ND	D	ND	D	ND	ND

As different bodies can have different capacities of the caffeine consumption so we should also know or estimate our body stamina of caffeine consumption. Even then we may be able to get caffeine benefits without completely prohibiting it due to its excepted side effects. As low to moderate amounts of caffeine consumption is usually tolerable so these amounts will benefit the whole human body but high amounts of caffeine may put on adverse effects on the body. So take caffeine only in low to moderate amounts and always try to avoid high caffeine intakes regularly.

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