Adverse Effects of Green Tea on Public Health the Untold whole Medical Story

Ameera Kamal Khaleel¹ amerakamal@student.usm.my , amera3kam@gmail.com Ramizu Bin Shaari¹ ramizu@usm.my Mohamad Arif Awang Nawi¹ mohamadarif@usm.my Ali Mihsen Hussein Al-yassiri² dralimihsen82@gmail.com

¹School of Dental Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, 16150 Kota Bharu, Kelantan, Malaysia ²Babylon University, Iraq

Corresponding author: Ramizu Bin Shaari

School of Dental Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, 16150 Kota Bharu, Kelantan, Malaysia, **Email**:<u>ramizu@usm.my</u>

ABSTRACT

In recent years, the uses of herbal products have increased significantly. Unfortunately, with the use of these used herbal products, an increase in number of reported adverse effects were seen. Green tea is made from steaming of the Camellia sinensis plant. The catechins in green tea consist of epicatechin (EC), epicatechin-3-gallate (ECG), epigallocatechin (GCG), and epigallocatechin-3-gallate (EGCG). They are responsible for green tea advantages like anti-inflammatory, antioxidant, anticarcinogenic, and antimicrobial activity. Despite these benefits, recently there have been several research that demonstrate several disadvantages and adverse effects following the consumption of a high dose of green tea extract which can lead to undesirable side effects like: Gastrointestinal disturbance and liver hepatotoxicity, nervous system stimulation, cardiovascular problems, disrupts renal function, interferences with some medications, impair thyroid function, iron deficiency anemia, hypokalemia, birth defects, and infertility. It is better to limit the green tea consumption to not more than two to three cups per day. Daily taking of too much green tea extract may have many side effects.

INTRODUCTION

The most common beverages consumed in the world is tea, which is from the plant Camellia sinensis. It is consumed as black, or Oolong or green tea (GT). To destroys the enzymes which are responsible for breaking down the pigments in the leaves, a freshly harvested leaves are steamed to produce GT, and to preserve the natural polyphenols which are responsible for the healthpromoting properties of GT ^[1]. Chemically, GT is composed from proteins; carbohydrates; amino acids; different elements; lipids; vitamins; sterols; and volatile compounds ^[2,3]. GT polyphenols (flavanols, flavandiols, flavonoids, and phenolic acids) account for about of 30% of its dry weight. The flavonoids are different catechins which are epicatechin (EC), epicatechin-3-gallate (ECG), epigallocatechin (GCG), and epigallocatechin-3-gallate (EGCG) ^[4].

Contrasting the positive and encouragingly results of GT uses, there are a recent research reporting that after the ingestion of a large amounts of GT or GT extract, the side effects appears and thus they encourage the GT drinkers to limit its consumption per day.

ADVERSE EFFECTS OF GREEN TEA (Figure-1).

Gastrointestinal disturbance and liver hepatotoxicity

Heartburn is caused by a bad food habits, an inactive lifestyle, and a high GT consumption. Scientists found that

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Correspondence:

Ramizu Bin Shaari School of Dental Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, 16150 Kota Bharu, Kelantan, Malaysia, Email: ramizu@usm.my

these factors_can increase the risk of heart burn and other gastroesophageal diseases ^[5]. Theophylline in GT can cause acid reflux ^[6]. The asymptomatic erosive esophagitis can also cause by excessive GT intake ^[7]. The utilization of high dosages of GT (more than five liters per day) can causes, stomachache, dyspepsia, flatulence and diarrhea, nausea, vomiting, and loss of appetite ^[8]. Other study also found that consumption of more than 400 mg/day of caffeine including that present in GT can cause nausea and vomiting ^[9].

After high consumption of GT, the liver toxicity is usually arising after three months. Most of the cases present with an acute hepatitis-like syndrome with a marked serum enzymes elevation. After stopping the extract, directly recovery occur, but fatal cases of acute liver failure have been also described ^[10]. Patel et al (2013) wrote a case report of acute liver failure in an adult male using a product containing GT extract to decrease the weight ^[11]. The liver hepatotoxicity may be caused by catechins. Histopathological examination showed inflammatory infiltrates, necrosis, and steatosis ^[12]. The major cytotoxicity is due to the formation of reactive oxygen species and destruction of mitochondrial membranes ^[13]. **Nervous system stimulation**

The excessive consumption of GT can cause stimulation to the central nervous system like tremors, dizziness, and confusion ^[14]. Caffeine in GT can cause a reduction in sleep quality and cause insomnia, anger, and anxiety. Bonnet

and Arand found that administration of 1200 mg/day of caffeine in adults for one week showed a significant increase in the level of fatigue due to a negative effect of caffeine on night sleep throughout the period of the study ^[15]. From a dose of caffeine as 80–87 mg, a significant increase in anxiety was seen by Vinader-Caerols et al (2012) ^[16].

Depending on the dose and the type of administration, caffeine can protect from seizures and increase the seizure susceptibility. In animal studies, it can decrease the antiepileptic potency of some drugs specially with topiramate ^[17]. Temple et al (2009) found that a dose of 2.32 mg/kg/day of caffeine did not increase irritability in adolescents in comparison to the placebo group ^[18]. Other also found that the administration of (70–80 mg/day) of caffeine from tea, or other caffeine sources did not cause any anxiety ^[19].

Cardiovascular problems

Hypertension is caused by increased catecholamine release by the adenosine antagonism or by the direct vasoconstrictive response due to adenosine antagonism after intake of therapeutic amounts of caffeine. This hypertensive effect of caffeine was seen diminishes with the chronic consumption ^[9]. Hypotension was also found associated with cases of severe overdose of caffeine including that of GT and phosphodiesterase inhibition may plays a role in this condition. This hypotension is attributed to tachydysrhythmias, reduction in cardiac filling, and decreased cardiac output which resulting in vasodilation ^[20].

Tachycardia was reported in cases of caffeine intoxication in a dose higher than 10mg/ kg/day, but bradycardia can be encountered from a dose within the therapeutic range [²¹]. Higher dosages of GT can also cause irregular heart rhythm ^[22], acutely harmful effects to the circulation system ^[23] and can modulate the cardiac function ^[24]. Taking the caffeine pills or supplements may cause atrial fibrillation, and even death ^[25]. The β 2-adrenergic pathway was involved in the EGCG induced cardiac effects ^[26].

Disrupts renal function

From the intracellular store, a high concentration of caffeine can release the calcium and result in a stronger muscular contraction and an increase in visceral sensation perception. Many different stimulators can release many substances, including prostaglandins, adenosine triphosphate, acetylcholine, and nitric oxide from urothelium, which contributes to the increased bladder sensation, and symptoms of overactive bladder ^[27,28].

Lohsiriwat et al (2011) study reported that caffeine can also decrease the bladder volume and increase the sensitivity to bladder filling ^[29]. Other study found that more than 4.5 mg / kg/day of GT can causes urgency of urination and increases its frequency, by increasing in the neuronal activation ^[30]. Inoue et al (2011) also reported that a high dose of GT polyphenols can disrupts the renal function, down adjust antioxidant enzymes, and prompting kidney impairment in mice ^[31].

Interferences with some medications

Warfarin drug can produce anticoagulation of the blood by inhibiting the production of vitamin K dependent clotting factors. The exogenous administration of vitamin K can inhibit the effect of warfarin. GT can be a significant source of vitamin K and thus, antagonize the action of warfarin ^[32]. Caffeine including that in GT can inhibit the metabolism of warfarin and increase its plasma concentration and anticoagulant effects. Thus, the patients during warfarin therapy must be advised to decrease the frequent use of GT ^[33]. In addition to that GT can keeps platelets from coagulation when taken with aspirin ^[34].

Some drugs like cimetidine, and ciprofloxacin. sparfloxacin, grepafloxacin, norfloxacin, trovafloxacin, and fluconazole can prevent caffeine breakdown and thus increases the caffeine elimination half-life. Decreases in caffeine elimination by using a high dose of ciprofloxacin was approximately 1.5 fold in comparison with the untreated control subjects, but in the case of enoxacin, it was a sixfold change, whereas in case of ofloxacin, the result showed the lowest inhibitory effect than others. This causing restlessness, increased heart rate, and sometimes arrhythmia [35,36]. GT caffeine can also inhibit the metabolism of antipsychotic drug like clozapine and can decrease the mean oral clearance of some drugs like clozapine during the concomitant intake of caffeine compared with that of alone,_and this can also cause toxicity [37].

GT tannins may also reduce the absorption of atropine, codeine, ephedrine, theophylline, aminophylline, lomotils, and can inhibit the adenosine hemodynamic effects, and increase the pharmacological effects of theophylline, pseudoephedrine, ephedrine, and aminophylline ^[38].

Impair thyroid function

As evidenced from in vitro and in vivo studies, the tea flavonoids possess a potent antithyroid activity [39]. At a high dose, the thyroid function can be impaired by GT extracts, and a significant decrease in serum T3 and T4 with a significant elevation of TSH was seen in response to dietary GT extract [40,41]. In postmenopausal women, GT can reduce the thyroid cancer risk. The caffeine can increase intracellular cyclic adenosine monophosphate and causes an inhibitory effect on tumor cell growth [42,43]. Other study was conducted at the National Cancer Center, in Japan, showed that a high GT consumption can increase the risk of thyroid cancer in premenopausal women, and this may be due to the estrogen-related mechanism. It was found that catechins can enhanced the estrogenic activity (alpha estrogen receptor) which is not found in normal thyroid glands, but it is present in thyroid cancer cells [44], and it is lesser in postmenopausal thyroid cancer than in premenopausal thyroid cancer [45]. Other study found that the anti-apoptotic protein Bcl-2 of human thyroid cancer cells was up-regulated by alpha estrogen receptor agonists and GT catechins can promote the growth of cancer cells through this receptor [46].

Iron deficiency anemia

More than billion people worldwide are affected by iron deficiency anemia. This anemia is due to iron deficiency and low levels of blood hemoglobin ^[47]. Some researches explain that EGCG can easily binds with iron and this can decrease its efficiency as a potent antioxidant and can also blocks the iron absorption causing iron deficiency anemia ^[48]. On human intestine, other study found that dietary polyphenolic compounds can interfere with absorption of iron in a dose-dependent inhibitory effect on heme iron absorption ^[49]. Any iron supplements must not be taken together with GT components. The tannin in GT can causes a reduction in the bioavailability of iron and all subjects which shows deficiency in iron or susceptibility to iron deficiency should use GT sparingly ^[48].

Hypokalemia

Potassium is important for the muscle contraction in the body. Low level of potassium in the blood is called hypokalemia. Excessive GT intake lower the potassium blood level and leading to a muscle weakness. There is a report of a 49-year-old Japanese man who developed hypokalemic myopathy after consuming large quantities of GT with chronic consumption of a cold remedy. Caffeine in GT can induce hypokalemia which is due to beta 2 adrenergic agonism stemming from catecholamine release, due to phosphodiesterase inhibition or adenosine antagonism ^[50]. Other study reported that some patients with hypokalemia were advised to decrease their GT consumption. After a few days, this decrease was allowed their potassium levels to return to normal levels ^[51].

Birth defects

Because of the possible antifolate properties of catechin, it can decrease the bioavailability of folate and can put the pregnant women at risk. The consumption of more than three cups/day of tea was seen associated with a high risk of birth defects like spina bifida [52,53].

Caffeine including that in GT can acts as a diuretic by stimulation of the central nervous system and increases the rate of elimination of water-soluble vitamins B, including folate. A high dose of caffeine intake can also affect the bioavailability of folic acid and reduce the serum folic acid levels. GT extract or EGCG can also inhibit the dihydrofolate reductase and decrease the circulating serum folate levels ^[54,55]. Caffeine can easly cross the placental barrier causing a decrease in placental blood supply to the fetus and affect the fetal growth ^[56]. An increased risk of preterm birth was also associated with

drinking GT. The risk of preterm birth was increased with a decrease in the age of starting tea drinking and increasing the duration, and this relationship is modified by gestational weight gain and maternal age ^[57]. **Infertility**

GT polyphenols have a therapeutic property, but excessive consumption have been associated with adverse effects. In cases of a higher consumption, it can cause infertility. Researchers reported that 10 mg/ml of GT can reduced the reproductive activity in Drosophila melanogaster. It can affect the development and reproduction of Drosophila *melanogaster* in both males (atrophic testes) and females (missing mature eggs) ^[58]. It was also reported that when the male albino rats were administered GT leaf extract for 26 days, a great influence on male reproductive system functionally as well as morphologically were seen. The testis weight was seen reduced, the sperm motility and count were decrease, and the testosterone level was reduced for the treated groups as compared with control rats' group. The LH and FSH levels were also changed accordingly in treated groups. The histopathological examination showed disintegration of seminiferous tubules of testis with inhibition of spermatogenesis [59]. Excessive caffeine can also negatively affect the male reproductive system by damaging the sperm DNA [60].

Adv	erse Effects of Green tea
	1 Gastrointestinal disturbances
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	5. Interferences with some medications. 6. Impair thyroid function.
The second	7. Iron deficiency anemia. 8. Hypokalemia.
No.	9. Birth defects.

Figure-1: Adverse effects of green tea.

CONCLUSION

One of the most used healthiest drinks is green tea. The source is from Camellia sinensis. It contains different antioxidants that can overcome various diseases like heart disease, diabetes, obesity, and cancers. But a new research shows that daily taking of too much green tea may have different side effects. Following the consumption of a high dose of GT extract, several disadvantages and adverse effects can be seen like: Gastrointestinal disturbance like heartburn and liver hepatotoxicity by mitochondrial cell damage, nervous system stimulation, cardiovascular problems, disrupts renal function, interferences with some medications by inhibiting the metabolism of these drugs, impair thyroid function, induce iron deficiency anemia by blocking iron absorption, lowering potassium levels in the blood, birth defects by its anti-folate effects, and infertility. For this reason, green tea is not recommended for individuals like those with gastrointestinal disturbances, insomnia, high blood pressure, compromised bladder, Warfarin treatment,

thyroid problems, iron deficiency anemia, and pregnant women.

CONFLICT OF INTEREST Non.

SOURCE OF FUNDING Self

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