

Review

Green tea extract and reproduction: A review

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Green tea is manufactured from the leaves of the plant *Camellia sinensis* and has been regarded to possess anti-cancer, anti-obesity, anti-atherosclerotic, antidiabetic, antimicrobial and antioxidant effects. The main bioactive components present in green tea are polysaccharides, flavonoids, vitamins B, catechin compounds, fluoride, etc. The credit for their useful antioxidant property lies with the huge collection of chemical substances called polyphenols and catechins. Green tea extracts exhibit stronger antioxidant protection for human body than vitamin C and vitamin E. Green tea has been found to aid in heavy metal detoxification by inhibiting its absorption and promoting excretion due to the antioxidant activities of green tea polyphenols such as catechin, which binds with heavy metals ions to form an insoluble complex –ionic salt that was used to remove them. Green tea components theanine and catechin have reproductive effects.

Keywords: Green tea extract, Reproduction, Antioxidant, Polyphenols

INTRODUCTION

Green tea is the nature's treasure to mankind, next to water as the most consumed beverage in the world (Gomikawa *et al.*, 2008). It is obtained from the tea plant *Camellia sinensis* which belongs to the family Theaceae and is cultivated in at least 30 countries around the world, commonly consumed in Japan, China, India and other Asian countries, some parts of North Africa, the United States, and Europe (Maruyama *et al.*, 2009; Chacko *et al.*, 2010; Namita *et al.*, 2012). Green tea is produced by inactivating the heat-labile enzyme polyphenol oxidase in the fresh leaves by either applying heat or steam, which prevents the enzymatic oxidation of catechins, the most abundant flavonoid compounds present in green tea extracts (Velayutham *et al.*, 2008).

The chemical composition of green tea varies with climate, season, horticultural practices, and the position of the leaf on the harvested shoot (Pastore, 2005). The active constituents in green tea are powerful antioxidants called polyphenols. Tea is reported to contain nearly 4000 bioactive compounds of which one third is contributed by polyphenols (Tariq *et al.*, 2010). Among the polyphenols in tea, is a family of compounds called the flavanoids. Flavanoids (and their fraction, catechins)

are the basic phenolic compounds in green tea responsible for antioxidant activities such as neutralization of free radicals that are formed in the process of metabolism (Horzic *et al.*, 2009). These flavanoids contain a substance called catechins. Major catechins present in green tea are epicatechin (EC), epigallocatechin gallate (EGCG), epigallocatechins (EGC) and epicatechin gallate (ECG).

The history of the medical effects of green tea starts on the early eighth century with the Buddhist monks who recognized green tea for its medicinal powers; therefore nowadays there is also an increasing interest in the beneficial effects of green tea on disease prevention (Neves *et al.*, 2010). Its active components are reported to have several biological properties, including cancer chemoprevention, inhibition of tumour cell growth, antiviral and anti-inflammatory activities (Yang *et al.*, 2000), antioxidant activity (Morel *et al.*, 1993; Guo *et al.*, 1996), antimutagenic and anticlastogenic effects (Gupta *et al.*, 2002) and inhibitory effects on several enzymes, such as aromatase (Satoh *et al.*, 2002), angiotensin converting enzyme (Actis-Goretta *et al.*, 2006) and thyroid peroxidase (Divi and Doerge, 1996). Also diminish

the risk of different illnesses, including diabetes, cancer and coronary heart disease (Dufresne and Farnworth, 2001; Chaiyasut *et al.*, 2011).

Green tea has recently become a subject of investigation in connection with the prevention of various diseases and also its effects on reproduction (Jiřina and Anton, 2013). Therefore, the aim of this review is to summarize research informations related to both beneficial and harmful properties of the green tea extracts on reproduction in both male and female.

Semen Quality and Testosterone Profile

The generation of reactive oxygen species (ROS) by sperm is a normal physiological process, however a shift between ROS production and scavenging activity is deleterious to sperm and it has been shown to be associated with male infertility (Sharma and Agarwal, 1996). Sheteifa and Morsy (2014) was able to demonstrate that green tea supplements improved semen volume of bucks. The epididymis is known to play a major role in the final development of motility, fertilizing ability and sperm storage. Sperm concentration can increase during epididymal transit with a simultaneous increase in sperm metabolism and the possibility of ROS threatens the survival of these male gametes (Dacheux *et al.*, 2003). The observed improvement in the their study in sperm characteristics, including motility, abnormality and concentration may be attributed to the prevention of excessive generation of free radicals produced by sperm by means of the antioxidant properties of green tea (Sheteifa and Morsy, 2014). The substantial increase in the glutathione (GSH, an intracellular antioxidant) level in the sperm and testicular tissue of rats that consumed green tea may suggest a decreased oxidative stress or an increased antioxidant capacity in the cell, thereby lowering the risk of oxidative damage (Awoniyi, 2010). Abshenas and his colleagues (2011) demonstrated the therapeutic effect of green tea extract against deleterious effects of heat (hyperthermia) on semen quality. According to them, green tea extract significantly improves sperm motility and concentration and sperm membrane integrity after 28 days of green tea extract administration. They hypothesized that extract contain high concentrations of polyphenols which have strong antioxidant properties (Abshenas *et al.*, 2011).

On the other hand, a study conducted by Shyamal and Soumendra (2015) in Indian, to assess the impact of green tea leaf extract (GTLE) on reproduction on adult male rats showed that GTLE is a potent herbal castrative agent when applied in a specific dose. According to this study, GTLE treated groups of animals showed decreased serum testosterone level, decreased sperm count and motility. The reduced concentration of testosterone may be due to decreased activity of steroidogenic enzymes (Shyamal and Soumendra, 2015).

Figueiroa *et al.* (2009) also indicated that green tea extract polyphenols mainly EGCG has inhibitory effect on leydig cell testosterone production probably through PKA/PKC signaling pathway, as well as direct or indirect inhibition of both P450_{scc} and 17 β -HSD, which are required for hormone synthesis (Figueiroa *et al.*, 2009). Furthermore, Chandra *et al.*, recorded a significant decrease in epididymal sperm number, serum testosterone level in dose dependent manner and testicular steroidogenic enzyme activities in GTE administered group of animals after 26days (Chandra *et al.*, 2011).

Ameliorative effect on reproductive toxicity and testicular damage

Lead being one of the reproductive toxicants can affect the gonadal structure and functions and can cause alterations in fertility (Dumitrescu *et al.*, 2009; Yousif and Adbullah, 2010; Qureshi and Sharma, 2012). Lead induced testicular toxicity has been shown to be ameliorated by the concurrent administration of herbal products such as green tea and garlic, which increased serum testosterone level and improves semen quality again due to their antioxidant activity (Thuppil and Tannir, 2013). According to Hassan *et al.* (2016) and Jassem *et al.* (2008), administration of green tea significantly increase sperm count, sperm motility and serum testosterone in lead treated rat comparing with control rats. Also lead acetate treated animals administered with green tea extract showed marked restoration of seminiferous tubules with active spermatogenesis within these tubules. The improvement of sperm motility of green tea treated rats was due to presence of isoflavones and other polyphenoles of green tea (Ly *et al.*, 2014), which are very efficient antioxidant, reduced the production of hydrogen peroxide, scavenger of oxygen free radicals (Fran *et al.*, 2000). Sha'bani *et al.* (2015) affirmed the detoxification effect of green tea extract on the reproductive system in rats exposed to lead acetate (Sha'bani *et al.*, 2015).

In investigating the possible protective effect of green tea on interferon (IFN)-induced spermatogonia apoptosis, Rezk and his colleagues (2014) documented that interferon produces obvious changes in testicular tissue structure and the co-administration of green tea produce significant improvement in the testicular architecture owing to its powerful antioxidant effects (Rezk *et al.*, 2014). Exposure to Lead and Cadmium is associated with various pathological conditions that include reproductive dysfunction and toxicity. The use of green tea in attenuating the damaged effects of Lead and Cadmium on reproduction of male rats, improved its testicular damage, decreased sperm count, testosterone level and inducing antioxidant defense (El-Betagy *et al.*, 2015). Green tea has been found to aid in heavy metal

detoxification by inhibiting its absorption and promoting excretion (Paul, 2008). The effectiveness of total green tea extract on oxidative stress and testicular tissue damage in malathion-induced infertility disorders was also studied. In this study, administration of total green tea extract improves the oxidative injuries such as lipid peroxidation, total antioxidant capacity and total thiol groups in testis tissue (Zadkhosh *et al.*, 2016). Antioxidative enzymes are activated by total green tea extract intake (Frei and Higdon, 2003), and the antioxidative strength of human plasma increases with continual ingestion of green tea (Kimura *et al.*, 2002; Coimbra *et al.*, 2006). Furthermore, oral administration of green tea, to rats for 7 weeks after or before and after I/p injection of the potent carcinogen benzo(a)pyrene, provided antimutagenic effect and therefore cancer chemoprotection and prevent testicular degeneration (Eldebaky *et al.*, 2015). In another study, Tarek *et al.* (2014), assessed the protective role of green tea extract in reproductive toxicity resulting from chlorpyrifos and cyromazine. Their study revealed that chlorpyrifos and cyromazine insecticides induces reproductive toxicity in male rats manifested by decreases in fertility index, weight of the sexual organs, semen characteristics and serum testosterone as well as testicular damage manifested by induction of lipid peroxidation and depletion of antioxidant enzymes in testes of rats. However, co administration of green tea extract with the insecticides antagonizes their reproductive toxicity and oxidative damage (Tarek *et al.*, 2014). Green tea extracts also exert protective effects against doxorubicin-induced spermatogenic disorders in increasing sperm density and motility and attenuating germ cell damage (Sato *et al.*, 2010).

Effect of green tea on polycystic ovarian syndrome and Uterine Fibroids

Polycystic ovary syndrome (PCOS) is a reproductive hormonal abnormality and a metabolic disorder which affects an estimated 5–10% of reproductive-age women and the main cause of infertility (Ehrmann 2005; Hassanzadeh *et al.*, 2013). Ghafurniyan and his colleague (2015) conducted a study in Iran, indicating the effect of green tea extract on reproductive improvement in estradiol valerate-induced polycystic ovary polycystic ovarian syndrome in rat. According to this study, Green tea consumption modulates gonadotropin levels, reducing insulin resistance, losing rats weights and improving the ovarian morphology. Due to these systemic effects and the ability to reduce metabolic features, green tea was able to increase the reproduction rate in PCOS rats through a reduction in ovarian cysts and an increase in the appearance of corpus luteum (Ghafurniyan *et al.*, 2015), Weight loss not only has a direct effect on the frequency of ovulation, but also increases the possibility

that the patients with PCOS respond to infertility treatment drugs such as clomiphene citrate and gonadotropins (Bhathena and Velasquez, 2002, Moran *et al.*, 2006). Catechins found in green tea directly can connect to the peroxisome proliferator-activated receptors (PPARs), regulates adipocyte differentiation and expression of adiponectin (Lim *et al.*, 2003). Green tea extract causes a decrease in the thickness of the follicular theca layer in PCOS rats, possibly mediated through increased lipolysis and decreased hypertrophy of this layer. Due to this decrease, the androgens and steroids produced by this layer would also decrease (Ghafurniyan *et al.*, 2015). PCOS is associated with changes in sex hormones, especially steroid. However, in polycystic group, sensitivity of the pituitary and hypothalamus changed due to increased level of estrogen (Balen *et al.*, 1995; Vigorito *et al.*, 2007). The effect of 10- day infusion of green tea extract on hormonal levels showed that luteinizing hormonal levels decreased significantly. As a result, consistent high levels of LH as well as constant low FSH levels were observed (Ghafurniyan *et al.*, 2015). Roshdy *et al.*, (2013) conducted a randomized, double-blinded, placebo-controlled pilot study; 800 mg of green tea extract was orally administered daily for 4 months to women with symptomatic fibroids confirmed by ultrasonography. There data demonstrated that subjects who used green tea extracts for 4 months experienced significant shrinkage in their total fibroid volume, significant reduction in fibroid-specific symptom severity, and significant consistent improvement in their quality of life. This fibroid-shrinking effect of EGCG was attributed to the inhibitory effect on proliferation of leiomyoma tumor cells and induction of apoptosis, as shown in previous preclinical work (Zhang *et al.*, 2010).

CONCLUSION

Different studies reviewed in this manuscript showed that green tea extract has effects on reproduction, in improving some of the reproductive parameters. On the other hand, few studies reported an adverse effect of green tea extract on reproductive indices. Therefore, future collaborative studies are needed to clarify optimum dosing amounts that will provide therapeutic benefits. Its ability to modulate, ameliorate and protect reproductive toxicity makes green tea extract a promising candidate for therapy in reproductive toxicity.

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