

A combination of Green Tea and Melatonin Consumption Improve Plasma Lipid Profiles in Adults

Mustafa Ghazi Alabbassi

College of Pharmacy/ Al-Mustansiriyah University/Dept. of Pharmacotherapeutics

الخلاصة

أمراض القلب والأوعية الدموية هي السبب الرئيسي للمرض والموت في العالم. تم تحضير الشاي الأخضر من أوراق زهرة الكاميليا والغنية بمضادات التأكسد، والذي يبدو أن للشاي الأخضر دور حاسم في خفض نسبة الدهون. الميلاتونيين أيضا له دور في العديد من الوظائف الفسلجية وكذلك مضادا للتأكسد.

الهدف من الدراسة هو تقييم تأثيرات شرب الشاي الأخضر والميلاتونيين على مستوى الدهون عند 36 شخصا. الصورة التوزيعية للدهون تشمل حساب الكوليسترول، الكوليسترول عالي الكثافة، الكوليسترول منخفض الكثافة، الترياكسرايد، الابولايبوبروتين a، الابولايبوبروتين b والايوبروتين a. صممت هذه الدراسة لحساب الصورة التوزيعية للدهون في بداية الدراسة، وبعد 3 أسابيع من شرب لتر ماء يوميا، كذلك بعد 4 أسابيع من شرب لتر من الشاي الأخضر يوميا والميلاتونيين 3 ملغم مساءً يوميا. تم تحضير الشاي يوميا بنفس الظروف. بعد شرب الشاي الأخضر اضافة للميلاتونيين وجد تحسن ملحوظ في الصورة التوزيعية للدهون. أظهرت النتائج أن شرب الشاي الأخضر والميلاتونيين له فائدة في الحماية من أمراض القلب والأوعية الدموية بواسطة تحسين الصورة التوزيعية للدهون في الدم.

Abstract

Cardiovascular diseases (CVDs) are the major cause of morbidity and mortality in the world. The green tea prepared with leaves of *Camellia sinensis* is particularly rich in antioxidants, which seems to have a crucial role in atherogenesis. Melatonin also participates in many physiological functions and exhibit antioxidant activity.

The aim of our investigation was to evaluate the effects of green tea drinking and melatonin on the lipid profile in 36 subjects. The lipid profile included the measurement of total cholesterol, high-density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), triglycerides (TGs), apolipoprotein A-I, apolipoprotein B, and lipoprotein (a). The measurements were performed at the beginning of the study, and after 3 weeks of drinking 1 L of water, and after 4 weeks of drinking 1 L of green tea daily

plus 3mg/day melatonin at night. Tea was prepared every day at the same conditions of temperature, time of infusion, and concentration. After drinking green tea plus melatonin a significant beneficial improvement in the lipid profile of subjects was observed. Our data suggest that drinking green tea plus melatonin have beneficial effects protecting against the risk for cardiovascular disease by improving blood lipid levels.

Keywords: Green tea, Melatonin, Lipid profile.

Introduction

Tea is an infusion prepared with the leaves of *Camellia sinensis*. Excluding water, tea is the most widely consumed beverage in the world. Green tea is different from black tea, that green tea is not fermented. Green tea is an important source of flavonoids, namely catechins, which are strong antioxidants. As well as, it contains minerals, vitamins, oils and caffeine ^[1]. There is considerable epidemiological evidence that tea drinking lowers the risk of heart disease. Researchers believed that daily consuming of green tea may improve cardiovascular health, by preventing blood platelets from sticking together and improving cholesterol level ^[2]. Also, green tea may prevent the oxidation of LDL-C, which, in turns, can reduce the buildup of plaques in arteries ^[3].

In addition melatonin is another antioxidant which has significant protective actions against cardiac damage, and these actions were apparent by reducing molecular damage and cellular loss through antioxidant effects ⁽⁴⁾. The importance of melatonin as an antioxidant depends on several characteristics: its lipophilic nature, ability to pass all bio-barriers with ease, and its availability to all tissues and cells. It distributes in all cell compartments being especially high in the nucleus and mitochondria ^[5]. Melatonin has also been shown to be an efficient protector of DNA ^[6], protein and lipids in cellular membrane ^[7] as well as antagonist of a number of endogenous and exogenous free radicals attach or during cellular processes ^[8].

Cardiovascular pathologies are one of the major causes of morbidity and mortality in that could decrease the prevalence of cardiovascular diseases (CVDs) continues as an active area of research ^[9]. Several epidemiological and clinical studies have shown that high levels of total cholesterol, triglycerides (TGs), LDL-C, apolipoprotein A-I (Apo A-I), and lipoprotein (a) [Lp(a)], and low levels of HDL-C and apolipoprotein B(Apo B), are risk factors for CVD, among several others ^[10,11]. According to the oxidative modification hypothesis for atherogenesis, reactive oxygen species may contribute to the events leading to the inception and progression of atherogenic lesions by promoting oxidation of LDL ^[12]. The most striking changes in atherogenic lesions include accumulation of lipids followed by infiltration, activation, and overgrowth of cells. In subendothelial space, LDL is oxidatively modified by reactive oxygen species produced by activated inflammatory cells, becoming a chemotactic factor for circulating monocytes, inhibiting the motility of the resident

macrophages, and being much more avidly phagocytosed by macrophages than the native LDL. The potential antioxidant bioactivities of both green tea and melatonin may, therefore have a crucial role in reducing the risk of atherogenesis. Several studies suggest that green and black tea drinking may offer a protection for CVD. The protection seems to increase with the volume of tea consumed daily^[13]. An increase in daily tea drinking of 711 ml was reported to reduce the risk of myocardial infarction by 11%^[14]. Endothelium-dependent vasodilatation, which is known to be impaired in heart disease patients and in subjects with high cholesterol levels, was reported to improve significantly after drinking tea daily for 4 weeks^[15]. Green tea drinking has also been associated with lowered serum levels of cholesterol, TGs, and LDL-C, and high serum levels of HDL-C^[16].

Considering the importance of tea drinking in human dietary habits worldwide and the high prevalence of CVD, researchers warranted further studies about the actions of tea. Therefore, the aim of the present study to evaluate the effects of combination of drinking green tea and melatonin on lipid risk factors associated with CVDs.

Materials and Methods

Thirty –six male subjects (50-60 years old) with a body mass index $25 \pm 4.8 \text{ kg/m}^2$ were participating in this study. The lipid profile included the measurement of total cholesterol, HDL-C, LDL-C, TGs, apolipoprotein A-I, apolipoprotein B, and lipoprotein (a). The measurements were performed at the beginning of the study, and after 3 weeks of drinking 1 L of water daily, and after 4 weeks of drinking 1 L of green tea daily plus 3mg/day melatonin. Tea was prepared every day at the same conditions of temperature, time of infusion, and concentration. None of the studied individuals presented known clinical, biochemical, or hematological manifestations of cardiovascular, hepatic, renal, or endocrine disorders. The subjects were not under any lipid-lowering medication or under any diet supplementation.

Green tea was prepared everyday at the same temperature (70-80°C), time of infusion (2.5 minutes), and concentration (1.75 g of tea leaves for 200ml of water). These conditions aimed to prepare a tea with a rich and adequate concentration, but also to obtain a pleasure beverage⁽¹⁷⁾. The subjects were asked to drink the water during the water period and the tea during the green tea period during the day, and asked to maintain their food and drinking habits at mealtime. No milk was added to the tea preparations. During green tea period the subjects were asked to take melatonin capsule in a dose of 3mg/day at bed time once a day.

Venous blood samples were collected at rest and fasted for 12 hours. After centrifugation, serum aliquots were prepared and stored at -30°C until assayed. The lipid measurements included cholesterol, TGs, HDL-C, LDL-C, Apo A-I, Apo B, and Lp (a). Cholesterol and TG were measured by enzymatic –

colorimetric assays using commercially available kits; HDL-C and LDL-C were performed by using direct methods; Apo A-1, Apo B, and Lp(a) were determined by immunoturbidimetric assays.

Results are expressed as mean \pm SD and as median values. To determine the differences occurring for each subject during the study, we used a paired Student *t* test whenever the parameters presented. A P value lower than 0.05 was considered significant.

Results

As shown in table-1, the evaluation of the lipid profile before and after 3 weeks of drinking 1 L of water daily (basal levels vs water drinking period), no effect was observed. When comparing the lipid profile presented after the water drinking period with those presented after drinking green tea and melatonin, we found a significant reduction in total cholesterol, LDL-C, TGs, Apo B, and Lp (a) and a significant increase in HDL-C and in Apo A-I (Table-1).

N= 36	Basal Level	After 3 Weeks of Drinking water	after 4 weeks of drinking 1 L of green tea daily plus 3mg/day melatonin
Cholesterol (mg/dL)	208.3 \pm 36.8 ^a	210.3 \pm 39.1 ^a	204.0 \pm 30.1 ^b
HDL-C (mg/dL)	52.2 \pm 10.6 ^a	50.7 \pm 9.2 ^a	59.6 \pm 8.7 ^b
LDL-C (mg/dL)	136.2 \pm 34.3 ^a	139.5 \pm 31.9 ^a	124.2 \pm 29.2 ^b
TG (mg/dL)	101.8 \pm 51.3 ^a	102.0 \pm 48.6 ^a	98.8 \pm 50.8 ^b
Apo A-I (mg/dL)	150.8 \pm 38.3 ^a	149.5 \pm 35.7 ^a	158.6 \pm 39.1 ^b
Apo B (mg/dL)	92.9 \pm 21.3 ^a	92.3 \pm 22.4 ^a	86.7 \pm 19.3 ^b
Lp (a) (mg/dL)	17.7 \pm 4.7 ^a	17.1 \pm 3.8 ^a	12.7 \pm 9.3 ^b
Cholesterol /HDL-C	4.0 \pm 1.0 ^a	4.1 \pm 1.0 ^a	3.4 \pm 1.0 ^b

Table 1: Effect of combination of green Tea and Melatonin on Lipid Profile (mean \pm SD).

Data were expressed as mean \pm SD; n= number of animals; values with non-identical superscripts (a, b) were considered significantly different (P<0.05)

Discussion

Tea appears to provide an important source of antioxidants, which seem to play a crucial role in several pathologies associated with oxidative stress, such as CVD^[18]. In the present study, we found that green tea drinking and melatonin imposed significant beneficial changes in the lipid profile of subjects. The effect of green tea is attributed to a reduction in cholesterol absorption and to an increased excretion of biliary acids and cholesterol; another proposed action is the inhibition of cholesterol synthesis in the liver^[19]. The protective effect of green tea has been attributed to its high content of flavonoids^[20], particularly in catechins, which are strong antioxidants. The antioxidants provided by green tea drinking may account for the inhibition in lipid peroxidation chain reactions that scavenge nitric and oxygen radical species^[21].

Previous researches show that green tea lower total cholesterol and raises HDL-C in both animals and human. When rats were fed 2.5% green tea leaves in their diet showed a drop in total cholesterol, LDL-C, and TGs, as well as, the body weight of green tea-fed rats was 10 to 18% lower than that of rats' not consuming green tea^[22].

Regarding the effects of melatonin on lipid profile parameters relevant to the antioxidant activity, it was shown that melatonin has ability to neutralize lipid free radicals thus breaking the chain of reactions where by lipid free radicals oxidize other fatty acids with reduction in the level of malondialdehyde being the product of lipid peroxidation^[23].

Our data suggest that green tea drinking and melatonin have beneficial effects, which protect against CVD by improving blood lipid profiles. Further studies that would examine additional parameters of green tea and melatonin consumption are needed.

References

1. Beecher, G.; Warden, B. and Merken, H. (1999). Analysis of tea polyphenols. *Proc Soc Exp Biol Med* 220(4):267-270.
2. Sano, J.; Inami, S. and Seimiya, K. (2004). Effect of green tea intake on the development of coronary artery disease. *Circ J.* 68:655-670.
3. Kuriyama, S.; Shimazu, T. and Ohmori, K. (2006). Green tea consumption and mortality due to cardiovascular disease, cancer, and all causes in Japan: Ohsaki study. *JAMA*; 296: 1255-1265.
4. Russel, J.R. (2003). Dun-Xian T. Melatonin: a novel protective agent against oxidative injury of the ischemic/reperfused heart. *Cardiovascular Research*; 58(1):10-19.
5. Martin, M.; Macias, M.; Escames, G.; Leon, J. and Acunacastroviejo, D. (2000). Melatonin but not vitamins C and E maintains glutathione homeostasis in t-butyl hydroperoxide-induced mitochondrial oxidative stress. *FASEB J*; 14: 1677-1679.

6. Lopez-Burrillo, S.; Tan DX; Mayo, J.C.; Sains, R.M.; Manchester, L.C. and Reiter, R.J. (2003). Melatonin, xanthurenic acid, resveratrol, vitamin C and alpha-lipoic acid differentially reduce oxidative DNA damage induced by fenton reagents: a study of their individual and synergistic actions. *J Pineal Res*; 34: 269-277.
7. Cuzzocrea, S. and Reiter, R.J. (2001). Pharmacological action of melatonin in shock, inflammation and ischemia/reperfusion injury. *Eur J Pharmacol*; 426: 1-10.
8. Zang, L.Y.; Cosma, G.; Gardner, H. and Vallyathan, V. (1998). Scavenging of reactive oxygen species by melatonin. *Biochem Biophys Acta*; 1425: 469-477.
9. Jan, H.; Jurgen, W.; Peter, U.; Klaus, K. and Ulrich, K. (2007). Mortality and morbidity from coronary heart disease attributable to passive smoking. *European Heart Journal*; 10: 1093.
10. Neki, N. (2002). Lipid profile in chronic smokers. *JACM*; 3(1):51-54.
11. Scott, M.; James, I.; Noel, B. and Bryan, B. et al. (2004). Implications of recent clinical trials for the national cholesterol education program adult treatment panel III guidelines. *Circulation*; 110: 227-239.
12. Helena, C.; Ricardo, G.; Luciane, C.; Evelise, N.; Alessandro, G.; Gabriel, G.; Jesus, A. and Amibal, V. (2005). Oxidative stress in atherosclerosis-prone mouse is due to low antioxidant capacity of mitochondria. *The FASEB Journal*; 19:278-280.
13. Nakachi, K.; Matsuyama, S.; Miyake, S.; Sugnuma, M. and Imai, K. (2000). Preventive effects of drinking green tea on cancer and cardiovascular disease: epidemiological evidence for multiple targeting prevention. *Biofactors*; 13(1-4): 49-54.
14. Peters, U.; Poole, C. and Arab, L. (2001). Does tea affect cardiovascular disease? A meta analysis. *Am J Epidemiol*; 154(6):495-503.
15. Hodgson, J.; Puddey, I.; Burke, V.; Watts, G. and Beilin, L. (2002). Regular ingestion of black tea improves brachial artery vasodilator function. *Clin Sci*; 102(2):195-201.
16. Kuhn, D.J.; Bums, A.C. and Kazi, A. (2004). Dou QP. Direct inhibition of the ubiquitin-proteasome pathway by ester bond-containing green tea polyphenols is associated with increased expression of sterol regulatory element-binding protein 2 and LDL receptor. *Biochim Biophys Acta*; 1682(1-3):1-10.
17. Astill, C.; Birch, M.R.; Dacombe, C.; Humphrey, P.G. and Martin, P.T. (2001). Factors affecting the caffeine and polyphenol contents of black and green tea infusions. *J Agric Food Chem*; 49(11):5340-5347.
18. Crespy, V. and Williamson, G. (2004). A review of the health effects of green tea catechins in in vivo animal models. *J Nutr*; 134(12): 3431 S-3440S.

19. Hasegawa, N.; Yamada, N. and Mori, M. (2003). Powdered green tea has antilipogenic effect on Zucker rats fed a high-fat diet. *Phytother Res*; 17(5): 477-480.
20. Peter, U.; Poole, C. and Arab, L. (2001). Does tea affect cardiovascular disease? A meta-analysis. *Am J Epidemiol*; 54(6): 495-503.
21. Feng, Q.; Torii, Y.; Uchida, K.; Nakamura, Y. and Osawa, T. (2002). Black tea polyphenols, theflavins, prevent cellular DNA damage by inhibiting oxidative stress and suppressing cytochrome P450 1A1 in cell cultures. *J Agric Food Chem*; 50(1):213-220.
22. Susana, C.; Alice, S.; Petronila, R.; Susana, R. and Elisabeth, C. (2006). Green tea consumption improves plasma lipid profiles in adults. *Nutrition Research*; 26: 604-607.
23. Barabio, V. (2000). Antioxidant and biological activity of melatonin. *UKr Biokhim Zh*; 72:5-11.