Review Article

Role of Black Tea in Type 2 Diabetes Mellitus and Metabolic Syndrome

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ABSTRACT

Consumption of black tea has been popular widely across the world. Tea (Camellia sinensis) has been used as a daily beverage since time immemorial. Tea is mainly available in three variants, approximately 76% to 78% of the tea produced and consumed worldwide is black, 20%-22% is green and less than 2% is oolong. Tea is an excellent source of poly phenolic compounds, particularly flavonoids. The catechins, also known as polyphenols present in the tea are mainly ascribed for the beneficial effect of tea in type 2 diabetes and metabolic syndrome. These active components (catechins) constitute seven forms including epigalocatechingallate (EGCg).The purpose of this review will focus on the effect of black tea catechins extracted from the Camelliasinensis plant on type 2 diabetes and metabolic syndrome.It is hoped that black tea can be consumed in a suitable manner as a supplement to prevent the advancement of type 2 diabetes, metabolic syndrome along with imparting other health benefits as well.

Keywords: Black tea, Metabolic syndrome, Insulin.

INTRODUCTION

Black tea is now consumed everywhere across the globe and is believed to have many beneficial effect on the health.[1] Notwithstanding many animal experiments have shown positive results, recently effectiveness of consumption of black tea on metabolic diseases are clearly demonstrated even in humans.[2] Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels.[2]

The global prevalence of diabetes is projected to increase, from 4% in 1995 to 5.4% by the year 2025.[2] World Health Organization has anticipated that the major surge will occur in developing countries.[3]

Inflammations and Diabetes

Various inflammatory pathways are indicated in the progression of type-2 diabetes which may accelerate insulin resistance and progressive beta cells dysfunction. In diabetic pathophysiology, the pancreatic beta cells are unable to secrete adequate insulin to overcome insulin resistance, thereby causing persistent hyperglycemia that may result in many macrovascular and microvascular complications. Recently, growing body of evidence have demonstrated that the propensity of developing type 2 diabetes is significantly associated with low-grade inflammation.[4,5] Moreover, nowadays chronic subclinical inflammation is accepted as an integral part of the insulin resistance syndrome[6,7] and also significantly correlate to features of the metabolic syndrome.[8,9] Many observational prospective studies have demonstrated that approximately 5-10% of the pre-diabetic subjects become diabetic every year.[10] Long-term inflammation of low grade intensity during pre-diabetic state facilitate onset of diabetes.[4]Recent epidemiological evidences also affirm the facts that inflammatory markers predict the development of diabetes and glucose disorders.[11] Two major pro-inflammatory cytokines TNF-a and IL-1ß have been culpably involved for obesity associated insulin resistance and pathogenesis of Type 2 diabetes (T2DM).

Evidences From Clinical Trials

Evidences generated from recent epidemiological studies demonstrates that daily consumption of black tea may be significantly associated with the reduced pro-inflammatory stress by altering the level of specific cytokines. In a recent study by Chatterjee *et al*., the authors had seen the effect of black tea on nine pre-diabetic subjects with metabolic syndrome. Their results demonstrated that the black tea consumption have a potential role in down regulating the serum lipid peroxides level, pro-inflammatory cytokines (TNF-a, IL-1ß) level and also may up regulate the anti-inflammatory cytokine (IL-10) significantly.[11] In addition, consumption of black tea for one month had resulted in significant changes ($p<0.05$) in the two indexes of insulin resistance and insulin sensitivity, namely HOMA-IR and QUICKI, although no significant change in fasting glucose level was noted.[12]In another study by Chattopadhyay *et al*. black tea decoction (10% and 20%) strength was found to cause substantial anti-inflammatory effects (64.8% and 77% reduction, respectively), on carrageenan-induced acute inflammatory models which has been commensurate as compared with the standard drug of indomethacin (89.1%). In a chronic anti-inflammatory model, black tea decoction (10% and 20%) has shown significant suppressive effects on rat paw edema (38.56% and 69.53%) observed on 21st day. Furthermore it was demonstrated that black tea increases the maximum number of T-lymphocytes at 72 h with a maximum strength of 20%. Maximum number of viable cells (T-lymphocytes) was found with black tea at 20% strength at 72 h. Thus the results of these studies corroborates with the effects of tea that was found to modulate the immune system which were recognized to stimulate the proliferation of cultured human peripheral blood mononuclear cells.[2] Todd and colleagues conducted a randomized study in type 2 diabetes to assess the effect of an extract of green and black tea on glucose control. In this double blinded study, they had recruited 49 subjects who were predominantly white. The average age of the study subjects were 65 years with a median duration of diabetes of 6 years, and 80% of them are reported using Antidiabetic medications. After 3 months of study, the mean changes in glycosylated hemoglobin

were +0.4 (95% confidence interval, 0.2-0.6), +0.3 (0.1-0.5), and +0.5 (0.1-0.9) in the placebo, 375-mg, and 750-mg arms, respectively. However, the difference in changes between the two arms failed to reach statistical significance. At the same time, the authors' failed to demonstrate hypoglycemic effect of extract of green and black tea in adults with type 2 diabetes mellitus.[13]However in another study by Bahorun and colleagues, 9 grams of black tea intake daily was associated with 18.4% reduction in fasting plasma glucose. In addition the authors also noted a significant rise plasma antioxidant propensity (FRAP: 418%; $p < 0.001$).[14] Satoh and associates, in 2015 demonstrated the effect of black tea on the carbohydrate digestion and absorption process in the gastrointestinal tract. They examined whether black tea can modulate postprandial hyperglycemia or not. The authors had used the freeze-dried powder of the aqueous extract of black tea leaves (JAT) for in vitro studies of a-amylase activity, a-glucosidase activity, and glucose uptake by glucose transporters in Caco-2 cells; ex vivo studies of small intestinal a-glucosidase activity; and in vivo studies of oral sugar tolerance in GK rats, an animal model of non-obese type 2 diabetes mellitus. JAT was demonstrated to subdue the degradation of disaccharides into monosaccharides by a-glucosidase in the small intestine. Thereby indirectly inhibiting the absorption of the dietary source of glucose mediated by SGLT1 and GLUT2 transporters localized at the apical side of enterocytes in the small intestine. The results indicated that black tea might be used as a functional food in the dietary therapy for borderline type 2 diabetes mellitus that could modulate postprandial hyper-glycemia.[15] In a recently published prospective randomized controlled study to investigate the effect of black tea on lipid levels, the author had recruited 87 subjects aged between 25 to 60 years. Participants were randomly assigned to drink either 3 cups of black tea (200 ml) per day or same volume of hot water for 12 weeks. The study results demonstrated that 9 grams of black tea consumption daily was linked with 36% decrease in triglyceride levels. Additionally, black tea intake demonstrated 17% reduction in the ratio of LDL to HDL cholesterol ratio, and a trend towards increasing HDL cholesterol level was also noted. The authors concluded that black tea when consumed within a normal diet contributes to a decrease of independent cardiovascular risk factors and improves the overall antioxidant status in humans.[15] Troup *et al*. investigated the effect of black tea intake on blood cholesterol concentrations in individuals with mild hypercholesterolemia in a diet-controlled double blind randomized trialamong 57 borderline hypercholesterolemic individuals. The authors concluded that intake of 5 cups of black tea per day did not alter the lipid profile of borderline hypercholesterolemic subjects significantly.[16] Biological mechanisms for beneficial effects of tea: Inspite of the conflicting results, several mechanisms have been proposed to explain the positive effect of black tea on glucose metabolism or obesity.

Epigallocatechingallate (EGCg), the most abundant form of catechin in black tea, is mainly ascribed for the beneficial effects of tea.[16] EGCG inhibits adipocyte development and differentiation in 3T3-L1 cells,[18] increases fat oxidation,[19] and stimulates expression of GLUT-4 in the adipose tissue of an animal model.[20] Inhuman studies, clear surge in energy expenditure were documented.[21] Also, some proposed the protective function of EGCG for cytokine-provoked ß-cell destruction mediated by inhibition of nuclear factor-?B activation.[21] Recently, Tian and associates demonstrated that tea polyphenols had anti-

obesity effect by up-regulating adiponectin levels in rats.[22]They suggested that the responsible pathways were the inhibition of Erk activation, alleviation of peroxisome proliferator-activated receptor ? (PPAR?) phosphorylation, and increases in the PPAR? expression.[23] Park *et al*. revealed the uncertain role of gallated catechin (GC) in tea, including EGCG, in glucose tolerance.[24] Kim and associates pointed out that GC acutely reduces blood glucose levels mainly through its activities in the alimentary tract while increasing the glucose level when in the circulation by blocking normal glucose uptake into the tissues. They also proposed development of non-absorbable derivatives of GC with only positive luminal effect as a prevention strategy of type 2diabetes and obesity.

CONCLUSION

Many studies are being carried out to define the precise molecular mechanisms of black tea and ultimately, its clinical application in type 2 diabetes and metabolic syndrome. Moderate black tea consumption seem to ameliorate the levels of risk factors which are independently linked with type 2 diabetes, obesity and cardiovascular disease. The beneficial effects of black tea are attributed mainly to the synergistic effects of tea phenolics and other antioxidant elements. Although the underlying plausible biological pathways for these effects warrants further extensive studies, black tea might provide an important source of dietary antioxidants in humans and seem to bestow protective effects against many metabolic diseases.

REFERENCES

1. Roy N, Chatterjee S, Bandhopadhyaya S, Maity C. Effect of tea on type 2 diabetes. *International Journal of Clinical Cases and Investigations*. 2014; 6(1): 61-68
2. Chattopadhyay C, Chakrabarti N, Black tea (Camellia sinensis) decoction shows immune modulatory properties on an experimental animal model and in human peripheral mononuclear cells, *Pharmacognosy Res*. 2012; 4(1): 15-21.
3. King H, Aubert RE, Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections, Diabetes Care. 1998; 21(9): 1414-31.
4. Badawi Alaa, Klip Amira, Type 2 diabetes mellitus and inflammation: Prospects for biomarkers of risk and nutritional intervention, Diabetes Metab Syndr Obes. 2010; 3: 173–186.
5. Deans KA, Sattar N, Anti-inflammatory" drugs and their effects on type 2 diabetes, Diabetes Technol Ther. 2006; 8(1):18-27.
6. Natali A, Ferrannini E, Hypertension, insulin resistance, and the metabolic syndrome, *Endocrinol Metab Clin North Am*. 2004; 33(2): 417-29.
7. Kohler HP, Insulin resistance syndrome: interaction with coagulation and fibrinolysis, Swiss Med Wkly. 2002; 18: 132 (19-20): 241-52.
8. Fukushima M, Usami M. Insulin secretion and insulin sensitivity at different stages of glucose tolerance: a cross sectional study of Japanese type 2 diabetes, Metabolism. 2004; 53 (7): 831-5.
9. Rudenski AS, Matthews DR, Understanding insulin resistance: both glucose resistance and insulin resistance are required to model human diabetes, Metabolism. 1991; 40(9): 908-17.
10. Lucas R, Parikh SJ, Cytokine profiling of young overweight and obese female African American adults with prediabetes. Cytokine. 2013; 64(1): 310-5.
11. Spranger J, Kroke A, Inflammatory Cytokines and the Risk to Develop Type 2 Diabetes Results of the Prospective Population-Based European Prospective Investigation into Cancer and Nutrition (EPIC)-Potsdam Study.*DIABETES*. 2003; 52: 812-817.
12. Chatterjee S, Roy N, Saha A, Roy S, Chatterjee A, Hazra N *et al*. Black Tea Consumption Enhance Antioxidant Status, Reduce Inflammatory Stress vis-à-vis Insulin resistance: Hint from a Small Clinical Cohort

Study on Pre-diabetic Subjects. *Int. J. Pharm. Sci. Rev. Res*. 2014; 28(2): 278-283
13. Todd M, Lisa L, Brooks BW. The effect of an extract of green and black tea on glucose control in adults with type 2 diabetes mellitus: double-blind randomized study. Metabolism. 2007;56(10):1340-1344
14. BahorunT, Luximon-Ramma A, Neergheen-Bhujun VS, Gunness TK, Googoolye K, Auger C *et al*. The effect of black tea on risk factors of cardiovascular disease in a normal population. *Preventive Medicine*. 2012;54 (Supplement): S98-S102
15. Satoh T, Igarashi M, Yamada S, Takahashi N, Watanabe K. Inhibitory effect of black tea and its combination with acarbose on small intestinal α-glucosidase activity. *Journal of Ethnopharmacology*. 2015; 161: 147-155
16. Troup R, Hayes JH, Raatz SK, Thyagarajan B, Khaliq W, Jacobs Jr. DR *et al*. Effect of Black Tea Intake on Blood Cholesterol Concentrations in Individuals with Mild Hypercholesterolemia: A Diet-Controlled Randomized Trial. *Journal of the Academy of Nutrition and Dietetics*. 2015; 115(2): Pages 264-271.e2
17. Higdon JV, Frei B. Tea catechins and polyphenols: health effects, metabolism,and antioxidant functions. *Crit Rev Food Sci Nutr*. 2003;43: 89–143.
18. Wu LY, Juan CC, Hwang LS, Hsu YP, Ho PH, Ho LT. Green tea supplementation ameliorates insulin resistance and increases glucose transporter IV content in a fructose-fed rat model. *Eur J Nutr*. 2004;43: 116–124.
19. Furuyashiki T, Nagayasu H, Aoki Y, Bessho H, Hashimoto T, Kanazawa K,Ashida H. Tea catechin suppresses adipocyte differentiation accompanied by down-regulation of PPARgamma2 and C/EBPalpha in 3T3-L1 cells. *Biosci Biotechnol Biochem*. 2004;68:2353–2359.
20. Klaus S, Pultz S, Thone-Reineke C, Wolfram S. Epigallocatechin gallate attenuates diet-induced obesity in mice by decreasing energy absorption and increasing fat oxidation. *Int J Obes (Lond)* 2005;29:615–623.
21. Rumpler W, Seale J, Clevidence B, Judd J, Wiley E, Yamamoto S *et al*. Oolong tea increases metabolic rate and fat oxidation in men. J Nutr. 2001; 131:2848–2852.
22. Tian C, Ye X, Zhang R, Long J, Ren W, Ding S *et al*. Green tea polyphenols reduced fat deposits in high fat-fed rats via erk1/2-PPARgamma-adiponectin pathway. PLoS One. 2013;8:e53796.
23. Han MK. Epigallocatechin gallate, a constituent of green tea, suppresses cytokine-induced pancreatic beta-cell damage. Exp Mol Med. 2003;35:136–139.
24. Park JH, Jin JY, Baek WK, Park SH, Sung HY, Kim YK *et al*. Ambivalent role of gallated catechins in glucose tolerance in humans: a novel insight into non-absorbable gallated catechin-derived inhibitors of glucose absorption. *J Physiol Pharmacol*. 2009; 60:101–109.