ORIGINAL ARTICLE

Reduction of post-prandial hyperglycemia by mulberry tea in type-2 diabetes patients

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Abstract   *Aim:* The dietary contents have a very important role in the management of metabolic syndrome along with type 2 diabetes mellitus (T2DM). Indian diet contains a large amount of carbohydrates that set off unpredictable blood sugar fluctuations and leads to increased risk of diabetic complications. The aim of the present study was to identify the effect of mulberry tea in the reduction of abnormally high postprandial blood glucose (PPG) levels in T2DM patients.

Methods: The study design was follow-up T2DM, 20 diabetic patients were given plain tea (control) and 28 diabetic patients were given mulberry tea (test subject) to measure the effect of mulberry tea on fasting blood glucose and PPG levels. Fasting blood glucose samples were collected after a standard breakfast. The PPG levels were recorded after the consumption of 70 ml tea along with 1 teaspoon of sugar after 90 min in all 48 patients.

Results: Fasting blood glucose levels in control and test group samples were found to be 178.55 ± 35.61 and 153.50 ± 48.10, respectively. After the consumption of plain tea and mulberry tea, the PPG values were recorded as 287.20 ± 56.37 and 210.21 ± 58.73, respectively. A highly significant ($p < 0.001$) change in the PPG level was observed in response to mulberry tea in all the test patients compared with control. Moreover, the effect size was also found to be very large (1.31).

Conclusion: Mulberry tea suppresses postprandial rise of blood glucose levels after 90 min of its consumption.

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1. Introduction

Due to its high prevalence and potential deleterious effects, type 2 diabetes mellitus (T2DM) continues to be a major medical concern worldwide, especially in the developing countries (Zimmet, 2011). Despite remarkable growth in this field of research, the diabetes occurrence has been increasing very rap-

idly with uncontrolled causative factors. Recent report suggests that approx. 150 million people worldwide are affected with diabetes and this number is expected to rise up to 300 million by the year 2025 (Kumar et al., 2012). The diabetic paradigm in India is also increasing rapidly and is expected to reach approx. 57.2 million by the year 2025 (Kumar et al., 2012). Some promising developments in the last decade in understanding the pathophysiology of T2DM have fueled new approaches toward its therapy and management. Recently, the usage of some naturally derived phytochemicals for the treatment of T2DM has been highlighted in the literature (Bulku et al., 2010; Dembinska-Kiec et al., 2008; Leiherer et al., 2013).

T2DM is a metabolic disorder of the endocrine system, primarily characterized by glycemic imbalance, which stimulates several metabolic turbulence and ultimately results into oxidative stress and chronic inflammation (American Diabetes Association, 2010). Uncontrolled hyperglycemia could also result in many chronic impediments such as micro-vascular complications like neuropathy, stroke and peripheral vascular disease (Cade, 2008). Medical complications of T2DM on the central nervous system such as increased risk of Alzheimer's disease and vascular dementia have also been reported (Banu et al., 2013; Helzner et al., 2009; Jabir et al., 2014; Kamal et al., 2014). Glycemic control is a primary concern in diabetic care as its impairment leads to several complications and mess up the prognosis among hospitalized diabetic patients (Kagansky et al., 2003; Solís et al., 2012; Turchin et al., 2009). Overall glycemic control could help and prevent the onset as well as delay in the progression of long term complications of diabetes. It also reduces morbidity and mortality of patients suffering from this disease (Solís et al., 2012). The abnormal insulin secretion by β-cells in response to a meal, impaired hepatic glucose production and defective glucose uptake by peripheral insulin-sensitive tissues (skeletal muscles) result into postprandial hyperglycemia (PPG), which is a serious issue in the management of glycemic patients. Moreover, control of the PPG level is critical in the treatment of not only diabetic patients but also in individuals with impaired glucose tolerance (Huang et al., 2012).

Recently, several treatment strategies for glycemic control have been implemented, viz. change in life style, diet therapy, use of synthetic and herbal agents (American Diabetes Association, 2011; Kumar et al., 2012; Painter et al., 2013). However, multiple medications are often needed to achieve adequate glycemic control in majority of the patients (American Diabetes Association, 2011; Painter et al., 2013; Rodbard et al., 2009). Due to their limited adverse effects, herbal agents have gained attention for the treatment of various diseases recently (Akilen et al., 2012; Kamboj et al., 2011; Kumar et al., 2012; Prince et al., 1998; Tabrez et al., 2013). The herbal agents as diabetic diet therapy could be quite effective in the management of carbohydrates in the normal diet. One such agent, mulberry (Morus alba) plant leaf extracts have been reported to possess several beneficial effects against various diseases. Glycemic control by mulberry leaf extracts due to their therapeutic potential has also been reported in various animal models (Chan et al., 2013; Jaruchotikamol and Pannangpetch, 2013; Kim et al., 2011; Kwon et al., 2011; Sharma et al., 2010). As far as our knowledge goes, there is no literature available on the glucose lowering effect of mulberry tea. This is the first research article reporting the effect of mulberry tea in reducing the PPG level in T2DM patients.

2. Materials and methods

In this study design, follow-up diabetic patients taking oral anti-diabetic drugs were selected at Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bangalore, India. Fasting blood glucose level was measured after routine standard breakfast and after consumption of 70 ml of mulberry tea with 1 teaspoon of sugar. The PPG levels were measured in total 48 patients after prior consent and Institutional ethics committee approval. Mulberry tea (Mulbericha green) was provided by Karnataka State Sericulture Research and Development Institute, Bangalore, India.

2.1. Methods

The first sample of fasting blood for glucose estimation was collected in morning. All the patients were instructed to consume routine standard breakfast (two idlis with chutney). Idli contains fermented mixture of ground rice and beans. Each idli contains approx. 1.67 g protein, 0.14 g fat, 9.12 g carbohydrates, 0.21 g minerals, 0.09 g fibers and 44.5 Kcal energy. Chutney is the coconut paste spiced up with chillies. The mulberry tea was prepared by the addition of one teaspoon of 'Mulbericha green' in one cup of hot water along with one teaspoon of sugar and given to diabetic patients for drinking. Similarly, the control group also consisted of diabetic patients and they were given normal tea (70 ml). After 90 min, the second blood sample was collected for the measurement of the PPG level. Analyses were carried out on a Roche Hitachi 912 analyzer.

2.2. Statistical analysis

Descriptive statistical analyses were performed in this study. Results on continuous measurements are presented as Mean $\pm$ SD and results on categorical measurements are presented in number (%). Student's t-test was performed to find out the significance of study parameters on continuous scale between two inter group analysis. Student's t-test and Chi-square test were also performed to identify the homogeneity of samples based on parameters on categorical scale between two groups. Significance was assessed at 5% level of significance.

2.3. Effect size

$$d = \frac{Mean1 - Mean2}{Pooled\ SD}$$

No effect (N)	$d < 0.20$
Small effect (S)	$0.20 < d < 0.50$
Moderate effect (M)	$0.50 < d < 0.80$
Large effect (L)	$0.80 < d < 1.20$
Very large effect (VL)	$d < 1.20$

3. Results

The age of the patients involved in this study was in the range of 30–70 years. The mean age of the control and test groups

was 53.80 ± 11.15 and 51.61 ± 8.59, respectively (Table 1). Samples were age matched with *P* value of 0.445. The selected subjects involved in this study were both males and females. The control group consists of 50% males and 50% females, and the test group consists of 57.1% males and 42.9% females. Samples were gender matched with *P* value of 0.624 (Table 1).

The present study is a case control study for the estimation of the effect of mulberry tea on the PPG level in 48 diabetic patients divided into a test group ($n = 28$) and a control group ($n = 20$). The subjects received a standardized breakfast together with tea containing one teaspoon of sugar. The tea was prepared from either mulberry leaf extract (test subjects) or normal black tea (controls). Blood glucose level was measured at fasting state and after 90 min post-prandial state. Fasting blood glucose levels in the control and test groups were found to be 178.55 ± 35.61 and 153.50 ± 48.10, respectively. After the consumption of plain tea and mulberry tea, the PPG levels were found to be 287.20 ± 56.37 and 210.21 ± 58.73, respectively (Table 2). Our data clearly indicate a significant decline in the PPG level after 90 min in the test subjects compared with that of the controls. The fasting and PPG levels are presented in Table 2. The mean fasting blood sugar level in the control and test groups was found to be 178.55 ± 35.61 and 153.50 ± 48.10, respectively. Moreover, a highly significant difference ($p < 0.001$) and very large size effect were also observed in mean PPG level in test group subjects. The mean PPG levels in the control and test groups were found to be 287.20 ± 56.37 and 210.21 ± 58.73, respectively.

4. Discussion

Post-prandial hyperglycemia represents a high risk factor for the development of T2DM and cerebrovascular disease, possibly due to its causative factors such as impaired insulin secretion, glucose production and/or defective glucose uptake by peripheral insulin-sensitive tissues (Blaak et al., 2012; Derosa and Maffioli, 2012). Elevated PPG level also contributes significantly toward the promotion of oxidative stress, inflammation and endothelial dysfunction; and leads to chronic diabetic complications, particularly cardiovascular disease and microvascular complications (Bell et al., 2008; Derosa and Maffioli, 2012; Shiraiwa et al., 2005). The underlying mechanisms of reduced PPG level in T2DM prevention is not completely understood till now. However, its role in appetite control or nutrient partitioning of markedly increased insulin and glucose concentrations (Brand-Miller et al., 2002) which assists in reducing total body weight has been reported in the literature recently (Blaak et al., 2012).

Several agents have been suggested in scientific literatures for the control of PPG level (Derosa and Maffioli, 2012; Ono et al., 2013; Tosh, 2013). Moreover, mammalian intestinal α-glucosidase inhibitors are one of the potential agents for the control of PPG levels (Huang et al., 2012). These agents could reduce the absorption of disaccharides and polysaccharides, which results in the decline of the PPG level (Huang et al., 2012). In the present study, we report PPG lowering potential of mulberry leaf extracts which could be beneficial for treatment, management and prognosis of diabetes. Furthermore, as a glucose lowering agent, mulberry tea could also prevent the progression and chronic complications to some extent.

Recently, herbal preparations have gained good attention toward the treatment of various diseases all over the globe (Devi et al., 2010). Recent developments in the field of phyto-pharmaceuticals have revealed the efficacy and toxicity associated with herbal agents and have become more popular among public (Zaidi et al., 2014). In the present study, we used leaf extracts of mulberry plant (*M. alba*) in a simple dietary form i.e., tea. Tea is a very common drink used alone or along with food. We believe that the mulberry plant derived extracts could easily be complemented with the foods because of its similar taste with normal tea.

Combined treatment approach is often considered to control glucose levels in diabetic patients (American Diabetes Association, 2011; Painter et al., 2013). Several patients require more than one treatment method to achieve adequate glycemic control and usually 2–3 average medications are given to patients with T2DM to reduce glucose levels. The primary therapeutic approaches toward a better glycemic control include proper diet management and changes in lifestyle. Synthetic agents used to reduce carbohydrate absorption from the intestine usually result in bloating gas and diarrhea (Chiasson et al., 2002). However, these symptoms were not observed after the consumption of mulberry tea. We, therefore, suggest the consumption of mulberry tea as a preferred method of glycemic control, which is also devoid of the side effects usually associated with common anti-diabetic drugs.

Table 1 Comparison of age distribution.

	Control group		Test group	
	No	%	No	%
Age in years				
30–40	3	15.0	3	10.7
41–50	4	20.0	11	39.3
51–60	8	40.0	9	32.1
61–70	5	25.0	5	17.9
Total	20	100.0	28	100.0
Mean ± SD	53.80 ± 11.15		51.61 ± 8.59	
Samples were age matched with $P = 0.445$				
Gender				
Male	10	50.0	16	57.1
Female	10	50.0	12	42.9
Total	20	100.0	28	100.0
Samples were gender matched with $P = 0.624$				

Table 2 Fasting blood glucose and PPG levels in the control and test groups.

Variables	Control group	Test group	Significance	Effect size
Fasting blood glucose	178.55 ± 35.61	153.50 ± 48.10	$t = 1.972$; $p = 0.055$	0.57 (M)
PPG	287.20 ± 56.37	210.21 ± 58.73	$t = 4.492$; $p < 0.001$	1.31 (VL)

Previously, mulberry leaf extracts have been reported for their beneficial effects against many diseases including cancer and atherosclerosis (Chan et al., 2013; Deepa et al., 2012; Jaruchotikamol and Pannangpetch, 2013; Park et al., 2012). Mulberry extracts have been reported to exert chemo-preventive potential on neuroblastoma cells, which could be helpful for controlling the cell growth (Park et al. (2012). Purified mulberry leaf lectins have been reported to induce apoptosis and cell cycle arrest in human breast and colon cancers (Deepa et al. (2012). Cytoprotective activity of mulberry leaf extract against oxidative stress induced cellular injury in rats has also been reported (Jaruchotikamol and Pannangpetch (2013). Moreover, the beneficial effect of mulberry leaf extract in the improvement of vascular endothelial functions has also been reported, which prevents atherosclerosis by reducing the atheroma burden (Chan et al. (2013).

Blood glucose lowering potential of mulberry leaf extract has also been reported in the scientific literature (Adisakwattana et al., 2012; Naowaboot et al., 2012; Oku et al., 2006). A previous study has reported the effect of mulberry tea on the inhibition of α-glucosidase, which in turn prolongs carbohydrate absorption process and helps to flatten blood glucose levels (Ye et al., 2002). Recently, one of the active components of mulberry leaf extract (1-deoxynojirimycin) and its derivatives has been reported to play an important role in delaying carbohydrate digestion by inhibiting intestinal α-glucosidases (Adisakwattana et al., 2012; Oku et al., 2006). Our study also supports the earlier reports of glucose lowering potential of mulberry extracts and that its consumption overcomes major side effects associated with anti-diabetic drugs (Adisakwattana and Chanathong, 2011; Adisakwattana et al., 2012; Park et al., 2009).

Having discussed our findings, we would like to mention some of the limitations of our study. Although, we are suggesting standard dietary intake of mulberry tea for the control of PPG level, there could be intra-individual variations in exerting the effect of mulberry tea toward various biological activities because of variations in the metabolic system of different individuals. Our study also does not provide mechanistic explanations on the active ingredients of mulberry extract, which needs to be further investigated and explored.

5. Conclusion

With unabated rise of diabetes all across the world, the prevention and management of this devastating disease are the need of hour. Control of glycemic level especially after a meal is crucial in both prevention as well as management of diabetes. The results of the present study highlight the hypoglycemic effect of mulberry tea after a routine standard breakfast. We believe that delayed carbohydrate digestion after the consumption of mulberry tea is due to the action of mulberry tea extract (1-deoxynojirimycin) on the enzyme α-glucosidase. However, the chemical complexity of mulberry tea and larger inter- and intra-individual responses need to be considered and explored in future studies.

Acknowledgements

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