Original Article

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Effect of Guava in Blood Glucose and Lipid Profile in Healthy Human Subjects: A Randomized Controlled Study

Biochemistry Section

SUCHITRA KUMARI[1], R RAKAVI[2], MANASWINI MANGARAJ[3]

ABSTRACT

Introduction: The fruit of *Psidium guajava (P.guajava)* is known to contain free sugars yet the fruit juice showed hypoglycaemic effect. Hypoglycaemic activity of guava leaves has been well documented but not for guava fruit.

Aim: So we aimed to evaluate the effect of ripe guava (with peel and without peel) fruit supplementation on blood glucose and lipid profile in healthy human subjects.

Materials and Methods: Randomized Controlled study undertaken in: 1) Baseline; 2) 6 weeks supplementation phase. Forty five healthy MBBS students were included and randomly enrolled into Group A, Group B and Group C. In Baseline phase: Fasting Plasma Glucose (FPG) and serum lipid profile was done in all 3 groups. Group A were supplemented with 400g of ripe guava with peel and group B without peel, for 6 weeks. Rest 15 treated as control i.e., Group C.

Result: Supplementation of ripe guava fruit with peel reduced BMI as well as blood pressure ($p<0.05$) in group A, whereas the FPG, Total cholesterol, Triglycerides were found significantly increased ($p<0.05$). Group B registered a significant fall ($p<0.05$) in BMI as well as blood pressure. Fall in FPG level after guava pulp supplementation was not significant. Serum Total cholesterol, Triglycerides and Low Density Lipoprotein Cholesterol (LDLc) levels decreased significantly ($p<0.05$) indicating that guava pulp without peel may have a favourable effect on lipid levels and blood sugar as well.

Conclusion: Guava fruit without peel is more effective in lowering blood sugar as well as serum total cholesterol, triglycerides and LDLc. It increases HDLc levels also.

Keywords: Blood sugar, *P guajava*, Randomized control trial, Supplementation

INTRODUCTION

Guava (*Psidium guajava Linn*.) is a small tropical tree that is widely grown for its fruit that is commonly known for its nutritional, medicinal and pharmacological values [1]. Guava fruit is included among the super-fruits with low calorie profile with high dietary fibre, rich in antioxidant vitamins [2] i.e., Vitamin C, Lutein, Beta carotene as well as minerals. So, it is considered as poor man's apple of tropical and sub-tropical countries.

Since long time, different parts of Guava tree have been extensively studied for its medicinal role. *Psidium guajava (P.guajava)* leaves have been reported to have hypoglycaemic effect [3] on blood glucose level of normal rats as well as Streptozotocin (STZ) induced diabetic rats. The administration of ethanolic extract of *P.guajava l*eaf showed hypolipidaemic and hypoglycaemic effect in Alloxan induced diabetic rats [4]. Though the hypoglycaemic activity of guava leaves is well documented [5] and guava leaf extract tea is available in market, the role of guava fruit in regulating blood sugar and lipid profile in human is still not clear.

Recently guava fruit water extract showed impressive efficacy in improving dyslipidaemia in animal models [6]. Although the fruit of *P.guajava is* known to contain free sugar, yet the fruit juice showed hypoglycaemic effect in Streptozotocin (STZ) induced diabetic rats [7]. The raw fruit peel of *P. guajava* had shown hypoglycaemic as well as hypolipidemic and hepatoprotective [8] effect but the ripe fruit peel has been found to have hyperglycaemic activity in diabetic rats [9]. Till now no human study has been conducted revealing the role of ripe guava fruit with peel and without peel on blood sugar and lipid profile.

As diabetes mellitus has emerged as a major urban health problem in India, observing the potential of natural products especially by supplementing fruits in regular diet and studying their effect in preventing diabetic complications has become important research avenue. So, this study was conducted with an objective to evaluate the effect of ripe guava (with peel and without peel) fruit supplementation on blood glucose and lipid profile in healthy human subjects. An attempt was also made to find the role of Guava fruit supplementation on Body Mass Index (BMI) and Blood Pressure (BP).

MATERIALS AND METHODS

This Randomized Controlled study was conducted in the Department of Biochemistry, All India Institute of Medical Sciences, Bhubaneswar. Forty five healthy MBBS students i.e., 31 male and 14 female MBBS students having routine diet of hostel canteen within the age group of 18 to 25 years were included in the study. They were randomly enrolled into Group A, Group B and Group C. Subjects suffering from any known chronic disorders, known diabetics, hypertensive with dyslipidaemia, addiction to alcoholism or tobacco smoking were excluded from the study. Subjects under medications like oral hypoglycaemic, hypolipidemic drugs i.e. statins, hormone replacements, antihypertensive drugs interfering with lipid profile or blood sugar were not included in this study.

This was a pre and post supplementation comparative study. This study was conducted for 4 months i.e., May - Aug 2015 (4 Months) and was undertaken in two phases i.e.,: 1) Baseline; and 2) 6 weeks supplementation.

Before the commencement of the study, all 45 participants were gathered together to inform the Aim & objective of the study, detailed study methodology, benefits expected and risks associated with the study as well as the freedom of individual to participate or withdraw from research at any point of time.

Baseline Phase

After obtaining informed written consent, all 45 healthy MBBS students reported after 12 hours overnight fast and 4ml venous blood sample was collected early morning. The sample collection and further processing was done in the AIIMS, Biochemistry laboratory, and weight, height, BMI, BP were measured at the AIIMS, OPD. Estimation of glucose was done by glucose oxidase-peroxidase

method [10] using glucose estimation kit in a semi-automatic analyser. The serum was used for estimation of total cholesterol by cholesterol esterase method [11], Triacylglyceride by lipoprotein lipase/glycerol kinase method [12], HDL_c by PEG precipitation method with a semi-automatic analyser. LDL_c value was estimated by calculation using the FriedeWald's formula i.e., LDL_c=Total cholesterol-(HDL_c + TAG/5). All data were recorded as the base line value.

Randomization Method

Out of 45 healthy subjects, random numbers were generated using Excel sheet, the list of participants were rearranged according to the random number obtained and a block of 15 participants were enrolled in group A, another 15 in group B and rest 15 in group C.

Supplementation: Fifteen subjects included in group A were supplemented with 400g of ripe guava with peel and another 15 subjects in group B were supplemented without peel ripe guava of 400 g everyday under direct supervision for 6 weeks. Rest 15 subjects were treated as control (group C) without any supplementation.

Post Supplementation Phase: After 6 weeks of guava supplementation, second round of investigations with fasting plasma glucose and lipid profile was conducted along with height, weight, BMI and BP measurement in all the 3 groups. The data was recorded as the post supplementation values.

STATISTICAL ANALYSIS

A comparative statistical analysis was done between the post supplementation values with the baseline values using SPSS Version 16.0. The values of continuous variables were expressed as mean±SD. Differences in variables between the post supplementation values with the baseline values were compared by using Paired t-test and Analysis of Variance (ANOVA) with post-hoc Tukey test. The p-value <0.05 was considered as statistically significant.

RESULTS

The clinical data of the study participants [Table/Fig-1] showed that all the three study groups (Group A, Group B and Group C) had more or less same BMI, Systolic Blood Pressure (SBP) as well as diastolic blood pressure (DBP). There was no significant difference in the mean value of High Density Lipoprotein (HDLc) and Very Low Density Lipoprotein (VLDLc) at the beginning of the study before guava fruit supplementation.

Sl. No.	Parameters	Group-A (n=15)	Group-B (n=15)	Group-C (n=15)
1	Height (cm)	164±8.2	164±8.6	167±9.6
2	Weight(Kg)	59±8.9	63±10.8	62±11.9
3	BMI(kg/m^2)	21.8±2.4	22.2±2.8	21.7±3.1
4	Systolic B.P(mm Hg)	123±8	124±10	114±10
5	Diastolic B.P(mm Hg)	77±8	76±9	72±7
6	Fasting Plasma sugar (mg/dl)	89.1±7.6	96.9±8.5	85.5±7.2
7	Total Cholesterol (mg/dl)	150.5±33.2	163.4±17.4	136.3±17.2
8	TAG (mg/dl)	79.4±19.2	110.6±28.1	95.2±29.1
9	HDLc (mg/dl)	52.3±8.8	49.6±5.8	46.9±14.8
10	LDLc (mg/dl)	85.6±30.1	92.4±15.3	71.3±15.7
11	VLDLc (mg/dl)	16.1±2.6	17.4±4.8	16.6±2.9

[Table/Fig-1]: Baseline characteristics of the study groups.

After 6 weeks of routine hostel diet, the control group registered an increase (p=0.016) in SBP which was statistically significant [Table/Fig-2]. However the FBP, TC, TAG were unaltered revealing the fact that regular hostel diet did not affect the study results even in Group A and Group B. These findings rule out the confounding effect of routine hostel diet and its nutrients on the study results.

Sl. No.	Parameters	Baseline value	After 6 weeks Routine Diet
1	Height (cm)	167±9.6	167±9.2
2	Weight (Kg)	62±11.9	62±12.1
3	BMI (kg/mt^2)	21.7±3.1	21.8±3.6
4	Systolic B.P(mm Hg)	114±10	122±14*
5	Diastolic B.P (mm Hg)	72±7	76±8
6	Fasting Plasma sugar (mg/dl)	85.5±7.2	84±5.5
7	Total Cholesterol (mg/dl)	136.3±17.2	141.4±20.5
8	TAG (mg/dl)	95.2±29.1	93.8±20.8
9	HDLc (mg/dl)	46.9±14.8	44.6±7.6
10	LDLc (mg/dl)	71.3±15.7	77.8±12.2
11	VLDLc (mg/dl)	16.6±2.9	17.8±5.3

[Table/Fig-2]: Primary outcome in control group after 6 weeks of routine hostel diet
*indicates p<0.05- Significant.

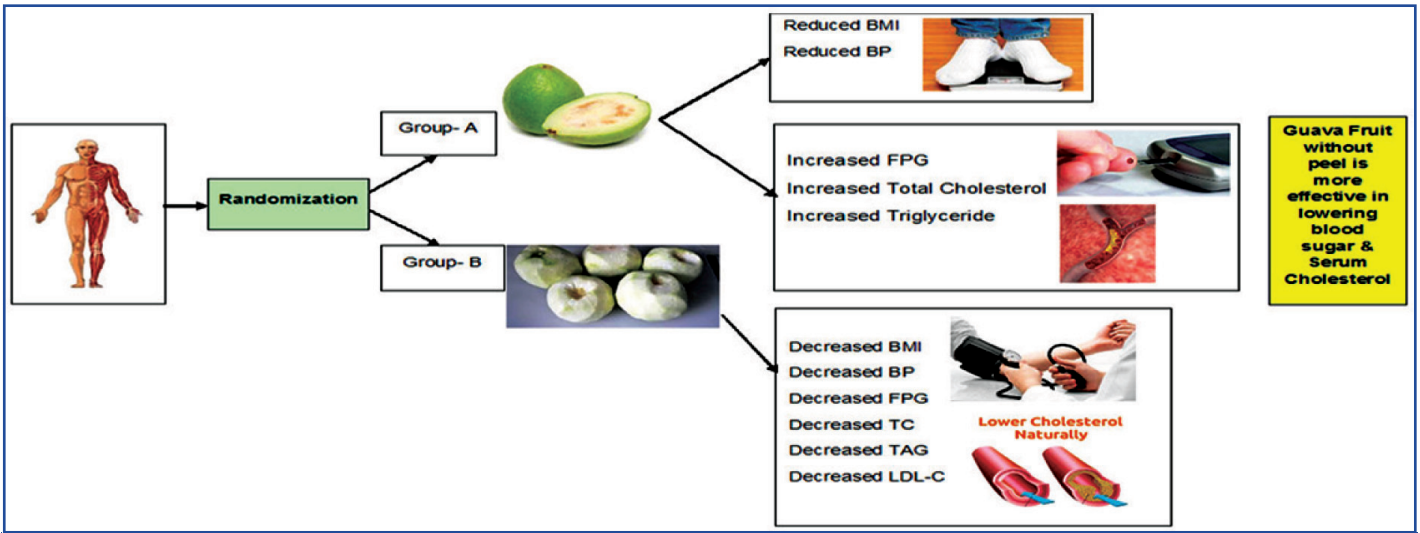
Supplementation of ripe guava fruit with peel reduced BMI as well as SBP and DBP (p<0.05) in group A [Table/Fig-3]. The FPG was found significantly increased (p<0.05) after guava fruit supplementation. TC was increased with a significant increase in TAG, LDLc levels with a fall in serum HDLc pointing towards the fact that guava fruit with peel could have a hyperglycaemic effect along with increasing TC, TAG as well as LDLc. In group B, supplementation of ripe guava without peel resulted in significant fall (p<0.05) in BMI as well as SBP and DBP. There was a fall in the mean FPG level after guava pulp supplementation but it was not statistically significant. Serum TC, TAG, LDLc levels decreased significantly (p<0.05) indicating that guava pulp without peel may have a favourable effect on lipid levels and blood sugar as well [Table/Fig-4].

Sl. No	Parameter	Group A		Group B	
		Group-A (n=15)	After 6 weeks Supplementation	Group-B (n=15)	After 6 weeks Supplementation
1	Height (cm)	164±8.2	164± 8.3	164±8.6	164±8.6
2	Weight(Kg)	59±8.9	57±9.1	63±10.8	60.4±11.2
3	BMI(kg/mt^2)	21.8±2.4	20.4±2.6*	22.2±2.8	20.9±3.2†
4	Systolic B.P (mm Hg)	123±8	111±9.9*	124±10	106±11†
5	Diastolic B.P (mm Hg)	77±8	69±6*	76±9	69±6†
6	Fasting Plasma sugar (mg/dl)	89.1±7.6	102.9±11.9*	96.9±8.5	93.8±8.4
7	Total Cholesterol (mg/dl)	150.5±33.2	170.2±31.5*	163.4±17.4	129.1±16.2†
8	TAG (mg/dl)	79.4±19.2	90.13±20.9*	110.6±28.1	86.6±24.5†
9	HDLc (mg/dl)	52.3±8.8	45.6±7.0*	49.6±5.8	57.9±4.4†
10	LDLc (mg/dl)	85.6±30.1	103±36.5*	92.4±15.3	62.2±10.9†
11	VLDLc (mg/dl)	16.1±2.6	18.1±3.9	17.4±4.8	16.9±3.9

[Table/Fig-3]: Primary outcome in supplementation groups after 6 weeks of ripe guava fruit supplementation.
*indicates p<0.05- Significant difference (6 weeks guava Supplementation and baseline in group A)
†indicates p<0.05- Significant difference (6 weeks guava Supplementation and baseline in group B)

DISCUSSION

Diabetes mellitus can cause a wide range of complications affecting almost any system of the body. Strict glycaemic control could prevent such complications in chronic diabetes. Various studies have shown that regular intake of fruits is associated with reduced risk of diabetic complications. Ayub MY, Norezmir MN et al., documented anti-hypertensive effect of Pink guava puree in hypertensive rats [13]. Our study also found significant fall in systolic and diastolic blood pressure in both group-A and group-B. Following ripe fruit



[Table/Fig-4]: Effect of guava fruit supplementation.

supplementation without peel (group-B) there was a fall in blood sugar. This could be due to high fibre content in guava fruit pulp. Dietary fibre (Pectin) delays the intestinal absorption of glucose, thus improving glucose tolerance. Invitro α-glucosidase inhibition performed by 0.05mg/ml guava fruit extract was about 70% [14]. So, hypoglycaemic effect of fruit pulp may be due to its ability to inhibit α-glucosidase enzyme in intestine. Guava fruit pulp is rich in flavonoid glycosides i.e., Strictinin, Isostrictinin and pedunculagin which have been used in clinical treatment of diabetes mellitus by improving sensitivity of insulin [15]. The Polyphenolic content i.e., Tannic acid, Gallic acid are directly related to anti-glycation activities of guava fruit pulp. There was a significant increase in blood sugar levels after guava fruit supplementation with peel. The raw fruit peel of *P. guajava* has higher concentration of Mg as compared to ripe fruit peel [16]. Mg favours insulin dependent uptake of glucose (GLUT-4)in peripheral tissues (i.e., Skeletal Muscles, Adipose tissue & Cardiac tissue) decreasing blood sugar level [7]. Low concentration of Mg in ripe guava fruit peel could be responsible for the hyperglycaemic effect observed in group-A. Hseuh-Chin Chao et al., documented a significant fall in LDLc and triglycerides in diabetic rats after administration of high doses of guava fruit water extract [6]. A significant fall in Total Cholesterol, Triglycerides and increase in HDLc was observed in hypertensive patients after guava fruit intake, a study conducted by Singh et al., [17]. Similar findings were observed in our study following guava fruit pulp supplementation in group-B subjects. High content of Pectin in guava fruit pulp is known to reduce total cholesterol, triglycerides as well as LDLc in serum. The phenolic and flavonoid contents in guava pulp may have an important role in inhibiting lipid peroxidation. Our study also showed that supplementation of guava fruit with peel in group-A led to significant increase in total cholesterol, triglycerides and LDLc in serum. Many enzymes of lipid metabolism are Mg^{++} dependent and low concentration of Mg^{++} in the ripe guava peel could affect these enzyme activities and increase serum total cholesterol level [18]. However the details of the nutraceutical composition of the ripe guava fruit peel is yet to be revealed in order to clearly explain its role in regulating lipid metabolism and serum lipid parameters.

CONCLUSION

Our study suggests that guava fruit without peel is more effective in lowering blood sugar as well as serum total cholesterol, triglycerides and LDLc. It increases HDLc levels. It could be a readily available dietary supplement in improving blood pressure, blood sugar and serum lipid parameters. Further study supplementing guava fruit in diabetes mellitus cases could establish the role of guava fruit in regulating blood sugar and preventing dyslipidaemia.

CURRENT RESEARCH QUESTION

1. How guava fruit supplementation with peel and without peel is effective in lowering blood sugar and improving lipid parameters?
2. Does guava fruit supplementation have anti-hypertensive and cardio-protective effect in healthy human being?
3. Could guava fruit supplementation improve Basal Metabolic Rate (BMI)?

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Biochemistry, All India Institute of Medical Sciences (AIIMS), Sijua, Bhubaneswar, Odisha, India.
2. Student, Department of Biochemistry, All India Institute of Medical Sciences (AIIMS), Sijua, Bhubaneswar, Odisha, India.
3. Professor and Head of Department, Department of Biochemistry, All India Institute of Medical Sciences (AIIMS), Sijua, Bhubaneswar, Odisha, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Suchitra Kumari,
Assistant Professor, Department of Biochemistry, All India Institute of Medical Sciences (AIIMS),
Sijua, Bhubaneswar-751019, Odisha, India.
E-mail: suchitrakumari76@gmail.com

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