Hypolipidaemic & hepatoprotective effects of *Psidium guajava* raw fruit peel in experimental diabetes

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**Background & objective:** The study evaluated the hypolipidaemic and hepatoprotective effects of unripe *Psidium guajava* fruit peel aqueous extract in streptozotocin (STZ) induced severely diabetic rats by assaying their triglyceride (TG), total cholesterol (TC), high density lipoprotein (HDL) cholesterol, alkaline phosphatase (ALKP), asperate amino transeferase (AST), alanine amino transferase (ALT) and creatanine (CRTN) levels.

**Method:** Severely diabetic albino Wister rats of same age group were treated orally once a day upto 3wk with a dose of 400 mg/kg bw of lyophilized extract. TG, TC, HDL, ALKP, AST, ALT and CRTN were estimated. LDL and VLDL cholesterol levels were calculated from the above measurements by using Friedwald formula.

**Results:** A significant decrease in TG ($P<0.01$), TC ($P<0.01$), HDL ($P<0.001$) VLDL ($P<0.001$) and LDL ($P<0.01$), ALKP ($P<0.01$), AST ($P<0.05$), ALT ($P<0.05$) and CRTN ($P<0.001$) levels were observed after 21 days treatment of aqeous extract of raw fruit peel compared to pre treatment levels.

**Interpretation & conclusion:** The extract showed significant hypolipidaemic activity in addition to its hypoglycaemic and antidiabetic activity. In view of its relative non-toxic nature *P. guajava* raw fruit peel may be a potential antidiabetic agent.

**Key words** Anti diabetic - glucose tolerance test - hypoglycaemic - *Psidium guajava*

*Psidium guajava* (Family: *Myrtaceae*) is an economically important plant of high medicinal value. *Psidium guajava* is commonly known as guava. It needs a tropical location and full sun for its healthy growth. Flavonoids, gallic acid and tannins are invariably present in all part of the plant viz., fruit, leaves, stem bark and heartwood. It has been reported earlier that the polyphenols and lucocynadines present in good amount in *P. guajava* may account for the marked astringent and medicinal properties of the different parts of the plant.

The guava fruit is a berry, which consists of a fleshy pericarp and seed cavity with fleshy pulp and numerous small seeds. *P. guajava* fruits are rich in dietary fiber associated with natural antioxidant compounds. Recently, the ripe fruit peel has been found to posses hyperglycaemic activity by our research group and diabetic patients are advised to peel off the ripe guava before eating. Antidiabetic activity based on higher concentration of Mg in the raw fruit peel of *P. guajava* has already been described. No reports are available on the hypolipidaemic activity of raw fruit peel. Hence,
we evaluated the hypolipidaemic and hepatoprotective effects of raw fruit peel of *P. guajava* in streptozotocin (STZ) diabetic rats.

**Material & Methods**

**Plant material:** Unripe fruits of *P. guajava* collected from the guava garden Khushrobagh, Allahabad, India, were authenticated by Dr Satya Narayan, Taxonomist, Department of Botany, University of Allahabad, India. A voucher specimen was submitted. The raw guavas were peeled off and the thin greenish peel of the unripe fruits was cut into small pieces. The pieces were mechanically crushed and continuously extracted for 48 h with hot water. The extract was filtered and concentrated in rotatory evaporator at 35 ± 5°C under reduced pressure, to obtain semisolid material, which was then lyophilized to get a powder (yield: 13.4%, w/v).

**Animal care and maintenance:** Experiments were performed in 6-8 wk old, healthy, male albino Wistar rats (150-200 g). Rats obtained from National Institute of Communicable Diseases (NICD), now National Centre for Disease Control (NCDC), Delhi, India, were housed under standard environmental conditions (at 25 ± 2°C, 50 ± 5% humidity with a 12 h each of dark and light cycle) and maintained with free access of water and a standard laboratory diet. The study protocol was approved by the Institutional Ethical Committee.

**Induction of diabetes:** Diabetes was induced by a single intraperitonial injection of freshly prepared streptozotocin (50 mg/kg bw) in 0.1 citrate buffer (*pH* 4.5) to a group of overnight fasted rats. After 3 days of STZ administration animal having marked hyperglycaemia (fasting blood sugar, FBG> 250 mg/dl) were selected for the study.

**Estimations:** Triglycerides (TG), total cholesterol (TC) and high density lipoprotein (HDL) cholesterol, alkaline phosphatase (ALKP), asperate amino transfeferase (AST), alanine amino transferase (ALT) and creatinine (CRTN) were estimated spectrophotometrically in blood serum by standard methods using kits of Bayer Diagnostic, India. Low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol levels were calculated from the above measurements by using Friedwald formula.

**Experimental design:** The dose of 400 mg/kg was identified as the most effective dose in our previous study and therefore selected for the present study in case of severe diabetic rats. The animals were divided into four groups of six rats each: Group I: normal control placebo treated; Group II: diabetic control placebo treated; Group III: diabetic treated with 400 mg/kg of extract; and Group IV: diabetic treated with 250 mg/kg of tolbutamide (positive control).

All biochemical parameters were estimated initially before the treatment and then weakly up to 21 days after the treatment.

**Statistical analysis:** Statistical analyses was performed using two-way analysis of variance (ANOVA), using statistical package PRISM 3.0 version. The significance of differences between and within various groups were determined. Differences were considered to be significant when *P*<0.05.

**Results & Discussion**

The triglyceride levels were increased by 2.86 per cent in diabetic control rats as compared to initial levels. However, it remained constant in normal control. The 21 days treatment of extract resulted in a significant (*P*<0.01) decrease of 47.47 per cent in TG levels of STZ induced diabetic rats. Whereas, in positive control, the reduction observed in TG level of rats was 48.06 per cent (Table I). The most common lipid abnormalities in diabetes are hypertriglyceridaemia and hypercholesterolaemia. Hypertriglyceridaemia

<table>
<thead>
<tr>
<th>Experimental rats</th>
<th>Treatment (Aq. extract)</th>
<th>Pre-treatment levels</th>
<th>Post-treatment levels</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>7 days</td>
<td>14 days</td>
</tr>
<tr>
<td>Normal (control)</td>
<td>Distilled water</td>
<td>90.32 ± 5.7</td>
<td>90.59 ± 5.4</td>
</tr>
<tr>
<td>SD (control)</td>
<td>Distilled water</td>
<td>185.79 ± 6.3</td>
<td>188.32 ± 6.1</td>
</tr>
<tr>
<td>SD (treated)</td>
<td>400 mg/kg</td>
<td>182.64 ± 6.3</td>
<td>136.43 ± 6.9</td>
</tr>
<tr>
<td>SD (Tolbutamide)</td>
<td>250 mg/kg</td>
<td>184.69 ± 6.9</td>
<td>122.47 ± 6.7</td>
</tr>
</tbody>
</table>

Values are mean ± SD (*n* = 6)

*P* < 0.05; **< 0.01 compared to pre-treatment levels
is also associated in metabolic consequences of hyperinsulinaemia, insulin resistance and glucose intolerance\(^1\). Thus, the improvement in TG levels of extract treated group indicates the hypotriglyceridaemic potential of *P. guajava* raw fruit peel and confirming thereby its usefulness for diabetic patients.

The levels of total cholesterol (TC) of both the controls, normal as well as diabetic, animals showed a slight increment of 1.67 and 2.86 per cent respectively, whereas, the treated diabetic animals showed a significant \((P<0.01)\) reduction of 19.08 per cent. The increased levels of TC reverted back to near normal range in diabetic treated group indicating thereby that on long term treatment the extract produced a significant decrease in total cholesterol level. A significant reduction of 16.03 per cent was observed in positive control \((P<0.01)\) compared to pretreatment level which was lesser than the extract treated group (Table II). High density lipoprotein (HDL) increased significantly by \((P<0.001)\) 26.34 per cent in diabetic treated groups which was higher than the positive control (17.53%). LDL and VLDL levels were found to be decreased significantly by 18.84 \((P<0.01)\) and 47.46 \((P<0.001)\) per cent respectively in diabetic treated group compared to pre-treatment level; increased by 12.21 and 2.55 per cent in diabetic control group, and remained constant in normal control group. In case of positive control the fall observed was 9.42 and 48.06 per cent in LDL and VLDL levels respectively (Table II). The risk of developing ischaemic heart disease is directly related to the raised levels of TC, LDL, VLDL and inversely related to the HDL levels\(^13\,14\). This extract, therefore, could be used for lowering TC, TG, LDL and VLDL levels and reducing thereby the risk of cardiovascular diseases by increasing HDL level.

Significant reduction \((P<0.05)\) of 27.5 and 43.94 per cent in AST and ALT levels respectively was observed in diabetic treated rats. In diabetic control AST and ALT levels were increased by 10.58 and 8.64 per cent respectively whereas, in normal control AST and ALT levels remains constant. In the positive control group fall of 27.38 and 25 per cent in AST and ALT levels respectively were found. Since, raised levels of AST and ALT enzymes increase the incidence of heart and liver diseases, decrease in their levels in diabetic treated group suggests that risk of liver and

### Table II. Effect of graded doses of *P. guajava* unripe fruit peel aqueous extract on TC, HDL, LDL and VLDL levels in severely diabetic (SD) rats

<table>
<thead>
<tr>
<th>Experimental rats</th>
<th>Treatment (Aq. extract)</th>
<th>Pre-treatment levels</th>
<th>Post-treatment levels</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 days</td>
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<td>14 days</td>
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<td></td>
<td></td>
<td></td>
<td>21 days</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (control)</td>
<td>Distilled water</td>
<td>95.3 ± 4.6</td>
<td>97.8 ± 4.2</td>
</tr>
<tr>
<td>SD (control)</td>
<td>Distilled water</td>
<td>122.4 ± 4.8</td>
<td>124.7 ± 5.2</td>
</tr>
<tr>
<td>SD (treated)</td>
<td>400 mgkg(^{-1})</td>
<td>124.97 ± 5.3</td>
<td>118.32 ± 5.8</td>
</tr>
<tr>
<td>SD (Tolbutamide)</td>
<td>250 mgkg(^{-1})</td>
<td>118.5 ± 5.4</td>
<td>109.7 ± 4.9</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Normal (control)</td>
<td>Distilled water</td>
<td>26.3 ± 3.2</td>
<td>26.6 ± 3.5</td>
</tr>
<tr>
<td>SD (control)</td>
<td>Distilled water</td>
<td>24.32 ± 3.5</td>
<td>20.14 ± 3.1</td>
</tr>
<tr>
<td>SD (treated)</td>
<td>400 mgkg(^{-1})</td>
<td>22.47 ± 2.4</td>
<td>24.94 ± 3.5</td>
</tr>
<tr>
<td>SD (Tolbutamide)</td>
<td>250 mgkg(^{-1})</td>
<td>23.84 ± 3.7</td>
<td>25.13 ± 3.2</td>
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<tr>
<td>VLDL (mg/dl)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Normal (control)</td>
<td>Distilled water</td>
<td>18.06 ± 2.5</td>
<td>18.18 ± 3.1</td>
</tr>
<tr>
<td>SD (control)</td>
<td>Distilled water</td>
<td>37.16 ± 2.2</td>
<td>37.66 ± 3.7</td>
</tr>
<tr>
<td>SD (treated)</td>
<td>400 mgkg(^{-1})</td>
<td>36.53 ± 2.7</td>
<td>27.29 ± 3.9</td>
</tr>
<tr>
<td>SD (Tolbutamide)</td>
<td>250 mgkg(^{-1})</td>
<td>36.93 ± 3.2</td>
<td>24.49 ± 3.1</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (control)</td>
<td>Distilled Water</td>
<td>51.0 ± 4.5</td>
<td>53.02 ± 4.8</td>
</tr>
<tr>
<td>SD (control)</td>
<td>Distilled Water</td>
<td>60.92 ± 5.7</td>
<td>66.90 ± 5.5</td>
</tr>
<tr>
<td>SD (treated)</td>
<td>400 mgkg(^{-1})</td>
<td>65.97 ± 3.7</td>
<td>66.10 ± 4.5</td>
</tr>
<tr>
<td>SD (Tolbutamide)</td>
<td>250 mgkg(^{-1})</td>
<td>57.73 ± 4.1</td>
<td>60.08 ± 5.1</td>
</tr>
</tbody>
</table>

\(P^*<0.05; \; **<0.01; \; ^*<0.001\) compared to pretreatment levels  
Values are mean ± SD \((n=6)\)
heart diseases can be reduced in diabetic patients by eating raw guavas. Increased level of ALKP indicates bone disease, liver disease or bile tract blockage. \textit{Psidium guajava} extract reduced ALKP level by 25.18 per cent indicating thereby, its protective effect over liver and improvement in liver function efficiency. These results are comparable with the dose of Tolbutamide treated group also showed a significant fall of 26 per cent (P<0.01). The serum creatinine level decreased significantly (P<0.001) in treated diabetic animals by 27.27 per cent as compared to initial values. Whereas, it increased slightly in case of controls, normal as well as diabetic, by 12.5 and 4.76 per cent respectively. Positive control showed a significant (P<0.001) fall of 31.82 per cent in creatinine levels (Table III).

Oral toxicity has already been checked in previous studies and the extract has been found to be relatively safe, as no mortality was associated with the single oral administration of 6000 mg/kg of the extract. Our results suggest that the raw fruit peel aqueous extract of \textit{Psidium guajava} showed significant hypolipidaemic and hepatoprotective effects and will be beneficial for type 2 diabetic patients.

### Table III. Effect of graded doses of \textit{P. guajava} unripe fruit peel aqueous extract on AST, ALT, ALKP and creatinin in severely diabetic (SD) rats

<table>
<thead>
<tr>
<th>Experimental rats</th>
<th>Treatment (Aq. extract)</th>
<th>Pre-treatment levels</th>
<th>7 days</th>
<th>14 days</th>
<th>21 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (control)</td>
<td>Distilled water</td>
<td>20.4 ± 2.4</td>
<td>21.3 ± 2.5</td>
<td>20.2 ± 2.3</td>
<td>20.9 ± 2.9</td>
</tr>
<tr>
<td>SD (control)</td>
<td>Distilled water</td>
<td>29.3 ± 2.6</td>
<td>30.2 ± 2.8</td>
<td>30.9 ± 2.7</td>
<td>32.4 ± 2.3</td>
</tr>
<tr>
<td>SD (treated)</td>
<td>400 mg/kg\textsuperscript{1}</td>
<td>30.9 ± 2.8</td>
<td>30.0 ± 3.2</td>
<td>25.6 ± 2.7*</td>
<td>22.4 ± 2.9*</td>
</tr>
<tr>
<td>SD (Tolbutamide)</td>
<td>250 mg/kg\textsuperscript{1}</td>
<td>31.4 ± 2.3</td>
<td>26.3 ± 2.5</td>
<td>25.4 ± 2.8*</td>
<td>22.8 ± 3.2*</td>
</tr>
<tr>
<td>ALT (U/l)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Normal (control)</td>
<td>Distilled water</td>
<td>22.4 ± 2.2</td>
<td>22.3 ± 2.5</td>
<td>22.5 ± 2.6</td>
<td>22.6 ± 2.9</td>
</tr>
<tr>
<td>SD (control)</td>
<td>Distilled water</td>
<td>32.4 ± 2.8</td>
<td>33.9 ± 3.2</td>
<td>34.2 ± 3.5</td>
<td>35.2 ± 2.6</td>
</tr>
<tr>
<td>SD (treated)</td>
<td>400 mg/kg\textsuperscript{1}</td>
<td>43.7 ± 2.9</td>
<td>30.1 ± 2.4</td>
<td>28.3 ± 2.1*</td>
<td>24.5 ± 3.2*</td>
</tr>
<tr>
<td>SD (Tolbutamide)</td>
<td>250 mg/kg\textsuperscript{1}</td>
<td>33.6 ± 3.1</td>
<td>30.2 ± 3.4</td>
<td>28.4 ± 2.4*</td>
<td>25.2 ± 2.5*</td>
</tr>
<tr>
<td>ALKP (U/l)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Normal (control)</td>
<td>Distilled water</td>
<td>86.8 ± 4.2</td>
<td>88.6 ± 4.5</td>
<td>87.1 ± 4.3</td>
<td>88.5 ± 4.1</td>
</tr>
<tr>
<td>SD (control)</td>
<td>Distilled water</td>
<td>145.9 ± 5.2</td>
<td>146.8 ± 5.3</td>
<td>147.2 ± 4.9</td>
<td>148.3 ± 5.1</td>
</tr>
<tr>
<td>SD (treated)</td>
<td>400 mg/kg\textsuperscript{1}</td>
<td>150.5 ± 5.7</td>
<td>146.4 ± 5.3</td>
<td>132.9 ± 5.9*</td>
<td>112.6 ± 4.8*</td>
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<tr>
<td>SD (Tolbutamide)</td>
<td>250 mg/kg\textsuperscript{1}</td>
<td>152.4 ± 5.6</td>
<td>140.2 ± 6.2</td>
<td>121.5 ± 5.3*</td>
<td>111.7 ± 5.5*</td>
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<td>Creatinine (U/l)</td>
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<tr>
<td>Normal (control)</td>
<td>Distilled water</td>
<td>0.8 ± 0.2</td>
<td>0.8 ± 0.3</td>
<td>0.9 ± 0.2</td>
<td>0.9 ± 0.3</td>
</tr>
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<td>SD (control)</td>
<td>Distilled water</td>
<td>2.1 ± 0.4</td>
<td>2.1 ± 0.3</td>
<td>2.1 ± 0.2</td>
<td>2.2 ± 0.3</td>
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<tr>
<td>SD (treated)</td>
<td>400 mg/kg\textsuperscript{1}</td>
<td>2.2 ± 0.2</td>
<td>2.0 ± 0.3</td>
<td>1.8 ± 0.4***</td>
<td>1.6 ± 0.2****</td>
</tr>
<tr>
<td>SD (Tolbutamide)</td>
<td>250 mg/kg\textsuperscript{1}</td>
<td>2.2 ± 0.3</td>
<td>1.9 ± 0.4</td>
<td>1.7 ± 0.2**</td>
<td>1.5 ± 0.4***</td>
</tr>
</tbody>
</table>

\(P^{*}<0.05; \ ^{**}<0.01; \ ^{***}<0.001\) as compared to pre-treatment levels

Values are mean ± SD (n= 6); AST, aspartate amino transferase; ALT, alanine amino transferase; ALKP, alkaline phosphatase

### References


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