Effects of selected herbal supplements in persons with type 2 diabetes

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Abstract
Diabetes mellitus is a metabolic abnormality leading to an increase in the plasma concentration of glucose and is a major cause of stroke and peripheral circulatory disorders. Momordica charantia (MC), commonly known as bitter gourd/Karela, and Trigonella foenum-graecum (TFG) (fenugreek/Methi) have several medicinal values like anti-diabetic, lipid-lowering property, anti-oxidant activity, anti-inflammatory, and anti-mutagenic activity. This is an open-label, four-parallel-group, prospective interventional clinical trial with a total number of 48 patients enrolled in the study and divided into four equal groups (12 in each group) viz; Group I (allopathic drug), Group II (allopathic drug and Karela (MC)), Group III (allopathic drug and Methi (TFG)) and Group IV (allopathic drug, methi, and karela). Blood sugar and lipid profile were measured at day 0 and day 90. One way ANOVA test was applied to find the significant difference between the groups and Tukey HSD post hoc test was applied for multiple comparisons among the four groups with probability p-value 0.05%. Multiple comparisons by post-hoc analysis between groups on day 90 showed a significant reduction of fasting blood sugar by 19.0% (p = 0.021), postprandial blood sugar by 35.0% (p = 0.001), total serum cholesterol by 14.0% (p = 0.000), serum triglyceride by 21.0% (p = 0.000), and serum LDL cholesterol by 17.0% (p = 0.000) in group receiving Karela and fenugreek seeds supplementation. Whereas serum HDL cholesterol on the 90th day was higher in the group by 10.0% (p = 0.015) receiving only fenugreek seeds as a supplementation. Fenugreek and karela, when given as a supplement, have a beneficial effect on blood sugar and lipid profile.

Keywords
Blood sugar, fenugreek, lipid profile, Momordica charantia, Nepal

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INTRODUCTION

Diabetes mellitus (DM), one of the major global health problems, has been rising rapidly in low-middle-income countries than in high-income countries. WHO estimated DM as the seventh leading cause of death in 2016. It is a complex disease, a leading cause of morbidity and mortality, resulting in stroke and peripheral circulatory disorders.

Momordica charantia (MC) (Bitter gourd or bitter melon or Karela) has been found to increase cellular glucose uptake by enhancing cellular insulin signaling pathways through the up regulation of GLUT4, PI3K and PPAR gamma. The active compound of MC is believed to be charantin, vicine and polypeptide, and the extracts are known to bear structural similarities to animal insulin.

Trigonella foenum-graecum (TFG) (fenugreek), stimulates the tyrosine phosphorylation of insulin receptor and enhances glucose uptake into cells. The leaves, chemical extracts and shoots of TFG have shown anti-oxidant, anti-diabetic and hypocholesterolemic properties.

This study was undertaken with the purpose of evaluating the effects of MC and TFG on blood sugar and lipid control of diabetic patients.

MATERIALS AND METHODS

This open label, four-parallel-group, prospective interventional clinical trial was conducted in BPKIHS, Dharan, Nepal from July 2015 to May 2016. Ethical approval was taken from Ethical Review Board, BPKIHS.

Sample size was calculated using the following formula:

\[
 n = \frac{2SD^2 (Z_{\alpha/2} + Z_{\beta})^2}{d^2}
\]

where, 
- \( n \) = sample size 
- \( SD \) = standard deviation of 17.6 
- \( Z_{\alpha/2} \) = 1.96 for 0.05 significance level 
- \( Z_{\beta} \) = 1.65 for 95% power 
- \( d \) = difference between mean values

After calculating the sample size, the total no. of subjects was 48 (12 in each group). Patients above 30 years with independent consciousness and behavior, who were diagnosed with DM type 2 by qualified physicians and taking anti-diabetic drugs prescribed by physicians, were included in the study. The MC used in this study was MC juice, which was prepared by crushing one medium-sized MC fruit with water in a mixer grinder and filtering through a tea filter. Participants were advised to take 200 ml of MC juice in the morning on an empty stomach. The TFG extract used was 6-7 gm of TFG seeds (one teaspoonful). The seeds were chewed and swallowed on an empty stomach once a day. MC+TFG extracts were 200ml of the MC juice and 6-7gm of the TFG seeds taken in a gap of half an hour on an empty stomach once a day.

RESULTS

A total of 48 uncomplicated type-2 DM patients participated in the study, of whom 42 completed the study. Six patients withdrew from the study; two each from groups II, III and IV as they were not willing to continue the treatment. Among 42 patients who completed the study, 18 were males and 24 females. The mean age of the patients was 56.6±1.5 years and mean BMI was 25.7±0.5 kg/m² (Table 1).

Add on treatment for 90 days with 200 ml/day of MC in Group II, 6-7 gm/day of TFG in Group III, and both 200 ml/day of MC and 6-7 gm/day of TFG in Group IV significantly reduced the serum FBS, PPBS, and total cholesterol in all the groups. There was significant reduction of fasting blood sugar by 19% (p = 0.021).
postprandial blood sugar by 35.0% (p= 0.001), total serum cholesterol by 14.0% (p= 0.000), and serum LDL-cholesterol by 17.0% (p= 0.000) in a group receiving karela and fenugreek seeds supplementation. Whereas serum HDL-cholesterol on the 90th day was higher in a group by 10% (p=0.015) receiving only fenugreek seeds as supplementation (Table 2).

Multiple comparison by Tukey HSD post-hoc analysis of serum FBS, PPBS, and total cholesterol, serum triglyceride, serum LDL-cholesterol and serum HDL-cholesterol on 90th day revealed that Group D receiving TFG + MC seeds supplementation has significant reduction in serum FBS (p = 0.021), PPBS (p =0.001), total serum cholesterol (p = 0.000*), serum triglyceride(p =0.000), serum LDL-cholesterol(0.000). Multiple comparison by Tukey HSD post-hoc analysis of total cholesterol, serum triglyceride, serum LDL-cholesterol and serum HDL-cholesterol on 90th day revealed that Group C receiving TFG supplementation also revealed significant reduction in total serum cholesterol (p =0.000), serum triglyceride (p =0.000), serum LDL-cholesterol (p =0.000), and significant increase in serum HDL-cholesterol (p= 0.015) (Table 2).

### DISCUSSION

Majority of the complication of diabetes mellitus can be prevented with adequate glycemic and lipid control. In spite of vigorous allopathic drug used in the prevention of these complications, it remains a challenge. Significant number of medicinal plants have hypoglycemic and hypolipidemic activity in experimental and clinical anti-diabetic models. This open-label, four-parallel group, prospective interventional clinical trial on the effects of M. charantia and T. foenum-graecum supplements in type 2 diabetics taking allopathic drug shows significant improvement in fasting blood sugar, post-prandial blood sugar, and lipid profile compared to its respective baseline.

This study found that FBS and PPBS are significantly reduced with add on therapy with both MC and TFG which is in consistent with the beneficial effects of MC and TFG in other studies. It has been proposed that fenugreek seeds in humans and animals attenuate glucose tolerance and improvement in glucose-induced insulin response, thereby ratifying the potential hypoglycemic activity of fenugreek seeds. Studies reveal the hypoglycemic effect of MC
due to its ability to maintain structural integrity of pancreatic islets and release of hormones and the presence of charantine, vicine, and polypeptide like active components that have structural similarity with human insulin.\(^8,12\)

The lipid lowering effect of TFG and MC has been extensively studied in animal models but only few clinical trials have been conducted. This study reveals significant improvement in lipid profile with MC and TFG when used as an adjuvant to anti diabetic drugs. This is in accordance with the other clinical trials.\(^13,14\)

A gel like soluble fiber present in fenugreek seeds combine with bile acids and lower the triglyceride levels and the amino acids present in the seeds boost insulin sensitization and glycogen synthesis. The hypoglycemic activity is enhanced by the dietary fibers and the saponins present in the fenugreek seeds.\(^15\)

It has been found that MC and TFG preparation were highly tolerable in all the trials and were associated with minimal or no side effects and can be considered as an add on therapy option with safety profile along with conventional cholesterol and sugar lowering agents. On the other hand MC and TFG also significantly increased the HDL cholesterol level in this study which is in accordance with other studies.\(^7,16,17\)

Patients enrolled in his study self-administered the extracts of MC and TFG. Thus, the relationship between various confounding

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**Table 2: Primary outcome following allopathic medication and MC and TFG (N=42)**

<table>
<thead>
<tr>
<th>Variables (Mean)</th>
<th>Groups</th>
<th>Baseline</th>
<th>7 days</th>
<th>15 days</th>
<th>30 days</th>
<th>90 days</th>
<th>P -value</th>
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<tbody>
<tr>
<td>Fasting blood sugar (mg/dl)</td>
<td>I</td>
<td>177.1</td>
<td>169.0</td>
<td>159.7</td>
<td>157.4</td>
<td>147.5</td>
<td>0.126</td>
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<td></td>
<td>II</td>
<td>156.9</td>
<td>134.7</td>
<td>137.0</td>
<td>124.8</td>
<td>108.7</td>
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<td>III</td>
<td>136.2</td>
<td>132.3</td>
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<td>122.6</td>
<td>115.4</td>
<td>0.992</td>
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<td></td>
<td>IV</td>
<td>188.7</td>
<td>173.4</td>
<td>152.2</td>
<td>139.8</td>
<td>122.2</td>
<td>0.021*</td>
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<td>Post prandial blood sugar (mg/dl)</td>
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<td>236.3</td>
<td>224.5</td>
<td>216.9</td>
<td>205.9</td>
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<td>II</td>
<td>227.5</td>
<td>208.1</td>
<td>205.2</td>
<td>184.0</td>
<td>154.51</td>
<td>0.608</td>
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<td>240.7</td>
<td>230.4</td>
<td>211.2</td>
<td>200.7</td>
<td>184.3</td>
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<td></td>
<td>IV</td>
<td>372.4</td>
<td>296.6</td>
<td>149.6</td>
<td>216.0</td>
<td>176.3</td>
<td>0.001*</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>I</td>
<td>201.1</td>
<td>200.0</td>
<td>200.9</td>
<td>200.0</td>
<td>197.9</td>
<td>0.924</td>
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<tr>
<td></td>
<td>II</td>
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<td>196.3</td>
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<td>III</td>
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<td>191.6</td>
<td>176.5</td>
<td>0.000*</td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td>209.7</td>
<td>206.1</td>
<td>200.8</td>
<td>192.7</td>
<td>172.4</td>
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<tr>
<td>Serum Triglyceride (mg/dl)</td>
<td>I</td>
<td>159.0</td>
<td>159.3</td>
<td>158.2</td>
<td>157.2</td>
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<td>191.0</td>
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<td>248.7</td>
<td>245.5</td>
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<td>220.8</td>
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<td>Serum LDL – Cholesterol (mg/dl)</td>
<td>I</td>
<td>114.6</td>
<td>114.0</td>
<td>114.8</td>
<td>116.5</td>
<td>114.3</td>
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<td>II</td>
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<td>99.5</td>
<td>97.4</td>
<td>96.4</td>
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<td>108.7</td>
<td>104.6</td>
<td>94.5</td>
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<tr>
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<td>IV</td>
<td>125.2</td>
<td>121.8</td>
<td>118.5</td>
<td>115.0</td>
<td>101.6</td>
<td>0.000*</td>
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<tr>
<td>Serum HDL-Cholesterol (mg/dl)</td>
<td>I</td>
<td>40.2</td>
<td>40.3</td>
<td>41.1</td>
<td>40.6</td>
<td>40.9</td>
<td>0.978</td>
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<td>41.1</td>
<td>41.0</td>
<td>41.8</td>
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<td></td>
<td>III</td>
<td>40.2</td>
<td>40.5</td>
<td>42.8</td>
<td>43.3</td>
<td>44.4</td>
<td>0.015*</td>
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<tr>
<td></td>
<td>IV</td>
<td>43.0</td>
<td>43.1</td>
<td>43.9</td>
<td>44.5</td>
<td>45.6</td>
<td>0.367</td>
</tr>
</tbody>
</table>

* P value (<0.05) was statistically significant (One –Way ANOVA test and Turkey HSD post hoc test)
Excluded (n=22)
  • Not meeting inclusion criteria (n=13)
  • Declined to participate (n=9)

Randomized (n=48)

Enrollment
Assesses for eligibility (n=64)

Fig. 1: Consort Flow Diagram

Group I (n=12)
(Received allopathic drug only)

Group II (n=12)
(Received allopathic drug and MC juice)

Group III (n=12)
(Received allopathic drug and fenugreek)

Group IV (n=12)
(Received allopathic drug, MC Juice and fenugreek)

Follow up

Lost to follow up (n=0)
Discontinued intervention (n=0)

Analysis

Analyzed (n=12)
Excluded from analysis (n=0)

Analyzed (n=12)
(Received allopathic drug only)

Analyzed (n=10)
Excluded from analysis (n=0)

Analyzed (n=10)
Excluded from analysis (n=0)

Analysis

Analyzed (n=10)
Excluded from analysis (n=0)

Analysis

Analyzed (n=10)
Excluded from analysis (n=0)

Analysis

Analyzed (n=10)
Excluded from analysis (n=0)

Analysis

Analyzed (n=10)
Excluded from analysis (n=0)

Analysis

Factors and the glycemic and lipid control in these patients cannot be overruled. This study further recommends the need of clinical trial exploring more of association of glycemic control, lipid profile control and various confounding factors with a larger sample size.

In conclusion, this study showed the significant improvement in the blood sugar and lipid profile after short term (90 days) treatment with add on therapy with oral supplementation of MC and TFG in patients with type 2 Diabetes Mellitus.

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REFERENCES


