Introduction:

Bitter melon has been used widely in Southeast Asia as a natural medicine to treat patients with diabetes (1-4). This is due to the insulin-like effect that bitter melon seems to have (1-4). The parts usually used are the fruit and seeds, while the less commonly used parts are the leaves and roots (3). The bitter melon fruit, seeds, and leaf extracts seem to have hypoglycemic effect in patients with diabetes (3). Bitter melon is used orally to treat other diseases such as ulcer, constipation, and urinary tract stones (3). It can be also used topically to treat some medical conditions such as skin abscesses (3).

Clinical Trials:

The hypoglycemic activity of bitter melon has been demonstrated in experimental animal studies (1, 4). Several clinical trials have tested different formulations of bitter melon (e.g. juice, powder, and extracts) (5). Although some patients with type 2 diabetes showed improvement in glycemic control, the results of clinical trials are considered inadequate to recommend bitter melon for the management of type 2 diabetes (1, 4-5). This is mainly because these trials do not meet proper methodological standards (1, 4). Examples include inadequate statistical methods, inadequate patient recruitment criteria, lack of randomization, lack of control groups, or short study duration (1).

An old study evaluated the efficacy and the safety of bitter melon extract as “vegetable insulin”, which was administered through the subcutaneous route (4, 6). This study reported that bitter melon extract was homologous to insulin taken from animal pancreas, and it showed that the average reduction in blood glucose level was statistically significant (6). The extract was considered safe to use as no hypersensitivity reaction was reported (6). Another study evaluated the effect of bitter melon juice on glucose tolerance in patients with type 2 diabetes, and it has been shown that glucose tolerance was improved in 73% of the participants (6).

Recently, in 2011, a randomized double-blind active control trial assessed the efficacy and the safety of three different doses of bitter melon (500, 1000, and 2000 mg per day) compared to metformin (1000 mg per day) in 143 newly diagnosed patients with type 2 diabetes for four weeks. At the end of the study, it was found that there was a significant decrease in fructosamine in the metformin group as well as the group receiving 2000 mg of bitter melon. However, the hypoglycemic effect of metformin was more than that of the 2000 mg dose of bitter melon per day. On the other hand, there was no significant change in fasting blood glucose (FBG) level and 2-hour plasma glucose level after oral glucose tolerance test (OGTT) in all bitter melon groups. Bitter melon was well tolerated in this study. However, some of the participants receiving the 2000 mg dose of bitter melon per day experienced increased appetite. Moreover, one patient, in the bitter melon group, experienced elevated liver function compared to baseline (1).

The following table summarizes the important aspects that the healthcare professional should know about bitter melon and its use for diabetes and related conditions.
Table 1: Summary of the important aspects that the healthcare professional should know about bitter melon and its use for diabetes and related conditions:

<table>
<thead>
<tr>
<th>Scientific Name</th>
<th>Momordica charantia, Momordica muricata (3-4)</th>
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<tbody>
<tr>
<td>Family</td>
<td>Cucurbitaceae (3)</td>
</tr>
</tbody>
</table>
| Active Constituents | • Insulin-like polypeptide called polypeptide-P (3, 7).  
                     • Plant insulin or p-insulin (3, 7).  
                     • Charantin: mixture of two steroid glycosides and vicine (3, 7).  
                     • Flavonoids (3).  
                     • Alpha- and beta-momocharin (3).  
                     • Proteins: MAP30 and MRK29 (3).  
                     • Others (e.g. Vitamins, elemental compounds, and fatty acids) (4). |
| Mechanism of Action | • Preliminary evidence suggests that bitter melon (1, 3, 7-9):  
                     ⇒ Increases pancreatic insulin secretion  
                     ⇒ Increases insulin sensitivity  
                     ⇒ Preserves β cells in the pancreatic islets  
                     ⇒ Depresses hepatic gluconeogenesis  
                     ⇒ Increases hepatic glycogen synthesis  
                     ⇒ Increases peripheral glucose utilization  
                     ⇒ Increases liver and muscle glycogen storage  
                     ⇒ Decreases glucose absorption  
                     • Polypeptide-P has insulin-like properties and similar pharmacokinetics of bovine insulin. Its onset is 30-60 minutes and peak effect is 4 hours (1-3, 5).  
                     • Charantin has a hypoglycemic effect (3).  
                     • Flavonoids have a cholesterol lowering effect (3). |
| Adverse Reactions | An oral dose of 1 g of bitter melon three times a day is considered well-tolerated. However, some patients may experience diarrhea, abdominal pain, and epigastric pain (3-4). Seeds consumption was associated with headache. Also, hypoglycemic coma and seizures were reported in two children after consuming bitter melon tea (3-4). Another case report showed that intake of the crushed bitter melon fruit resulted in atrial fibrillation (4). The effect of bitter melon on liver function is not known in the clinical setting, despite the fact that an increase in liver function tests was reported experimentally in animal studies (3-4). |
| Toxicity        | The red arils around the seeds of bitter melon are reported to be toxic to children. One case resulted in vomiting, diarrhea, and eventually death (4). |
| Interactions with Drugs | Hypoglycemic drugs: Risk of hypoglycemia might increase by concomitant use of hypoglycemic drugs such as insulin, glimepiride, metformin, and rosiglitazone (3). Therefore, patients with diabetes who take hypoglycemic drugs should be counseled about the increased risk of hypoglycemia when eating foods that contain bitter melon concomitantly (5). It is worthy to mention that bitter melon is included widely in traditional Asian and Indian cuisine (5). Furthermore, a decrease in blood glucose level after eating food containing bitter melon by a patient taking chlorpropamide was reported (3, 5). One experiment showed that bitter melon had minor effects on cytochrome P450 enzymes and glutathione S-transferase (4). |
| Interactions with Herbs/Supplements | Hypoglycemic herbs and supplements: Risk of hypoglycemia might be increased by concomitant use of hypoglycemic herbs and supplements such as fenugreek, alpha-lipoic acid, and chromium (3). |
Table 2: Evidence-based Safety Rating Standards (Adapted from the Natural Medicines Comprehensive Database) (10)

<table>
<thead>
<tr>
<th>Interactions with Foods</th>
<th>Unknown (3)</th>
</tr>
</thead>
</table>

**Interactions With Medical Conditions**
- **Diabetes:** Bitter melon might affect blood glucose level in patients with diabetes. Accordingly, close monitoring of blood glucose level is required (3).
- **Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency:** Vicine that is found in the bitter melon seeds can increase the risk of favism after consuming food containing these seeds (3-4).
- **Surgery:** As bitter melon might affect the glycemic control in patients with diabetes, patients should discontinue bitter melon consumption at least two weeks before the surgery (3).

**Interactions with Lab Tests**
- **Blood glucose level:** bitter melon fruit, fruit juice, and extracts can alter blood glucose level results in patients with type 2 diabetes (3).
- **Glycosylated hemoglobin (HbA1c):** Treatment with bitter melon extract for seven weeks can lower HbA1c in patients with type 2 diabetes (3).

**Dosage Administration**
Natural Medicines Comprehensive Database reported that there is no typical dose (3). On the other hand, Lexicomp database reported that 50-100 ml per day of bitter melon juice, or 900 mg of bitter melon fruit three times per day have been recommended and/or given for patients with diabetes (4). However, evidence is insufficient to rely on in prescribing these doses (4).

**Safety (See Table 2)**
- "POSSIBLY SAFE" when consumed orally and in an appropriate way. It has been reported that bitter melon fruit seems to be safe when used for three months at most (3).

**Effectiveness (See Table 3)**
There is insufficient evidence that bitter melon is effective for diabetes (3).

**Pregnancy**
Using bitter melon should be avoided as it is "LIKELY UNSAFE" because it was documented that it stimulated menstruation, and had an abortifacient effect (3-4).

**Lactation**
Using bitter melon should be avoided as the available information is insufficient (3-4).

<table>
<thead>
<tr>
<th>LIKELY SAFE</th>
<th>This product has a very high level of reliable clinical evidence showing its safe use when used appropriately. Products rated Likely Safe are generally considered appropriate to recommend.</th>
</tr>
</thead>
<tbody>
<tr>
<td>POSSIBLY SAFE</td>
<td>This product has some clinical evidence showing its safe use when used appropriately; however, the evidence is limited by quantity, quality, or contradictory findings. Products rated “Possibly Safe” appear to be safe, but do not have enough high-quality evidence to recommend for most people.</td>
</tr>
<tr>
<td>POSSIBLY UNSAFE</td>
<td>This product has some clinical evidence showing safety concerns or significant adverse outcomes; however, the evidence is limited by quantity, quality, or contradictory findings. People should be advised NOT to take products with a “Possibly Unsafe” rating.</td>
</tr>
<tr>
<td>LIKELY UNSAFE</td>
<td>This product has a very high level of reliable clinical evidence showing safety concerns or significant adverse outcomes. People should be discouraged from taking products with a “Likely Unsafe” rating.</td>
</tr>
<tr>
<td>UNSAFE</td>
<td>This product has a very high level of reliable clinical evidence showing safety concerns or significant adverse outcomes. People should be discouraged from taking products with an Unsafe rating.</td>
</tr>
</tbody>
</table>
als that bitter melon is effective for diabetes is insufficient. Therefore, bitter melon should not be used as a pharmacological therapy for type 2 diabetes. Further double-blind randomized clinical trials on bitter melon are needed in a large sample of the population in order to assess the efficacy and safety issues.

**Conclusion:**

Bitter melon is considered "POSSIBLY SAFE" when consumed orally in a proper way. The evidence from quality clinical trials that bitter melon is effective for diabetes is insufficient. Therefore, bitter melon should not be used as a pharmacological therapy for type 2 diabetes. Further double-blind randomized clinical trials on bitter melon are needed in a large sample of the population in order to assess the efficacy and safety issues.

**References:**


Pharmacotherapy Services Department

Drug Information Services

Listed below are the Drug Information Services that we offer:

- Update and manage drug information resources
- Update healthcare providers when new information is available on drugs
- Provide trainings and workshops to healthcare providers on drug information and medication safety
- Respond to drug information questions

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