

## **To take or not to take – the controversial role of *Momordica charantia* extracts in improving symptoms of diabetes mellitus**

### **Introduction**

In 2010, the global prevalence of diabetes was found to be 6.4% and this percentage is projected to reach 7.7% by 2030. It results in significant mortality and morbidity, apart from being an important risk factor for cardiovascular disease. Diabetes mellitus is characterized by a gradual decline in pancreatic  $\beta$ -cell function and increase in insulin resistance in the body. It is the most common endocrine metabolic disorder and affects all categories of people in all parts of the world. Therapeutic interventions for this disease mostly comprise of insulin, glinides, biguanides, and sulfonylureas; however, most of these medications have harmful side effects and deplete the body of essential nutrients. Current medical guidelines recommend enhancing glucose tolerance in the body through diet control and physical exercise apart from anti-diabetic medications (Yin et al., 2014).

*Momordica charantia*, also known as bitter melon or bitter melon, is a plant that belongs to the Cucurbitaceae family and it has widely been used by indigenous populations of South America, Asia, East Africa, and the Caribbean as a hypoglycemic agent. Several animal studies have proved its anti-diabetic effects; however, its evidence in clinical trials is limited and its mode of action in controlling blood glucose is not well-characterized (Blum et al., 2012). Chemical analysis of these extracts have found that this plant has several phytochemicals which delays gastric transient time and prevents damage to organs such as the liver and pancreas that are involved in glucose metabolism. Preliminary clinical studies have also found that *M. charantia* extracts can reduce serum glucose in diabetic individuals. However, clinical studies are limited and the results are extremely varied making it difficult to incorporate it into medical therapeutic guidelines (Kasbia et al., 2009).

This paper aims to evaluate the scientific literature pertaining to the use of *M. charantia* extracts in lowering blood glucose levels of diabetic people. While it is strongly recommended that therapeutic interventions that have passed clinical trials should be preferred for most diseases, knowledge of ancient plants is abundant with several useful substances that can help in curing most elusive ailments for which there is no definitive treatment currently. Both are important points to be considered while designing intervention regimes for diabetes and both these points are argued in this essay making use of data from the literature.

## **Use of *M. charantia* extracts for diabetic treatment lacks scientific basis**

The scientific knowledge pertaining to the strength and efficacy of anti-diabetic uses of *M. charantia* extracts in the treatment of diabetes mellitus is highly limited. A study conducted by Kasbia et al. (2009) sought to understand the efficacy of these extracts in appetite, energy expenditure, and postprandial glucose levels in overweight non-diabetic men after treating them with an oral glucose load, and it found that the administration of these extracts had no significant effect on glucose and insulin levels in these participants. This was the first study that was done using healthy men and administration of two different doses of the extract found no physiologic effects pertaining to these extracts. According to this study, most claims are theoretical and derived from preliminary animal studies with little evidence in clinical studies with diabetic patients. Additionally, all studies that have been performed until now use different participant characteristics, species of *Momordica*, doses, mode of administration, and parameters studied. As a result of these inconsistencies between study designs, the findings cannot be extrapolated to the larger population which makes its use in diabetic people unreliable as compared to standard anti-diabetic medication (Kasbia et al., 2009).

Another study conducted by Dans et al. (2006) sought to evaluate the efficacy of *M. charantia* extracts in addition to standard anti-diabetic therapy in patients with poor glycemic control in a large clinical trial. This study found that when compared with placebo, administration of *M. charantia* capsules had no significant effect over fasting blood sugar, cholesterol, weight, sodium, potassium, and serum creatinine. The hypothesized effect was a 1% decline in A1c levels; however, the observed effect was just 0.24% decline in A1c in 40 patients when investigated over 3 months. Therefore, even after 3 months of therapy with *M. charantia* capsules, no significant effect was noticed in diabetic patients. Additionally, some of the patients reported gastrointestinal discomfort as a side effect of the capsules, which indicates that while having no significant therapeutic effect, this therapy may cause adverse effects in users (Dans et al., 2006).

A comparative study conducted by Fuangchan et al. (2011) evaluated the effects of different doses of *M. charantia* extracts and metformin on the levels of fructosamine in diabetic patients over a period of 4 weeks. This study found that although *M. charantia* extracts exerted hypoglycemic effects in patients, it was significantly lesser as compared to the hypoglycemic effects of metformin. Also, the dose at which *M. charantia* extract exerted its effect was 2000 mg/day as compared to 1000 mg/day for metformin. This shows that although *M. charantia* has beneficial effects, it cannot be considered a suitable alternative for metformin for diabetic patients who require effective and rapid hypoglycemic control (Fuangchan et al., 2011).

A meta-analysis carried out by Yin et al. (2014) using the limited number of studies available on the effects of *M. charantia* extracts on glucose tolerance found that there is no significant effect exerted by this plant in diabetic patients. The limited number of studies is definitely a limitation; however, the studies that have been conducted lack experimental strength due to differences in doses used and duration of the study. As this is a plant-based extract, it may be reasonably expected that the beneficial effects may become apparent after prolonged use; however, the longest study has been conducted over just 12 weeks. As a result, the current scientific evidence for use of *M. charantia* extracts in diabetes is inconclusive and cannot be relied upon to replace anti-diabetic therapy (Yin et al., 2014).

### ***M. charantia* has the potential to be a natural therapeutic intervention for diabetes**

Despite the handful of studies that indicate a non-significant effect of *M. charantia* extracts on the control of diabetes, there is also significant evidence that prove its effectiveness as an anti-diabetic agent. Although several animal studies have showed the glucose lowering effects of *M. charantia* extracts, a few population-based clinical trials have also indicated the efficacy of these extracts in controlling blood glucose levels. While it may, as of yet, not be advisable to replace standard anti-diabetic therapy completely with *M. charantia* extracts, these extracts may be used as a supplementary therapy especially in patients showing poor glycemic control. As it is natural, it lacks the side effects of chemically synthesized medications and may potentially have many more beneficial effects in the body apart from lowering blood sugar levels.

Apart from hyperglycemia, the other adverse effects of diabetes include abnormal fat, protein, and carbohydrate metabolism, complications regarding the body's vasculature, and several other metabolic abnormalities. Additionally, with the increased global burden of diabetes, there is a growing population of middle-aged diabetics who cannot afford anti-diabetic medications and who face several decades of living with this chronic condition. As a result, in order to reduce the health outcomes and economic impacts of this disease especially in developing nations, modern medicine has turned to alternative and complementary therapies, including herbal medicines, to achieve glycemic control in diabetics. Currently, 400 plants are known to possess hypoglycemic activity and *M. charantia* is one of the few plants that have been extensively characterized for their anti-diabetic potential (Ooi et al., 2012).

An early study conducted by Baldwa et al. (1977) evaluated the beneficial effects of *M. charantia* extracts administered to diabetics and controls through a subcutaneous injection. Analysis of blood glucose levels at different time points following the injection found a reduction of 49.2% after 4 hours as compared to 5% in participants who had received a placebo injection. Although this study had several methodological limitations,

the results are nevertheless promising given the high percentage of blood glucose reduction in participants who received the *M. charantia* injection (Baldwa et al., 1977).

A study conducted by Tongia et al. (2004) evaluated the anti-diabetic effects of *M. charantia* extracts in addition to metformin, glibenclamide, or metformin + glibenclamide in three groups of participants, and measured levels of fasting blood sugar and postprandial sugar before and after administration of the intervention. This study found that introduction of *M. charantia* extracts to the anti-diabetic therapy led to a significantly higher reduction in the measured parameters as compared to administration of the anti-diabetic therapy alone. The only flaw of this study was that the sample size was very small with just 15 participants; however, the preliminary results were promising and indicative of a potential beneficial effect of *M. charantia* in diabetes (Tongia et al., 2004).

A meta-analysis conducted by Phimarn et al. (2018) found that use of *M. charantia* extracts had the potential to regulate HDL and LDL levels, fasting blood sugar, A1c, and weight in diabetic patients. This is the first meta-analysis that has demonstrated potentially beneficial therapeutic effects of *M. charantia* extracts in diabetic patients. The active ingredients that confer these properties to the plant extracts include charantin, momorcharin, and mormordicin, and studies have shown that these ingredients can promote insulin secretion in the body and prevent damage to pancreatic  $\beta$  cells (Xu et al., 2015).

Also, in contrast to chemically synthesized medications, *M. charantia* extracts have not been reported to have any critical adverse events or withdrawal effects, and they are deemed to be safe for oral administration. These extracts have not been shown to have any severe or life-threatening effects on the skin, central nervous system, or the digestive system, which are most commonly the victim of side effects of chemically synthesized medications (Phimarn et al., 2018).

## **Discussion**

The literature abounds with several studies that prove the beneficial effects of *M. charantia* extracts in controlling diabetes as well as studies that do not report a significant effect of these extracts in controlling blood sugar levels in diabetic subjects. While complementary and alternative therapies are widely preferred by a lot of people especially for medications that need to be taken life-long, it is also important to note that chronic conditions such as diabetes, if not controlled appropriately, can lead to other complications such as cardiovascular and cerebrovascular diseases. Several diabetics also prefer a combination of herbal and chemically synthesized medication; however, this does not serve to fulfill the purpose of going natural and avoiding the adverse effects of long-term synthetic medications. In order to truly demonstrate the efficacy of

*M. charantia* extracts, there needs to be studies where subjects wholly undergo plant-based treatments and avoid synthetic medication altogether for a prolonged duration with blood glucose measurements at regular intervals. Only then will it be possible to prove the viability of treatment with *M. charantia* in place of standard anti-diabetic therapies. On the other hand, the science of Ayurveda has been using and prescribing plant-based medications for years with several beneficial effects in diseases where chemically synthesized medications have failed. Often, these herbal medicines do not have strong evidence in scientific literature, except for the fact that they have minimal side effects and the least possible harm they can do to a person is to not have any beneficial effect at all.

## **Conclusion**

This paper evaluated the scientific literature pertaining to the use of *M. charantia* extracts in the treatment of diabetes either alone or in combination with other anti-diabetic interventions. While several studies show beneficial effects of *M. charantia* in diabetes, a few studies also indicate no significant effect of this plant in controlling blood sugar levels. The main issue that is apparent from the literature is that the studies that have been conducted in this regard lack consensus relating to dosage of the extract, dosage of synthetic medications if used, mode of administration, parameters measured, time intervals at which parameters are measured, participant selection, and randomization method of participants. As a result, it has become difficult to extrapolate the results of any study to a larger population. In general, *M. charantia* extracts have shown beneficial effects in diabetes with minimal adverse events and can be used either alone or as a supplement to other anti-diabetic interventions in diabetic patients.

## References

- Baldwa, V. S., Bhandari, C. M., Pangaria, A., & Goyal, R. K. (1977). Clinical trial in patients with diabetes mellitus of an insulin-like compound obtained from plant source. *Upsala Journal of Medical Sciences*, 82(1), 39-41. doi:10.3109/03009737709179057
- Blum, A., Loerz, C., Martin, H., Staab-Weijnitz, C. A., & Maser, E. (2012). *Momordica charantia* extract, a herbal remedy for type 2 diabetes, contains a specific 11 $\beta$ -hydroxysteroid dehydrogenase type 1 inhibitor. *The Journal of Steroid Biochemistry and Molecular Biology*, 128(1-2), 51-55. doi:10.1016/j.jsbmb.2011.09.003
- Dans, A. M., Villarruz, M. V., Jimeno, C. A., Javelosa, M. A., Chua, J., Bautista, R., & Velez, G. G. (2007). The effect of *Momordica charantia* capsule preparation on glycemic control in type 2 diabetes mellitus needs further studies. *Journal of Clinical Epidemiology*, 60(6), 554-559. doi:10.1016/j.jclinepi.2006.07.009
- Fuangchan, A., Sonthisombat, P., Seubnukarn, T., Chanouan, R., Chotchaisuwat, P., Sirigulsatien, V., . . . Haines, S. T. (2011). Hypoglycemic effect of bitter melon compared with metformin in newly diagnosed type 2 diabetes patients. *Journal of Ethnopharmacology*, 134(2), 422-428. doi:10.1016/j.jep.2010.12.045
- Kasbia, G. S., Arnason, J. T., & Imbeault, P. (2009). No effect of acute, single dose oral administration of *Momordica charantia* Linn., on glycemia, energy expenditure and appetite: A pilot study in non-diabetic overweight men. *Journal of Ethnopharmacology*, 126(1), 127-133. doi:10.1016/j.jep.2009.07.035
- Ooi, C. P., Yassin, Z., & Hamid, T. (2009). *Momordica charantia* for type 2 diabetes mellitus. *Cochrane Database of Systematic Reviews*. doi:10.1002/14651858.cd007845
- Phimarn, W., Sungthong, B., Saramunee, K., & Caichompoo, W. (2018). Efficacy of *Momordica charantia* l. on blood glucose, blood lipid, and body weight: A meta-analysis of randomized controlled trials. *Pharmacognosy Magazine*, 14(56), 351. doi:10.4103/pm.pm\_215\_17
- Tongia, A., Tongia, S. K., & Dave, M. (2004). Phytochemical determination and extraction of *Momordica charantia* fruit and its hypoglycemic potentiation of oral hypoglycemic drugs in diabetes mellitus (NIDDM). *Indian J Physiol Pharmacol*, 48(2), 241-244.
- Xu, X., Shan, B., Liao, C., Xie, J., Wen, P., & Shi, J. (2015). Anti-diabetic properties of *Momordica charantia* l. polysaccharide in alloxan-induced diabetic mice. *International Journal of Biological Macromolecules*, 81, 538-543. doi:10.1016/j.ijbiomac.2015.08.049

Yin, R. V., Lee, N. C., Hirpara, H., & Phung, O. J. (2014). The effect of bitter Melon (*Mormordica charantia*) in patients with diabetes mellitus: A systematic review and meta-analysis. *Nutrition & Diabetes*, 4(12). doi:10.1038/nutd.2014.42