

# ABSTRACT

---

The prevalence of diabetes is rapidly rising globally, with 69.1 million cases of diabetes in India in 2015. Besides oral glucose lowering drugs and insulin injections, several complementary medicines and therapies including Ayurveda, Naturopathic and Unani for the treatment and control of diabetes are also being practiced.

*Aegle Marmelos* (L.) Correa (bael leaves), described in ancient medical treatise *Charak Samhita* for the treatment of diabetes '*madhumeh*' is one such complimentary therapy. Animal studies have indicated a hypoglycaemic effect of *Aegle Marmelos* (L.) Correa leaf extract with a high margin of drug safety and no short term toxicity. However evidence based research on humans is lacking. Thus to fill in this gap in existing knowledge, present study was planned with the broad objective: "In-Depth Study Of The Antioxidant Profile Of *Aegle Marmelos* (L.) Correa (Bael) And Its Impact On Type II Diabetes Mellitus Subjects".

The specific objectives were 1) In-depth antioxidant profile, proximate composition and minerals in the cultivated variety ('*Gomayasi*') and wild variety of *Aegle Marmelos* (L.) Correa leaves; 2) Knowledge, practice and use (KPU) of *Aegle Marmelos* (L.) Correa leaves with practitioners of Ayurveda and Naturopathy; and 3) Impact of *Aegle Marmelos* (L.) Correa (bael) leaf juice supplementation on blood sugar levels, lipid profile, liver and kidney functions of Type II diabetes subjects.

Phase I- Samples of the cultivated variety of *Aegle Marmelos* (L.) Correa leaves (*Gomayasi*) were collected from Central Horticultural Experiment Station (CIAH), Vejalpur (Godhra), Panchmahal, Gujarat, India and wild variety was collected from the identified zone (21004'49.7"N 70035'10.6"E) of Gir forest, Talala, Gir Somnath, Gujarat, India. The physico-chemical analysis of proximate principles were done using suitable methods: ash, moisture, protein, fat, fibre (AOAC methods), mineral content (AOAC methods), heavy metals- lead, arsenic, mercury and cadmium (AAS), total antioxidant capacity (FRAP/DPPH), total phenol content (Folin-Ciocalteu method) and individual phenolic compounds (HPLC) of dry powdered samples.

Results revealed that proximate principles (ash, moisture, protein, carbohydrate, fat and crude fibre content) of wild variety of Gir were more than the cultivated variety called *Gomayasi* (6.5% and 6%; 53.96% and 52.14%; 7.6% and 2.22% ; 10.38% and 5.42%; 8.18% and 12.78% and 30.14% and 25.10% resp). Similar trend was reported for minerals (copper-12 and 11ppm; iron-181 and 165 ppm; manganese-62 and 56 ppm and zinc-49 and 38 ppm) for wild and cultivated bael leaves respectively. No heavy metals (Cadmium, Arsenic, Lead and Mercury) were detected in any variety. Total polyphenol content was 7.6% (wild) and 6.5% (cultivated), quantification of individual phenolic compounds (HPLC) revealed the presence of Gallic acid, Chlorogenic acid and Ferullic acid in wild variety whereas Gallic acid, Ferullic acid and Pyrocatechol in cultivated variety. Total antioxidant capacity (FRAP value-14.65  $\mu\text{mol/l}$  and 11.80 $\mu\text{mol/l}$ ) and (DPPH-  $\text{IC}_{50}$  value -437  $\mu\text{g/ml}$  and 620 $\mu\text{g/ml}$ ) for wild and cultivated variety respectively and thus it can be used as potential inhibitor of free radicals.

To conclude, the wild variety was found to be superior to cultivated variety in terms of its rich antioxidant content, total phenol content and polyphenol composition, trace elements and free from heavy metal contamination and was thus selected for supplementation in the clinical trial.

In Phase II, using snow ball sampling technique, 20 practitioners (10 each from Naturopathy and Ayurveda) were enrolled from in and around Vadodara and key informant interviews were conducted to assess Knowledge, Practice and Use (KPU) of bael leaves along with desk reviews on its various commercial uses in different diseases specially diabetes through personal visits to various university libraries across the state of Gujarat and other internet sources.

The results revealed that Ayurveda practitioners used 5-10g/day of bael leaves for the treatment of diabetes in various forms such as powder, decoction and dry extract while Naturopathic practitioners used 40-50g bael leaves in the form of juice mixed with water to make a volume of around 100ml, which was selected for the clinical trial.

Phase III was a randomized controlled clinical trial. For final dose selection sensory evaluation using 10g, 20g and 30g bael leaves juice in 100 ml water using 30 T2DM

subjects (19 M, 11 F) using a 9-point Hedonic rating test and based on the results, 20g *Aegle Marmelos* (L.) *Correa* leaf juice was selected.

Sixty confirmed T2DM subjects on oral hypoglycaemic drugs were enrolled from largest private hospital of Veraval city of Gir Somnath district after their written consent. Baseline data on socio-economic status, anthropometric details, medical history, 24 hour diet recall, food frequency questionnaire, biophysical (blood pressure) and biochemical parameters (FBS, PPBS, HbA1c, Creatinine, HsCRP, SGPT, SGOT, TC, HDL, LDL, TG, VLDL, total proteins and total antioxidant capacity by FRAP assay) were elicited from the subjects following which they were randomly divided into two groups i.e. Experimental group (n=30, received 100 ml of freshly prepared 20g bael juice) and Control group (n=30). Post data was collected after 60 days. This study was approved by the department ethical committee (Ethical code: IECHR/13/20).

Post 60 day supplementation results revealed that there was significant reduction ( $p \leq 0.0001$ ) in FBS level by 20%, HbA1c by 20%, PPBS by 15.5%, TC by 8.4%, TG ( $p < 0.01$ ) by 10.9%, LDL-C ( $p < 0.001$ ) by 15%, VLDL-C ( $p < 0.05$ ) by 12.6% and an increase in HDL-C of males ( $p < 0.05$ ) by 13.42% and in serum antioxidant activity (serum FRAP) ( $p < 0.0001$ ) by 17.7% in the subjects of Experimental group post supplementation.

There was no significant alteration in HsCRP and serum creatinine ( $p > 0.05$ ) but there was significant reduction ( $p < 0.01$ ) in liver enzymes (SGPT and SGOT) by 13% and 19% respectively post supplementation. The findings of the present study indicate that supplementation of 20 g *Aegle Marmelos* (L.) *Correa* (bael) leaf juice had beneficial impact on blood sugar values and lipid profile along with liver functions of the diabetic subjects.

**Conclusion:** *Aegle Marmelos* (L.) *Correa* leaf juice intake could have a beneficial role in improving the glycemic profile of type II diabetic subjects. Also the use of *Aegle Marmelos* (L.) *Correa* fresh leaf juice should be encouraged as a supportive or complementary therapy for the management of type II diabetes mellitus and its associated co-morbidities. It can be supplemented along with Oral Hypoglycaemic Drugs (OHD) to keep the above parameters in control.