

SUMMARY AND CONCLUSION

Diabetes has reached epidemic proportions worldwide, posing a substantial burden on healthcare system. Historically, diabetes was considered as a disease confined to developed countries and affluent people. However, recent estimates suggest that the prevalence of diabetes is rising globally, particularly in developing countries. The progression and decline in glycemic control are also more rapid among South Asians when compared to Europeans. Population based studies showed high rate of urbanization and its impact on people's dietary habit, mode of entertainment and physical activity together lead to an increasing prevalence of Type II diabetes in India over the past few decades. Statistically, about 50 per cent of people with diabetes remain undiagnosed and approximately 20-30 per cent already has developed complications before being diagnosed. Dietary management is an essential component in managing diabetes.

Bitter gourd is one of the traditional medicine that helps to prevent or counteract Type II diabetes. Most of the scientific studies suggest that a regular consumption of bitter gourd certainly can circumvent various health related problems either by its prophylactic or therapeutic actions (Anilakumar *et al*, 2015). In the latest count, approximately 228 different compounds with proven medicinal properties acting alone or in combination with other, have been isolated from bitter gourd fruit, seeds, leaves, stems, pericarps, endosperm, callus tissues and cotyledons (Singh *et al.*, 2011). Research highlights that *Momordica charantia* may either have insulin like secretagogue effect and it can stimulate peripheral glucose utilization or it may inhibit key gluconeogenic enzymes such as glucose-6- phosphatase and fructose biphosphatase (Parma *et al.*, 2011).

Hence, the present research was undertaken with the focus on prediabetic populations who are at a higher risk of developing diabetes, for establishing preventive strategies with traditional herbal remedy using bitter gourd on Type II

diabetics to reduce the complications through the hypoglycemic effect of bitter gourd.

The present research was designed with the following objectives:

- Collect baseline data on the consumption pattern of bitter gourd
- Develop bitter gourd recipes and analyze the antioxidants
- Elicit details on the prevalence of prediabetics
- Conduct an intervention study using bitter gourd juice on selected prediabetics and
- Evaluate the impact of bitter gourd intervention on Type II diabetics

The methodology involved in the present study is given below:

Phase I

A group of 332 Type II diabetics, above the age of 30 years were selected and socio-economic, dietary profile of the subjects was collected by administering a pre-tested interview schedule. The family and personal diabetic history of the subjects were recorded. Awareness of the participants about the control and management of diabetes, consumption of functional foods like bitter gourd and other vegetables was recorded. For all the selected diabetics anthropometric measurements namely height and weight were recorded and Body Mass Index (BMI), waist circumference, Waist to Height Ratio (WHtR) and Conicity Index(CI) was calculated. At the time of personal interview, fasting, postprandial blood glucose levels, glycosylated haemoglobin levels and lipid profile were noted from the medical reports of the 332 diabetics.

Phase II

The common domestic cooking methods namely boiling, pan-frying, stir-frying, braising and microwave cooking were selected and fifteen different bitter gourd recipes were standardized. Antioxidant capacity was analysed by ABTS assay in five triplicate samples in duplicates for the bitter gourd extracts. The sensory evaluation of the recipes was carried out with 10 each of non diabetic and diabetic adults as taste panel members using nine point hedonic rating scale for appearance, taste,

texture, aroma and overall acceptability and a bitter gourd recipe book was also developed.

Phase III

A total of 948 prediabetics were screened in Government and private industries in Coimbatore District, TamilNadu, India using IDRS (Indian Diabetic Risk Score). About 12.6 per cent were found to be prediabetics having the Fasting Blood Glucose (FBG) level 100-125 mg/dl as per the American Diabetes Association (ADA). Only 9.5 per cent (N=90) were willing to participate in the clinical trial.

Phase IV

A single blinded, placebo-controlled, randomized, cross-over designed intervention study was planned to find out hypoglycemic effect of bitter gourd with cucumber for placebo treatment.

The daily dosage of 2.5 g freeze dried bitter gourd powder (50 g fresh equivalent) was calculated according to Human Equivalent Dosage (HED) by the Center for Drug Evaluation and Research (CDER,2005).

On the basis of the animal trial, the supplement was prepared for human feeding trial. Freeze dried bitter gourd and cucumber powders of 2.5 g was packed in aluminum sachets (6 x 10 cm) sealed and tested for food grade quality. Required quantity of bitter gourd and placebo sachets were shipped from Taiwan to India (study area) to conduct the clinical trial and there it was stored at -20°C in a deep freezer. Before starting the clinical trial, the study design was registered in the Clinical Trial Registry of India (CTRI), Indian Council of Medical Research (ICMR). CTRI registration No. is CTRI/2013/06/003759. It was presented before the Institutional Human Ethical Committee (IHEC) of AUW and the approval number is AUW/IHEC-2013 AP-01.

Prediabetics aged >25 and having FBG between 100 – 125 mg/dl or HbA1c >5.7-6.4 per cent and those willing to participate in the study with written consent were included in the study. Fifty-three male and 37 female participants were selected for the clinical trial. Clinical trial was carried out as AB-BA sequence. Group 1 (AB)

started the intervention with sample Mary (A) followed by John (B), while the Group 2 (BA) started the supplementation with John (B) followed by Mary (A). The intervention continued for a period of eight weeks. Mary or John sachets were mixed freshly in 150 ml water and were consumed during their lunch time throughout the eight weeks period of respective intervention phase. In order to measure 150 ml of water, measuring cups were given to the participants. Participants were provided with sachets on a weekly basis to ensure the intake. Between the two arms, 4 weeks was left as wash-out period to minimize the carry-over effect of one phase to the other. Cross over was done after this wash out period. The trial was successfully completed with 65 pre diabetics after a drop out of 25 participants during the study period.

Phase V

Among the 332 Type II diabetics, 40 Type II diabetics were selected for dietary intervention using the following inclusion criteria:

- Fasting blood glucose level within the range of 140-200 mg/dl
- Post prandial blood glucose level within the range of 160-260 mg/dl
- HbA1c level 7-8.5%
- Willing to give written consent and participate in the dietary intervention

The selected forty Type II diabetics were randomly divided into two groups namely an intervention group (N=20) and a nutrition education group (N=20). For the intervention group 15 g of bitter gourd dhal powder was supplemented for a period of eight weeks along with nutrition education. For the nutrition education group nutrition and health education on dietary management of diabetes was given once in 15 days.

Impact of intervention is evaluated through anthropometric measurements and biochemical parameters before and after the 60 days of bitter gourd intervention as per the standard procedures.

The salient findings arising from the present study are summarized and presented below:

Baseline survey

- Among the 332 Type II diabetics surveyed, 173 participants (52.1 per cent) were male and 159 participants (47.9 per cent) were female.
- Of the selected 332 Type II diabetics, 34.3 per cent were in the age group ranged between 41-50 years. Higher percentage (34.1) of male diabetics were in the age group between 41-50 years and majority of the selected female Type II diabetics (34.6 per cent) were in the age group between 41-50 years.
- It was saddening to note that around 13.3 per cent of the selected Type II diabetics were uneducated. About 28.3 per cent were educated up to high school and 25.6 per cent were graduates and 13.3 were highly qualified with a professional degree.
- With regard to the occupation, higher percentages (36.4 per cent) of selected male Type II diabetics were doing farming followed by 20.2 per cent employed in Government offices. Most (47.2 per cent) of the selected female Type II diabetics were housewives. About 15.1 per cent of the female participants were working in private industries.
- Almost 45.8 per cent of the selected diabetics were in the middle income group earning ₹7500-14500 per month as their family income followed by 21.7 per cent of them belonging to high income group earning more than ₹14500 per month. Among the selected diabetics, 17.5 per cent were in low income group and 15.1 per cent of the diabetics belong to economically weaker section.
- From the survey, it is revealed that around 75.7 per cent of male and 71.1 per cent of female diabetics were non vegetarians. Refined sunflower oil was preferred and used by 53 per cent of the diabetics followed by 35.5 per cent groundnut oil. Around 9.6 per cent of the diabetics were using vanaspathy and 7.5 per cent were using ghee.

- With regard to the family history, 32 male and 25 female diabetics, both parents were affected with diabetes followed by 89 male and 64 female diabetics were having single parental history of the disease.
- About 42.8 per cent of the selected diabetics were health conscious and knew the importance of visiting the clinics regularly and were visiting the clinics once in a month.
- The mean expenditure incurred by the male and female diabetes were ₹ 1641 and ₹1536 per month respectively. About 12.3 per cent and 9 per cent of the monthly income was spent towards hypoglycemic drugs, doctors fee and blood analysis by the male and female participants respectively.
- From the 173 male diabetics surveyed, 81 diabetics were having the habit of smoking cigarette or beedi. Out of 153 female diabetics surveyed, 46 participants had the habit of chewing betel leaves with tobacco.
- It is saddening to note that only 35.3 per cent male and 30.2 female diabetics were doing regular exercise.
- The mean weight of the screened male and female were 71.37 and 62.59 kg which were well above to the reference weight as recommended by ICMR. Mean body mass index determined for the screened male and female were 26.05 and 25.23 respectively which shows that they were in pre obese category which is also associated with increased risk of diabetes
- The mean waist circumference of the female participants were much higher (88.42 cm) than the reference value and the male diabetics also showed a elevated waist circumference compared to the reference value.
- Data on biochemical parameters showed that the mean fasting blood glucose level of the female diabetics were higher (144.23 mg/dl) than male diabetics (142 mg/dl) which was well above the reference value. Mean post prandial levels of the male and female participants were 224.29 and 226.75 mg/dl respectively.
- The poor glycemic control was recorded from the female and male Type II diabetics with mean HbA1c levels of 8.29 per cent and 8.10 per cent respectively.

- Data on lipid profile of the surveyed 332 Type II diabetics revealed that the mean serum total cholesterol of the 173 male participants was found to have 222.98 mg/dl, HDL cholesterol 41.82 mg/dl, 145.1 mg/dl as their mean LDL cholesterol, 189.25 mg/dl was recorded for triglycerides and an average of 36.76 mg/dl for VLDL cholesterol.
- Out of the 159 female participants, mean total cholesterol level was found to be 224.16 mg/dl, average HDL cholesterol values were found to be 40.86 mg/dl, mean LDL cholesterol was 148.38 mg/dl, triglyceride level was 172.57 mg/dl and the average VLDL cholesterol level recorded was 34.14 mg/dl.
- With regard to the bitter gourd consumption, the data revealed that, 60 female and 52 male diabetics were consuming 100 g of bitter gourd once in a week, followed by 38 female and 35 male participants consuming 100-200 g of bitter gourd once in a week, a minimum of 12 female and 5 male participants consuming more than 200 g of bitter gourd weekly. Around 84 male and 60 female diabetics consumed bitter gourd in the form of gravy or curry.
- It is evident from the results that 41.6 per cent of the diabetics believed that bitter gourd is good for general health, 34.3 per cent reported that it helps to decrease the blood sugar level and 13.3 per cent informed that it reduces the stomach infection.

Development and evaluation of bitter gourd recipes

- The antioxidant values of bitter gourd ranged from 2.91 in raw samples to 6.69 in pan fried samples. In raw as well as boiled samples, the process of cooking reduced the antioxidant level to the extent of 38 per cent and 2 per cent respectively when compared to control sample. This reduction might be due to the loss of water soluble vitamins which are essential for antioxidant content of samples.
- From the results, it is revealed that the crude residue obtained from the bitter gourd extracts ranged from 1.35 to 2.85 g fresh percentage. Pan

frying method of cooking increased the antioxidant content to the extent of 45 per cent and braising to six per cent.

- Acceptability scores for raw preparations given by the diabetic taste panel was significantly greater when compared to that of non diabetics ($P < 0.05$). The mean scores revealed that the pan fried recipes are well accepted by the diabetic participants when compared to non diabetics though the difference was not significant.
- Three different curries were prepared using braising method in which bitter gourd absorbed the taste of other ingredients and in turn reduced the bitterness. Crispy karela, bitter gourd dhal powder and the microwave cooked recipe were well accepted by the non diabetics compared to diabetic taste panel.

Identification and screening of prediabetics by IDRS

- To identify the prediabetics around 948 participants aged >25 years from different industries were screened using IDRS. Of these 540 (57 per cent) were males and 408 (43 per cent) were females. 35.4 per cent of the selected participants were in the age group between 31-40 years followed by 30.6 per cent in the age group of 41-50 years. Among the female participants screened, a higher percentage (47.1) was in the age between 31-40 years and 31.1 per cent were less than 30 years of age.
- It was noticed from the result, that almost 28.7 per cent and 36.5 per cent of the male and female participants were in preobese category and considered to be overweight.
- About 37.7 per cent of female participants were having their waist circumference of 80-89 cm and falls in the risk category. About 27.5 per cent of the female participants were having ≥ 90 cm as their waist circumference which in turn increases the metabolic rate. With regard to the family history, 126 (23.3 per cent) males and 122 (29.9 per cent) females were having positive history of diabetes in either of the parent.

- Among the 948 participants screened, a total of 337 participants were in the high risk category with the IDRS score ≥ 60 .

Preface data of the selected prediabetics

- From the selected 90 prediabetics for the clinical trial, most (N=34) of the selected prediabetics were in the age group of 31-40 years, 41 belonged to middle income group followed by 28 in high income group and nine prediabetics were in economically weaker section.
- With regard to the dietary habits of the selected prediabetics, 49 males and 31 females were found to be non vegetarians consuming only chicken and lamb. Sunflower oil was preferred and used by 72 prediabetics followed by 15 using palm oil.
- Only 21 male and 9 female prediabetics were doing regular exercise. Sixteen male pre diabetics out of 53 had the habit of smoking cigarette.
- Around 51 selected prediabetics were having a history of diabetes in their family. Majority of prediabetics (N=34) were having a single parental history of the disease.

Impact of intervention on prediabetics

- Clinical trial on 65 prediabetics revealed that the consumption of bitter gourd led to a significant ($p<0.01$) reduction in body weight thereby reducing the BMI significantly ($p<0.01$) whereas placebo treatment had no effect on BMI.
- The prediabetics in AB group showed a statistically significant ($p<0.01$) decline in waist circumference during bitter gourd and placebo intervention. BA group revealed no significant change in waist circumference after the placebo intervention whereas during bitter gourd intervention it had reduced from 92.01 cm to 90.87 cm which was statistically significant ($p<0.01$).
- In the case of Waist to Height Ratio of the AB group, initial value of 0.565 per cent declined to 0.554 per cent after eight weeks of bitter gourd

intervention and the difference was found to be significant at ($p<0.01$) level in the same group after the wash out period, the waist to height ratio reduced from 0.566 to 0.564 per cent. In BA group, the placebo intervention did not show significant reduction in waist to height ratio whereas bitter gourd intervention proved to have an impact on waist to height ratio and the difference was found to be significant at ($p<0.01$) level.

- Conicity index of the AB group exhibit a difference of 0.02 from initial value and it was found to be significant at ($p<0.01$) level during bitter gourd intervention. In BA group, it is clear that there is no change in the conicity index of placebo intervention whereas bitter gourd intervention had an impact and the difference was found to be significant at ($p<0.01$) level.
- Anthropometric measures of both AB and BA group ($N=65$) enlightens that bitter gourd intervention had a positive impact with significant ($p<0.01$) reduction in body weight, BMI, waist circumference, waist to height ratio and conicity index. It was also observed that there was an affirmative cutback in body fat which was significant at five per cent level ($p<0.05$).
- No trend in the reduction or increase in blood pressure was noted among the subjects in both AB and BA groups.
- The mean body fat percentage of the selected prediabetics showed a significant reduction ($p<0.01$) during bitter gourd intervention and no significant difference in case of placebo intervention in AB group. BA group did not show any significant difference with regard to bitter gourd as well as placebo intervention. However, the overall reduction recorded in BA group was significant at one per cent level.
- The mean initial fasting blood glucose level of prediabetics in AB group was 110.66 mg/dl which got reduced significantly ($p<0.01$) to 99.86 mg/dl at the end of bitter gourd intervention. In the case of BA group the placebo treatment did not bring forth any appreciable change in FBG where as the bitter gourd treatment was found to have a significant ($p<0.01$) impact.

- With respect to the glycosylated hemoglobin level of the AB group, initial value (6.37 per cent) significantly ($p<0.01$) trimmed down to 5.53 per cent after eight weeks of bitter gourd treatment and in placebo treatment the glycosylated hemoglobin reduced from 6.42 to 5.93 per cent which was also significant at 1 per cent level. In case of BA group, no significant difference was observed both during placebo and bitter gourd treatment, however when compared to the initial glycosylated hemoglobin level, it was found to be significantly ($p<0.01$) less after the intervention period of five months. Since the HbA1c levels reflect the blood sugar levels of past three months, every measurement reflects the impact of intervention as well as the past values.
- It is inferred that the mean fructosamine level did not significantly change during bitter gourd treatment but significant increase was noted during placebo treatment in AB group as well as in BA group. Significant reduction ($p<0.01$) was observed from the baseline to the final level of fructosamine in both the groups.
- It is evident that AB group showed an increase in insulin level from 9.55 to 10.57 $\mu\text{U/dl}$ during bitter gourd treatment and a reduction of 0.33 $\mu\text{U/dl}$ during the placebo treatment.
- With regard to the lipid profile, the total cholesterol and LDL cholesterol had reduced significantly ($p<0.05$) in AB group whereas in BA group there was a significant reduction only in total cholesterol.
- With regard to the fasting blood glucose and glycosylated hemoglobin of the pooled data a significant ($p<0.01$) reduction was observed whereas contradictory increase in fructosamine level was noticed on bitter gourd consumption. In case of insulin, slight increase was found with no statistical significance.
- The pooled data reveals that triglyceride ($p<0.05$), total cholesterol ($p<0.01$) and LDL cholesterol ($p<0.01$) reduced significantly where as

HDL cholesterol increased and VLDL cholesterol reduced without any significant impact due to bitter gourd treatment.

- The body weight had a positive correlation with fasting blood glucose and total cholesterol whereas the glycosylated hemoglobin was negatively correlated.
- In case of BMI a high degree of positive association was found with fasting blood glucose and negative association was observed with glycosylated hemoglobin and total cholesterol.

Effect of dietary intervention on Type II diabetics

Out of the 332 Type II diabetics surveyed, 40 were selected for the dietary intervention program. Data on anthropometry, dietary intake and lipid profile were collected before and after the intervention and the findings were summarized as follows:

- The mean body weight of the experimental group was 67.5 kg before the intervention and was reduced to 66.8 kg after the intervention period. The difference between the initial and final body weight were statistically analyzed and recorded to be significant at ($p < 0.01$) level. Body weight changes may also result in significant ($p < 0.01$) BMI reduction in the experimental group after the intervention.
- The mean waist circumference was 91.06 cm before supplementation which decreased to 90.22 cm after the supplementation and the difference between two levels was found to be statistically significant at ($p < 0.01$) level whereas the control group did not show any significant reduction in waist circumference.
- It is evident from the result that the same trend of difference (0.01) was observed with waist to height ratio and conicity index before and after the bitter gourd supplementation in the experimental group.
- Diabetic subjects were found to exhibit significant ($p < 0.01$) hypoglycemia compared to control groups. The mean fasting blood glucose level of the

experimental group was 159.85 mg/dl which had reduced to 150.9 mg/dl after a period of two months of bitter gourd intervention. The initial and final values were analyzed statistically and found to be significant at ($p<0.01$) level. In the control group, there was significant increase between the initial (162.81 mg/dl) and final (167.32 mg/dl) levels of fasting blood glucose. Significant difference was observed between experimental and control at ($p<0.01$) level and when initial values of the experimental and control group were compared, it showed significant difference at ($p<0.01$) level.

- The mean post prandial blood glucose level of experimental group before supplementation was 231 mg/dl and had reduced to 221.05 mg/dl after supplementation for 60 days and the difference was statistically significant at ($p<0.01$) level. The mean post prandial blood glucose level of control is 240.38 mg/dl before supplementation and it was 255.26 mg/dl after supplementation which reveals a significant increase statistically.
- The glycosylated hemoglobin level before the supplementation was 7.53 percent and declined to 7.29 per cent after the bitter gourd supplementation. The difference was found to be statistically significant ($p<0.01$) level. In case of control group glycosylated hemoglobin was reduced but without any statistical significance.
- From the results, it was apparent that the mean total cholesterol level of the experimental group was 218.75 mg/dl which was reduced to 211.10 mg/dl after the intervention period and found to be statistically significant at ($p<0.01$) level. No significant difference was found between the initial (219.68 mg/dl) and final (220.53 mg/dl) levels of the total cholesterol with regard to the control group.
- With regard to the mean HDL cholesterol level of the experimental group, 39 mg/dl was recorded before the intervention and had been increased to 39.85 mg/dl after the end of the intervention period with a statistical significance at ($p<0.01$) level.

- The mean LDL cholesterol level of experimental group had declined significantly ($p < 0.01$) from 145.95 mg/dl to 138.55 mg/dl. Though there was an decrease from 145.57 mg/dl to 137.73 mg/dl in the control group, the difference was found to be not significant between the initial and final levels.
- The VLDL cholesterol level which depends on the level of triglyceride showed reduction with 1.05 mg/dl difference and was statistically proved to be significant at ($p < 0.01$) level. It was found that statistically no significant difference was recorded between the initial and final levels of the control group during the intervention period.
- The mean triglyceride level of the experimental group of the selected diabetics was found to be decreased (5.8 mg/dl) after the intervention with a statistical significant difference at ($p < 0.01$) level. In case of control group no significant difference was observed between the initial and final levels after the intervention period.

Conclusion

The concept of food as medicine is a central theme in dietetics and nutritional sciences. *M. charantia* has been used as dietary supplements and ethno medicine throughout centuries for relieving symptoms and conditions related to what we know in modern days as diabetes. In relation to diabetes, only charantin, insulin-like peptide and alkaloid-like extracts possess hypoglycemic properties similar to the plant itself or its crude extracts.

The present study proves that the consumption of bitter gourd juice prepared with 2.5 g freeze-dried bitter gourd powder (50g of the vegetable) reduced the fasting blood glucose and total cholesterol level among the prediabetics. In addition, this also helps to alleviate several components of metabolic syndrome, mainly by reduction of waist circumference. Thus, the concept of bitter gourd as a remedy for pre diabetics can be used as a natural treatment for diabetes mellitus without side effects. In addition, supplementation of bitter gourd powder for diabetics created

hypoglycemic and hypolipidemic effect and proves that locally available and low cost vegetable is acting as cardio protective food. Hence, the vegetable may be pursued for their clinical usefulness in the management of diabetes mellitus and its associated complications. In conclusion, bitter gourd juice act as an adjunct therapy for oral hypoglycemic agents marking the beneficial effects in the treatment of diabetes mellitus.

Recommendations

- Prevalence of pre diabetes may be studied on a large-scale.
- Raising awareness among prediabetics to evade a remaining lifetime burdened diabetes.
- Awareness and consumption of bitter gourd for pre diabetes and diabetes has to be created among rural and tribal population.
- Extraction of bitter gourd nanoparticles and its efficacy need to be investigated.