INTRODUCTION

“It is alarming that world leaders stand by while the diabetes fuse gradually burn. The severe impact on families, nations and healthcare continue with struggle. Governments, supporting agencies and the International Society must take intensive action to resolve the threat now, before the diabetes time bomb burst out.”

- IDF President Mbanya, 2014

Health is a resource for everyday's life and is a positive concept highlighting social and personal resources as well as physical abilities (Irvine et al., 2006). Over the past 50 years, the threats from rapidly changing environments have increased at an exceptional rate. Environmental degradation has significantly affected the ecosystem of our world.

The globe today faces an epidemic of Non Communicable Diseases (NCD), which will soon exceed communicable diseases both in the developing and developed countries, particularly native and migrant Asian Indian is ethnically the vulnerable race (WHO, 2014).

Non communicable diseases are becoming a major public health problem in the country due to changing lifestyles, increasing stress and tensions results in social and cultural systems in the society. Other factors like decline in child mortality, control of infectious diseases, extensive use of antibiotics, improvement in nutritional standards and access to health services have also contributed to increase in life expectancy in the population. Around 36 million people die each year and nearly 80 per cent of NCD deaths (29 million) occur in low- and middle-income countries (WHO, 2012).

Srivastava et al.,(2012) opines that the diabetes is a heterogeneous metabolic disorder characterized by altered carbohydrate, fat and protein metabolism, which causes hyperglycemia resulting from inadequate insulin secretion, insulin action or
both. Insulin is a hormone secreted by the beta cells of the pancreas, which is required to utilize glucose from digested food as an energy source.

Diabetes mellitus is becoming a pandemic worldwide. Being a major degenerative disease, diabetes is found in all parts of the world and it is becoming the third most lethal disease of mankind and increasing rapidly. The high burden of diabetes presents a formidable challenge not only in developing countries, but also to a developing nation.

IDF (2014) Diabetes Atlas Sixth Edition revealed the key findings about the diabetes as follows:

- 387 million people have diabetes in 2014 and by 2035 this will rise to 592 million
- About 77 per cent of people with diabetes live in low- and middle-income countries
- Maximum number of people with diabetes are between 40 and 59 years of age
- Around 179 million people with diabetes remain undiagnosed
- Diabetes caused 4.9 million deaths in 2014; Every seven seconds a person dies because of diabetes
- In 2014, 11 per cent of total expenditure of adults was due to diabetes
- In 2013, more than 21 million live births were affected by diabetes during pregnancy.

According to Bhagyalaxmi et al. (2013) NCDs, particularly diabetes, cardiovascular disease and stroke have emerged as a major public-health problem in India. The morbidity and mortality in the most productive phase of life are posing serious challenges to Indian society and economy.

India is the second most populous country, with considerable diversity in caste, religion, habitat, socioeconomic status, lifestyle and food habits. Although several infectious and parasitic diseases have been controlled successfully in India,
non-communicable diseases are becoming increasingly common, resulting in an
enormous burden on the health care system (Ramachandran and Snehalatha, 2009).

In India, NCDs were responsible for 53 per cent of deaths and 44 per cent of
disability adjusted life years lost. There is a gradual transition from infectious
to chronic diseases as the population grows older, richer and more urbanized.
Sedentary lifestyles and increased consumption of high fat foods such as fast foods are
contributing to the growing prevalence of chronic diseases like hypertension and

Diabetes is one of the most common non-communicable disease in which
approximately 85–95 per cent of all cases of diabetes are Type II diabetes and the
worldwide explosion of this disorder is a major health care burden (Badran and
Laher, 2012).

The increase of life-expectancy has induced higher disease prevalence in
elderly population together with a strong financial contribution, which sometimes
exceeds their means. Several studies estimated the economic cost of diabetes,
especially in the US, pointing on the increased health resource employed and lost
productivity due to complications in Type II diabetes (ADA, 2013).

The prevalence among adults aged 20-70 years are expected to rise from 285
million in 2010 to 438 million by the year 2030 (Unwin et al., 2009). The escalating
prevalence of diabetes noticed in the last two to three decades can be attributed
mainly to lifestyle changes due to the rapid socioeconomic growth. The highest
prevalence is a result of environmental and behavioral changes and cannot be
attributed to altered gene frequencies since the increase has occurred within a few
decades (Ramachandra, 2012). The highest percentage of increase in disease
prevalence are likely to be in developing nations, with major increases in the South
Asia, Sub-Saharan Africa, Middle-East and Latin America (Wild et al., 2004).

Recent data indicate that South Asia is one of the major sites of this epidemic
of Type II Diabetes with a projected 72 per cent increase in the next 20 years.
According to International Diabetes Federation (2014) the top five countries in
Southeast Asia with diabetes is India (66.847 M), Bangladesh (5.982 M), Sri Lanka
(1.177 M) Nepal (0.7 M) and Mauritius (0.21 M) in the age group of 20-79 years. South Asian people with Type II diabetes also have a greater risk of developing cardiovascular disease and renal problems and a higher diabetes-related mortality rate is seen among this group than in the general population. In India, the recent ICMR INdia DIABetes (ICMRINDIAB) study revealed that the prevalence of diabetes (both known and newly diagnosed) in 4 regions of the country: 10.4 per cent in Tamil Nadu, 8.4 per cent in Maharashtra, 5.3 per cent in Jharkhand, and 13.6 per cent in Chandigarh (Anjana et al., 2011).

Population based studies from India point out that in addition to genetic predisposition the lifestyle changes, sedentary life, lack of exercise and associated excess weight, diet and related epidemiological transition are the major factors in the development of diabetes (Arunachalam et al, 2002 and Valliyot et al., 2013).

Misra et al.,(2011) reported that the prevalence of diabetes is rising in rural India at a rate of 2.02 per 1000 population per year and the rate of increase was high in men (3.33 per 1000) per year as compared to women (0.88 per 1000) per year.

Diabetic subjects have a two to four fold higher risk of developing coronary artery disease than non-diabetic individuals and the frequency of stroke is three times higher than that of matched controls. The risk of stroke is increased by 150 per cent to 400 per cent in subjects with diabetes, while the risk of dementia associated with stroke increases by more than three fold in these patients (Badran and Lehar, 2012).

Generally, diabetes is characterized by chronic hyperglycemia and alterations of cellular homeostasis, which lead to diffused vascular damage. These adverse effects of hyperglycemia are separated into macrovascular complications (peripheral arterial disease, coronary artery disease and stroke) and microvascular complications (diabetic nephropathy, neuropathy and retinopathy) pose a serious threat to the morbidity and mortality of diabetic population (Forbes and Cooper, 2013).

Growing evidence implies that increased oxidative stress, induced due to several activated pathways, is a main reason in the pathogenesis of endothelial
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dysfunction and vascular disease (Chiarelli and Marcovechio, 2013). The UK Prospective Diabetes Study (UKPDS) found that every one per cent decline in glycated haemoglobin (HbA1c) was associated with a 37 and 14 per cent reduction in microvascular disease and myocardial infarction respectively (Litwak et al., 2013).

Epidemiological studies have demonstrated that Type II diabetes results from an interaction between a genetic predisposition and lifestyle factors including patterns of eating and sedentary behavior that lead to obesity. Providentially, there is increasing evidence that Type II diabetes can be delayed or prevented by changes in these lifestyle factors (Pottie et al., 2011). Strategies targeting interventions aimed at the entire population to reduce key diabetes risk factors, such as abdominal obesity and physical inactivity are important. However, these need to be complemented with diabetes prevention strategies specifically aimed at prediabetic and other high-risk individuals.

About 50 per cent of people with diabetes remain undiagnosed and approximately 20 to 30 per cent patients usually have already developed complications before being diagnosed. The high prevalence of prediabetes observed in many South Asian countries highlights a potential indicator of further progression of the epidemic in the region (Jayawardena et al., 2012).

In parallel there is an epidemic of prediabetes is Impaired Glucose Tolerance (IGT) and Impaired Fasting Glycemia (IFG) with prevalence rates between 10 to 15 per cent reported in South Asian adult populations (Ramachandran et al., 2012).

Prediabetes is a high risk state for diabetes that is defined by glycemic variables that are higher than normal, but lower than diabetes threshold. American Diabetes Association criteria for prediabetes is fasting blood sugar (glucose) level 100 to 125 mg/dl (5.6 mM to 6.9 mM); two hour glucose tolerance test after ingesting the standardized 75 g glucose solution the blood sugar level of 140 to 199 mg/dl (7.8 to 11.0 mM) (Jellinger and Paul, 2009) and glycosylated hemoglobin level between 5.7 and 6.4 per cent.

Prevalence of prediabetes is increasing worldwide and experts have projected that more than 472 million people will have prediabetes by 2030 (IDF, 2011).
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Yang et al., (2010) reported that the total prevalence of diabetes and prediabetes in China had now reached 9.7 per cent and 15.5 per cent among adults.

Prediabetes is also associated with the simultaneous presence of insulin resistance and β-cell dysfunction-abnormalities that start before glucose changes are detectable. In the 20 year follow-up of the DaQing Diabetes Prevention Study, lifestyle intervention reduces 43 per cent of diabetes risk, translating to a mean 3.6 year delay in development of diabetes (Gong et al., 2011).

According to Bajai et al., (2015) prevalence of impaired glucose tolerance was distinctly higher in women (14.2 per cent) compared to men (6.3 per cent) in urban areas and 10.9 per cent in women compared to 6.9 per cent in men in rural areas.

Recent ICMR–INDIAB study has shown urban, rural and overall prediabetes prevalence was low i.e. 9.8 per cent, 7.1 per cent and 8.3 per cent respectively in urban, rural and overall population (Anjana et al., 2011).

Several affidavits may accord to top prevalence of diabetes in these areas. Firstly, Asian populations, abnormally those of SEAR descent, are added decumbent abdominal obesity and low muscle mass with increased insulin resistance. Secondly, accelerated socioeconomic development has led to concurrent shift in infrastructure, technology, and food supply that promote over nutrition and sedentary lifestyles (Pan, 2005). Refined wheat and polished rice are the staple Asian diets with peak glycemic load and glycemic index. Added urbanization and use of automobiles accept acquired abounding citizenry to about-face from a physically active, agrarian lifestyle marked by energy scarcity to a sedentary lifestyle.

There was a lack of diabetes awareness, which led to high prevalence of undiagnosed diabetes. A diagnosis of prediabetes increases the risk for developing Type II diabetes and without lifestyle interventions to improve health, 15 per cent to 30 per cent of people with prediabetes will develop Type II diabetes within 5 years (CDCP, 2011)

The Indian Diabetes Prevention Programme-1 (IDPP-1) a 3 year prospective study in IGT subjects in India showed a very high conversion rate to diabetes
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Hypoglycemic Effect of Bitter Gourd (*Momordica charantia* L.) on Prediabetics and Type II Diabetics (18 per cent per year). Recent epidemiological studies in Chennai have indicated a rapid conversion of IGT to diabetes, resulting in increased prevalence of diabetes with a concomitant reduction in the number of IGT subjects (Ramachandran, 2007).

Around 5 to 10 per cent of people with prediabetes will progress to diabetes per year, with the same proportion converting back to normoglycemia (Forouhi *et al.*, 2007 and Nathan *et al.*, 2007). Prediabetes is not only related to an increased risk of diabetes and its complications, but also might cause damage to kidney and nerves, according to accumulating evidence.

Prediabetes is coupled with the concurrent presence of β-cell dysfunction and insulin resistance that start before glucose changes are detectable. The majority people with prediabetes do not show symptoms but are considered to be at a high risk of developing cardio vascular disease. Recent research has shown that some long term damage to the cardiovascular system could start even in the prediabetic stage. With prediabetes the subtle balance between glucose and insulin has been thrown off. Impaired fasting glucose (IFG) is a prediabetic state with insulin resistance and cardiovascular risk, although it carries a lesser risk than impaired glucose tolerance (Nichols *et al.*, 2007).

Identification and treatment of prediabetic individuals is therefore crucial. On the basis of randomized trials that the effectiveness of lifestyle intervention and several anti diabetic drugs in the prevention of diabetes, lifestyle intervention aimed at achieving more than seven per cent weight reduction and 150 min per week of moderate intensity physical activity is recommended for all people with prediabetes (Heianza *et al.*, 2011).

The diabetes prevention program and other randomized trials have demonstrated that lifestyle intervention (structured diet and physical activity) among subjects with prediabetes significantly reduces the progression to diabetes (Gillies *et al.*, 2007). Making small changes in the lifestyle will prevent or delay the onset of diabetes.

Ozougwu *et al.*, (2013) noted that the changes in dietary energy sources, particularly the increase in fat and sugar intake, the decrease of starch intake and
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dietary fiber, contribute to obesity and cause deterioration of glucose tolerance. Even mild obesity (BMI > 25) causes four to five fold increases in the risk of developing diabetes, if accompanied by the increase in visceral fat mass.

The major obstacle in diabetes care is lack of awareness common amongst not only the general population, but the patients also. CURES study reported that approximately 25 per cent of the population was unaware of diabetes and only 41 per cent of diabetic patients knew that diabetes could be prevented (Poudel and Adhikari, 2013).

The most crucial need in India currently is the primary prevention of diabetes. Screening for glucose intolerance as a precautionary measure, even in those younger than 30 years of age, is necessary in Asian Indians since they develop hyperglycemia at a younger age (Ramachandran and Snehalatha, 2009).

Economic considerations are important for policy makers, public health agencies, insurers and health-care providers and consumers, but few studies have assessed prediabetes screening and treatment strategies in terms of cost-effectiveness and health benefits (Tabák, 2012).

Effective management of diabetes requires sustained glycemic control over many years to lower the risk of macro and micro vascular complications in people with diabetes. As diabetes is a multifactorial disease leading to several complications, it therefore demands a multiple therapeutic approach.

Although several therapies are in use for treatment, there are certain limitations due to high cost and side effects such as development of hypoglycemia, weight gain, gastrointestinal disturbances and liver toxicity (Dey et al., 2002). Based on recent advances and the involvement of oxidative stress in complicating diabetes mellitus, efforts are on to find out suitable antidiabetic and antioxidant therapy. Alternative and affordable approaches to manage diabetes are needed for subjects in developing countries.

Complementary and alternative medicine involves the use of herbs and other dietary supplements as alternatives to mainstream Western medical treatment.
According to World Health Organization (WHO), medicinal herbs are an handy, affordable and culturally appropriate source of primary health care for more than 80 per cent of Asia’s population (Tabish, 2008).

Herbal medicine also called as botanical medicine or phytomedicine, refers to the use of any plant's seeds, berries, roots, leaves, bark or flowers for medicinal purposes. Scientific validation of several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level could be considered as of possible therapeutic value (Dwivedi and Daspaul, 2013).

Despite all the progress, plants are still an indispensable source of medicinal preparations having a protective and curative effect. Numerous species are having medicinal significance and many of those are commonly used to treat and prevent specific ailments and diseases (Scartezzini and Sproni, 2002).

In the context of using traditional medicinal plants for treating diabetes, extensive screening has been performed in many ethnomedical systems within the Indian subcontinent (Ocvirk et al., 2013). Making healthy food choices and tracking eating habits can help to manage the blood sugar level within a safe range.

*Momordica charantia* (bitter gourd or bitter melon or karella) thrives in hot and humid climates so it is a tropical and subtropical vine of the family Cucurbitaceae, widely grown in Asia, Africa and the Caribbean for its edible fruit, one of the well known medicinal plants (Altinterim, 2012).

Generally people of Asian origin are more aware of bitter gourd’s health benefits than their Western counterparts. Bitter gourd is quite bitter when eaten as raw but has a wonderful taste once it is cooked properly. It is a low calorie vegetable which has many nutritional benefits. Bitter gourd is one of the powerful nutrient-dense vegetable composed of a complex array of beneficial compound. These include vitamins, minerals, phytochemicals and antioxidants, all which contribute to its remarkable versatility in treating a broad range of diseases. Bitter gourd contains high amounts of ascorbic acid, vitamin A, vitamin E, vitamins B1, B2 and B3 as well as vitamin B9 (Bakare et al., 2010).
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Bitter gourd is a popular vegetable all over the South Asia. Bitter gourd prepared with a blend of spices makes it very palatable and is used in many regions of India.. In Southern India, bitter gourd is used in the dishes like curry with tamarind, sambar and fry. One of the special preparation namely pagarkai pitla, a kind of sour curry with tamarind is very popular in Tamil Nadu (Singh et al., 2011). Raw green form of bitter gourd is more commonly used for cooking than the ripe yellow form. As the name implies bitter gourd is bitter to the taste buds and hence excluded from most of the meals. One of the best ways to obtain essential nutrients in bitter gourd for diabetics is having vegetable juice, particularly bitter gourd juice to reduce the blood sugar level.

Bitter gourd extracts are currently being used the clinical conditions which include diabetes, dyslipidemia, microbial infections and certain types of cancer potentially as a cytotoxic agent. In numerous studies, at least three different groups of constituents found in all parts of Momordica have clinically demonstrated hypoglycemic properties or other actions of potential benefit against diabetes mellitus (Sharma et al., 2009).

Polypeptide P, isolated from fruit, seeds and tissues of Momordica charantia showed a significant hypoglycemic effect when administered subcutaneously to languish and humans. Ethanolic extracts of Momordica charantia (200 mg/kg) showed an antihyperglycemic and also hypoglycemic effect in normal and STZ diabetic rats. This may be because of inhibition of glucose-6-phosphatase besides fructose-1, 6-biphosphatase in the liver and stimulation of hepatic glucose-6-phosphate dehydrogenase activities (Patel et al., 2012).

Bitter gourd extract exerts a significant impact on inhibition of cell growth and induction of apoptosis in breast cancer cells mediated by cell cycle and apoptosis regulatory proteins (Ray et al., 2010). Bitter melon offers a novel adjunct therapeutic approach to ameliorate obesity-associated peripheral inflammation and neuroinflammation (Nerurkar et al., 2011).

Researchers have demonstrated that bitter melon reduces adiposity in rodents fed a high fat diet, lowers plasma and hepatic lipids, insulin and leptin levels and normalizes glucose tolerance (Shih et al., 2009).
Bitter gourd has reduced blood glucose and lipids in both normal and diabetic animals, protected beta cells, enhanced insulin sensitivity and reduced oxidative stress (Shih et al., 2009). *Momordica charantia* fruit juice acts like insulin to exert its hypoglycemic effect and moreover, it can stimulate amino acid uptake into skeletal muscle cells just like insulin. Several studies have suggested that *Momordica charantia* juice and its extract can stimulate peripheral glucose uptake and regulate the amount of glucose taken up by the gut (Platel and Srinivasan, 1997).

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 (Parmar et al., 2011).

Bitter gourd is used mainly for the treatment of Type II diabetes. Some preliminary evidence suggests that the consumption of bitter gourd as a whole fruit, extract or dried powder may reduce blood sugar levels. Green bitter gourd varieties that are not too immature and gently processed can be considered for the prevention and treatment of diabetes mellitus (Habicht et al., 2011).

Overall, there remains a need for effective therapeutic approaches that will not only normalize blood glucose and improve insulin sensitivity but also improve the plasma lipid profile (Verspohl, 2012). However, only a few have been subjected to detailed scientific investigation due to a lack of mechanism-based available *in vitro* assays.

Major hindrance in the incorporation of this vegetable in modern medical practices is the lack of scientific and clinical data proving their efficacy and safety. Although the bitter gourd has a bitter taste, it is enriched with several health and nutritional benefits that improves the overall health. Bitter gourd has always been a neglected food among a large part of the population. But it has wonderful health benefits that are hidden in and is not so frequently used vegetable.

As compared to animal studies, only few clinical trials have been conducted so far regarding the hypoglycemic potential of bitter melon and majority of these studies lack proper control and have conflicting results (Fuangchan et al., 2011).
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For medical nutritional therapy, further observational trials evaluating the effects of *Momordica charantia* are needed to guide any recommendations in clinical practice.

Hence 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
- Supplement bitter gourd juice to pre diabetics and evaluate its efficacy
- Evaluate the impact of bitter gourd intervention on Type II diabetics.