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MOMORDICA CHARANTIA L.: PANCREATIC B CELLS PROTECTIVE AND REGENERATIVE PROPERTIES A REVIEW

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ABSTRACT

Momordica charantia Linn. is used as herbal drug for the treatment of Diabetes mellitus. In Ayurveda the antidiabetic properties and the protective mechanism to reverse diabetic condition is claimed since time immemorial. In this review article the regenerative capacity and the protective properties of Momordica charantia Linn. on the pancreatic β cells (Islets of Langeranhs) is discussed. Different form of Momordica charantia Linn fruits are used as anti diabetic drugs e.g. fruit pulp and seed powder, fruit juice, whole fruit etc. Different form of extracts has also anti diabetic properties and proven out to have regenerative capacity upon damaged pancreatic β cells e.g. Ethanolic/Methanolic extracts, aqueous extracts, Acetone extracts etc. The inductive efficacy on the regenerative properties upon damaged pancreatic β cells has been proven by trial on animal models after triggering artificial diabetic condition with alloxan or streptozotocine treatment. The histo pathological studies of the pancreases of these animals also confirmed the regeneration of the pancreatic β cells after the treatment of Momordica charantia Linn.

Key words: Momordica charantia Linn, Pancreatic β cells, Ethanolic/methanolic extracts, Acetone extracts, Alloxan, Streptozotocine, Diabetes mellitus.

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases in which a person usually gets high blood sugar (hyperglycemia) due to lack of insulin or because cells do not respond to the insulin that is produced (Shoback *et al*., 2011). One measure cause or etiology of diabetes is due to the beta cells in the islets of Langerhans are selectively destroyed by an autoimmune response in type 1 diabetes or due to some other idiopathic causes. The islets of Langerhans are the regions of the pancreas that contain its endocrine cells. Hormones produced in the islets of Langerhans are secreted directly into the blood flow by five different types of cells out of which 65-80% are β cells responsible for insulin secretion (Elayat AA *et al*., 1995). From centuries and in the history of Indian system of medicines Momordica charantia has been used as one of the treatments for diabetes mellitus. Momordica charantia, called bitter melon, bitter gourd or bitter squash in English, Karela in Hindi and *Karavellaka* in Sanskrit, belongs to the family Cucurbitaceae (Anonymous 1), found and grows in plenty in Asia, Africa, and the Caribbean and throughout India. In view of the wide spread popularity of Bitter melon as a medicinal plant for the treatment of diabetes present review is to provide validated information about the protecting and regenerating property of Momordia charantia extracts on β-cells of islets of Langerhans in references through pharmacological and animal model trial studies results.

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Treatment of diabetes

Many individuals with type-2 diabetes can control their blood glucose levels by proper nutrition and exercise, these healthy lifestyle changes alone are often not enough. Type-1 diabetics need daily insulin injection to be normoglycemic. But exogenous intake of insulin has no stimulatory effect upon pancreas therefore the symptoms are only suppressed while the insulin secreting

beta cells of the pancreas continue to malfunction. Apart from insulin oral anti-diabetic medications to lower blood glucose levels, such as sulfonylureas, biguanides, alphaglucoside inhibitors, thiazolidinediones and meglititinides meglititinides are the well accepted present day drugs.

Use of bitter melon in diabetes

Momordica charantia (bitter melon) fruit extract (MCE) has been used in India for a long time and has been shown to have a hypoglycemic effect in diabetes mellitus. The fruits, stems and leaves are all effective. Bitter melon contains the chemicals charantin (a steroid glycoside), vicine and polypeptide –P(4). Polypeptide-p, has been isolated from fruit, seeds and tissue of Momordica charantia Linn (bitter gourd). It is a hypoglycemic peptide. Polypeptide-p is a very effective hypoglycemic agent when administered subcutaneously to gerbils, langurs and humans (Khanna P *et al*., 1981). One study reported that subcutaneous injection of p-insulin significantly lowered blood glucose levels in type-1 diabetics. This indicates that p-insulin works by mimicking the action of human insulin in the body and thus may be used as plant-based insulin replacement in patients with type-1 diabetes. The fruit and seeds of bitter melon are thought to exert hypoglycemic effects in normal and diabetic animal models (Jellin JM *et al*., 1999). The specific components thought to contribute to its hypoglycemic activity include charantin, polypeptide P and vicine. Other theoretical actions include extra pancreatic activity, such as increased tissue glucose uptake, liver/muscle glycogen synthesis, and decreased blood glucose synthesis through depression of the enzymes glucose-6-phosphatase, fructose-1, and 6 bisphosphatase and enhanced glucose oxidation by enzyme G6PDH pathway (Anonymous 2).

The Pancreatic β cells regenerative properties were studied through taking into consideration of different animal model trials .The effect of Momordica charantia fruit juice, aqueous extract, ethanolic extract, acetone extracts were studied on streptozotocin (STZ) and alloxan induced diabetes in rats .

The fruit juice increases the number of beta cells in the pancreas of the streptozotocin-diabetic rat (Ahmed I *et al*., 1998)

An investigation was made of the effect of Momordica charantia fruit juice on the distribution and number of alpha, beta and delta cells in the pancreas of streptozotocin (STZ)-induced diabetic rats using immune-histochemical methods. The results indicated that there was a significant (Student's t-test, $P < 0.004$) increase in the number of beta cells in M. charantia-treated animals when compared with untreated diabetics, however, their number was still significantly less than that obtained for normal rats. The results suggest that oral feeding of M. charantia fruit juice have a role in the renewal of beta cells in STZ-diabetic rats or alternately may permit the recovery of partially destroyed beta cells.

Momordica charantia fruit aqueous extract regenerates the pancreatic β-cells in streptozotocin-induced diabetes in neonatal rats (Abdollahi M *et al*., 2011)

In an experiment using the Sprague-Dawley neonatal rats, the Momordica charantia (MC) fruit aqueous extract exhibited regenerating/renewal property on the pancreatic β-cells in the nSTZ rats. Diabetes mellitus was induced in one day Sprague-Dawley neonatal rats using a single intrapretoneal injection of streptozotocin (STZ) (85 mg/kg body weight) and monitored for 12 weeks thereafter. The diabetic rats were separated into three groups, as follows: the diabetic control group (i.e. nSTZ), the diabetic group (i.e. nSTZ/M) - which was orally given 20 mg/kg of MC fruit extract and the diabetic group (i.e. nSTZ/G) - that was treated with glibenclamide, 0.1 mg/kg for a period of four weeks. At the end of treatment, the animals were sacrificed and blood samples were collected from the saphenous vein to measure the blood glucose and serum insulin level. The pancreatic specimens were removed and processed for light microscopy, electron microscopy examination and immunohistochemical study. The results of this study showed that MC fruit aqueous extract reduced the blood glucose level as well as glibenclamide and increased the serum insulin level in the treated diabetic rats ($P<0.05$). The fruit extract of MC alleviated pancreatic damage and increased the number of β-cells in the diabetic treated rats ($P<0.05$). These results suggest that oral feeding of MC fruit extract may have a significant role in the renewal of pancreatic β-cells in the nSTZ rats.

Regenerative effect of Momordica charantia fruit pulp ethanolic extract on pancreatic β-cells in neonatally streptozotocin-induced type 2 diabetic rats (Hafizur RM *et al*., 2008)

In an animal model trial experiment upon neonatal streptozotocin-induced type 2 diabetic rats ethanolic extract of Momordica charantia fruit pulp exhibited significant modulation in pancreatic β-cells. On assessment of Fasting glucose, serum insulin (by ELISA) and β-cell function (HOMA % B by homeostasis model assessment) and β-cell size and number by morphometry; significant improvement of fasting blood glucose, serum insulin and β-cell function was observed with the MCF ethanolic extract for the diabetic rat model. The islet size, total β-cell area and number of β-cells were increased to almost double in the diabetic rats treated with MCF

extract as compared to the untreated diabetic rats. Insulin granules in β-cells were notably reduced in diabetic islets as compared to control islets. However, extract-treated diabetic rat β-cells were abundant with insulin granules, which was comparable to non-diabetic control islets. The modulation of pancreatic β-cells may be due to M. charantia ethanolic extract.

Effects of alcoholic extract of Momordica charantia (Linn.) whole fruit powder on the pancreatic islets of alloxan diabetic albino rats (Singh N *et al*., 2008)

Upon oral administration alcoholic extract of whole fruit of Momordica charantia on alloxan induced diabetic adult albino rats the blood sugar level significantly decreased. The study was done by using 4 groups of albino rats. Animals of group I served as diabetic control group. The animals of II, III, and IV groups received 25 mg, 50 mg and 75 mg doses of the extract respectively for different durations. 75 mg dose showed increase in body weight. All doses of alcoholic extract of M. charantia were able to decrease the blood sugar level significantly. Extract feeding showed definite improvement in the islets of Langerhans. No toxic effect was observed in the liver .The significant features of the study was that ; the blood glucose once lowered by the treatment with M. charantia fruit extract remained static even after discontinuation of drug for 15 days and in pancreatic islets, beta cells also showed definite improvement.

Histopathological studies (Singh N *et al*., 2008)

Intravenous injection of alloxan monohydrate results in selective damage of beta cells of islets resulting in elevation of blood sugar level upto 4 times the normal range. Histological examination of islets of Langerhans from the pancreas of diabetic control group showed varying degree of damages. Regular arrangement of alpha and beta cells was disturbed. Islets showed reduced granulation of beta cells, hydropic degeneration, clumping of beta cells, pyknosis and necrosis.

After 15 days extract feeding islets showed no improvement. After 30 days feeding of the alcoholic extract of M. charantia, no hydropic degeneration was found in all the three dose groups (i.e. 25 mg, 50 mg and 75 mg). Large and some medium sized islets were present containing beta cells with cytoplasmic granules and areas of necrosis were very few. Necrosed areas in islets indicate damage caused by alloxan injection. Islets of Langerhans were generally large in size. Small islets were comparatively fewer. Some islets showed disfigurement also but alpha and beta cells were clearly distinguishable and normal in appearance and arrangement. When after 30 days extract feeding, it was discontinued for 15 days, beta cell granulation remained intact along with necrosed areas. There was not much difference in the islet picture in all the three dose groups.

Acetone extract of Momordica charantia (Linn.) (bitter gourd) fruits regenerates beta cells in islets of Langerhans (Singh N *et al*., 2007)

Acetone extract of whole fruit powder of M. charantia (bitter gourd) in doses 25, 50 and 75 mg/100 g body weight lowered the blood glucose from 13.30 to 50% after 8 to 30 days treatment in alloxan diabetic albino rats, confirming anti hyperglycemic effect of this plant in diabetic animals and humans. Histological observations with acetone extract showed different phases of recovery of beta cells of the islets of Langerhans of pancreas, which in the untreated diabetic rats were less in number and showed varied degree of atrophy. The most important finding of this study was observation of the presence of small scattered islets among the acinar tissue in some experimental animals, which may reflect neo formation of islets from pre-existing islet cells

DISCUSSION AND CONCLUSION

In all the above cited experiments it is obvious that in case of the streptozotocin and alloxan induced diabetic rats results in selective damage of beta cells of islets resulting in elevation of blood sugar level. Histological examination (Singh N *et al*., 2007) of islets of Langerhans from the pancreas of diabetic control group also showed varying degree of damages e.g. disturbed arrangement of alpha and beta cells, reduced granulation of beta cells, hydropic degeneration, clumping of beta cells, pyknosis and necrosis etc. After oral administration of different form of Momordica charantia (Linn.) extract, fruit juices etc. showed recovery and regeneration of those scattered islet cells.

Regranulation of islets of Langerhans β cells, alpha and beta cells were again clearly distinguishable and normal in appearance and arrangement. The histological studies also indicate the presence of small scattered islets among the acinar tissue in some experimental animals, which indicates neo formation of islets from pre-existing islet cells.

From the above reviewed (Singh N *et al*., 2008) trials study based upon the observation on animal models it is obvious that different form of Momordica charantia (Linn.) e.g ethanolic extract, acetone extract, aqueous extracts, fruit juice etc. all have been shown to regenerate the damaged pancreatic islets of Langerhans β cells which are responsible for the secretion of insulin. Momordica charantia (Linn.) (bitter gourd) has the good potential to develop anti diabetic drugs for both IDDM (type-1) and NIDDM(type-2) diabetes.

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