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"A Comprehensive Analysis Of Previous Research Works Done On Homoeopathic Medicines In Type 2 Diabetes Mellitus – An Overview"

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ABSTRACT-

A class of metabolic illnesses known as diabetes mellitus is typified by persistently high blood sugar levels that arise from abnormalities in either insulin secretion, insulin action, or both. The significance of insulin as an anabolic hormone leads to anomalies in the metabolism of proteins, lipids, and carbohydrates. The numerous studies findings have shown that patients with diabetes may benefit from homoeopathy. Therefore, our goal is to draw attention to a few of the key elements of homoeopathic treatment for diabetic patients.

Keywords: Diabetes, Homoeopathy, Insulin, Polyuria, Polydipsia, Polyphagia.

INTRODUCTION –

Among the oldest diseases that humans have ever encountered is likely diabetes mellitus (DM). About 3000 years ago, it was first mentioned in an Egyptian manuscript.[1] The distinction between type 1 and type 2 diabetes was established in 1936.[2] In 1988, type 2 diabetes was initially identified as a part of the metabolic syndrome.[3] The most prevalent kind of diabetes mellitus (DM) is type 2, also referred to as non-insulin dependent DM. It is characterized by hyperglycemia, insulin resistance, and relative insulin insufficiency.[4] The combination of behavioral, environmental, and genetic risk factors leads to type 2 diabetes.[5-6]
Individuals with type 2 diabetes are more susceptible to a range of immediate and long-term consequences, many of which result in an early death. Patients with type 2 diabetes are more likely to have increased morbidity and mortality due to the type's prevalence, sneaky onset, and delayed diagnosis, particularly in underdeveloped nations with limited resources like Africa.[7]
A class of metabolic disorders known as diabetes is defined by elevated blood sugar levels brought on by deficiencies in either insulin production, insulin action, or both. Diabetes's chronic hyperglycemia is linked to long-term harm, malfunction, and organ failure, particularly to the kidneys, eyes, heart, nerves, and blood vessels.

Definition of Diabetes Mellitus: A class of metabolic illnesses known as diabetes mellitus is typified by persistently high blood sugar levels that arise from abnormalities in either insulin secretion, insulin action, or both. The significance of insulin as an anabolic hormone leads to anomalies in the metabolism of proteins, lipids, and carbohydrates. These metabolic abnormalities are caused by insufficient insulin to produce an adequate response and/or insulin resistance of target tissues, primarily the liver, adipose tissue, and skeletal muscles, at the level of insulin receptors, signal transduction system, and/or effector enzymes or genes.[8-10] Diagnosis kind and duration determine the severity of symptoms. Some diabetics, particularly those with type 2 diabetes in its early stages, have no symptoms at all. Others have severe hyperglycemia, and children who have complete insulin insufficiency are particularly susceptible to

symptoms like polyuria, Polydipsia, Polyphagia, weight loss, and blurred vision. Uncontrolled diabetes can cause ketoacidosis, a rare form of nonketotic hyperosmolar syndrome, stupor, coma, and, if left untreated, death.[11-14]

Classification of Diabetes Mellitus:

1. Insulin Dependent Diabetes Mellitus (Type1 IDDM)

This type of diabetes mellitus is also called autoimmune diabetes and previously known as juvenile-onset or ketosis-prone diabetes. The individual may also seek with other autoimmune disorders such as Graves' discase, Hashimoto's thyroiditis, and Addison's disease, Type 1 diabetes mellitus is also known as insulin- dependent diabetes mellitus (IDDM). this occurs mainly in children and young adults; the onset is usually sudden and can be life threatening . Type 1 is usually characterized by the presence of anti glutamic acid decarboxylasc, islet cell or insulin antibodics which identify the autoimmune processes which leads to beta-cell destruction.

Type I diabetes (caused by b-cell breakdown, which typically results in a complete lack of insulin) (American Diabetes Association, 2014). There is a severe shortage or absence of insulin secretion as a result of the loss of the pancreatic B-islets cells. The rate of beta-cell destruction varies greatly amongst persons. Insulin injections are necessary for treatment. When fasting diabetic hyperglycemia is first discovered, 85–90% of people with Type 1 diabetes mellitus have markers of immunological damage, such as islet cell auto-antibodies, auto antibodies to insulin, and auto antibodies to glutamic acid decarboxylase (GAD). Although the precise origin of diabetes mellitus is still unknown, auto-antibodies that damage beta-islet cells in most cases have been linked to an autoimmune process.

2. Non-Insulin Dependent Diabetes Mellitus(Type2 NIDDM)

Adult-onset diabetes is another name for type 2 diabetes mellitus.According to the American Diabetes Association (2014), people with this kind of diabetes typically have a progressive insulin secretor malfunction and are resistant to the effects of insulin.Both forms of diabetes are associated with long-term issues in the kidneys, eyes, nerves, and blood vessels, which are the main sources of morbidity and death from the disease.

The causes are multifaceted, and risk factors for middle-aged and older adults include obesity, a sedentary lifestyle, aging, and genetics (Ross and Wilson, 2010). Patients in these categories are more likely to experience macro and microvascular problems.

3. Gestational Diabetes Mellitus

Gestational diabetes mellitus (CMD) 1d is the term used to describe glucose intolerance that is identified for the first time. Gestational Diabetes Mellitus (GDM) is the term used to describe women who acquire type-1 diabetes mellitus during pregnancy as well as women who have undiagnosed asymptomatic Type 2 diabetes mellitus that is identified during pregnancy. Regarding gestational diabetes mellitus (GDM) (diabetes not definitely over diagnosed as gestational diabetes) Gestational diabetes mellitus can arise throughout pregnancy and go away after giving birth. The effects of intrauterine exposure to hyperglycemia are thought to be the cause of the longer-term increased risk of obesity and type 2 diabetes in offspring born to mothers with GDM.

4. Other Specific Type (Monogenic Types)

Hepatocyte nuclear factor (HNF)-la, a hepatic transcription factor, has mutations on chromosome 12 that cause the most prevalent type of monogenic types of diabetes. They also called these hereditary beta cell defects:

The early onset of hyperglycemia (usually before the age of 25) is a common characteristic of several kinds of diabetes. The terms "mature onset diabetes of the young" (MODY) (12), "mature onset diabetes in youth," or "dysfunction associated with other endocrinopathies" (e.g., acromegaly), are also used to describe them. People with exocrine pancreas diseases like pancreatitis or cystic fibrosis as well as those who have pancreatic dysfunction brought on by substances, medications, or infections. Certain medications are often used in conjunction with HIV AIDS treatment or following organ donation.

A few families have been found to have genic defects that prevent proinsulin from being converted to insulin; these features are inherited in an autosomal dominant way. Less than 10% of DM cases consist of these.

Past research work on Type 2 DM:

When diabetes is brought on by streptozotocin (STZ), the islets' β-cells are partially destroyed, which results in insufficient insulin release and elevated blood glucose levels, or hyperglycemia. When the homeopathic remedy Syzygium jambolanum was administered to diabetic animals, the elevated blood glucose level was significantly reduced. This could be attributed to the stimulatory effect of S. jambolanum on the remaining β-cells of the islets of Langerhans to produce insulin or the regeneration of pancreatic β-cells, as other reports in this line have concurred.[14]

The assessment of the activities of hepatic hexokinase and glucose-6-phosphate dehydrogenase, which are significantly elevated in the mother tincture treated diabetic group, revealed the corrective effect of S. jambolanum. This suggests an insulin tropic effect, as these enzymes are positively regulated by insulin. Given that insulin adversely regulates hepatic glucose-6-phosphatase, a significant decrease in the enzyme's activity is indicative of the drug's insulin tropic action.[14]

The impact of homeopathic formulations of Syzygium jambolanum and Cephalandra indica on the gastrocnemius muscle of type-2 diabetic rats treated with high fat and high sugar was evaluated by Sampath S et al. Homeopathy is a comprehensive therapeutic approach that employs minuscule amounts of organic compounds derived from plants, minerals, or animal components. In homeopathy, Syzygium jambolanum and Cephalandra indica are used to treat type-2 diabetes. The molecular pathways underlying these effects are unknown, though. Rats with high fat and fructose-induced type-2 diabetes mellitus were utilized as test subjects, and the molecular mechanism of the antidiabetic actions in their skeletal muscle was investigated using homeopathic formulations of S. jambolanum and Cephalandra indica in mother tincture, 6c and 30c.

Following a 30-day course of therapy, measurements were made of the insulin signaling molecules in the gastrocnemius skeletal muscle, serum insulin, and fasting blood glucose. In comparison to the control group, diabetic rats exhibited a significant increase in fasting blood glucose level ($p < 0.05$) and a significant decrease in serum insulin and lipid profile, as well as low levels of insulin receptor (IR), vakt murine thymoma viral oncogene homolog (Akt), p-Akt (ser473), and glucose transporter-4 (GLUT4) protein expression ($p < 0.05$). In comparison to diabetic rats, treatment with homeopathic remedies resulted in a significant drop in fasting blood glucose ($p < 0.05$) and an increase in serum insulin and the expression of these proteins ($p < 0.05$).

The skeletal muscle of type-2 diabetic rats was used in the study to examine the antidiabetic effects of homeopathic preparations of S. jambolanum and C. indica, including ultramolecular dilutions. These preparations improve insulin action by activating insulin signaling molecules.[15]

KLA et al looked at the efficiency of customized homeopathic therapy for glycemic management. From 2012 to 2015, a total of twenty-seven adults, ages 37 to 84, received customized homeopathic treatments. As a control, published data from 40 T2DM patients in Hong Kong receiving normal conventional treatment was utilised. Changes in glycated haemoglobin (HbA1c) and fasting plasma glucose (FPG) at the 12-month mark or the most recent follow-up, whichever comes first.

In comparison to the group receiving just conventional treatment, the homeopathic group exhibited a higher baseline FPG ($p = 0.044$), and a greater number of patients had a history of cardiac events ($p = 0.022$) and long-term diabetes (>20 years) ($p = 0.006$). After a year, the homeopathic group's mean FPG difference from the control group was much higher: $p = 0.001$ for the difference between -2.24 mmol/L (95% confidence interval [CI]: -3.47 to -1.01) and 0.16 mmol/L (95% CI: -1.72 to 2.04). Glycated haemoglobin (HbA1c) mean difference was likewise substantially larger, $p = 0.046$; -1.11% (95% CI: -2.17 to -0.05) vs 0.08% (95% CI: -1.37 to 1.53). Better results were linked to lower baseline glycaemic control ($r = -0.750$, $p < 0.001$), but not the length of diabetes ($r = 0.058$, $p = 0.772$).

The improvement held up well under sensitivity tests. When individualized homeopathic medication was utilized instead of only basic conventional treatment, better glycaemic control was observed.[16]

Pal, et al.: Antidiabetic effect of Cephalandra indica study revealed that Cephalandra indica MT is a potential antidiabetic medicine. The testing of biological activities in vivo in rats and in vitro in 3T3 cell lines has indicated that Cephalandra indica MT reduced the blood sugar level in diabetic rats significantly and inhibited the uptake of radioactive glucose, respectively. The partial recovery of altered islets of Langerhans and interlobular ducts in the pancreas of STZ and Cephalandra indica MT-treated rats also support this observation. Evaluation of antidiabetic activity of Cephalandra indica MT was conducted in STZ-induced diabetic rats. The blood glucose level for diabetic rats untreated with any drug reached up to ~485 mg/dL at the end of the fourth week, whereas diabetic rats treated with glibenclamide at a concentration of 1mg/kg body weight showed a blood glucose concentration of ~278 mg/dL. The oral administration of MT for 28 days (75 µL/100 g) showed a much lower glucose (~269 mg/dL) at the end of the fourth week. The characteristic loss of body weight associated with diabetes is due to increased muscle wasting or loss of muscle proteins due to hyperglycaemia. By the conclusion of the fourth week, the blood glucose level in diabetic rats receiving no medication had increased to approximately 485 mg/dL, while the blood glucose level in diabetic rats receiving glibenclamide at a dose of 1 mg/kg body weight had decreased to around 278 mg/dL. At the end of the fourth week, there was a significant decrease in glucose (~269 mg/dL) following the 28-day oral dose of MT (75 µL/100 g). The typical weight loss linked to diabetes is caused by either enhanced muscular atrophy or muscle protein loss as a result of hyperglycemia.[17-18]

When compared to rats treated with glibenclamide and rats not receiving any treatment, the body weight of diabetic rats (a secondary consequence of diabetes) treated with MT did not vary greatly, indicating that MT may prevent muscle wasting. Untreated diabetic rats' body weight dropped from approximately 115 to 86 g, while treated rats' body weight dropped from approximately 110 to 78 g. There have been varying reports on how glibenclamide and antihyperglycemic plant extracts affected the body weight of diabetic rats. Rats given sandalwood oil gained weight at a rate of 59.2% more than rats given vehicles, while rats given glibenclamide gained weight at a rate of 3.5% less than expected.[19]

In one study, diabetic rats given Momordica charantia (bitter melon, karela) had a 4-6% rise in body weight over control; whereas, rats given glibenclamide did not exhibit any net weight gain.[20] When glibenclamide's hypoglycemic effects were compared to those of Syzygium cumini (jamun) and Tinospora cordifolia (giloi), all of the animals' body weight increased by 12% over that of normal rats.[21-22] Rats given fenugreek did not see a change in body weight.[23]

Compared to rats treated with glibenclamide and rats left untreated, the liver and pancreas biopsies of the MT-treated

rats revealed a partial recovery. The glucose uptake experiment further shown that 3T3 cells treated with MT absorb less glucose than cells not treated. The current study concluded that Cephalandra indica can be used to treat diabetes. The antidiabetic effect of Cephalandra indica MT appears to be able to reverse the effect of glucose levels generated by STZ. The restoration of pancreas and liver tissue may be the cause of the antidiabetic action, which lowers the risk of diabetes-related secondary problems. The components causing the antidiabetic action of Cephalandra indica MT may be identified through more in-depth analysis of the separated molecules' activity. Using LC MS and HPTLC, the active ingredients in Cephalandra indica were found. While all other dilutions (6 to 30C) had nondetectable quantities of active components, terpenoids were not detected in MT.
While the precise chemicals causing the weight gain in the rats treated with MT have not been found, it is possible that these molecules, which are abundant in phenolics, play a part, maybe by blocking the breakdown of proteins and fats. This is the first study to detect several compounds in Cephalandra indica MT. The findings will spur more investigation into the potential applications of certain compounds having antidiabetic properties. A thorough analysis of 108 clinical studies.[23] research on well-known herbs (often used in glycemic control) such aloe, ginseng, garlic, tulsi, fenugreek, gurmar, karela, and ivy gourd (Cephalandra indica) showed that all of these plants have similar efficacies to those of prescription medications. However, there was inconsistency in these studies' experimental setup, protocols, chemical compositions, and dosages. As a result, the evidence was deemed preliminary and called for more investigation. As early as 1988, reports of Cephalandra indica MT's effectiveness as a homoeopathic antidiabetic therapy were made.[24]

Additionally, pancreatic beta cell regrowth was noted. Nothing in the literature indicated that further progress had been made through later study. More specific information regarding its therapeutic role is provided by the current study on the same homoeopathic medicine, which uses both in vivo and in vitro model experiments with similar observations of reduced blood sugar levels and altered appearance of the spoke wheel and central vein in the liver, as well as the islets of Langerhans and interlobular duct in the pancreas, after receiving treatment with STZ. Many phenolic compounds in hypoglycaemic herbal constituents may modulate signal transduction pathways, and they are reported to have an insulin secretagogue role in stimulating skeletal muscles, preventing neurological deficits, suppressing stress activated protein kinase, and regenerating beta cells in the islets of Langerhans.[25] There are numerous natural antidiabetic medications on the market worldwide. However, due to uncertainty over safe dosage and a lack of knowledge about the actual bioactive chemicals in such medications, the United Kingdom has issued a caution against taking them.

The results of this study showed that Cephalandra indica MT contains a significant amount of phenolics, which are beneficial to health. Overall, these reports from contemporary biological investigations confirm that Cephalandra indica MT's effectiveness. As early as 1966, glibenclamide was described as an antidiabetic medication for type II diabetes. However, within the past 40 years, its more recent mechanism of action and utility have been proven,[26] making it an indispensable molecule. Metformin is the only other widely used substitute. Therefore, it is essential to support more research in order to increase the market share of homoeopathic medications for serious illnesses like diabetes. The poorer segments of the Indian population will benefit greatly from this effort because homoeopathic drugs are significantly less expensive. As the usage of complementary and alternative therapies rises, The US Preventive Services Task Force and the American Diabetes Association Guidelines, which use powdered Cephalandra indica to demonstrate insulin-mimetic properties comparable to those of conventional medicines, have encouraged further research on Cephalandra indica, even in wealthy nations like the United States.[23] Similar to Gymnema sylvestre, Cephalandra indica has no negative effects on the kidneys or liver.

To draw in the worldwide market for such affordable medications, it is necessary to identify the precise bioactive ingredients and their dosages. This is probably going to improve the financial situation of Indian homoeopathic medicine manufacturers.

CONCLUSION-

Results pooled from the included previous research works provided strong evidence that Homoeopathic interventions led to statistically significant improvement in glycaemic control in humans and lower animals especially for Type2 diabetes mellitus. The idea that diabetic patients can effectively employ homeopathic treatment has been strengthened by the findings of previous research work overviewed. However, more research is advised.

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