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Exploration of Novel Therapeutic Strategies for the Treatment of Diabetes Mellitus

Exploración de Nuevas Estrategias Terapéuticas para el Tratamiento de la Diabetes Mellitus

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ABSTRACT

Diabetes mellitus (DM) is a disorder in which the body does not produce enough or respond to insulin normally, resulting in an abnormal increase in blood glucose levels. 90% of diabetes cases in pregnant women are gestational diabetes mellitus (GDM). It is known that fluctuations in the level of glucose and its irregularity led to disturbances in the health of both mother and fetus.The therapeutic strategies and options for the treatment of gestational diabetes are highlighted in this review. We havereviewed medicinal plants used in the treatment of gestational diabetes. Literature review indicates that medicinal plants are effective in treating osteoarthritis and have been clinically and scientifically proven. Natural medicines have been the subject of chemical studies and many plants are the subject of clinical trials. Their results are remarkable and significant. However, scientific exploration for bioactive constituents is becoming increasingly important and their mechanisms of actions to treat GDM are still ongoing.

Keywords: Medicinal Plants; Pregnant Female; Gestational Diabetes; Plant Efficacy.

RESUMEN

La diabetes mellitus (DM) es un trastorno en el cual el cuerpo no produce suficiente insulina o no responde normalmente a ella, lo que resulta en un aumento anormal de los niveles de glucosa en sangre. El 90% de los casos de diabetes en mujeres embarazadas son diabetes mellitus gestacional (DMG). Se sabe que las fluctuaciones en el nivel de glucosa y su irregularidad provocan alteraciones en la salud tanto de la madre como del feto. En esta revisión se destacan las estrategias y opciones terapéuticas para el tratamiento de la diabetes gestacional. Hemos revisado las plantas medicinales utilizadas en el tratamiento de la diabetes gestacional. La revisión de la literatura indica que las plantas

medicinales son efectivas en el tratamiento de la artrosis y han sido probadas clínica y científicamente. Las medicinas naturales han sido objeto de estudios químicos y muchas plantas son objeto de ensayos clínicos. Sus resultados son notables y significativos. Sin embargo, la exploración científica de los constituyentes bioactivos se está volviendo cada vez más importante y sus mecanismos de acción para tratar la GDM aún están en curso.

Palabras llave: Plantas Medicinales; mujer embarazada; Diabetes gestacional; Eficacia de la planta.

INTRODUCTION

Gestational diabetes affects 14% of pregnant women annually, and 90% of diabetes cases are in pregnant women. GDM is defined as an imbalance in glucose levels during pregnancy, and this imbalance may be the result of type 1 or type 2 diabetes or as a result of gestational diabetes. There are risk factors which Contribute to the development of GDM, including obesity, genetic history of diabetes in the family, type 2 diabetes, and maternal age. Gestational diabetes has a negative effect on both the mother, such as preeclampsia, miscarriage, high blood pressure, and on the fetus, such as low oxygen, high bilirubin, obesity, diabetes, and microgliosis. In addition, 50% of these cases progress to type 2 diabetes (Figure.1) [1].

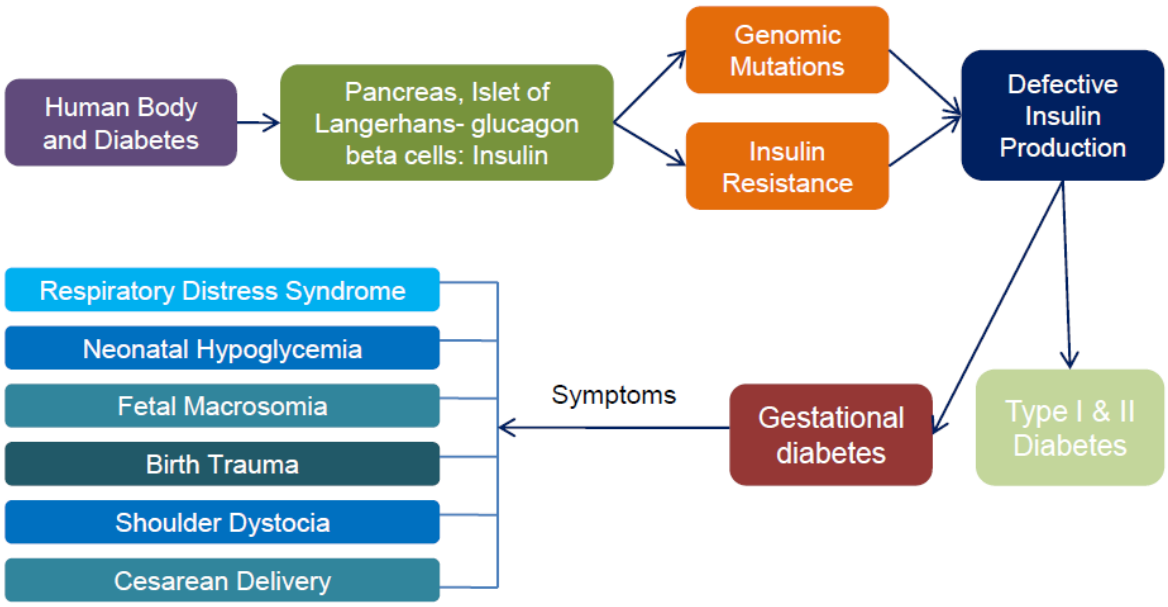

Figure1. Process and effect of gestational diabetes in pregnant women and neonatal

Reasonable planning, resource allocationand prevention strategies for the future depends on data on the epidemiology of gestational diabetes mellitus (GDM) and number of women affected (Hughes*et al.*, 2017). The criteria for screening for gestational diabetes vary according to different individuals and institutions, but the majority agrees on the necessity of testing in the 24-28 weeks of pregnancy. The examination is done especially in pregnant women who have a family history of diabetes, obesity, and previous gestational diabetes. It is considered the most important method for examining gestational diabetes (Teresa et al., 2020). The glucose challenge test (GCT), which is followed by measurement of the glucose curve oral glucose tolerance test (OGTT) in the case of high GCT.

We find that the American College of Obstetricians and Gynecologists has set standards for screening gestational diabetes, which is that there should be a history of gestational diabetes before that, BMI ≥30 kg/m2, and an abnormality in glucose levels(Ravi et al., 2019).While the American Diabetes Association has set criteria for diagnosis based on the presence of a previous history of gestational diabetes, the presence of obesity and the presence of diabetic urine (American Diabetes Association,2020).As for the criteria of the Canadian Diabetes Association, the presence of a history of gestational diabetes, BMI ≥30 kg/m2, the birth of children with macrosomia, the mother's age over 35 years, the presence of ovarian cysts, and treatment with corticoids. As for the criteria of the International Diabetes Federation, it was the presence of a family history of diabetes, high maternal age, and obesity (Lobna et al., 2021).In the case of the National Institute for Health and Care Excellence criteria, it is based on the child's weight gain of more than 4.5 kg, obesity, and previous gestational diabetes (Charnley et al., 2021)

Gestational diabetes is a temporary form of diabetes that occurs during pregnancy when the pancreas stops secreting insulin, or is not working enough. In the absence of response to insulin, this leads to the accumulation of glucose in the blood, and causes symptoms of diabetes (Plows et al., 2018).Gestational diabetes may not show symptoms, but some signs and symptoms may appear, such as: Fatigue, blurred vision, Hands or feet numbness, extreme thirst, bladder and vaginal infections, frequent urination, and the presence of glucose in the urine. In addition to the appearance of urinary tract infections, clots in the heart (Figure2) (The Royal Australian College of General Practitioners,2016).

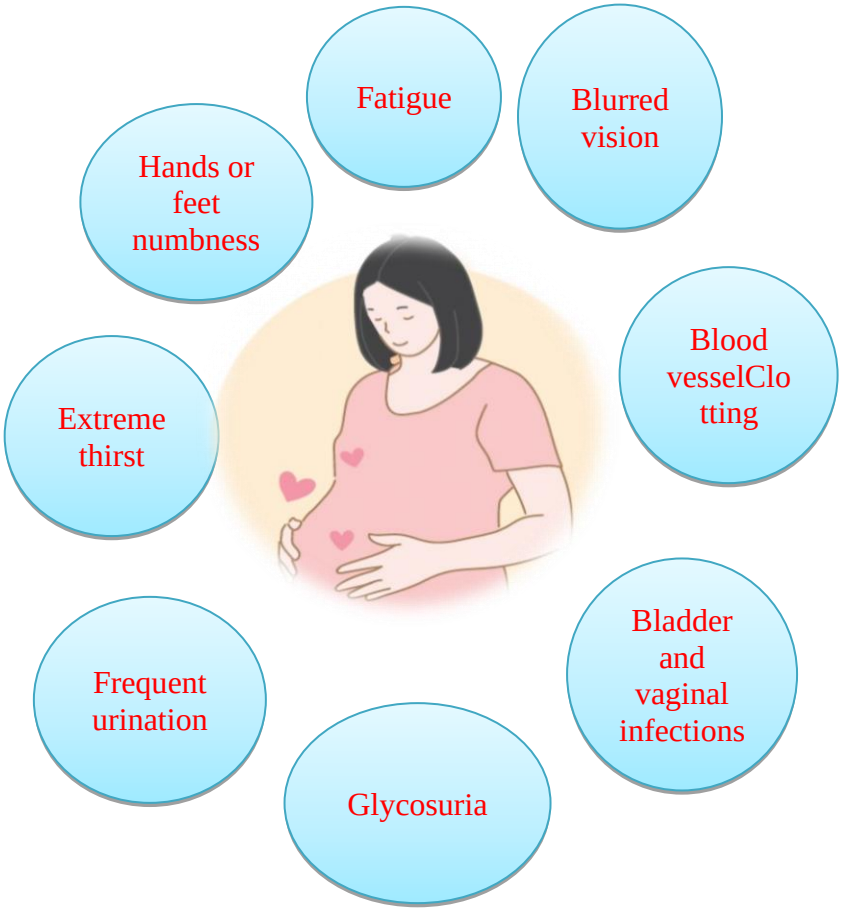

Figure2. Symptoms of Gestational diabetes

Management of Gestational Diabetes

There are different ways to manage gestational diabetes, the last one may be taking oral medications such as Glyburide and metformin, and the best option may be insulin injections. In some cases, especially in the case of obesity, the best option may be a diet (Alfadhli, 2015).

Dietary Nutrition

Diabetic pregnant women should be subject to nutritional counseling by a nutritionist. Diets depend on the weight and height of the mother, with the addition of the nutritional components

needed for the mother and fetus, with the exclusion of sugars and can be replaced by using artificial sweeteners. In one study, it was found that these women who Suffering from BMI >30 kg/m2, restricting calories in meals to 30-33%, reducing sugar and triglyceride levels. Also, restricting calories to 35-40% led to a reduction in maternal diabetes and improved fetal health. Meals to medium meals and two meals or four snacks. With the need to reduce the amount of carbohydrates contained in the meal to reduce the high rate of glucose in the blood. Some foods that are not allowed include white sugar, flour, sweets, canned foods, fast food (Itani et al., 2020)

Exercises

Exercise plays an important role in reducing high glucose, so it is recommended to exercise at least 10 times a week. One of the most important types of exercise for a diabetic is walking for at least 30 minutes every day, as this increases the burning rates and thus contributes to lowering the blood sugar rate (Colberg et al., 2010).

Oral Sugar Lowering Drugs

Glyburide

It is a sulfonylurea compound that stimulates the pancreas to produce enough insulin. Dosage starts at 2.5-20 mg per day and should not exceed 30 mg per day. A comparison was made between treatment using Glyburide and insulin for pregnant women with diabetes, who were examined at week 11-33, and the results were similar, as there was an improvement in the levels of fasting diabetes, postprandial glucose, and A1C (Ganesan et al., 2021).

Metformin

It is a biguanide drug that reduces intestinal glucose absorption and the formation of glucose in the liver. This drug is indicated in the treatment of women in pre-diabetes, in addition to being used in the treatment of ovarian cysts that reduce fertility. Metformin can pass through the placenta, but it is not it does not cause any harm to the fetus. Metformin treatment begins with 500 mg in the first week, and then the dose begins to increase until it reaches 2500-3000 mg divided throughout the day (Tarry-Adkins et al., 2020).

It was the first clinical trial using metformin compared to insulin in the treatment of diabetic pregnant women, and it was found that there was no difference between both groups except for higher rates of premature birth in those who were treated with metformin compared to insulin (Priya et al., 2018).

Injection Insulin Drugs

Despite the effective results of using Glyburide and Metformin in reducing high blood sugar levels, in some cases, insulin is required as the first line of treatment, especially in cases where treatment with oral anti-diabetic drugs is likely to fail (Huhtala et al., 2020).

After the birth process and after the regularity of glucose levels, it may be necessary to stop the treatment with oral tablets and insulin as well, so it is necessary to review the indicators of diabetes, especially in the early hours after birth. Women with gestational diabetes are encouraged to breastfeed for the benefit of both the mother and the newborn. It requires continuation of treatment. It is preferable to use metformin, glyburide, glipizide, and insulin. Although they are excreted in milk, they have a low effect on the fetus. This requires measuring the level of glucose in the blood of infants to ensure that the level of glucose does not drop. After giving birth, the mother should be subjected to medical care to monitor the level of glucose in the blood, as gestational diabetes may turn into type 2 diabetes (Tarry-Adkins et al., 2021).

Medicinal Plants Used to Treatment of Gestational Diabetes

Alternative medicine uses some medicinal plants in the treatment of diabetes. Some medicinal plants have proven effective in treating diabetes, and this effectiveness is due to the fact that these medicinal plants contain phytochemical compounds that have anti-diabetic properties (Fig.3) (Abu-Odeh et al., 2021).

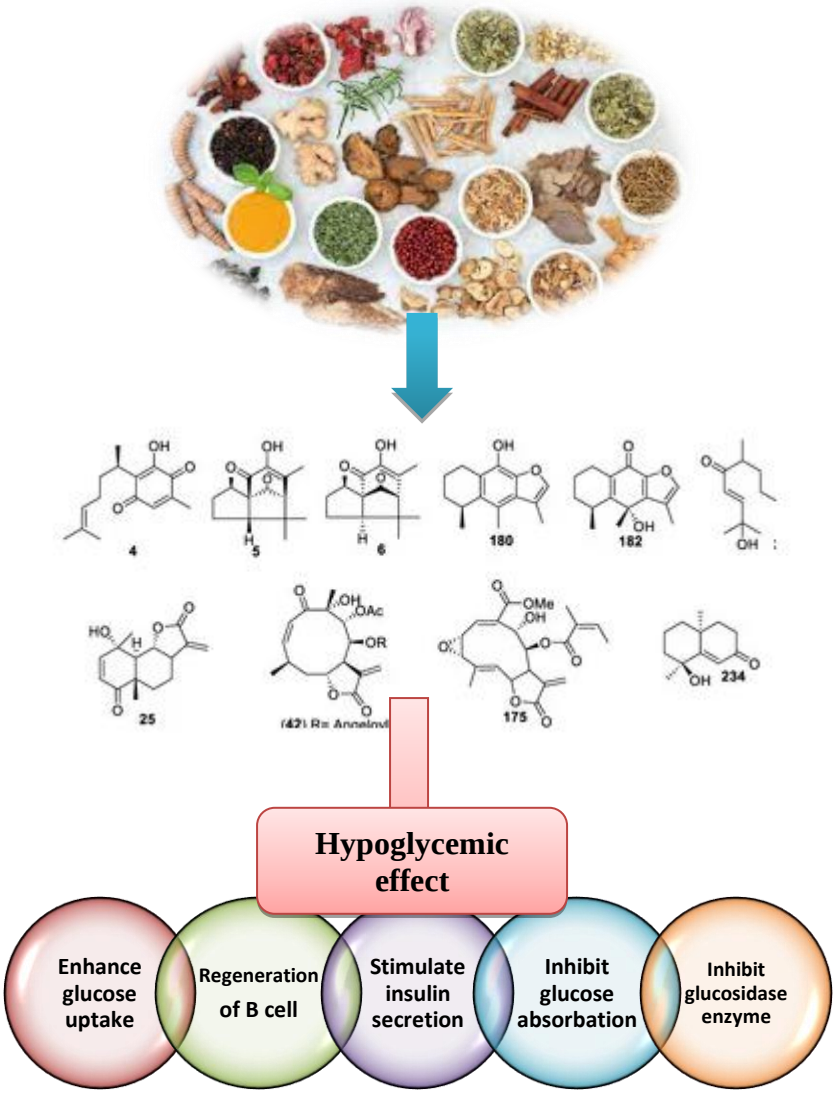

Figure3. Mechanism action of traditional plants as hypoglycemic

Humans are increasingly using medicinal plants to treat a variety of diseases; these medicinal plants are known to the general public as herbal medicines.According to ANVISA (National Health Surveillance Agency), all medicine made from plant raw materials is herbal medicine. Of course, analyzing its pharmacological properties and having a broad understanding of its efficacy and safety for a qualified drug is required, because every plant carries the risk of toxicity, so scientific studies are becoming more advanced (Walaa,2020). Most of the time, the population that uses medicinal plants for disease treatment is unaware of the proper care that must be taken from cultivation to preparation,

as well as the therapeutic action of the plant, its toxicity, indications, and contraindications. Each plant has theoretical values that benefit health as well as values that can harm the patient's health because, while the plant can heal, it also has a high risk of intoxication if the proper form of proper preparation is not followed. Traditional medicines from all over the world include a wide range of natural drugs for the treatment of symptoms associated with chronic diseases such as diabetes mellitus. Several of these herbs have been shown to have anti-diabetic activity when tested using various types of experimental techniques. A wide range of plant-derived action principles representing various types of biological activity, including alkaloids, glycosides, amino acids, polysaccharides, hypoglycins, peptidoglycans, steroids, guanidine, glycopeptides, carbohydrates, inorganic ions, and terpenoids, have shown activity, including treatment of diabetes (Abdellatif et al.,2021).

Several plants are popularly known for treating diabetes mellitus, but there has been little scientific research proving their effectiveness and use in gestational diabetes. Table 1 presents a list of medicinal plants with anti-gestational diabetes potential based on the different parts used and mode of action *(*Walaa, 2021*).*

Table 1. Some of the most commonly used medicinal plants in pregnant diabetic women.

Local Name	Botanical Name (Family)	Used Plant Part	Formulation/ Route of Administration	Mechanism of Action	Active Constituents	Reference
Garlic/ Lahshun	*Allium sativum* (Amaryllidaceae)	Rhizome	Aqueous homogenate of garlic	Glycogen synthesis and Stimulate secretion of insulin	Allicin	Singh,2011
Brown mustard/ Sarso	*Brassica juncea* (Brassicaceae)	Seeds	Oil	Stimulate insulin secretion	Isorhamnetin	Grover,2002
Kondor	*Boswellia carterii* (Burseraceae)	Oleo-gum resin	-	Increase in serum insulin and liver glycogen	Boswellic acid	Helal et al.,2005
Duckweed/ Nonia	*Portulaca oleracea* (Portulacaceae)	Seeds	Powdered	Improvement of insulin secretion and regeneration of diabeticendothelial dysfunction	-	Lee et al.,2012
Indian Aloe/ Gheekumari	*Aloe vera* (Liliaceae)	Leaves	Aloe Juice	Stimulate insulin secretion from β-cell	PseudoprototinosaponinAI II andprototinosaponins AIII	Bnouham et al.,2006
Mukkootti	*Biophytumsensitivum* (Oxalidaceae)	Leaves	Decoction	Stimulate insulin secretion from β-cell	-	Puri,2001
Jambolao/ Jamun/ black olive	*Eugenia jambolana*(Myrtaceae)	Leaves and seeds	Decoction	Decrease the amount of glucose in the blood and Enhancement of insulin release from cell	Pandanus odorus (Toei-hom) a 4-hydroxybenzoic acid	Singh,2011

Lotus, Kamal	*Nelumbo nucifera* (Nymphaeaceae)	Leaves	Extract	Decrease of fasting blood glucose and fasting blood insulin levels	Selenium (Se)-polysaccharide	Zeng et al.,2007
Canton/ Ginger	*Zingiber officinale* Lin. (Zingiberaceae)	Rhizome	Extract/ capsule	Stimulate insulin secretion	Gingerols, shogaols, paradols, and zingiberene	Rudge et al.,2013
Cathedral bells	*Kalanchoe pinnata* Lam. (Crassulaceae)	Seeds	Extract	Reduce fasting blood glucose and Stimulate insulin secretion	Aphenyl alkyl ether	Ute et al.,2013
Babul/ Babhul	*Acacia arabica* (Leguminosae)	Seeds	Powdered (4 g/kg body weight)	Stimulate insulin secretion from β-cell	Quercetin	Champion et al. ,1980
Coriander/ Dhaniya	*Coriandrum sativum* (Apiaceae)	Fruits	Fruits as supplement in diet and drinking water	Enhancement of insulin release from β-cell	-	Eidi,2009
Banana	*Musa sapientum* (Musaceae)	Flowers	Extract	Stimulate insulin secretion	Flavonoids (Epicatechin and gallocatechin)	Ganugapati et al.,2012
Bel	*Aegle Marmelos* (Rutaceae)	Leaves	Extract	Reduce fasting blood glucose	Flavonoids, tannins	Sabiu et al.,2004
Red Raspberry	*Rubus idaeus* (Rosaceae)	Leaves	Leaf tea	Reduce fasting blood glucose	Phenolic compounds and flavonoids	Cheang et al.,2016

As conclusion, due to the importance of testing gestational diabetes because of its negative effects on the mother and fetus, so it is recommended that the care provider for pregnant women review glucose levels, especially in the 24-28 week of pregnancy, to speed up decision-making and control the issue in the event of gestational diabetes.There are many strategies of institutions responsible for following up on pregnant women and safe treatment methods, but the majority prefer to take glyburide and metformin, although taking metformin is the first and best option compared to using glyburide because of its side effects. However, in some cases where the glucose level is significantly high. It cannot be controlled, so it is recommended to give insulin to control the condition and prevent complications for both mother and fetus.

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