

A Review On Therapeutic Potentials Of Plant Based Nanocomposites For Diabetes Mellitus

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Abstract: *Diabetic is the dangerous diseases in the world it causes major public health problems. Despite the great advances in diabetic treatment and drug, the prevalence and mortality rates of diabetic remain high. Therefore, the pursuit for more efficient and less toxic diabetic treatment strategies is still at the spearhead current research. Plant based nanocomposites is one of the best active ingredients of the biological nanomaterial, and it has a potential effect on antioxidant, antiinflammatory, antibacterial, anticancer, and antidiabetic properties. In this review, the medicinal properties and pharmaceutical effects of plants based nanomaterial derivatives for the potential effect on biological activities.*

1. INTRODUCTION

Diabetes is a chronic metabolic disorder and causes severe illness in animals (1). Due to lower quantity secretion of insulin by pancreas or body of organisms improperly use the insulin (Glucose converted into glycogen) hyperglycaemia occurs in blood and sometimes leads to failure of homeostasis (2). In the global range the case of diabetes rates increases every year. Prolonged diabetics leads to the chance of other disorders such as eye disturbance(3,4 & 5) diabetic wound (6), artheroclesis (7) and other disease. Administration of chemotherapeutic based diabetic drugs leads to chemical residue accumulates in the patient body and causes side effects and mortality complications (8,9). Due to this condition, we need to find the suitable and bioavailability efficiency drugs consists following salient features such as to control or promote the insulin secretions, proper use of insulin and prevent the side effects, mortality rate in patients.

Based on the earlier findings, medicinal plant compounds have been treated as therapeutic potential for diabetic wound-healing (10-15). Medicinal plant extracts were biochemical compounds in managing the complications associated with diabetes mellitus such as hypercholesterolemia and impaired renal function(16-23). Plant nanocomposites are considerable interest in finding safer antioxidants from natural sources to replace the synthetic ones (24-32). The active components from herbal plants are used for growth promotion and oxidation of cells (33-38). The introduction of biocompatible materials and devices that are engineered on the nanometer scale that interact with biological molecules and cells and provide specified diagnostic, therapeutic, and imaging functions will utterly change the way in which health care is provided in the future (39-43).

Mechanism and action of Diabetes mellitus

Diabetes, a chronic disease caused by insulin dependent and independent Insulin is a hormone that bind with glucose and transport to cell for energy production (44). Depends upon the insulin secretion, it can be classified as Type I diabetes mellitus (insufficient secretion of insulin) mostly affect children and adolescent and Type II diabetic mellitus is one the most important metabolic disorders associated with significant morbidity and mortality. In worldwide, it is estimated that more than 326 million patients have type 2 diabetes mellitus, Types II Diabetes affects frequently in adult and it causes severe effect when the body parts not able to use the secreted insulin properly. Gestational diabetes is one of the diabetes which is occurring in the stage of pregnancy (45). During pregnancy, the blood glucose level is increased because of placenta of mother. This type of diabetes is called (GDM) and the blood glucose level is normal after the delivery.

Despite that this the risk stage of both maternal and the child. The child has the chance to get the type II disease after the 5 to 6 years of the delivery. For the prevention of these types of diabetes there are many chemotherapeutic drugs are available to treat such an illness. But it causes mortality and the opportunistic disease (46). Because of their chemical nature and residue present in the drug because of this pandemic situation we need a alter at the same time; the effective and chemical free drug is the need of current scenario to eradicate and cure the diabetes in worldwide.

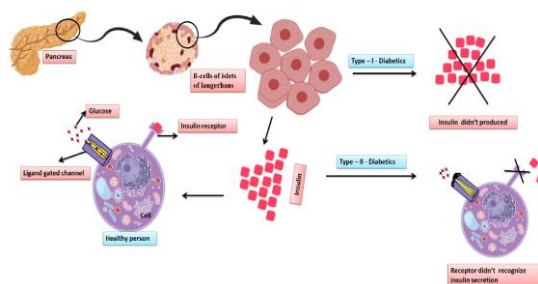


Figure 1: Mechanism of insulin secretion in healthy & diabetic person

Mechanism of insulin secretion

Diabetes mellitus is a metabolic condition that considered by high blood glucose. A large number of people are suffering by Type II diabetes in all over the world(47). Diabetes is a lifelong disorder, which is noticeably affected by humans. These factors have to be addressed on daily basis while managing diabetes and the patient is the person best equipped to deal with the situation. Diabetes is a disease in which our blood glucose (or) blood sugar levels are too high. In our daily food diet, Glucose is rich source of foods like, rice, bread, potatoes, fruit, sugar, yogurt and milk. When we eat too much of glucose rich food and lack of physical work we surely affected by diabetics. Not only the food, there is lot of reasons for the cause of diabetics. Being overweight or obese increase our risk too. When we have a high blood pressure, high cholesterol or high triglycerides may we have a diabetic parent or ancestry (48). Insulin is the hormone that helps the glucose get into cells to give them energy. There a few types of diabetics, types I diabetes is an autoimmune disease type II diabetes occurs, when our body becomes resistant to insulin and sugar builds up in your blood. The number of people with diabetes in India wildly increased from 26 million in 1990 to 65 million in 2016 (MHFW). In 2020, according to the (IDF) international diabetes federation, 463 million people have diabetes in the world. 88 million people in south Asia of this 88 million, 77

million belong to India. Diabetes causes more effects on our body (ex) loss of consciousness, risk of stroke, extreme thirst, visual disturbances, sweet- smelling breath, cataracts and glaucoma, risk of heart disease, risk of infections, fatigue and lack of energy, high blood pressure, pancreas malfunction, gastroparesis, excessive urination, protein in the urine, damaged blood vessels, ketoacidosis, nerve damage, dry- cracked skin and 15–25% of diabetic people have diabetic foot ulcers. These are the problems caused by diabetic disease. An internationally coordinated effort is required to improve human behaviour and lifestyle to halt the global diabetes epidemic and the development of such complications as retinopathy, nephropathy, neuropathy, cardiovascular diseases, peripheral vascular diseases and stroke. Awareness of diabetes, its complications and better health care has proved to improve the long-term outlook of this disease. The management of diabetes is intimately linked to food therefore; knowledge about food and nutrition and the scientific base of biochemistry, physiology, and pathogenesis go a long way towards the understanding and dealing with the disorder (49) Diabetes mellitus is one the most important metabolic disorders associated with significant morbidity and mortality. It is estimated that more than 326 million patients worldwide have type 2 diabetes mellitus, and 15–25% of these will develop diabetic foot ulcers(50).

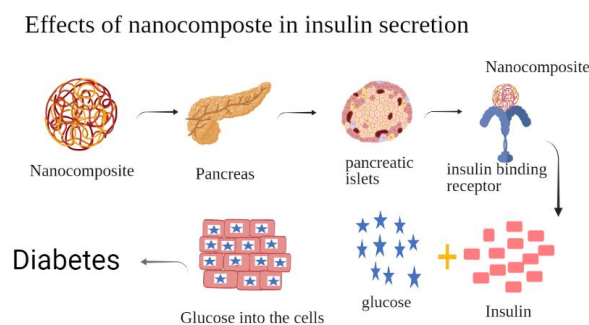


Figure 2: Mechanism of nanocomposite in insulin secretion

Diabetes causes by the main reason of our genetic makeup, family history of our ancestor, ethnicity of people, health and environmental factors. There is lot of reason is therefore people getting diabetes (51). The most common causes are food habit and the genetic makeup of the people. People are eating too much of junk food and unsaturated fatty foods, and eat lot amount of rice and the glucose containing food(52). In the ancestor way people have the genes of their ancestor if their ancestor has the disorder and it's transported to their young ones through their genes.

Effects of nanocomposites in insulin secretion

Nowadays “nanocomposite” which (at least) two solid constituents provide not only average higher than additive (53). These nanomaterials are should be in nanofiber, nanoparticles, and nano clays. Nanocomposites is a solid material and they have the 10^{-9} nm scale range. These types of nanomaterial's are composed with metallic, non-metallic or polymeric materials. Example, (zinc, chitosan, silica or carbon-based nanoparticles). The nanocomposites are having the single binding sites and the particular targeting regions. But the nanocomposites of the nanomaterial have the controlled and multitargeting regions and the high effects on the compositing material (54). Based upon the nature, incorporation of nanomaterial and the function of nanocomposites are classified into further types (55, 56).

Polymer-based nanocomposites

Polymer based nanocomposite is one of the emerging synthesized materials because of their bio and polymer nature for the adherence(57). Polymer based nanocomposite is composed by polymer with any metal or non-metal substance. The polymers are may be a chitosan, gelatine, or any other substance which have the polymer substance in their nature. (58). Because of their mechanical property and thermal property, the polymer as well as the polymer matrix are combined with the other nanomaterials(59). The polymer-based nanocomposites are having the better anti-diabetic activity because of their potential value and the mechanical property (60). Earlier proposed the comparative study of different nanocomposites for the anti-diabetic assays of α -Amylase inhibitory activity and α Glucosidase inhibitory activity(61) Proved the effects of chitosan polymer nanoparticle in the activity of anti-diabetic in db/db mice. In this study the chitosan is used to reduce the glucose level of mice and it have the lower molecular weight (2.0×10^4 Da)(62) reported the anti-diabetic activity of essential oil encapsulated in gelatine pectin particles against sugar. And the do the glycosidic activity. The gelatine pectin oil particle was prepared by the method of electrospray and these particles are used against the glucose oxidation(63) Proposed the statement the gelatine is isolates form the Atlantic salmon fish and that one is used in dipeptidyl- peptidase IV inhibitor in streptozotocin induced diabetic rats. (64)

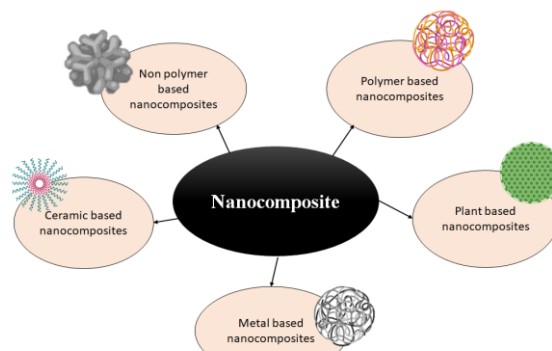


Fig3: Different types of Nanocomposites

Non-polymer- based nanocomposite

In this composite the composites do not contain any polymer or polymer derived substance. In this type of nanocomposite, the nanomaterial is may be a metal or ceramic. Accordingly, to this way the nanocomposite is further classified into two types. Namely metal based nanocomposites and ceramic based nanocomposites (65) expose the study of nanocomposite which been synthesised from the nanomaterial of the same compound. According to Pouran et al. (2020) Proposed the study of synthesised integrated ZnO/Ag nanocomposite and the surface analysis and the in vivo studies for the management of type I diabetes suspicions and the study of enzyme@ metal -organic framework and oxidase, $\text{IrO}_2/\text{MnO}_2$ nanocomposite for α - glucosidase inhibitor screening technique (66).

Metal based nanocomposite

In the nanomaterial synthesis the noble metal, metal oxide and metal-based nanocomposite is an attracting great interest. They report the electromagnetic activity of metal-based nanocomposite in the medicinal field. The functional nanomaterials, nanocomposites consisting of metal nanoparticles dispersed in a dielectric matrix are of particular interest due to their novel properties offering hosts of new application (67). Food

packaging is protecting the product from the contamination for long time storage. The metal oxide nanocomposite is used as a food packaging substance. Titanium based nanocomposite are the best composite material in advance study of diabetes. The metal nanoparticles are synthesised by the green chemistry method because it's synthesised from the various plant extract and they propose the *in vitro* and *in vivo* anti-diabetic activity. The *in vitro* activity is further divided into two types based on the enzymatic reaction such as enzymatic activity and non-enzymatic activity. In enzymatic activity they state the following assays like α - amylase, α -glucosidase, sucrose inhibitory activity, protein tyrosine phosphatase IB (PTP IB) and Dipeptidyl peptidase IV (DPPIV). And the non-enzymatic activity like glycated haemoglobin, glucose uptake methodology, and cultured cell lines studies of cytotoxicity method (MTT reagent), glucose transport method, and peroxisome proliferator-activated receptor- λ luciferase assays. And they propose the *in vivo* antidiabetic activity in animals like in Invertebrates they choose the silkworms, in aquatic environment in zebra fish, and lower beings rodents (rats& mice) and the large beings rabbits and dog. Here, the CuO nanomaterial is capped with PVP (polyvinyl-pyrrolidone) and PEG (polyethylene-glycol) and do the antidiabetic α - amylase enzyme inhibitory activity. They synthesis silver nanoparticles using outer peels of two varieties of Ipomoea batatas (L.) and do the α -glucosidase enzyme activity (69-71).

Ceramic based nanocomposite

Ceramic nanocomposite is defined as ceramic composites with more than one solid phase, in which at least one of the phases has dimensions in the nanoscale range (<50–100nm). In the past several decades, much effort has been concentrated on improving the fracture toughness of ceramics (72). Ceramic nanoparticle has the high thermal resistance, chemical durability, and mechanical strength as well as the medicinal property. Nanoscale ceramics such as hydroxyapatite (HA), zirconia (ZrO₂), silica (SiO₂), titanium oxide (TiO₂), and alumina (Al₂O₃). These materials are made up from the new synthetic method for the improvement of physical-chemical properties for reducing their toxicity in the biological systems (73). The hydroxyapatite is synthesised by the method of core shell and characterized then this nanoparticle is having the insulin and gallic acid for the insulin oral delivery. Hydroxyapatite (HAP-NPs) is synthesised by the green chemistry technique and these have the antidiabetic activity(74).

Plant based nanocomposite

Many reports showed the plants-based composite are efficaciously treat the diabetic patient more than the other nanocomposites because of their biocompatibility and non-toxic efficiency. The silver nanoparticle is synthesised from *Allium Cepa* by the process of green synthesis to make the nanocompositethese materials are highly effective for the diabetic and proved by the *in vitro* antidiabetic assay. The following flowchart is used to know the plants and the combination of the nanomaterial to used synthesis of the plant based nanocomposites.

Plant species used to synthesis	Nanomaterial	Activity	Reference
<i>Trigorella foenum graecum</i>	Green- silver nanocomposite	Antidiabetic activity in Streptozotocin Induced Diabetic Rats	Virk et al.2018 (75)

<i>Portulaca oleracea</i>	Functionalized silver nanocomposite	α -amylase and α -glucosidase enzyme inhibition activity	Saratale et al.2020 (76)
<i>Murssraya Koenigii</i>	Ag/CuO	α -glucosidase enzyme inhibition activity	Selvan et al.2021 (77)
<i>Xanthoxylum armatum</i>	Pd- rGO	α -glucosidase enzyme inhibition activity	Hazarika et al.2019 (78)
<i>Zingiber officinale</i>	Ag/ CuO	α -amylase and α -glucosidase enzyme inhibition activity	Selvan et al.2021 (77)
<i>Urtica dioica</i>	ZnO	α -amylase and α -glucosidase enzyme inhibition activity	Bayrami et al.2020 (79)
<i>Vaccinium arctostaphylos</i>	ZnO	Anti-diabetic activity in Alloxan induced Diabetic rats	Alioghli et al.2019 (80)
<i>Fritillaria cirrhosa</i>	Au	Anti-diabetic activity in Streptozotocin induced diabetic rats	Guo et al.2020 (81)
<i>Azadirachta indica</i> <i>Hibiscus rosasinensis</i> <i>Murraya koengii</i> <i>Moringa oleifera</i>	ZnO	α -amylase and α -glucosidase enzyme inhibition activity	Rehana et al.2017 (82)
<i>Hibiscus subbariffa</i>	ZnO	Anti-diabetic activity in Streptozotocin (STZ) induced diabetic mice	Bala et al.2015 (83)
<i>Silybum marianum</i>	ZnO	Anti-diabetic activity in Alloxan induced diabetic mice	Arvanag et al.2019) (84)
<i>Andrographis paniculata</i>	ZnO	α -amylase enzyme inhibitory activity	Rajakumar et al.2018 (85)
<i>Nigiella sativa</i>	Ag	α -amylase enzyme inhibitory activity	Subha et al.2021 (86)
<i>Eclipta alba</i>	Ag	Anti-diabetic activity in Streptozotocin induced pancreatic cell line	Vijayakumar et al.2020 (87)
<i>Leucosidase sericea</i>	Ag	α -amylase enzyme inhibitory activity	Kumar et al.2011 (88)
<i>Cassia auriculata</i>	Ag	α -amylase and α -glucosidase enzyme inhibition activity	Karthick et al.2014 (89)
<i>Gymnema sylvestre</i> <i>Tamarindus indica</i>	Ag / SiO ₂	α -amylase and α -glucosidase enzyme inhibition activity	Arunachalam et al.2015 (90-91)
<i>Rhizophora apiculata</i>	Ag	Hepatoprotective activity	Ghosh et al.2014 (92)
<i>Costus speciosus koen</i>	nanocrystalline	photocatalytic activity	Chinnasamy et al.2019 (93)

Recently, nanocomposites based on nano-sized inorganic particles and clusters have been paid more attention due to the interesting nano-sized effects of the particles (94-97). The

nanocomposites is classified into many ways depending upon the nature, incorporating materials as well as the binding site of the nanomaterials and most of the reports are exploring the nanocomposites are having a better result than the nanoparticles (98-102).

Insulin and Insulin Analogues and Secretagogues

Secretagogues tend to interact with particular cell receptors on beta cells (B), resulting, discharge of insulin (103-105). Drugs of this class cover sulfonylureas and rapid action on glinides. Several observational studies speculated that secretagogues elevate the high risk of HCC in diabetes patients (106-109). For the better performance of B cell functionality, insulin is eventually needed, thereby, usage of insulin with long term diabetes patients causes more complications. Earlier studies reported their findings in Meta analyses that 161% of elevated HCC risk was noticed in the patients injected with insulin. Enormous accounts of studies have been shown that free radicals implicate against disorders covering diabetes, cancer, antidiarrheal, anti-inflammatory, antimicrobial, antibiofilm and wound healing (110-111). Similarly, duration of DM before, on set of HCC, has played a critical role in the linking at DM and HCC.

2. CONCLUSION

Nanocomposites from plant products have been shown to possess good therapeutic potential as anti-inflammatory agents and as a wound healing promoter, due to the presence of terpenes, and flavonoids. So, for that the plant and bio-based plant nanocomposite is the alter drug for the above-sided statement.

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