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Need of silver nanoparticles for better antidiabetic drug delivery - an overview

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ABSTRACT

Growth and applications of nano science and nanoparticles have a great footprint in recent years. There is increasing optimism that nanotechnology, as applied to medicine, will bring significant advances in the diagnosis and treatment of disease. Working with these extremely small structures is very much interesting due to its unique properties. Drug delivery and related pharmaceutical development in the context of nanomedicine should be viewed as science and technology of nanometer scale complex systems, consisting of at least two components, one of which is a pharmaceutically active ingredient. Hyperglycemia occurs because of uncontrolled hepatic glucose output and reduced uptake of glucose by skeletal muscle with reduced glycogen synthesis. Nowadays, to develop nanoscaled systems has become a prominent strategy to improve the drug delivery of phytochemicals. In this review, we primarily summarized the significance of nanotechnology followed by its importance in herbal antidiabetic drug delivery. Equipped With high scale production possibility, Long stability and Freeze dried to form powder formulation silver nanoparticles are determined for better herbal drug targeting in Diabetes Mellitus.

Keywords: *Nanoparticles, Hyperglycaemia, Silver Nanoparticles, Phytochemicals.*

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INTRODUCTION

Nanotechnology is one of the fastest developing sciences over the last few years. This is an interdisciplinary science that connects knowledge of biology, chemistry, physics, engineering and material science.[1] Nano word comes from the Greek word "nanos" meaning "dwarf". Nano typically is defined as one billionth of a quantity or term that represents mathematically as 1 x 10-9 or simply as 10-9. It is the science of very small, virtually any science that involves understanding the world at the atomic level, manipulating material on the scale of atoms and molecules. [2] Nanoparticles are small solid colloidal particles which are available in range from 10 to 1000 nm (1.0 µm), in which the active drug or biologically active material are dissolved, entrapped, and/or to which the active principle is adsorbed or attached. Goal of nanotechnology is same as that of medicine, to diagnose as accurately and early as possible and to treat as effectively as possible without any side effects using controlled and targeted drug delivery approach.[3]

Advantages of Nanoparticles: Nanoparticles deliver drugs through oral, nasal, parenteral, intra-ocular routes etc. Ability to control and sustain the drug release before reaching the specific site of action. Protects the drug from rapid degradation and maintains the drug at specific site. Lower doses of drug show high therapeutic efficacy and reduced side- effects. Drugs can be incorporated without any chemical reaction resulting in the preservation of pharmacological activity of the drug. [4]

Based on their importance and unique features of nano particles, such as surface to mass ratio of nanoparticles is much larger than that of other particles, their quantum properties and their ability to adsorb and carry other compounds, nanoparticles (NPs) are more attractive. NPs have large surface area which is able to bind, adsorb and carry other compounds such as drugs, probes and proteins. Although the definition identifies nanoparticles as having dimensions below 0.1µmor 100nm, especially in the area of drug delivery relatively large (size>100nm) sufficient amount of drug loaded on to the particles.

Nanoparticles and Drug Delivery: Drug delivery and related pharmaceutical development in the context of nano medicine should be viewed as science and technology of nano meter scale complex systems (10–1000 nm), consisting of at least two components, one of them is a pharmaceutically active ingredient. The whole system leads to a special function related to treating, preventing or diagnosing diseases sometimes called smart drugs. The primary goals for research of nano-bio-technologies in drug delivery include More specific drug targeting and delivery, Reduction in toxicity while maintaining therapeutic effects, Greater safety and biocompatibility, Faster development of new safe medicines. [5]

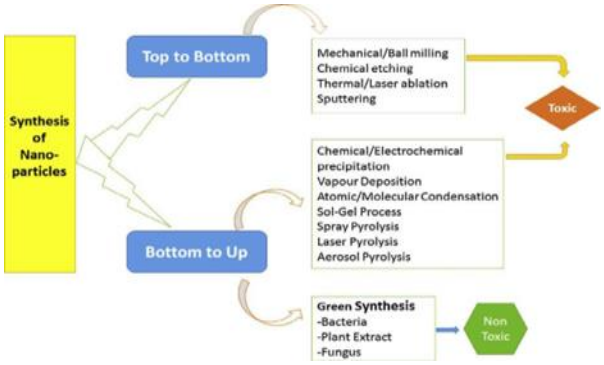

Figure1: Synthesis of Nanoparticles

Advantages of Herbal Drug As Nanoparticl[6]: Herbal nanoparticles were used to target specific organs which improve the drug delivery, safety, effectiveness, selectivity. High concentration drugs can be delivered to target site due to its unique size and loading capacity. Drug dissolution rate in blood increases because of small particle size and large surface area of nanoparticles. Decrease side effects, Widespread availability, Lower cost, Exhibits passive targeting to the disease site of action without the addition of any particular ligand moiety.

Silver Nanoparticles: Silver is a soft white lustrous element. Metallic silver itself is insoluble in water, but metallic salts such as AgNO3 and silver chloride are soluble in water. AgNPs are unique in nanoscale system due to the ease in its synthesis and chemical modifications. AgNPs are used in the development of new technologies in the areas of electronics, material sciences and medicine and because of their extensive applications in various areas more research is being conducted on the AgNPs by the scientists throughout the world.

Synthesis of Silver nanoparticles: Silver nanoparticles (AgNPs) are increasingly used due to their unique physical and chemical properties in various fields such as medical, food, health care, consumer, and industrial purposes. These include optical, electrical, and thermal, high electrical conductivity and biological properties. Due to their peculiar properties, they have been used for several applications. Syntheses of silver nanoparticles are carried out using three methods physical, chemical, and biological methods. [7]

Physical methods: Nanoparticles are prepared by evaporation-condensation using a tube furnace at atmospheric pressure. Conventional physical methods including spark discharging and pyrolysis were used for the synthesis of AgNPs. The advantages of physical methods are speed, radiation used as reducing agents and no hazardous chemicals involved, but the downsides are low yield and high energy consumption, solvent contamination, and lack of uniform distribution.

Chemical methods: This method uses water or organic solvents to prepare the silver nanoparticles. This process usually employs three main components, such as metal precursors, reducing agents, and stabilizing/capping agents. Basically, the reduction of silver salts involves two stages Nucleation and Subsequent growth. In general, “top-down” and “bottom-up” are the two methods by which Nanoparticles can be prepared. In “top-down” method mechanical grinding of bulk metals with subsequent stabilization using colloidal protecting agents occurs. “Bottom-up” methods include chemical reduction, electrochemical methods, and so no decomposition. High yield is the major advantage of chemical method compare to physical method. These methods are extremely expensive and the chemical reagents used are Thio-glycerol, 2-mercaptoethanol, citrate, borohydride are toxic and hazardous. And also the manufactured particles are not of expected purity, as their surfaces were found to be settled with chemicals. Preparation of silver nano particles with definite size along with the prevention of agglomeration is very difficult as well as in chemical method toxic and hazardous chemicals are excised out as byproducts. [8]

Biological methods: Biological methods have emerged to overcome all the problems related to physical and chemical methods. Silver nanoparticles are synthesized with definite size using different biological systems including bacteria, fungi, plant extracts, and small biomolecules like vitamins and amino acids as an alternative method to chemical methods not only for AgNPs, but also for the synthesis of several other nanoparticles.

Advantages of silver nanoparticles

1. High scale production possibility.
2. Long stability
3. Freeze dried to form powder formulation9

Table 1: Different plants used for the synthesis of silver nanoparticles

Plants	Plant part used	Size (nm)	Shape
Alternanthera dentate	Leaves	50-100	Spherical
Acoruscalamus	Rhizome	31.83	Spherical
Boerhaavia-diffusa	Wholeplant	25	Spherical

Teaextract	Leaves	20- 90	Spherical
Tribuluster-restris	Fruit	16-28	Spherical
Psoraleacoryli-folia	Seed	100-110	Spherical
Hevetiaperuvi-ana	Latex	10-30	Spherical
Aloevera	Leaves	50-350	Spherical, Tri-angular
Nelumbonucif-era	Leaves	25- 80	Spherical, Tri-angular
Citrussinensis	Peel	10-35	Spherical
Meliadubia	Leaves	35	Spherical
Centellaasiatica	Leaves	30-50	Spherical
Abutilon indi-cum	Leaves	7-17	Spherical
Premnaher-bacea	Leaves	10-30	Spherical

The recent emergence of nanotechnology has provided a new therapeutic modality in silver nanoparticles for use in medicine. Silver powder was believed by Hippocrates, father of modern medicine, to have beneficial healing and anti-disease properties and listed as a treatment for ulcers. Silver compounds were major weapons against wound infection in World War I until the advent of antibiotics upon reaching nanoscale, like other nanomaterials and primarily by virtue of extremely small size, silver particles exhibit remarkably unusual physicochemical properties and biological activities. These distinctive properties extend its application in antibacterial, antifungal, anti-viral and anti-inflammatory therapy.

Applications of Nano Silver: Due to the multifunctional properties of Nano silver, it is widely used in all fields such as electronics, food products, personal care & cosmetics, household products, medicinal products etc., The application of nano silver in the consumer products is mainly based on the antibacterial property of silver. Currently the application of nano silver in medical products is emerging in the field of medical devices and pharmaceutical research and development. Emerging Application of nano-silver in medical products like Cardiology, Dentistry, Drug delivery, Imaging, Orthopedics, Pharmaceutics, Surgery, Wound care, Diagnostics, etc..

Significance of Silver nanoparticles [10]**:**

Silver is the basic element which can exists in three different forms Ag0, Ag2+, Ag3+. Pure silver has the highest electrical, optical and thermal conductivity and has lowest contact resistance.

Patients with diabetes mellitus have an increased prevalence of vascular disease. Pathologic thrombosis associated with atherosclerotic plaque rupture is a major cause of morbidity and mortality. Platelets are intimately involved in the initiation and propagation of thrombosis. Evidence suggests that platelets from patients with type 2 diabetes have increased reactivity and baseline activation compared to healthy controls. This is associated with biochemical factors such as hyperglycemia, hyperlipidemia, insulin resistance. So anti platelet should be prescribed to DM patients at >10% 10-year risk of cardiovascular disease and considered in patients at intermediate (5%–10%) risk according to the recent position statement of the American Diabetes Association. Silver nanoparticles inhibit thrombin-induced platelet aggregation in a concentration-dependent manner. Clumping of blood platelets is often a serious problem for diabetic patients which may lead to heart problem. [10]

Silver nanoparticles inhibit the aggregation of platelets obtained from patients with noninsulin-dependent diabetes mellitus by nearly 50%. Moreover, intravenous administration of nanoparticles (218 mg/kg body weight) in two different mice strains led to significant inhibition of platelet aggregation in mouse whole blood (studied by electronic impedance) in a dose-dependent manner. Studies found that aggregation was significantly reduced in platelets exposed to silver nanoparticles. [11]

Diabetes Mellitus and Silver nanoparticles:

Diabetes mellitus is a chronic metabolic disorder characterized by a high blood glucose concentration – hyperglycemia caused by insulin deficiency, often combined with insulin resistance. Hyperglycemia occurs because of uncontrolled hepatic glucose output and reduced uptake of glucose by skeletal muscle with reduced glycogen synthesis. When the renal threshold for glucose reabsorption is exceeded, glucose spills over into the urine (glycosuria) and causes an osmotic diuresis (polyuria) which, in turn, results in dehydration, thirst and increased drinking (polydipsia). [12]

Pterocarpus marsupium Roxb is a medicinal plant widely distributed in India. Pterocarpus marsupium, Roxb (pm) is also known as Indian kino, Bijasal, Vijaysar, belongs to the family Leguminosae. Pterocarpus marsupium Roxb is grown in central, western and southern regions of India. The heart wood, leaves, flowers and bark have useful medicinal properties.[13] The plant is traditionally used for various disease like diabetics, angina, cancer, and used as cardiotonic, brain tonic, etc. [14]

Silver nanoparticles were prepared by green synthesis method using Pterocarpus marsupium Roxb. bark and wood extract. Biosynthesis of nanoparticles is a kind of bottom- up approach where the main reaction occurring is reduction. The reduction of silver ions leads to the formation of stable silver nanoparticles. These nanoparticles were characterized and evaluated for various tests such as visual examination, uv-visible spectral analysis, FTIR

spectroscopy, drug entrapment, determination of particle size, determination of zeta protentional, SEM analysis, in- vitro anti diabetic study and invitro drug release and kinetic study. The results of the above tests were showing promising results which can be a lead to develop Pterocarpus marsupium Roxb.as silver nanoparticles so as to enhance its anti diabetic activity. [15]

Piper beetle leaves were chosen to decipher their impact on modulating the level of glucose by studies on the inhibition of α-amylase activity and glucose diffusion. Research with organic extracts of plant material is widespread. Aqueous leaf extracts were employed for the present study to infer a simple way of acquiring phytonutrients to manage DM. The application of plant extracts in the native form is restricted due to its decreased solubility and reduced bioavailability. These hindrances can be overcome by capping them on heavy metal like silver resulting in the production of bioactive components of plant material. [16]

Biogenic silver nanoparticles thus serve as potent inhibitors of such digestive enzymes.[17] The synthesis and efficiency of nanoparticles depends on the amount of reducing compounds like phenols, flavonoids and terpenes, etc., in the plant extracts. One of these plants is Thymus serpyllum, commonly known as Breck land thyme, which belongs to the family Lamiaceae and it possess several important compounds like minerals, phenols, flavonoids, and many other reducing agents. [18]

The medicinal plant "Thymus serpyllum" has an aqueous extract rich in bioactive compounds, which served as a reducing agent to synthesize and then as a capping agent to stabilize the nanoparticles. The newly biosynthesized silver nanoparticles were confirmed via characterization techniques such as SEM, XRD, EDS, and FTIR, depicting spherical 42 nm size nanoparticles with JCPDS Card No. 00-04-0783. Smaller size nanoparticles show better antioxidant and alpha amylase inhibition activity, and increasing the dose of AgNPs increased the scavenging ability as well as amylase inhibition. The synthesized nanoparticles improved the insulin sensitivity and glucose tolerance in treated mice and reduced the fasting glucose levels significantly. [19]

The AgNPs that were derived from the leaf extract of F. cretic demonstrated properties that were anti-oxidant, anti-hyperlipidemic, and antidiabetic. Additionally, they have a protective effect on the kidneys and the liver. The findings of the study were evaluated in-vitro and in-vivo using methods that are intended to treat diabetes. It was discovered that the AgNPs that were generated from the leaf extract might have qualities that could help treat diabetes. Therefore, the AgNPs found in leaf extract can be utilised to protect tissues from oxidative stress, which is possibly the root cause of the glycemic effects of the extract. AgNPs, which are obtained from leaf extract, might 1 day be manufactured on a commercial scale and put to use in the treatment of diabetes. [20]

CONCLUSION:

Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. Herbs are also effective in prevention and treatment of the toxicity induced by other drugs or toxins. Certain bioactive substances, flavonoids, antioxidants and phenolic substances are rich in medicinal plants which are regarded as a vital source in developing drugs for variety of diseases like Type II diabetes Mellitus, cancer, atherosclerosis and cardiovascular diseases. Indeed, these reported and ongoing strategies have shown that plant products (crude extracts or isolated compounds) incorporated into nano formulations (either encapsulated with in, through, or attached to the nanocarrier) are largely more effective on diabetes than when in unencapsulated form. Lipid nanocarriers, namely liposomes, solid lipid nanoparticles, and nanostructured lipid carriers, have shown significant encapsulation efficiency or loading capacity of plant products, which can make them preferred carriers for large amounts of drugs. The reported studies have shown that increased activity can be achieved with a low dose of drug carried by lipid nanocarriers.

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