



Exploring the Potential of Silver Nanoparticles for Diabetes: A Review

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ABSTRACT:

Various academic disciplines are influenced by progress in science and technology, particularly in the field of nanotechnology. The synthesis of green silver nanoparticles is vital for this sector because plant extracts are less toxic, cheaper, and environmentally friendlier. After years of chronic non-communicable illnesses like diabetes mellitus, the practices of using nanoparticles as a treatment give birth to nanomedicine. Researchers aim to harness nanomaterials and nanostructures to combat these diseases while avoiding adverse effects. By 2045, diabetes mellitus is expected to become the lead in cause of death in India and the second most common cause of death globally, following cardiovascular diseases. Because the action mechanisms of silver nanoparticles can be predicted, nanotechnology helps to better comprehend the complexities involved in their biological application. This review covers recent studies on green-synthesized silver nanoparticles, their characterization, and their antidiabetic properties in both in vitro and in vivo settings.

1. INTRODUCTION

Nanotechnology is a crucial field of study that focus on the desing , alteration, and evaluation of particles ranging from 1 to 100nm in size. It explores the chemical, physical, and biological characteristics of atoms both individually and in bulk. The swift advancement of nanoparticles and nanomaterials has opened new avenues in both fundamental research and practical applications across multiple fields. These include healthcare, Cosmetics, biomedicine, food and feed, drug delivery, environmental science , mechanics, optics, chemical industries, electronics, space technology, energy science, Catalysis, light emission, electronics, single- electron transistors, nonlinear optical devices, and photo-electrochemical application [1,2,3].Using nanostructures as encapsulation and delivery systems, functional food components are carried, protected, and delivered to their exact place of action in the human body [4]. Proteins, vitamins, and antioxidants are among the functional components that are delivered by nanocapsules, which also regulate their release and conceal their flavor [5].

Insufficient insulin production, inadequate body cell response to insulin, or both are characteristics of diabetes mellitus, a metabolic disease [6]. Glucose is mostly derived from lipids and carbohydrates and is stored in the liver before being released into the circulation when insulin levels drop[7].Type 2 and type

1 diabetes have different etiologies and patho-physiologies, despite the fact that both can result in hyperglycemia[8]. Type 1 diabetes necessitates rapid glycemic management since it is an insulin-dependent, incurable metabolic disease that results in hyperglycemia [9]. Before the discovery of insulin a Century ago, type1 diabetes, which accounts for 5-10% of all diabetes Cases, was linked to a significantly reduced life expectancy [10].The body makes glucose through the breakdown of foods high in carbohydrates, sugar, and sweets, as well as from the liver [11]. The condition known as "adult-onset diabetes mellitus" (AODM), or type 2 diabetes, typically appears after the age of 40 and is typified by inadequate insulin production for normal body function [12]. Insulin resistance is characterized by decreased insulin production from pancreatic β -cells and the failure of insulin-sensitive tissue to respond effectively to insulin [13]. Type2 diabetes is influenced by various genetic, metabolic, and environmental risk factors, including age, obesity, genetic susceptibility, family history, gut microbiome balance, epigenetic changes, mitochondrial dysfunction, and ethnic background [14][15]. If therapy is not administered, diabetic ketoacidosis may develop, which may lead to severe consequences and, in some cases, death. Among the treatments include consistent exercise, weight loss, healthy diet, continual medical attention, and a risk reduction strategy. [16,17,18,19].

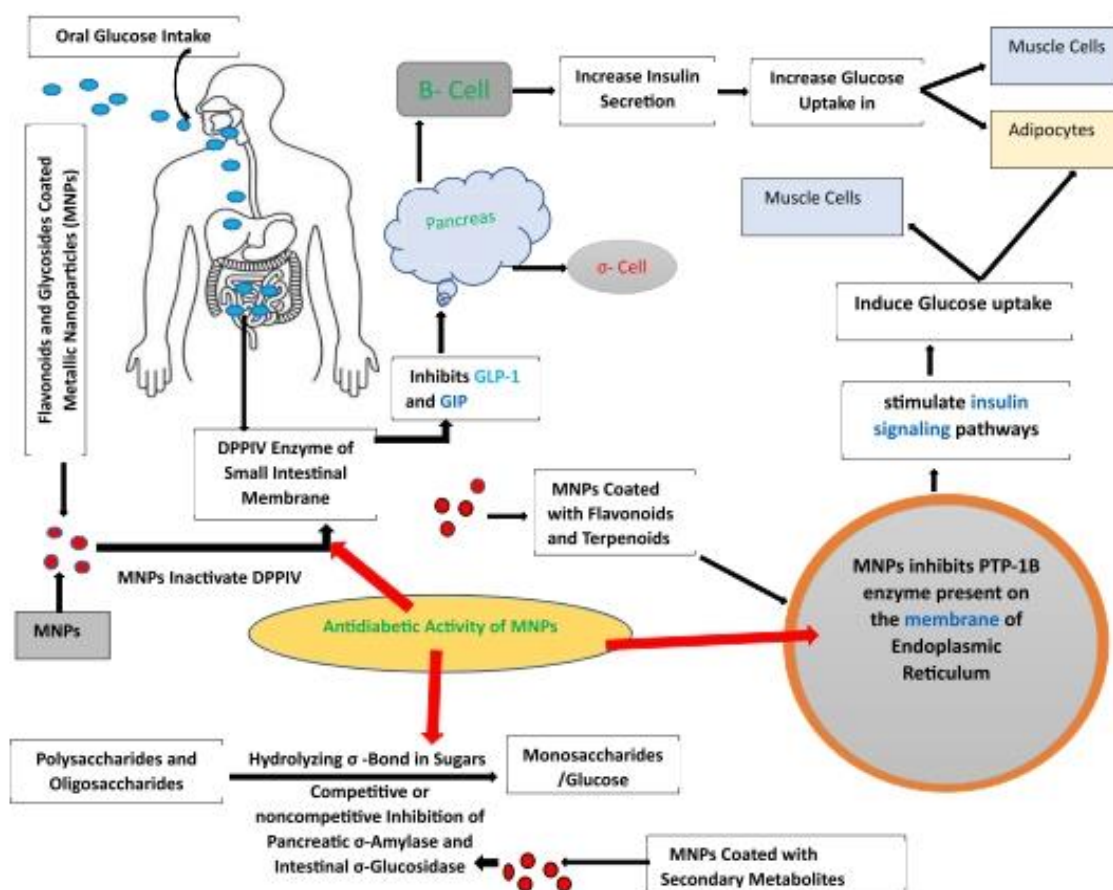


Fig. 1 : The work illustrates how silver nanoparticles (AgNPs) produced using plant-mediated processes have an anti-diabetic effect.

Conductivity, chemical stability, and biological and catalytic activities, such as antibacterial, antiviral, antifungal, and anti-inflammatory qualities, are some of the special qualities of silver nanoparticles [20]. Among the medical applications of AgNPs are vaccine adjuvants, anti-diabetic drugs, bone and wound healing, biosensors, and anticancer therapy [21]. Recent studies suggest that AgNPs derived from plant extracts may be used as anti-diabetic medications [22]. Researchers created AgNPs using leaf extract from *Solanum nigrum* and examined their ability to prevent hyperglycemia in rats with diabetes induced by alloxan. They found that AgNPs had a superior hypoglycemic effect and lowered blood glucose levels without producing overt acute toxicity when contrasted with the popular anti-diabetic drug glibenclamide [23]. Nanotechnology enables the creation of nano-sized materials like nanopores [24], liposomes [25], quantum dots [26], nanotube [27],

polymeric nanoparticles [28], dendrimers [29], fullerenes [30], nanoemulsion [31], nanofibers [32], and AgNPs and gold [33] as superior treatment options compared to conventional therapies.

2. SYNTHESIS AND CHARACTERIZATION OF SILVER NANOPARTICLES

Numerous analytical techniques, such as atomic force microscopy (AFM), transmission electron microscopy (TEM), scanning electron microscopy (SEM), energy dispersive analysis (EDAX) of X-rays, X-ray diffractometry (XRD), Fourier transform infrared spectroscopy (FTIR), and ultraviolet-visible spectroscopy (UV-vis), have been used to characterize nanoparticles. Metallic nanoparticles are created using top-down methods - slicing and serial cutting of bulk material into nanosize particles - and are also made using bottom-up methods - which imply atom-by-atom



construction of the material [34]. The bottom-up method is, however, recommended when preparing nanoparticles in homogenous systems, where catalysis forms the nanostructures. However, in order to scale down materials, the top-down operations used in bulk materials use particular methods such as etching, mechanical grinding, thermal decomposition, cutting, and sputtering. Surface structural defects, which alter the physical properties and surface chemistry of metallic Ag nanoparticles, are the major disadvantages of top-down approaches [35,36,37,38], biological methods [39,40,41], and physical methods [42,43].

2.1 Some Methods for Synthesizing Silver-Nanoparticles

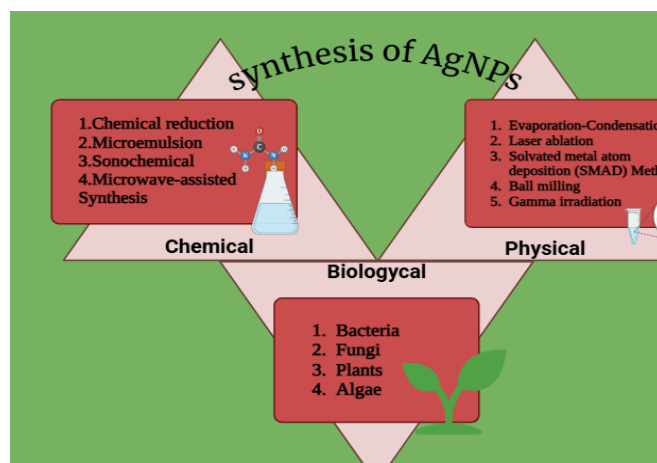


Figure:- 2 Synthesis of Silver-Nanoparticles

An easy, affordable, or ecological way to create AgNPs is by biological synthesis. However, for a successful use, the surface components of nanoparticles must be carefully considered. Typical techniques include chemical, biological, and physical procedures.

Table 1: AgNPs Made From Biological Resources Have Antidiabetic Properties.

Biological origin of NP	Shape or size o	Secondary metabolites	Parameters	Significant discoveries	Reference
(Leaves) <i>Argyrea nervosa</i>	Round and 15 nm in size	phenols, sterols, flavonoids, sugars, triterpenoids, and saponins; tannins	assay for α -glucosidase and α -amylase inhibition	About 70% of both enzymes were inhibited at 100 μ g/ml.	62,63
<i>Allium-cepa</i>	spherical and 49–73 nm in size	Quercetin, kaempferol, organic acids, chlorogenic	The assay for α -glucosidase and α -amylase	At 100 μ g/mL, α -amylase ($P \leq 0.05$) and α -glucosidase (P	64,65

2.2 Mechanism of plant-mediated synthesis of AgNPs

There is a lot of interest in the quick, low-cost, non-pathogenic, and ecologically benign method of producing AgNPs from plants [44]. Unlike chemical and physical methods, plant-mediated synthesis of AgNPs allows for development and is easily scaled up for large-scale manufacture [45]. As a forerunner to plant-mediated nanotechnology, the first study on the synthesis of AgNPs using Alfalfa (*Medicago sativa*) was published in 2003 [46]. Certain plant parts, such as bark, roots, stems, fruit, seeds, calluses, peels, leaves, and flowers, have been used to create silver nanoparticles [47]. Medicinal plants like Nim tree [48], Aloe vera Linne [49], tulsi [50], Ceylon cinnamon [51], Coconut palm [52], Harad [53], Giloy [54], Black paper [55], Rosy periwinkle [56], and Red gum [57] have been used in studies on plant-mediated synthesis of AgNPs. Most plant material extracts can both reduce and stabilize, with a few exceptions, when exogenous compounds such as sodium-do-decyl sulphate are employed as stabilizing agents [58]. Proteins [59], chlorophyll [60], and metabolites [61] found in plant material extracts have been demonstrated to serve as capping agents during the AgNP production process.

3. ANTI-DIABETIC POTENTIAL OF AG NANOPARTICLES

Silver nanoparticles (AgNPs) have shown promising anti-diabetic potential by modulating glucose metabolism, improving insulin sensitivity, and reducing oxidative stress.



		acid, polyphenols, and flavonoids, ferulic acid, gallic acid	enzyme inhibition	> 0.05) were inhibited by approximately 74% and 60%, respectively.	
<i>Avicennia officinalis</i>	Distributed and 181.4 nm in size	glycosides, reducing sugar, proteins, resins, sterols, tannins, and cardiac glycosides; catechol	test for the inhibition of α -amylase and α -glucosidase	At 0.5 mg/mL, α -amylase (IC ₅₀ = 0.28) and α -glucosidase (IC ₅₀ = 0.15) showed 98% and 90% inhibition, respectively.	66,67
<i>Tomentosum Callophylum</i> (Leaves)	Spherical and 24 nm in size	Phenols, alkaloids, terpenoids, glycosides, coumarins, flavonoids, saponins, or tannins	DPPIV, and α -glucosidase, α -amylase inhibitory evaluation	At 500 μ g/mL, DPPIV, α -amylase, and α -glucosidase were inhibited by approximately 18%, 52%, and 58%, respectively.	68
Asiatica Cantella (leaves)	Round and 30–50 nm in size	proteins, glycosides, steroids, alkaloids, carbohydrates, and saponins.	Tests for yeast cell absorption of glucose, non-enzymatic hemoglobin glycosylation inhibition, and suppression of α -amylase activity	52.91 \pm 0.421% more Hb was non-enzymatically glycosylated, 43.96 \pm 0.91% more α -amylase was blocked at 1000 μ g/ml, and 63.27 \pm 0.57% more glucose was absorbed at 200 μ g/ml.	69
<i>Anisata Clausena</i> (Roots)	Round and 32.75 nm in size	Terpenoids, flavonoids, or alkaloids	Tests for glucose 17 diffusion, yeast cell absorption of glucose, and α -amylase inhibition	Glucose uptake peaked at 69.51% (10 mM), α -amylase inhibition at 83.60% (500 μ g/mL, P < 0.001), and GDRI at 78.33% (600 μ g/mL, P < 0.001).	70
(Leaves) <i>Enhalus acaroides</i>	Triangular, hexagonal, and spherical and 2–100 nm	p-hydroxybenzaldehyde, daucosterol hexacosyl alcohol, apigenin, luteolin,	α -glucosidase enzyme	The enzyme showed 76% inhibition at 100 μ g/mL with an IC ₅₀ of 47 μ g/mL.	71
(Leaves) <i>Lonicera</i>	Round and hexagonal and 53	polysaccharides, flavonoids, phenols,	The α -amylase or α -	At a concentration of 100 μ g/mL, AgNPs	72,73



<i>japonica</i>	nm in size	or saponins.	glucosidase enzyme	exhibited non-competitive inhibition of both enzymes, resulting in IC ₅₀ values of 54.56 and 37.86 μg. This inhibition led to 80% suppression of α-amylase activity and 96% inhibition of α-glucosidase. This represented increases of 20 and 24% over the effects of plant extracts.	
<i>Asoca saraca</i>	Round and 36 nm in size	Saponins, tannins, flavonoids or amino acids, carbohydrates, proteins	Assessment of α-amylase suppression	α-Amylase inhibition with an IC ₅₀ value of 0.35 mM	74
<i>Zingiber officinale</i>	Round and 123.8 nm in size	such as monoterpenes, Gingerols, primarily neral as well as geranial, and sesquiterpenes, such as (-) zingiberene and bbisabolene.	Biochemical characteristics of rats with STZ-induced diabetes	After seven days of treatment, blood glucose levels recovered to normal (86 mg/dl), and body weight climbed to 200 mg/kg.	75,76
<i>Ocimum sanctum</i> (Leaves)	Round and 15.0 ± 12.34 nm in size	Organic chemicals, phenols, terpenes, terpenoids, and amine compounds	The enzyme kinetics and inhibition studies of α-glucosidase and α-amylase.	αamylase and α-glucosidase showed competitive inhibitions of 59.57 ± 3.72% and 89.31 ± 5.32% at 3 mg/ml, respectively; A reduction in crude extract-induced inhibition of -1.66 (α-amylase) and 27.06% (α-glucosidase)	77
<i>Zingiber officinales</i>	Round and 123.8 nm in size	Gingerols and other volatile oils, such as monoterpenes, primarily neral and geranial, and sesquiterpenes, such	Biochemical characteristics of rats with STZ-induced diabetes	After seven days of treatment, blood glucose levels recovered to normal (86 mg/dl), and body weight climbed to	78



		as (-) zingiberene and bbisabolene		200 mg/kg.	
<i>Aloe barbadensis</i>	Spherical and 10-30 nm in size	Aloe-emodin, aloin	alpha-glucosidase and antioxidant activity	lowering of blood glucose, enhancement of insulin sensitivity, and inhibition of the α -glucosidase enzyme	79

Table 2: Silver nanoparticles' green production and in vitro antidiabetic effects.

Source	Plant Parts (stem, roots, leaves, flower)	NPs Form (Ag)	Approach	Characterization	size	Antidiabetic activity	Reference
<i>Z. officinale</i> and <i>C. amada</i>	Area of sprouting	AgNP	Ten minutes of centrifugation at 5000 rpm	FTIR, SEM, XRD, EDS, and UV/Vis	round in form (25–30 nm)	<i>Z. officinale</i> has 55.10% and 57.50% α -glucosidase or α -amylase activity, respectively, whereas <i>C. amada</i> AgNPs exhibit 65.40% and 68.78%.	80
<i>P. marsupium</i>	wood and bark	AgNP	The aqueous solution of AgNO ₃ and its yellow-to-brown color change	FTIR and UV/Vis	148.5 nm is the average particle size.	<i>Pterocarpus marsupium</i> , with an IC ₅₀ value of 700 μ g/ml, exhibited amylase inhibition of 41.44% at a lower concentration and 71.14% at a higher concentration.	81
<i>A. cepa</i>	Bulbs	AgNP	After centrifuging 20 mL of extract and 50 mL of 0.1M AgNO ₃ for 30 minutes at 3000 rpm, the color changed from yellow to	TEM, UV/Vis and SEM	Round form (49–73 nm)	The suppression activity of 40 μ g/mL on α -amylase and α -glucosidase was found to be 23% and 45%, respectively, in	82



			brown.			an in vitro assessment.	
<i>P. guajava</i>	Leaf extract	AgNP	Psidium guajava extract (5 mL), AgNO ₃ solution (1 mL), followed by centrifugation at 15,000 rpm for 20 minutes, and then incubation at 38°C	SEM, FTIR, and UV/Vis,	round in form (52.12–65.02 nm)	BGL decreased from 243 ± 1.6 to 109.7 ± 0.88 while body weight rose from 196.7 ± 3.8 to 209 ± 2.38 after in vivo evaluation of Psidium guajava NPs (400 mg/kg) on the twenty-first day.	83
<i>P. niveum</i>	Whole plant	AgNP	At pH 11, an alcoholic (100 mg) extract and an AgNO ₃ solution (1 mM) showed green hue.	FTIR, XRD, SEM, EDS, and UV/Vis	Shaped like a sphere (21 nm)	Body weight lose from 142 to 150 on the twenty-first day of the in vivo study, while blood glucose levels decreased from 265 mg/dL to 140 mg/dL at a dosage of 10mg/kg.	84
<i>G. pomace</i>	Extract from fruit waste	AgNP	AgNO ₃ (1 mM), grape extract, stirring, centrifugation at 12,000 rpm, and light to dark brown coloring	Zeta potential, FTIR, UV/Vis, EDS, and HTEM	spherical form (15–20 nm)	The IC ₅₀ values for α-glucosidase and α-amylase are 43.94 μg/mL and 48.5 μg/mL respectively.	85
<i>A. officinalis</i> , <i>L. and X. granatum</i> , <i>m J.</i>	Extract from leaves and bark	AgNP	Before being rinsed with water and dried at 50 OC, the AgNO ₃ solution (10Mm) and extracts were centrifuged at 10,000rpm for 20 minutes.	DLS, FTIR, UV/Vis, SEM and XRD	Clusters as well as polydispersed (0–1000 nm)	AgNPs from X. granatum and A. officinalis have α-amylase activities of 35.51 to 89.5% and 18.21 to 76.13%, respectively.	86
<i>C. viscosa</i>	the entire plant	AgNP	When heated to 26 ± 2°C, the aqueous extract +	FTIR, TEM, SEM, XRD, and UV/Vis	circular, rod-shaped,	α-glucosidase or α-amylase inhibition with 3	87



			1, 2, and 3 mL AgNO ₃ turned from light green to dark brown.		and triangular, with an average size of 24 nm	mL. AgNPs have respective IC ₅₀ values measured at 21.92 ± 1.74 mg/mL along with 1.76 ± 1.91 mg/mL, with 57.62% and 90.14%.	
<i>E. phyllanthus</i>	Extract from leaves	AgNP	Following the extraction of 5 mL of AgNO ₃ solution, stirring, and The tint shifted from pale yellow to brownish after centrifugation at 5000 rpm.	XRD, AFM, SEM, EDX, and UV/Vis	globular form (25–55 nm)	The level of glucose dropped from 280.83 ± 4.17 to 151.17 ± 3.54 mg/dL.	88
<i>C. tsoi</i>	Extract from leaves	AgNP	Heat two milliliters of 5 mM AgNO ₃ with leaf extract, and stir the mixture.	DLS, SAED, XRD, UV/Vis, TEM, SEM	spherical, triangular, and hexagonal (10 nm to 20 nm)	The activity of α -amylase and α -Glucosidase activity rose from 45 ± 0.83 to 93 ± 1.09 and from 57 ± 1.35 to 80 ± 1.54 as the concentration increased from 10 to 75 μ g/mL.	89
<i>E. thyrsoideum</i>	Complete plant extract	AgNP	Centrifugation at 12,000 rpm with plant extract, 15 mL of AgNO ₃ , and a yellow color change	UV/Vis, SEM, FTIR, TEM, EDX and XRD	Round form (10 nm)	On the seventh and fifteenth days after receiving AgNPs, diabetic rats' fasting blood sugar (FBS) dropped.	90
<i>C. tomentosum</i>	Extract from leaves	AgNP	After adding 10 mL of AgNO ₃ , 5g of desiccated leaf, and 20 mL of distilled water, the color turned from pale green to dark	FTIR, XRD, EDX, and UV/Vis	Face-centered cubic form	β -glucosidase and α -amylase are 19% and 50%, respectively.	91



			brown.				
<i>S. enterica</i>	Filter of culture	AgNPs	The production of NPs is confirmed by AgNO ₃ , centrifugation, stirring for 12 hours, and color change.	SEM, EDX, or UV/Vis, FTIR, TEM	Round form (7.18–13.24 nm)	When AgNPs (3 mL) were utilized, the IC ₅₀ values for α -amylase and α -glucosidase were 428.60 μ g/mL and 562.02 μ g/mL, respectively.	92

Table 3: Silver nanoparticles' green production and in-vitro antidiabetic effects.

Plant	Nanoparticles	Pharmacological activity	Dose	Model used	Reference
<i>Azadirachta indica</i> (Neem), Seeds	AgNPs	antidiabetic activity	(10 to 40 mg/kg b.w)	Mice	93
<i>Phagnalon niveum</i> belongs to the family Asteraceae.	AgNPs	Anti-diabetic activity	12 to 28 nm, with an average of 21 nm	Wistar rats	94
<i>Thymus serpyllum</i>	AgNPs	Anti-diabetic activity	42 nm , 10 mg/kg	BALB/c mice	95
<i>Psidium guajava</i> Leaf Extract	AgNPs	Anti-diabetic activity	(100 mg/kg) w	(STZ) rats	96
<i>Momordica charantia</i> (MC)	AgNPs	Anti-diabetic activity	Both 100 and 200 mg kg ⁻¹ are commonly used.	The study involved Wistar rats with diabetes, which was induced by streptozotocin.	97
<i>Tribulus terrestris</i> Seeds	AgNPs	Anti-diabetic activity	75.68 \pm 0.11% at 100 μ g/ml	streptozotocin-induced diabetic mice	98



4. CHALLENGES ASSOCIATED WITH AgNPs

Although research has been promising in relation to the antidiabetic potential of AgNPs, there are notable barriers to their use. One big issue is the potential toxicity of AgNPs which leads to cytotoxicity and genotoxicity.

Second, there is some challenge in that AgNPs are poorly pharmacokinetically characterized in terms of bioavailability which hampers their maximum performance in exhibiting antidiabetic properties.

Furthermore, their antidiabetic efficacy could be decreased if they interact with other pharmaceutical preparations. Cost and scalability of AgNP manufacturing is also a significant concern.

Finally, regulations-permitting approval and safety standards-must support the use of AgNPs as antidiabetic agents [99].

5. FUTURE PROSPECTIVES

Silver nanoparticles (AgNPs) are recently gaining huge spotlight for their role in treating diabetes and other pathologies. AgNPs have been given significant opportunities in biology and medicine due to their minute dimensions, extensive surface area, and ability to engage with biomolecules. Furthermore, it has been reported that AgNPs exert antidiabetic effects by modulating a wide array of metabolic processes associated with glucose metabolism. In conclusion, silver nanoparticles might become the perfect and available antidiabetic drug in the future, offering better patient results and safety and efficacy.

The increasing recognition of green chemistry and the utilization of plant extracts in metal nanoparticle synthesis are driving the advancement of eco-friendly methods. The economical, energy saving, and eco-friendly approach of synthesizing silver nanoparticles using plant extracts offers numerous benefits, including healthier work environments, reduced waste, and safer products. This approach can overcome the lengthy process of utilizing microbes, which may diminish their effectiveness in nanoparticle synthesis.

CONCLUSION

The aim of this study is to deliver a comprehensive and relevant analysis of the current research status on the

synthesis, biological activities, and characterization of AgNPs in the management of diabetes. It also reports the challenges faced in using AgNPs as antidiabetic drugs and their mode of action toward glucose metabolism.

Medicinal plants are known to manufacture hundreds of bioactive compound, which can be use for eco-friendly synthesis of silver nanoparticles. With rapid increase in global population, diseases are becoming more and more common, making the green synthesis more economical, safe, and viable for mankind. Among the metallic nanoparticles, silver has been extensively researched owing to its anticancer properties against diabetes. Although the action modes of these nanomaterials are similar to those of standard preparations, this still needs additional investigation into their mechanism of action in diabetes.

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