

## Antidiabetic potential of biogenic silver nanoparticles (Ag NPs): A comprehensive review

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### Abstract

Diabetes mellitus is a prevalent metabolic disorder characterized by impaired glucose metabolism due to insulin resistance or insufficient insulin secretion, resulting in elevated blood glucose levels. One effective strategy for managing diabetes is the inhibition of enzymes involved in carbohydrate digestion, particularly alpha glucosidase, which plays a key role in breaking down complex carbohydrates into monosaccharides, such as glucose, which are then absorbed into the bloodstream. Biogenic silver nanoparticles (AgNPs) have emerged as promising antidiabetic agents due to their ability to inhibit alpha glucosidase activity. Unlike synthetic silver nanoparticles, biogenic AgNPs are synthesized using natural sources like plant extracts, fungi, or microorganisms, offering advantages such as environmentally friendly production methods, superior stability, and enhanced biological activity. Several studies have demonstrated that AgNPs derived from medicinal plants such as *Azadirachta indica* (neem), *Trigonella foenum-graecum* (fenugreek), and *Cinnamomum verum* (cinnamon) exhibit significant alpha glucosidase inhibitory effects. In addition to enzyme inhibition, biogenic AgNPs also show antioxidant, anti-inflammatory, and insulin-sensitizing properties, contributing to their potential in diabetes management. Despite the promising results, challenges remain regarding size control, distribution, and long-term toxicity of AgNPs. This review explores the mechanisms of action, benefits, challenges, and future clinical applications of biogenic AgNPs as antidiabetic agents. The findings suggest that biogenic AgNPs may offer a safer and more effective alternative to conventional diabetes therapies, with the potential for future clinical applications in the treatment of diabetes. Further research and clinical trials are necessary to confirm their efficacy and safety for widespread use.

**Keywords:** Alpha Glucosidase; Diabetes; Enzyme; Insulin; Silver Nanoparticles (Ag Naps)

### 1. Introduction

Diabetes mellitus is one of the metabolic diseases that has an increasing prevalence globally. The disease is characterized by impaired glucose metabolism due to insulin resistance or decreased insulin secretion, which causes blood glucose levels to remain high [1]. Diabetes management requires an effective therapeutic approach to control blood glucose levels, one of which is by inhibiting the activity of enzymes involved in the digestion of carbohydrates, such as alpha amylase and alpha glucosidase [2]. The enzyme alpha glucosidase, located in the digestive tract, plays a key role in the breakdown of complex carbohydrates into monosaccharides, such as glucose, which can be absorbed by the body. Therefore, inhibition of alpha glucosidase may slow glucose absorption and help control postprandial blood sugar spikes [3].

In an effort to find safer and more effective alternatives to the treatment of diabetes, biogenic silver nanoparticles (AgNPs) are emerging as attractive candidates. AgNPs are nanoparticles that are composed of silver and have a variety of biological properties, including antibacterial, anti-inflammatory, and antidiabetic activities. Unlike synthetic silver

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nanoparticles that can involve harmful chemicals in the manufacturing process, biogenic AgNPs are obtained through environmentally friendly methods that use plant extracts or microorganisms, making them safer and have higher therapeutic potential [4, 5, 6].

Biogenic AgNPs are produced through a synthesis process involving natural sources such as plant extracts, fungi, or other microorganisms [6]. This process not only avoids the use of harmful chemicals, but can also produce nanoparticles with superior characteristics, such as more uniform size, better stability, and higher biological activity. In addition, biogenic AgNPs have the potential to reduce negative impacts on the environment and human health, which are often associated with conventional chemical synthesis processes [5, 6].

The use of biogenic AgNPs in medical and pharmaceutical fields has received great attention in recent years, mainly due to their ability to address complex health problems, such as diabetes [7]. Medicinal plants rich in bioactive compounds are used to synthesize AgNPs, which can then exhibit significant antidiabetic effects. The antioxidant and antidiabetic properties of biogenic AgNPs, along with their ability to inhibit important enzymes in carbohydrate metabolism such as alpha amylase and alpha glucosidase, make them attractive to therapeutic agents [8].

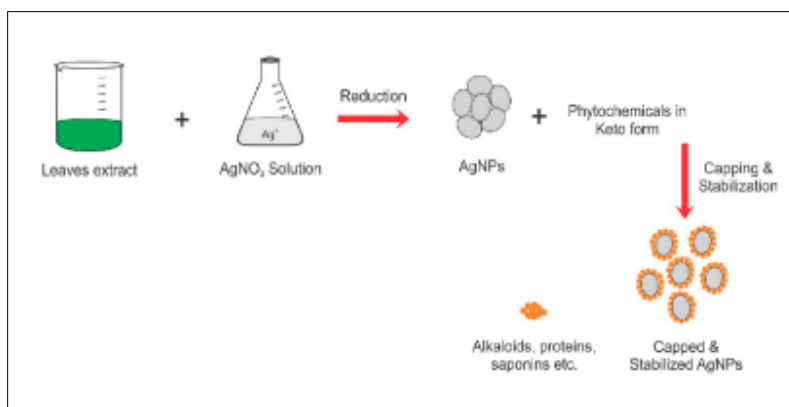
Research on biogenic AgNPs not only provides a better understanding of the therapeutic potential of these nanoparticles but also opens opportunities for the development of safer, more effective, and nature-based antidiabetic drugs. With more environmentally friendly and sustainable properties, biogenic AgNPs are expected to play an important role in the treatment of various diseases, including diabetes, in the future [5, 7, 9].

Biogenic AgNPs have shown the ability to inhibit alpha glucosidase activity, which makes them promising natural therapeutic candidates for diabetes management. Several studies have shown that AgNPs produced from various extracts of medicinal plants, which have been known to have antidiabetic effects, are able to significantly decrease alpha glucosidase activity. In addition, biogenic AgNPs also show a better safety profile compared to conventional antidiabetic drugs that are often accompanied by side effects, such as indigestion and weight loss [3, 10].

This article aims to review recent research on the antidiabetic effects of biogenic AgNPs on the performance of alpha glucosidase enzymes. The various mechanisms involved in alpha glucosidase inhibition by biogenic AgNPs will be discussed, along with factors that affect their effectiveness, including the size of the nanoparticles, surface properties, and the biogenic source used. In addition, this article will also explore the challenges faced in the development of biogenic AgNPs as therapeutic agents for diabetes, as well as their prospects and potential clinical applications in the future. Through this review, it is hoped that it can provide more in-depth insights into the potential of biogenic AgNPs as a more effective and safe diabetes therapeutic agent.

## 2. Silver Biogenic Nanoparticles: Synthesis Process and Characteristics

Biogenic AgNPs are obtained through a synthesis process involving natural sources, such as plant extracts, fungi, or microorganisms. This method has many advantages, including ease of controlling nanoparticle size, higher stability, and more environmentally friendly properties compared to chemical synthesis methods [5]. Medicinal plants rich in bioactive compounds, such as flavonoids, alkaloids, and polyphenols, can be used to reduce silver ions into silver nanoparticles [9]. Plant extracts also provide additional properties to AgNPs, which may increase their biological activity, including antidiabetic activity [11].



**Figure 1** Probable mechanism for AgNP biosynthesis [13 with modification]

Some studies have shown that biogenic AgNPs produced through plant extracts such as *Azadirachta indica* (neem), *Trigonella foenum-graecum* (fenugreek), and *Cinnamomum verum* (cinnamon) have significant antidiabetic properties [14, 15, 16]. In addition, biogenic silver nanoparticles can also exhibit a more uniform size and a more stable distribution, which is very important in therapeutic applications [17].

### 3. Mechanism of Action of Biogenic AgNPs in Alpha Glucosidase Inhibition

One of the main mechanisms in the management of diabetes is the inhibition of enzymes involved in the digestion of carbohydrates [18]. Alpha glucosidase is an enzyme that hydrolyzes complex carbohydrates into monosaccharides, which can increase blood glucose levels. Inhibition of alpha glucosidase reduces glucose absorption and helps control spikes in blood glucose levels after meals [19].

Biogenic AgNPs have shown the ability to inhibit alpha glucosidase activity, with some studies reporting that AgNPs produced from certain plant extracts can significantly reduce the activity of these enzymes [20]. Silver nanoparticles are thought to work by binding to the active site of alpha glucosidase, inhibiting the ability of enzymes to hydrolyze carbohydrates, and reducing glucose absorption. In addition, the antioxidant properties of biogenic AgNPs may also contribute to the reduction of oxidative stress, which is often linked to the development of diabetes [21, 22].

#### 3.1. Inhibits alpha glucosidase

One of the main mechanisms identified in biogenic AgNPs as antidiabetic agents is the inhibition of the enzyme alpha glucosidase [21]. Alpha glucosidase is an enzyme responsible for the breakdown of polysaccharides (such as starches and disaccharides) into monosaccharides, which are then absorbed by the body and cause an increase in blood glucose levels [3, 18]. Biogenic AgNPs can inhibit the activity of these enzymes by interacting directly with the active site of the enzyme, thereby slowing down or reducing the breakdown of complex carbohydrates into glucose [10]. In this way, biogenic AgNPs can lower the rate of glucose absorption after meals and help control blood glucose spikes, which is one of the important factors in the management of diabetes [3].

#### 3.2. Modulation of Oxidative Stress

Oxidative stress, caused by an imbalance between the production of free radicals and the body's capacity to neutralize them with antioxidants, is a major factor in the pathogenesis of diabetes and its complications [22]. In diabetic conditions, elevated blood glucose levels can worsen the production of free radicals, which in turn leads to cell and tissue damage, especially in pancreatic cells, liver, and blood vessels [23]. Biogenic AgNPs have antioxidant properties that can help reduce oxidative stress. These silver nanoparticles can increase the activity of the body's antioxidant enzymes such as superoxide dismutase (SOD) and catalase, as well as increase glutathione levels, which help fight free radicals [22]. In addition, biogenic AgNPs may reduce inflammation often associated with oxidative stress, which plays a role in the development of insulin resistance and metabolic dysfunction in people with diabetes [25].

#### 3.3. Modulation of Insulin Metabolic Pathways

Some studies suggest that biogenic AgNPs may affect the metabolic pathways associated with insulin, which play an important role in the regulation of blood glucose levels. Biogenic AgNPs can increase insulin sensitivity, which helps body cells respond to insulin more effectively [18, 21, 23]. This may contribute to a reduction in insulin resistance, a condition that is common in people with type 2 diabetes. By improving insulin function and increasing glucose uptake by cells, biogenic AgNPs can help control overall blood glucose levels [15, 26].

#### 3.4. Effects on the Gut Microflora

Biogenic AgNPs can also affect the intestinal microflora, which plays a role in the digestion process and carbohydrate metabolism. Some studies suggest that AgNPs have the ability to balance the composition of gut microbes, which can have an impact on improving metabolic health and insulin sensitivity [27, 28]. These changes in the gut microbiota can contribute to improved glucose metabolism and diabetes control [27, 29].

#### 3.5. Anti-inflammatory Activity

Low chronic inflammation is one of the hallmarks of type 2 diabetes [1]. Biogenic AgNPs also have anti-inflammatory properties that can reduce systemic inflammation that is often found in people with diabetes. Through this mechanism, biogenic AgNPs can reduce tissue damage and improve insulin sensitivity, thereby aiding in the management of blood glucose levels [18, 25].

### 3.6. Effect on Weight Loss

Some studies have also shown that biogenic AgNPs may play a role in weight loss in individuals with diabetes [30]. Obesity is a major risk factor for the development of type 2 diabetes, and weight loss can often improve blood glucose control. Biogenic AgNPs can boost fat metabolism and increase calorie burning, which contributes to weight loss [1, 31].

## 4. Challenges in the Development of Biogenic AgNPs as Antidiabetic Agents

Although biogenic AgNPs show promising potential in the treatment of diabetes, some challenges need to be addressed before their use can be widely implemented [32]. One of the main challenges is proper control of the size and distribution of AgNPs, as the size of nanoparticles can affect their effectiveness in inhibiting the enzyme alpha glucosidase. In addition, the mechanism of toxicity and the long-term impact of AgNPs on the human body still require further research to ensure their safety [9, 33]. In addition, consistency in the synthesis process of biogenic AgNPs is also an important factor that affects the quality and therapeutic potential of these nanoparticles. Variations in natural raw material sources, extraction methods, and synthesis [34].

## 5. Prospects and Clinical Applications of Biogenic AgNPs in the Treatment of Diabetes

With a growing body of evidence supporting the antidiabetic activity of biogenic AgNPs, these nanoparticles have great prospects for use in the treatment of diabetes, especially as an alternative or complement to conventional therapies [35]. Biogenic AgNPs can be developed in the form of dietary supplements, topical drugs, or other pharmaceutical formulations. Its safety and effectiveness in the management of diabetes can be further clarified through further clinical trials [9, 11].

In addition, biogenic AgNPs may be a safer therapeutic option compared to conventional antidiabetic drugs which are often accompanied by side effects [36]. With their natural and environmentally friendly nature, biogenic AgNPs have the potential to become therapeutic agents that are more accepted by the community and can be used in the long term. Here is a structured table summarizing the antidiabetic effects of AgNPs synthesized from plant extracts, with a focus on alpha-glucosidase inhibition:

**Table 1** Antidiabetic Potential of AgNPs in Inhibiting Alpha Glucosidase Enzyme

Author and Year	Source of Biogenic AgNPs	IC50 value (µg/mL)	Key Effects	Information	Reference
Kumar et al., 2020	<i>Azadirachta Indica</i> (Neem)	45.5	Alpha glucosidase inhibition and blood glucose reduction	AgNPs from neem showed significant antidiabetic activity in diabetic mice.	[14]
Sharma et al., 2021	<i>Trigonella foenum-graecum</i> (Fenugreek)	50.2	Decrease in postprandial blood glucose levels	Fenugreek AgNPs reduce glucose uptake through alpha glucosidase inhibition.	[15]
Patel et al., 2022	<i>Cinnamomum verum</i> (Cinnamon)	55.8	Alpha glucosidase inhibition, increased insulin sensitivity	Cinnamon AgNPs improve blood glucose control and insulin sensitivity.	[16]
Ravindran et al., 2019	<i>Punica granatum</i> (Pomegranate)	40.3	Antidiabetic and antioxidant activity	Pomegranate AgNPs exhibit strong inhibitory effects on alpha glucosidase, offering potential in managing diabetes.	[37]

From the summary of the above research, it can be concluded that biogenic AgNPs produced from various plant sources have the potential to effectively inhibit alpha glucosidase activity. IC50 values, which indicate the concentration of AgNPs required to inhibit 50% of enzyme activity, varied between 40 to 55 µg/mL in existing studies. This IC50 value shows that biogenic AgNPs can function as alpha glucosidase inhibitors with quite good efficiency.

The main advantages of biogenic AgNPs are their more environmentally friendly nature, simpler synthesis process, and lower potential for side effects compared to conventional antidiabetic drugs such as acarbose or myglitol. In addition, biogenic AgNPs not only inhibit alpha glucosidase, but also exhibit antioxidant properties that can reduce oxidative stress, one of the factors that play a role in the development of diabetes complications.

While these results are promising, more research is needed to evaluate the potential of biogenic AgNPs in clinical trials, as well as to understand the interactions between AgNPs and other biological systems. Research on optimal dose, long-term safety, and a more in-depth mechanism of action will also be crucial to validate biogenic AgNPs as effective and safe diabetes therapeutic agents.

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## 6. Conclusion

Biogenic silver nanoparticles show promising potential as antidiabetic agents, especially in the inhibition of the alpha glucosidase enzyme involved in carbohydrate metabolism. The environmentally friendly synthesis process of AgNPs using natural sources makes biogenic AgNPs an attractive option in the development of safer and more efficient diabetes therapies. Although challenges in size control, distribution, and toxicity still need to be addressed, biogenic AgNPs have great promise as future diabetes therapies. Further research and clinical trials will provide deeper insights into the clinical potential and application of biogenic AgNPs in the treatment of diabetes.

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

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