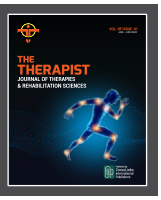
DOI: https://doi.org/10.54393/tt.v7i01.301

THE THERAPIST
JOURNAL OF THERAPIES & REHABILITATION SCIENCES
https://thetherapist.com.pk/index.php/tt
ISSN (E): 2790-7406, (P): 2790-7414
Volume 07, Issue 01 (Jan - Mar 2026)



Review Article

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Diet Therapy of Diabetes Type II by Paneer Dodi (*Withania coagulans*): A Review

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ARTICLE INFO

Keywords:
Withania coagulans, *Withanolides*, Diet Therapy, Diabetes Mellitus, *Ecoagulin*

How to Cite:
Saeed, M. K., Zahra, N., Khan, A., Anjum, S., Ijaz, A., Shahzad, K., & Ahmad, I. (2026). Diet Therapy of Diabetes Type II by Paneer Dodi (Withania coagulans): A Review: Diet Therapy of Diabetes Type II by Paneer Dodi (Withania coagulans). THE THERAPIST (Journal of Therapies &Amp; Rehabilitation Sciences), 7(01), 03-10. https://doi.org/10.54393/tt.v7i01.301

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Received Date: 4th February, 2026
Revised Date: 26th March, 2026
Acceptance Date: 29th March, 2026
Published Date: 31st March, 2026

ABSTRACT

Globally, chronic non-communicable diseases are currently the leading cause of mortality and disability. People of various ages and socioeconomic backgrounds are affected by this diverse set of illnesses, which includes diabetes, cancer, chronic respiratory disorders, and cardiovascular diseases. Paneer Dodi is a member of the *Solanaceae* family and is scientifically known as *Withania coagulans*. Patients with diabetes, particularly those with type-2 diabetes, can benefit greatly from this enchanted herb. It aids in controlling oxidant status, kidney pro-inflammatory indicators, and blood sugar levels. The plant contains free amino acids, esterases, alkaloids, and a variety of *withanolides*, including *withanolide A*, *withanolide D*, *withanolide E*, *coagulins*, and *withacoagulins*. *W. Coagulans* is a potential natural substitute for synthetic drugs, which often have adverse effects, given the high incidence of diabetes mellitus. It works as an efficient antidiabetic by inhibiting the enzymes α-glucosidase and α-amylase, stimulating insulin secretion, increasing glucose absorption, and regenerating pancreatic β-cells. In diabetic patients, these measures help control hyperglycemia and improve lipid profiles. According to the review, *W. coagulans* shows promise for research and development of novel therapeutic products, such as antidiabetic tea, for diabetes diet therapy.

INTRODUCTION

Herbal remedies are a priceless gift from nature and are in high demand on the global market. According to estimates from the World Health Organization (WHO), over 80% of people worldwide use plant-based medications on a regular basis due to their high efficacy and relatively low adverse effects when compared to synthetic medications. Plant-based medications are often seen as more environmentally friendly and humane than synthetic medicines. Plants are potent therapeutic agents because they contain antioxidants and beneficial compounds. One of the most significant medicinal plants is *Withania coagulans* (Paneer Dodi), which is a member of the *Solanaceae* family and genus Withania [1]. The two species of *Withania*, *W. somnifera* and *W. coagulans*, are found throughout South Asia, the Eastern Mediterranean, and Pakistan. The plant's greyish-yellowish branches can be used to identify it. It usually has tall calyx, corolla, petioles, and leaves (Figure 1).

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Figure 1: *Withania coagulans* (Paneer Dodi) Plant

The berries are yellowish brown, the seeds are brown, and the flowers are dioecious [2]. Coagulin L from *W. coagulans* fruits exhibits antihyperglycemic activity, and the fruit of *W. coagulans* (Paneer Dodi), also known as "tukhm-e-hayat" ("fruit of life"), showed hypoglycemic activity, which is a safe and effective alternative treatment for diabetes. In type II diabetic mice, it demonstrated pharmacological effects on blood glucose, lipid profile, and body weight, resulting in a considerable reduction in blood glucose and total cholesterol [3, 4] (Figure 2).

Figure 2: *Withania coagulans* (Paneer Dodi) fruit and Source

Additionally, the plant has been shown to have a variety of other properties, such as hepatoprotective, immunosuppressive, cytotoxic, antifungal, antibacterial, anti-inflammatory, wound healing, and free radical scavenging (Figure 3).

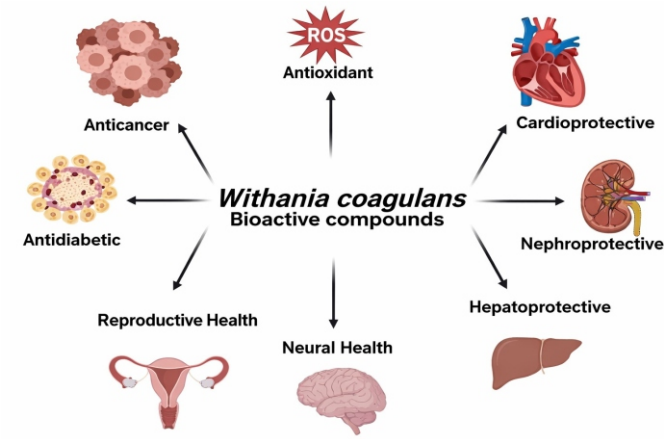

Figure 3: Pharmacological Activities of *Withaniacoagulans* (Paneer Dodi)

Different plant parts exhibit multiple pharmacological effects; however, antidiabetic activity is specifically evaluated using biomarkers such as fasting blood glucose, HbA1c, insulin levels, and lipid profiles to ensure disease-specific assessment [6]. This plant exhibits a wide range of biological activities in several sections. Wounds are frequently treated with the sweet-tasting fruits of *W. coagulans*. The fruits are also used to treat asthma and liver problems. The seeds are used as an emmenagogue and diuretic, as well as to cure liver disease, piles, and ophthalmia. The leaves and roots of *W. coagulans* are used locally to cure a range of illnesses, although flowers have been traditionally reported for antidiabetic use, studies indicate that fruits are the most commonly used part for managing diabetes due to their higher concentration of bioactive compounds [7]. This herb is typically prescribed by practitioners of herbal medicine, including Ayurvedic and Unani specialists, as well as integrative medicine professionals. One of the most common and well-known metabolic diseases, diabetes mellitus, has a variety of causes, such as chronic hyperglycemia and abnormalities in the body's metabolism of carbohydrates, fats, and other substances brought on by low blood insulin levels or insensitivity of specific organs to insulin [8]. *Withani acoagulans* is primarily found in South Asia and the Middle East. Although not universally available, it can be accessed globally through herbal markets and commercial formulations. It is a chronic illness that affects people from all walks of life. The number of people with diabetes is rising due to modern, busy lifestyles; some of these people are even in their 30s and 40s. Increased stress and poor eating habits with a growing reliance on junk food are among the culprits. Other variables that are contributing to the rising incidence of diabetes in young people include smoking and increased tobacco use, pollution, and heredity. It is a multifactorial human metabolic disorder that is a global concern and is typified by high blood glucose levels. Many

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people have been affected, especially in developing countries like Pakistan, which currently has the third-highest diabetes burden globally [9]. According to estimates from the International Diabetes Federation (IDF), 537 million people worldwide had diabetes in 2021, making up 10.5% of the population and requiring $966 billion in medical treatment. By 2045, this healthcare cost is predicted to surpass $1054 billion. Diabetes is expected to affect 529 million people globally by 2023 and 1.3 billion by 2050 [10].

Roughly 90–95% of all cases of diabetes are type 2 diabetes mellitus (T2DM), the most common kind. It is mainly associated with genetic predisposition, sedentary lifestyle, and obesity. T2DM results in pancreatic β-cell dysfunction and peripheral organ resistance to insulin, which impairs glucose absorption and raises blood glucose levels [11]. Due to the complex relationship between these conditions and increased susceptibility to CVD, stroke, and other co-morbidities, effective management strategies would need to be implemented. Among metabolic syndrome instances, hypoglycemic or hypolipidemic medications that lower blood sugar or cholesterol rate highly effective [12]. Pharmaceutical sciences have recently synthesized numerous new antidiabetics and antidyslipidemic medications, which are described during the development process from various natural product chemistries. The search for safe, effective, and natural therapeutic approaches has coincided with the rising global prevalence of diabetes and hyperlipidemia [13]. Insulin therapy, oral hypoglycemic medications, and lifestyle modifications are current methods for managing diabetes. Due to adverse effects, high prices, and the progressive nature of the disease, many patients still struggle to attain adequate glycemic control despite the availability of these medications. To provide safer and more effective antidiabetic drugs, there is an increasing interest in studying alternative therapies, especially those that come from natural sources [14]. Diabetes has long been treated using herbal medicine in traditional systems. The plant *Withania coagulans,* often known as Paneer dodi, has drawn interest due to its possible ability to prevent diabetes. According to a preliminary study, *Withania coagulans* exhibits notable hypoglycemic activity, which is attributed to its bioactive constituents, including withanolides. This study is noteworthy because it integrates conventional knowledge with modern pharmaceutical methods, which may lead to a safe and efficient substitute for managing diabetes [15]. To improve patient participation, awareness programs, physician guidance, and integration of herbal medicine with conventional therapy are essential. Ensuring safety, scientific validation, and regulatory approval can further enhance public trust in herbal-based interventions. The main objective of the various antidiabetic medications that have been reported in the literature is to control the glycemic state in individuals with diabetes. Many synthetic antidiabetic drugs have significant side effects that restrict their long-term use, despite their effectiveness. For instance, metformin is widely used, but up to 50% of people may have nausea, diarrhea, or stomach discomfort. While Glipizide may cause hypoglycemia, weight gain, nausea, diarrhea, allergic reactions (including rash or eczema), and, in rare instances, SIADH with hyponatremia, thiazolidines (TZDS) may cause weight gain, fluid retention, and congestive heart failure [16]. Synthetic medications are not appropriate for long-term or widespread use due to their side effects and their high cost, particularly in low-income settings. Interest in affordable and well-tolerated plant-derived antihyperglycemic drugs has increased due to these disadvantages as well as the rising prevalence of drug-induced hypoglycemia and the cost of long-term therapy [17]. In this regard, herbal remedies like *Withania coagulans* and nutraceuticals have become viable options for treating diabetes. Because of their natural origin, multi-targeted strategy, and few side effects, they are perfect for long-term use, particularly in places with limited resources.

The number of large-scale, context-specific, and longitudinal studies that evaluate the effectiveness of therapeutic interventions in the long term in different populations is insufficient. The most crucial issue is to find out whether these interventions are effective and consistent in various clinical settings and patient differences. Although *Withania coagulans* fruit is widely used in traditional medicine, little is known about its bioactive components. This study aims to outline what is already known about its antidiabetic potential and to promote further research on diet therapy as a safe and effective alternative treatment for diabetes mellitus.

Withanolides Compounds

The chemical name for a lactone, "olide," is combined with "withan" from the genus Withania to create the structural identifier "withanolide." The withanolide skeleton is 22-hydroxyergostan-26-acid-26,22-lactone, 3, in addition to withanolides A, D, and E (Figure 3).

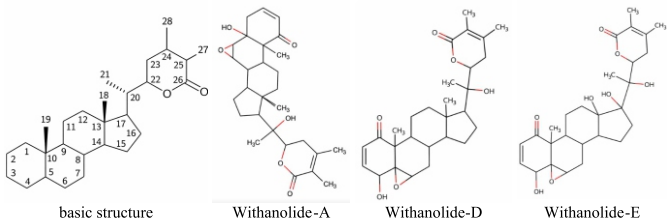

Figure 4: The Chemical Name for a Lactone

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Numerous novel structural variations, including anodizations, result from changes to the carbocyclic backbone or side chains. Lactone steroids known as withanolides are the main bioactive phytoconstituents that were extracted from *W. coagulans*. Several withanolides, including as *coagulin F, coagulanolide, withacoagulin*, and *coagulin G*, are found throughout the entire *W. coagulans* plant. These withanolides have anti-inflammatory, anti-diabetic, antimicrobial, and immunosuppressive properties. Furthermore, examples of withanolides include *withaferin A, withanolide D, withanolide E, withanolide H, withanolide K, withanolide A, withacoagulin H, withanolide J*, and *withanolide I. Pharmacological* effects of all the steroidal lactones [18]. The study presents the chemical components of *W. coagulans* (Paneer Dodi) fruits (Table 1).

Table 1: Demographic Characteristics (Age and BMI)

Sr. No.	Chemical Constituent	Specific Chemicals	Role
1	Withanolides	- Coagulin F (27-hydroxy-14,20-epoxy-1-oxo-(22R) -witha-3,5,24-trienolide)-Coagulin G (17beta,27-dihydroxy-14,20 -epoxy-1-oxo-(22R)-witha-2,5,24-trienolide) -Withacoagulin (20(β)-hydroxy-1-oxo-(22R)-witha-2,5,24 -trienolide)	These steroidal lactones have adaptogenic, anti-inflammatory and anti-cancer effects. They improve immunity and help control stress reactions.
2	Esterases	- Various Esterase Enzymes	Aids in the coagulation of milk, which is necessary for the production of cheese.
3	Free Amino Acids	-Proline -Tyrosine - Glycine	Vital for metabolic processes and the production of proteins.
4	Fatty Acids	- Linoleic acid (C18H32O2) - Oleic acid (C18H34O2)	Vital for supplying energy and preserving the integrity of cell membranes; they also contain anti-inflammatory properties.
5	Alkaloids	- Withanine	It is utilized in traditional medicine and has analgesic and anti-inflammatory properties.

Mechanism of Action of Withanolide

Withanolide A works as an effective antidiabetic by inhibiting the enzymes α-glucosidase and α-amylase, suppressing hemoglobin glycosylation, stimulating insulin synthesis, increasing glucose absorption, and regenerating pancreatic β-cells. These actions serve to manage hyperglycemia and enhance lipid profiles by lowering LDL, VLDL, and triglycerides while boosting HDL levels [19]. Another researcher described how the plant *W. coagulans's* aqueous extract stimulated the release of insulin from pancreatic β-cells, which resulted in a glucose-lowering effect. When compared to untreated cells, cells treated with the extract secreted nearly twice as much insulin [20].

Antihyperglycemic Activity of Paneer Dodi

There have been reports of plant extracts exhibiting anti-diabetic qualities throughout the last ten years. Indian cheese has historically been made by coagulating milk with its extract. One of the plants that has been utilized in medicine is this one. its many medicinal qualities. If these extracts are proven to be safer and more successful than current medications, their use in the treatment of diabetes may be chosen. The traditional method of consuming the extract is to soak the fruit in water for the entire night. However, the strong odor and bitter taste make it difficult to consume the amounts required to produce health benefits. The fruits of *W. coagulans* may be causing the increased glucose level to drop. After a detailed investigation of the powdered ethanolic extract of *Withania coagulants* fruits, a formulation containing the plant material was created, making it more palatable and suitable for diabetics. The efficacy of this plant in the treatment of diabetes is demonstrated by notable outcomes from an in vitro anti-diabetic analysis of a tablet formulation [20]. The important presence of Mg and Ca in *W. coagulans* fruits may be responsible for their hypoglycemic and antidiabetic properties. Because of its advantageous qualities as a medication and functional food, the system is functional [21]. Most studies on Withania coagulans have been conducted in animal models, with limited clinical trials in humans, particularly in Pakistan. Available evidence suggests mild gastrointestinal discomfort in some cases; however, comprehensive safety profiling in humans is still lacking. *Withania coagulans* is a safe and effective alternative treatment for diabetes since it has hypoglycemic qualities. Vital signs, blood glucose, and lipid peroxidation are considerably reduced by an aqueous extract of *Withania coagulans* berries (1gm/kg; P.O.). It encourages the proper level of insulin secretion. *Withania coagulans* lowers blood glucose by enhancing glucose utilization and carbohydrate metabolism. It lowers hyperglycemia. In both streptozotocin-induced diabetic rats and normoglycemic rats, treatment with coagulanolide in addition to four known withanolides 1-3 and 5 isolated from four fruits of *W. coagulans* significantly inhibits the postprandial rise in hyperglycemia after sucrose load. *Withania coagulans* is therefore regarded as an antihyperglycemic and

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antidyslipidemic medication. Type-2 diabetes mellitus is frequently treated with *Withania coagulans* [22]. In type 2 diabetic rats, *W. coagulans* fruits showed notable pharmacological effects on body weight, lipid profile, and blood glucose. These extracts significantly reduced glucose, triglyceride, total cholesterol, LDL, and VLDL levels while increasing HDL when given at a dose of 1 g/kg body weight for 14 days. Additionally, the extracts decreased hepatic and serum lipid peroxidation in db/db mice and diabetic rats. With a maximum reduction of 33.2% in normal rats, 1g/kg was found to be the most effective dose for lowering fasting blood glucose. Along with other withanolides, coagulanolides significantly reduced postprandial hyperglycemia and enhanced glucose tolerance, indicating their potential as an antidiabetic and antidyslipidemic drug [23]. Due to its significant hypoglycemic properties, *Withania coagulans* offers a safe and effective alternative to diabetes treatment. In STZ-induced diabetic rats, the aqueous and chloroform extracts have an impact on body weight, lipid profiles, and blood glucose; they increase HDL levels and the atherogenic index while decreasing total cholesterol, triglycerides, glucose, LDL, and VLDL [24]. According to the researcher, the extract also showed effectiveness in the Nicotinamide/STZ model, with the most advantageous dosage being 250 mg/kg [25]. In STZ-induced diabetes mice, Arslan *et al.* found that the extract had a substantial impact on GLP-1 levels and combination therapy [26]. The histological analysis by Wickramasinghe *et al.* revealed enhanced pancreatic islet architecture when extract + glipizide was used, suggesting cell regeneration properties as well as anti-diabetic and antihyperlipidemic activities [27]. By increasing glucose tolerance and lowering postprandial hyperglycemia, coagulanolide and other withanolides have been demonstrated to have antidiabetic and antidyslipidemic qualities [28-30].

Additional Health Advantages of *Withania coagulans* (Paneer Dodi): Reduces oxidative stress and inflammation

Withania coagulans lowers lipid peroxidation, boosts glutathione, superoxide dismutase, and catalase, and lessens oxidative stress. This keeps the pancreas and kidneys from being harmed by free radicals [31]. The benefits of paneer phool also help reduce joint inflammation symptoms, such as swelling, redness, and soreness. This makes it especially helpful for people with gout or arthritis. Its withanolides block NF-κB and nitric oxide pathways, while it lowers proinflammatory cytokines (IL-1β, IL-6, TNF-α) in the kidneys and other tissues [32].

Hepatoprotective Qualities and Asthma Management

These conditions can be inherited or brought on by several liver-damaging factors, including infections, excessive alcohol consumption, and obesity. Chronic liver problems are treated with paneer dodi. Due to its hepatoprotective qualities, this herbal remedy may aid with liver issues. The advantages of paneer phool for asthma management are also becoming more well-known. This enchanted herb helps treat respiratory issues and improve lung function. Including paneer doda in a person's diet may help reduce asthma symptoms and may prevent an asthma attack from happening suddenly [33].

Menstruation Disorders and Wound Healing

Among the doda's many applications, its ability to treat menstruation issues is becoming more well acknowledged. Menstrual issues may be treated with medications, although they may have adverse consequences. A non-healing wound can result from diseases like diabetes that interfere with and potentially slow down the body's healing process. Paneer Dodi, an Ayurvedic substance with antiplatelet (wound-healing) qualities, may aid in accelerating the healing process. Paneer Dodi may boost the number of proteins and collagen that aid in quicker healing, according to some research [34].

High Cholesterol and Low Urine Output

To create healthy cells, the human body needs cholesterol. On the other hand, elevated cholesterol levels can raise your risk of heart disease. According to research on Paneer Dodi, the plant's anti-hyperlipidemic properties may help lower cholesterol levels. The consumption of paneer flowers is also well known for boosting the body's urine production. The therapeutic herb's diuretic qualities reduce urination-related pain [5].

Anthelmintic Activity and Cardiovascular Effects

The essential oil from the steam distillation of the petroleum ether extract of *Withania coagulans* fruits seems to have anthelmintic qualities. In ruminants, the upper portions of *Withania coagulans* have anthelmintic properties. The aqueous extract of Paneer Dodi fruits yields withanolide, a steroidal lactone with cardiovascular effects. The aglycones of cardiac glycosides and this withanolide substitute, which was extracted from the fruits of *Withania coagulans*, share a similar chemical structure [35].

Anticancer

Withaferin (3β-hydroxy-2, 3-dihydro-withanolide F) has anticancer properties. The aqueous extract of *Withania coagulans* contains anticytotoxic properties. The extract significantly reduces the generation of TNF-α in chicken lymphocytes and inhibits DMSO-induced cytotoxicity [36].

Central Nervous System and Alzheimer's Disease

Numerous illnesses of the central nervous system, including epilepsy, anxiety, depression, catalepsy, and sleep, can be effectively treated by the bioactive metabolites extracted from Withania. In rats, rabbits, and

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dogs, the whole extract of *Withania coagulans* Dunal fruit has been shown to exhibit central nervous system (CNS) depressive activity. Alzheimer's disease is a degenerative neurological condition that causes neuronal loss and cognitive deterioration. The illness, which is categorized as a neurodegenerative dementia, starts out mildly and gets worse with time. According to studies, withanolides—compounds present in several plants, such as *Withania coagulans*—have an inhibitory effect on quinine reductase and metastatic activity. These results suggest that withanolides may be used to treat Alzheimer's. To investigate and confirm their therapeutic efficacy in treating the intricacies of this neurodegenerative illness, more research is necessary [37]. Even though it has excellent medical qualities, it is fairly affordable and widely accessible. To put it briefly, this herb has a number of health benefits and therapeutic potential.

Use Caution

Although paneer dodi has several health benefits, the herb should be used sparingly. This is especially true for women who are pregnant or nursing: before using this herb, they should speak with a gynecologist.

Study Limitations and Future Recommendations

The research is hampered by a small sample size, a limited study period, and a single-centre location that could restrict the extrapolation of the results. In future research, the sample sizes, cross-center methods, and follow-up time should be increased to improve the validity and applicability of findings.

CONCLUSIONS

In this conclusion, the substantial pharmacological potential of *Withania coagulans* (Paneer Dodi) in the treatment of diabetes mellitus and several other illnesses. Rich in bioactive substances, including coagulins and withanolides, although *Withania coagulans* exhibits multiple pharmacological effects, its disease-specific efficacy depends on dosage, extract type, and target pathway. Currently, most dosage data are derived from preclinical studies, and standardized therapeutic doses for different diseases in humans remain to be established through clinical trials, including anti-diabetic. As a natural product (antidiabetic tea), *Withania coagulans* shows potential for diabetes diet therapy. It offers directions for further investigation and study in the fields of pharmaceutical science and herbal medicine.

Authors' Contribution

Conceptualization: MKS
Methodology: MKS, NZ
Formal analysis: AK, SA, AI
Writing and Drafting: KS, IA
Review and Editing: MKS, NZ, AK, SA, AI, KS, IA

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The authors received no financial support for the research, authorship and/or publication of this article.

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