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REVIEW ARTICLE

Withania coagulans: A Comprehensive Exploration of Its Phytochemical Constituents and Pharmacological Properties within Traditional and Modern Herbal Medicine Frameworks

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ABSTRACT
Withania coagulans (Indian Rennet) is a medicinal plant widely recognized for its rich content of withanolides, which contribute to its diverse pharmacological activities. Traditionally used in Ayurveda and Unani medicine, this plant exhibits antifungal, anthelmintic, antibacterial, hypolipidemic, antioxidant, and hypoglycaemic properties. Notably, its antidiabetic potential has attracted considerable attention in modern research, with several studies highlighting its role in glucose metabolism and insulin sensitivity. This review comprehensively explores the chemical composition, pharmacological effects, traditional applications, geographical distribution, and economic significance of Withania coagulans. A detailed examination of its bioactive compounds and mechanisms of action underscores its therapeutic relevance. Furthermore, this article discusses the plant's potential in drug development and herbal formulations, positioning it as a promising candidate for future pharmaceutical and nutraceutical applications. Given the increasing prevalence of diabetes and metabolic disorders, Withania coagulans holds significant potential as a natural antidiabetic agent, warranting further investigation through clinical trials and advanced pharmacological studies.
***Keywords**: Hyperglycaemic, Wound healing, Withania coagulans, Antidiabetic, Anti-inflammatory, Withanolide.*

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INTRODUCTION

Traditional medicine is grounded in the knowledge, skills, and customs that are unique to diverse cultures, shaped by distinct beliefs, experiences, and practices. It serves as a means to prevent, diagnose, alleviate, or manage physical and mental ailments while also enhancing overall well-being. Presently, traditional medicine remains prevalent due to various factors such as the exorbitant costs and prolonged timelines associated with novel drug development, apprehensions regarding toxicity, and the limited availability of sustainable sources for essential raw materials [1].

Plants continue to hold promise as a valuable reservoir of therapeutic agents within traditional healthcare frameworks, having been harnessed for medicinal purposes over the course of millennia [2]. The robust interest displayed by the pharmaceutical industry in herbal medicine's efficacy and safety has spurred an expansion in research on medicinal plants. With a focus on *Withania coagulans*, this review aims to furnish contemporary insights on medicinal plants to cater to the growing interest in their utilization, drawing upon botanical, commercial, ethnopharmacological, phytochemical, and pharmacological investigations currently documented in scholarly works.

TAXONOMICAL CLASSIFICATION [3]:

Kingdom: "Plante; Plant"
Sub kingdom: "Tracheobionta", Vascucular plant;
Division : "Angiosperms"

Class: “Mangnolipsida”
Family: “Solanacae”
Genus : “Withania”
Species : “*Withania coagulans* dunal”
Cougnals you withania dunal is a stiff, Asian subshrub that reaches a height of 60 to 120 cm and is predominantly situated in the arid regions of Punjab. Moreover, records of its presence have been documented in the proximity of Simla, Garhwal, and Kumaun. The maturation of the berries occurs between January and May, with blossoms emerging from November to April. The plant relies on its seeds for propagation through natural means. Its dioecious flowers exhibit auxiliary clusters and slender, downward-pointing pedicels measuring 0.6 mm in length. The calyx is roughly 6 mm long, bell-shaped, and adorned with triangular teeth that are 2.5 mm in size. It is covered with delicate, star-shaped grey tomentum. The bloom is approximately 8 mm long, divided to about one-third of its length, featuring sub-acute ovate-oblong lobes. The outer surface of the corolla is densely covered in a star-like mealy texture. The stamens of the male flowers are positioned at the top of the corolla-tube, with anthers measuring 3–4 mm in length and possessing spherical filaments that are 2 mm long. The ovary is spherical and lacks both stigma and style. Female flowers, in contrast to their male counterparts, bear smaller non-fertile anthers and stamens it only reaches halfway up the corolla-tube. The stamen filaments are regarding 0.85 mm in length. The ovary assumes a spherical shape, exhibiting a 2-lamellate stigma resembling a mushroom and a globular style. The fruit is sleek and round, with a diameter ranging from 6 to 8 mm. The enlarged membranous calyx, covered in a scaly down on the outside, envelops the berry closely. The texture of the kidney-shaped, spherical seeds varies from 2.5 to 3.0 mm in diameter [4].

Synonyms [5]:
-Arabic: Javzuhnizaja, Kaknajehindi
- English: chease maker
-Punjabi: Kharmjaria,Spinbajia
-Hindi:Akri,Punir
-Marathi: Panir fool
- Sindhi: Punirband, Punirjafota
- Telgu :Pennerugadda

Economical important:
Withania coagulans, commonly recognized as "paneer" in Punjab (Pakistan), is also identified as "the cheese maker" or "vegetable rennet" due to its milk-coagulating characteristics. The coagulation of milk by berries are said to include an enzyme in their husk and pulp that makes this process easier. A concoction prepared using one ounce of *W. coagulans* fruit and one quart of boiling water has the capability to coagulate a gallon of warm milk in approximately sixty minutes. The berries of *W.coagulans ,* known as "paneer," serve as the origin of the coagulating enzyme utilized in Punjab for milk coagulation. The crushed berries of this plant are infused in heated (approximately 100°F) sheep or buffalo milk, followed by covering it with a cloth. The curdling of milk typically necessitates a duration of 30 to 40 minutes [6].
Economical uses:
There are documented accounts of diuretic, sedative, emetic, and alterative effects associated with *W. coagulans* fruits. Various digestive issues, such as strangury, asthma, biliousness, dyspepsia, and flatulent colic, have been historically managed with these fruits. Specific regions in the subcontinent have long utilized these berries as a remedy for purifying the blood. *W. coagulans* holds a significant position in traditional medicine for its efficacious medication of ulcers, rheumatism, dropsy, consumption, and senile weakness [7].
Properties of Paneer Dodi [8]:
The medicinal attributes of paneer dodi encompass the following:
It possesses sedative characteristics conducive to inducing sleep. It exhibits diuretic properties that enhance urine production in the kidneys. It may manifest emetic features capable of inducing vomiting. It could aid in wound healing. It may assist in alleviating inflammation. It might demonstrate potential in lowering blood cholesterol levels (anti-hyperlipidaemic). It may showcase activity in eradicating fungi (antifungal). It may exhibit antibacterial properties. It may display efficacy in eliminating worms and parasites (anti-helminthic activity).

- Potential uses of panner phool for overall health:
- Potential applications of panner phool for diabetics:

The fruits and flowers of the paneer dodi plant have been extensively employed in traditional medicine for managing diabetes. In an experimental model of type 2 diabetes, paneer dodi exhibited symptom alleviation and restoration of normal blood glucose levels. Consequently, paneer dodi could aid in regulating blood sugar levels. However, consultation with a healthcare provider before utilizing paneer dodi or any herbal remedies for addressing health concerns is advisable. Furthermore, herbal supplements should not be used as a substitute for contemporary medical interventions.

- Potential uses of panner phool for liver:

Laboratory investigations have substantiated the hepatoprotective attributes of paneer dodi fruit extract. Evaluation of blood enzyme levels during the study provided evidence of this protective effect. Individuals with liver conditions should seek medical advice prior to incorporating paneer dodi into their diet. Ingesting herbal supplements without medical consultation could potentially exacerbate the existing liver condition.

- Potential Uses of paneer dodi for reduced urine output:

An animal investigation was conducted to explore the diuretic properties of paneer dodi fruit extract. Results indicating increased urine volume and electrolyte excretion underscored the diuretic effects of the fruit extract. Prior to using paneer dodi for its health benefits, individuals are advised to consult a healthcare provider for an accurate diagnosis and recommended course of action treatment.

- Potential uses of paneer flower for wound management:

The application of paneer dodi fruit extract on wounds resulted in accelerated wound healing (wound contraction) in an animal trial. This indicates the potential of paneer dodi in wound healing. However, consultation with a healthcare professional is recommended prior to using paneer dodi on wounds to avoid the risk of wound infection.

- Exploration of the potential uses of paneer flower for combating infections:

An evaluation was conducted on the bactericidal properties of paneer dodi fruit extract, revealing its effectiveness against Staphylococcus aureus and Vibrio cholera. Moreover, it exhibited anti-helminthic characteristics and demonstrated antifungal activity against various harmful fungi. These attributes have been observed in laboratory experiments. Nevertheless, further research is essential to validate the therapeutic application of paneer dodi in human health. Therefore, seeking medical advice before incorporating paneer dodi for any medical condition is strongly advised.

The advantageous effects of *Withania coagulans* [9]:

1. Gastrointestinal Health: Traditionally utilized to support optimal digestion and alleviate gastrointestinal issues such as bloating and indigestion.
2. Glycaemic Control: Research indicates that it may have the ability to control blood sugar levels, which may be advantageous for people who already have diabetes or are at risk of getting it.
3. Anti-Inflammatory Characteristics: *Withania coagulans* contains anti-inflammatory properties that may mitigate inflammation within the body and alleviate symptoms of inflammatory disorders.
4. Antioxidant Properties:
   Possessing antioxidant attributes, it can secure cells from oxidative stress either harm caused by free radicals.
5. Immune System Support: By enhancing the immune system, it may assist in defending the body against infections and illnesses.
6. Cholesterol Regulation: Initial research indicates a positive impact on cholesterol levels, potentially beneficial for heart health.
7. Potential Anticancer Properties: While further research is necessary for a comprehensive understanding, several studies suggest anticancer properties of *Withania coagulans*.

Drawbacks and potential adverse effects of *Withania coagulans* :

1. Allergic Responses: Certain individuals may experience allergies to plants from the Solanaceae family, including *Withania coagulans*, leading to reactions like rash, itching, or respiratory issues.
2. Gastrointestinal Distress: High intake may occasionally result in digestive problems such as nausea, vomiting, or diarrhoea.
3. Drug Interactions: Interaction with medications for diabetes, hypertension, and immunosuppression is possible, underscoring the importance of consulting a healthcare provider before usage, especially if on medication.
4. Pregnancy and Lactation: Limited information exists on the safety of *Withania coagulans* during pregnancy and breastfeeding, warranting caution or consultation with a healthcare professional.
5. Potential Blood Sugar Effects: While beneficial for blood sugar control, concurrent use with diabetic medications may lead to hypoglycaemia due to excessive blood sugar lowering effects.

6. Hepatic Impact: Although further investigation is needed for a comprehensive understanding, studies suggest potential alterations in liver function due *to Withania coagulans.*

PHYTOCHEMICAL ANALYSIS

Due to the extensive array of phytoconstituents present in its fruits, both aqueous and methanol extracts of *W. coagulans* are renowned for their traditional medicinal uses. Upon conducting phytochemical analysis, these extracts were found to contain alkaloids, tannins, saponins, steroids, phenolic compounds, carbohydrates, proteins, amino acids, and organic acids. Noteworthy discoveries encompass a diverse range of withanolides, which are steroidal lactones like coagulin F, coagulin G, coagulanolide, among others. The extraction of 20β-hydroxy-1-oxo-(22R)-witha-2,5,24-trienolide and withacoagulin was performed using the entire *Withania coagulans* herb, with their structures explained through different spectroscopic methods. Prior research on phytochemicals indicates a potential correlation between the plant's hypoglycaemic effect and the steroids, as well as alkaloids, derived from plant sources [2, 3].

Analysis of Defatted Meal:

In the defatted meal derived from *Withania coagulans* dunal seeds, 17.8% of the free sugars primarily consist of d-galactose and d-arabinose in a 1:1 ratio, with minor amounts of maltose. Enzymatic assessments have indicated the lack of a β-galactosidic linkage within the polysaccharide Furthermore, approximately 12–14% of these seeds comprise fatty oil sourced from the unsaponifiable part of the fruits, containing the hydrocarbon triacontaine and the sterol dihydrostigmasterol. The hypocholesterolaemia effect exhibited is akin to maize oil, attributed to notably high levels of β-sitosterol and linoleic acid present in oil [7, 9].

Presence of Withanolides in *Withania coagulans:*

Considerable quantities of steroidal lactones, known as withanolides, are identified in W. coagulans. These natural occurring polyhydroxy C28 steroidal lactones, also known as withanolides, are linked to an undamaged or rearranged ergostane skeleton by a crucial structural element consisting of a six or five membered lactone or lactol ring. They pass the Dragendorff test even though they are nitrogen-deficient. An identifiable blue spot forms on TLC following treatment with H2SO4–MeOH. While not universally distributed in all Solanaceae plants, withanolides have been documented in marine organisms such as soft corals, as well as plants from the Taccaceae and Leguminoseae families [10].

PHARMACOLOGICAL ASPECTS

Antidiabetic and Antioxidant Effects:

Withania coagulans fruit extract (1g/kg; oral; 7 days) has been shown to causes hypoglycaemia reactions in both normal and streptozotocin-induced diabetic mice. In diabetic rats, this extract dramatically reduced high levels of cholesterol, blood glucose and lipid peroxidation (LPO). It also showed effective in vitro free radical scavenging using DPPH. *Withania coagulans* aqueous extract improves peripheral cell, tissue, and islet glucose absorption [11].

Antifungal properties

The steroidal lactone 17 beta-hydroxywithanolide K (20S, 22R) as well as 14 alpha, 17 beta, and 20 beta-trihydroxy-1-oxo-with-2,5, 24-trienolide, which were extracted from the ethanolic extract of the whole *W. coagulans* plant, had antifungal properties [12].

Anti-inflammatory Attributes:

The extract of *Withania coagulans* demonstrates notable anti-inflammatory results, particularly beneficial for acute inflammation caused by egg albumin and the cotton pellet granuloma technique. In a rat paw edema model caused by carrageenan, significant anti-inflammatory properties were observed in the hydroalcoholic extract of *Withania coagulans* fruit [13].

Antitumor Properties:

The demonstration of the anti-tumour results of withaferin 3β-hydroxy-2,3 dihydro-withanolide F is highlighted. Moreover, an investigation into the anti-cytotoxic action of the aqueous extract of *Withania coagulans* was conducted, revealing a significant reduced in TNF-α generation in chicken lymphocytes, along with a substantial prevention of cytotoxicity induced by DMSO [14, 22].

Cardiovascular Effects:

Reports have emerged regarding the cardiovascular system impacts of a withanolide isolated from *Withania coagulans* fruits. The administration of Withanolide at a dosage of 5 mg/kg body weight resulted in reduced blood pressure in dogs; this effect was prevented by atropine, while propranolol or mepyramine did not. In rabbit Langendorff preparation and ECG investigations, myocardial depressive results were observed, although minor positive inotropic and chronotropic effects were noted in an injected in frog heart [15].

Wound healing activity:
The significant benefits of the aqueous-methanolic extract *Withania coagulans* were demonstrated in both open and cut wound models. Additionally, it was revealed that the extract enhanced DNA synthesis, proteins, collagen, and mucopolysaccharides [16, 21]].
Anthelmintic activity:
The anthelmintic properties of *Withania coagulans* berries appear to be associated with the essential oil extracted from the pulp via vaporizing petroleum ether. Notably, the anthelmintic effects of this essential oil are most prominent in ruminating animals, particularly those consuming the upper parts of the *Withania coagulans* plant [17].
Immunosuppressive effects:
In rats treated with thymocytes and human B and T cells, both withanolide E and ashwagandha exhibit immunosuppressive properties through distinct mechanisms. Withanolides, comprising coagulin-H, modulate various cellular processes linked to immunological responses, including lymphoid cell proliferation and IL-2 mediator synthesis. This mechanism mirrors the action of prednisolone due to the potent inhibition of lymphocyte proliferation, leading to the production of coagulin-H, Th-1, and other anti-tumour cell cytokines [18, 20].
Anticancer activities:
The cytotoxic potential of *W. coagulans* root, leaf, petiole, and fruit CME was evaluated at a dose of 20 g/mL, targeting HeLa, MCF-7, RD, INS-1, and RG2 cells. Various chemicals (such as DMSO, CCM, and MTX) were assessed at a similar concentration for reference, indicating an enabling effect for one component and serving as negative controls for the other two. Following a 72-hour incubation period, neither DMSO nor CCM exhibited any significant ($p < 0.05$) impact on HeLa, RD, MCF-7, RG2, or INS-1 cells. Petioles displayed the highest activity levels in HeLa cells, followed by *W. coagulans* berries extracts (>80% cell killing). There was minimal variation in activity between petiole and fruit extracts. However, both fruit and petiole extracts showed a similar pattern of action, resulting in >80% cell killing in RG2 and RD cells at 20µg/mL after 24 to 72 hours of incubation [19].

CONCLUSION

In conclusion, the extensive historical background of herbal medicine spans multiple centuries and remains an essential component of worldwide healthcare. The utilization of herbal therapy serves as a substantial supplementary and substitute option for diverse health and well-being requirements, in conjunction with the notable progressions of contemporary medicine which are vital for critical and severe ailments. Nevertheless, it is crucial to acknowledge that the effectiveness and safety of herbal medicinal products may vary, leading to potential interactions with other pharmaceuticals or underlying medical conditions. Therefore, it is imperative to seek advice from a healthcare professional who possesses expertise in herbal remedies to formulate an individualized treatment regimen. *Withania coagulans* comprises a range of chemically and biologically active compounds, demonstrating adaptability and auspicious therapeutic capabilities. Despite this, its biological functions and medical applications have not been extensively examined. As a result, further comprehensive investigations are imperative to leverage its therapeutic advantages in the management of diseases.
This analysis accentuates *Withania coagulans* and its therapeutic properties, encompassing anti-diabetic, anti-inflammatory, hepatoprotective, cardiovascular, diuretic, anti-bacterial, anti-cancer, wound healing, antioxidant, immunosuppressive, antitumor, anthelmintic, antifungal, and anti-arteriosclerosis effects. It also demonstrates a potential for augmenting testosterone levels in males. Nonetheless, additional research is necessary to substantiate its medicinal utilization thoroughly. Consequently, there exists a notable requirement for forthcoming scientific inquiries into *Withania coagulans* to ascertain both its medicinal effectiveness and economic viability.

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