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## Withania Coagulans in Treatment of Diabetics and Some Other Diseases: A Review

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### ABSTRACT

Ayurvedic medicines are largely used for treatment of many diseases. Using of herbal drugs are the traditional system in India for healing & curing. Due to many adverse effect of modern drugs people used to prefer herbal drugs. The traditional medicines are increasingly solicited through the traditional practitioners and herbalists in the treatment of infectious diseases. Medicinal plants play a vital role for the development of new drugs. Withania is a small genus of shrubs, which are distributed in the East of the Mediterranean region and extend to South Asia. The berries of the shrub are used for milk coagulation. It is popularly known as Indian cheese maker. In Punjab, the fruits of W. Coagulans are used as the source of coagulating enzyme for clotting the milk which is called "paneer".

**Keywords:** Diabetes, hypoglycemic agents, herbal medicines, Withania coagulans, Doda Paneer

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## INTRODUCTION

Diabetes is a chronic disease which affects all groups of people in world. Modern, hectic lifestyle is contributing to increase the diabetics, some even in the age group of 30 to 40 years. The reasons are increased tension, faulty eating habits with increasing dependence of junk foods. Smoking and increased use of tobacco, pollution, hereditary causes, can be inducted as the other factors which are increasing the incidence of diabetes in the young.

Treatment includes insulin supplementation; diet control and use of hypoglycemic agents like Metformin . Insulin supplementation is the common mode of treatment in Type I diabetes while oral drugs like Metformin is used in Type II diabetes. Disadvantage with insulin supplementation is that the dosage of insulin needed steadily increases with passage of time. Oral anti- diabetics have serious side effects which includes hepatotoxicity and renal damage.

The use of alternative and herbal treatment of Diabetes is increasing and new research has given promising results with many herbs. One such herb which has been studied is *Withania coagulans*.

The patients are advised by the traditional healers to dip the flowers in a cup of water overnight and take the leachate internally next morning. Although the traditional healers are in favour of its long term use but by seeing initial progress they fix the duration of medication. Paneer plants are collected on special days after performing worship and uttering of Mantras. According to the traditional healers this worship makes the plants medicinally rich. They also offer specific herbal solution to the plants few days before the collection. The traditional healers of Southern Chhattisgarh use the insects feeding on paneer plants for the treatment.

### Taxonomical Classification

Kingdom : Plantae  
Division : Magnoliophyta  
Order : Solanales  
Family : Solanaceae  
Genus : *Withania*

### Botanical Description

Shrub branched, 2-3m in length, ridge and furrows are present, slightly hairy stem cylindrical, 0.5-0.16cm length, hair curved. Fruit berry, globose, 1.5-1 cm long, 0.7-1 cm width, Sepals covers the fruit and ended into crown like structure. Seeds oval to rounded, yellowish brown, 41-59 in number, 0.1-0.3cm long, 0.2-0.3cm wide, dotted. Flowering period is from January to April. The pulp and husk of the berry contain an enzyme. The main component of berries are esterases, fatty oil, amino acids such as proline, hydroxyproline, valine, tyrosine, aspartic acid, glycines, aspargines, cysteine and glutamic acid and alkaloids are the phytoconstituents 30. The most of the activities of the plants is due to the presence of an active

component as, *Withanolide*. *Withanolides* are steroidal lactones with an ergostane skeleton 4. The fruits are diuretic hypolipidemic.



Figure of *Withania coagulans*

### **Synonyms:**

English: Vegetable Rennet, Indian-Cheese-maker,  
Unani- Desi Asgandh, Kaaknaj-e-Hindi, Paneer, Paneer-band, Akri (fruit),  
Siddha/Tamil-Ammukkura.

Local names: This plant is known by different names, in different local languages, such as 'Akri' or 'Puni-ke-bij' in Hindi, 'Tukhmekaknaje- hidi' in Persian. 'Spiubajja' in Af-ghan, 'Khamjira' in Punjabi and 'Punirband' or 'Punir- ja-fota' in Sindhi.

*Useable Part:* Whole plant, roots, leaves, stem, green berries, fruits, seeds and bark are used.

### **Structures**

Withanolides of ergostan steroids are four-ring triterpenes. The plant steroids are derived from sterols and comprise steroid saponins, steroid alkaloids, pregnanes, androstanes, estranes, ecdysteroids, withanolides and cardiac glycosides (Kreis and Muller-Uri 2010). "Withanolide" represents the term for the C28-skeleton 22-hydroxyergostan-26-oic acid -22, 26-olide; this  $\gamma$ -lactones residue containing the structure is a theoretical (Lavie et al 1965 a, b). Basically there are two major groups of withanolides as follows:

A- Withanolides with an unmodified skeleton

- a) With a regular  $\beta$  -oriented side chain
- b) With an unusual  $\alpha$  -oriented side chain.

B- Withanolides with modified carbocyclic skeletons or side chains.

These withanolides are initially classified on the basis of the chemotypes of the *Withania* species depending on the region of the collected plant. Chemically, these compounds may be classified as ergostane derivatives from their structural pattern; these can be broadly divided into seven groups.

1.  $5\beta$ ,  $6\beta$  -epoxides
2.  $6\alpha$ ,  $7\alpha$  -epoxides
3. 5-enes
4. Intermediate compounds
5.  $5\alpha$ ,  $6\alpha$  -epoxides
6.  $6\beta$ ,  $7\beta$  -epoxides
7. Phenolic withanolides (Glotter 1991).

Among these, the  $5\beta$ ,  $6\beta$  -epoxides are most common. Most of the compounds possess a  $4\beta$  -hydroxy group. Purushothaman and Vasanth (1989) extracted four-ring compound which possess  $\alpha$ ,  $\beta$  -unsaturated- $\gamma$ -lactone system, in e.g. ixocarpa- lactone A. (Refer into Atta-ur-Rahman 1998e). Ray (1989) showed that the withanolides which possess  $6\alpha$  and  $7\alpha$ -epoxides generally contain  $5\alpha$  -hydroxyl and are believed to originate from  $5\beta$ ,  $6\beta$  -epoxides (Refer to Atta-ur- Rahman 1998e).

#### **Medicinal Uses of *Withania Coagulans* :**

*Withania coagulans* (Paneer Doda) has been used since time immemorial in Indian Ayurvedic medicines. The method of use is very simple. You need to drop 10 of those seed like flowers in a glass of water overnight. Filter the water through a sieve and drink it in the morning. Paneer Doda is available easily from any decent Ayurvedic specialist shop and costs about 50 cents for 100 gms. Continue this treatment and control of blood sugar is achieved in a fortnight.

*Withania coagulans* is used in chronic complaints of liver. A composite Ayurvedic herbal hepatoprotective medicine 'Liv-52' contains extracts of *Withania coagulans* and *W. somnifera*. They are also used in dyspepsia, flatulent colic and other intestinal infections. The berries are used as a blood purifier. The twigs are chewed for cleaning of teeth and the smoke of the plant is inhaled for relief in toothache. *Withania coagulans* (Stocks) Dunal is used to treat nervous exhaustion, debility, insomnia, wasting diseases, failure to thrive in children, impotence. Its fruits are used for liver complaints, asthma. Flowers of *Coagulans* (Stocks) Dunal are used in the treatment of diabetes. The root is harvested in autumn and dried for later use. Some caution is advised in the use of these plants since it is toxic. Antimicrobial, anti-inflammatory, hepatoprotective, anti-hyperglycemic, cardiovascular, immunosuppressive, free radical scavenging and central nervous system depressant activities of the plant have been reported.

*Withania coagulans* act as diuretic because they increase urinary potassium level and alter urinary  $\text{Na}^+/\text{K}^+$  output. Diuresis induced by *Withania coagulans* extract at 500 mg/kg dose

is strong with similar intensity comparable to furosemide. Phytochemically, *Withania coagulans* fruits are shown to contain steroidal lactones, withanolides, amino acids and essential oils.

However amino acids are reabsorbed in proximal convoluted tubules of nephron and cannot function as diuretic. Withanolides are steroidal lactones with an ergostane skeleton found as chief chemical constituent of the plant. These withanolides are more polar in nature as compared to other withania species. Finally this diuretic effect may be associated with the presence of active principles of polar nature where withanolides may be the main chemical protagonist of this activity.

The volatile oil obtained from fruits of *W. coagulans* had antibacterial activity against *S. aureus* and *Vibrio cholera* and also found to have antihelminthic activity. Withanolides isolated from ethanolic extract of the whole plant showed antifungal properties.

The aqueous extract of the plant have shown an anti-inflammatory activity in various rodent models.

*W. coagulans* has wound healing activities in streptozotocin-induced diabetic rats. The hydroalcoholic fraction of *W. coagulans* in oral form is found to be more effective than the aerial part of *Aloe barbadensis* Miller which is used as a local demulcent in wounded diabetic rats. Prasad et al (2010) showed that withaferin-A is responsible for increasing the collagen significant levels, protein, DNA, SOD, CAT and hexosamine decreasing.

Siddiqui et al (1963) studies showed the extract of *Withania coagulans* is muscular relaxing in experimental animals and is also a hypotensive, respiratory stimulant.

The protective effect of obtained 3F-hydroxy-2, 3 dihydro-withanolide F from *W. coagulans* fruits was studied against the hepatotoxicity, induced by CCl<sub>4</sub>. Budhiraja et al (1984) showed that the protective effect of withanolide F was more active than hydrocortisone.

The aqueous extract exhibited free radical scavenging activity in an *in vitro* system using DPPH (Budhiraja et al 1986). Fruits extracts of *W. coagulans* have antioxidant potential against several diseases such as ageing, arteriosclerosis etc. which caused due to ROS. ( Mathur et al. 2011)

Based on Karami et al (2006) the root extract of *W. coagulans* had significant effects on the withdrawal syndrome in mice. It also showed significant suppression of morphine withdrawal jump, induced by naloxone, and decreased the development of morphine dependence.

An isolated new withanolide with a special chemical structure that was similar to the aglycones of the cardiac glycosides was examined for its cardiovascular effects of *W. coagulans* fruits. The withanolide caused a moderate drop of blood pressure in dogs (34 +/- 2.1, mm Hg) which was blocked by atropine and not by mepyramine or propranolol. In rabbits Langendorff

preparation and ECG studies, produced myocardial depressant effects but in perfused frogs hearts it caused mild positive inotropic and chronotropic effects (Budhiraja et al 1983).

A known withanolide, coagulin-H, was evaluated for its effect on various cellular functions related to immune responses including lymphocyte proliferation, interleukin-2 (IL-2) cytokine expression. These results were compared with prednisolone. Coagulin-H was found to have a powerful inhibitory effect on lymphocyte proliferation and the Th-1 cytokine production. The inhibition of the phytohaemagglutinin (PHA) activated T-cell proliferation by coagulin-H (Mesaik et al 2006).

Withanolides are known as plant hormones, which can be used instead of physiological human hormones. Withanolides are amphiphilic compounds which are able to regulate activities and the physiological body hormones processes. According to a theory, when these plant hormones enter the human body, they occupy the active receptor of the cell wall, and don't allow the animal hormones to get binding to this site and express their true activities. COX-2 enzyme receptors are interested in being occupied by plant steroid hormones (Alternative Medicine Review, Monograph, 2004). Molecular docking of cyclooxygenase with a set of ligands revealed that as compared to NSAIDs, withanolides were better inhibitors of COX-2. Withanoside glycans and withanolides showed selective interaction with COX-2 better than COX-1. Therefore withanoside glycans and withanolides could be the next substitutes of NSAIDs (Nithya et al 2010).

The alcoholic extract of *W. coagulans* showed significant anti-inflammatory effects in acute inflammation induced with egg albumin. Sub-acute inflammation induced with formalin and granulation tissues were formed by cotton pellet method (Budhiraja et al 1977). Budhiraja et al (1986) reported Anti-inflammatory activity of a withanolide from *W. coagulans*.

This plant contains different phytoconstituents like steroids, alkaloids, phenolic compounds, tannins, saponins, carbohydrates, proteins, amino acids and organic acids. Pharmacological investigations have elucidated association of these activities with the specific steroidal lactones known as Withanolides present in *Withania*. Withaferin A and Withanolide A and Withanone are the major Withanolides present in *Withania somnifera* and *Withania coagulans*.

## CONCLUSION

The fruit, leaves and root of *Withania coagulans* have been used as a treatment in many disorders. It's found to be rich source of esterases, free amino acids, fatty oils, essential oils and withanolides. Withanolides are steroidal lactones and several of them possess significant pharmacological activities. Hence, further structure–activity relationship investigations and possible optimization of their non-toxic and diffusion properties would be interesting. In addition, future studies should lead to synthesis of these complex and fascinating chemical structures and their generics via modification/addition of different functional groups. It is also

important to reveal the bio-efficacy of isolated compounds in combination with other herbs or drugs.

The plant *doda paneer* is a very good drug to treat diabetes mellitus, It not only lowers the blood sugar level but it also minimizes the future complication of diabetes such as neuropathy, retinopathy, nephropathy and cardiovascular pathologies by its very potent antioxidant action. It also possess a very good hepato-protective, anti-tumor, anti-angiogenic, chemopreventive and anti-inflammatory activities. In spite of its very good medicinal properties it is very economical, easily available, easily consumable all these properties make it a best drug for Diabetes Mellitus.

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