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# *WITHANIA COAGULANS DUNAL.* (PANEER DODA): A REVIEW

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**ABSTRACT:** plant based medicines have created much awareness in the today's society due to their various well proven therapeutic effects and lack of side effects which has provoked the human to go back towards nature for safer herbal remedies. The plant, *Withania coagulans Dunal* is one of them which is used to cure various ailments and used in folk medicine. *Withania coagulans Dunal* commonly known as Indian cheese maker has been used for preparing a vegetable rennet ferment for making cheese in different parts of India. Different parts of this plant have been reported to possess a variety of biological activities. In Nothern India traditional healers use dry fruits of Withania coagulans for the treatment of diabetic patients. *Withania coagulans Dunal.* has been shown to exert hypoglycemic, hypolipidemic, free radical scavanging, cardiovascular, central nervous system depressant, hepatoprotective, anti-inflamatory, wound healing, antitumor, immuno-suppressive, cytotoxic, antifungal and antibacterial properties. The twigs are chewed for cleaning of teeth and the smokes of the plant is inhaled for relief in toothache. A large numbers of phytochemicals have been isolated from *Withania coagulans* which are responsible for various pharmacological action of this plant. The present article aims in projecting a detailed review of the plant regarding its morphology, chemical constituents and pharmacological properties. It has also included therapeutic effects of the whole plant and its extracts and isolated withanolides.

**Key Words**: Chemical constituents, morphology, pharmacological properties, *Withania coagulans Dunal.*

**INTRODUCTION:** Ayurveda is the science of life. The basic aim of Ayurveda is maintenance of health and treatment of various diseases. The plants are the key source of medicine in Ayurveda for treatment and prevention of diseases and maintenance of healthy life. The plants are used in medicine since antiquity. Much of the medicinal plants are documented in the Ancient Ayurvedic classics and these plants are still used successfully to treat different ailments. One of these plants which is used to treat various disease is *Withania coagulans Dunal*. The shrub is important for the property of coagulating milk, possessed by its berries; they are used for this purpose in North-West India and adjoining country. The milk-coagulating activity is due to the presence of an enzyme, which can easily be isolated by extracting the berries with water and precipitating the enzyme either by ammonium sulphate or by adding two volumes of acetone. The precipitate is dried at low temperature and the enzyme is obtained as a brownish white powder.

**Aims and Objectives:**

- Detailed review of the plant regarding its morphology, chemical constituents and pharmacological properties.
- To study the therapeutic effects of the whole plant and its extracts and isolated withanolides.

**Botanical description of Withania coagulans:**

Botanical Name :*Withania coagulans Dunal*

Family : Solanaceae

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| Subfamily | :Solanoideae |
| Tribe | :Physaleae |
| Subtribe | :Withaninae |
| Sanskrita Name | :Rishyagandha[1&2] |
| Hindi Name | :Punir, Punir bandh, Akri, Binputakah, Paneer doda |
| English Name | :Indian Cheese maker, Indian Rennet, Vegetable Rennet |
| Trade Name | : Paneer dodi, Panner, doda, Panir bed, Paneer dhodi. |

**Vernacular Name of Withania coagulans :** The plant is known by different names in different local languages such as;

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|---|---|---|
| Bengal | - | Asvagandha |
| Bombay | - | Kaknaj |
| Gwalior | - | Asgandha |
| Panjab | - | Khamjaria, Khamjira, Panir |
| Sindhi | - | Punirjafota, Punirband |
| Persian | - | Kaknajehindi, Punirbad |
| Arabic | - | Javzulmizaja, Kaknajehindi |
| Canares | - | Asvagandhi |
| Telgu | - | Panneru-gadda |
| Urdu | - | Hab kaknaj |

**Distribution :** This shrub is, common in , East India, Nepal and Afghanistan,. In India it occurs in Punjab, Rajasthan, Simla, Kumaun and Garhwal.

**Morphological Discription:** A rigid grey- tomentose undershrub 0.3-0.9 m. high, branches terete, clothed with dense grey or yellowish white tomentum. **Leaves :** 2.5-5.7 by 1-2.2 cm., lanceolate-oblong, obtuse, entire, clothed with a persistent not easily detachable greyish tomentum, of a uniform colour on both sides, thick, more or less rugose, base acute, running down into an often obscure petiole; petiole 6 mm. long but often indistinct. **Flowers :** Dioecious, in axillary clusters; pedicles 0-6mm. long, deflexed, slender. Calyx 6 mm. long, campanulate, clothed with fine stellate grey tomentum; teeth triangular, 2.5 mm. long. Corolla 8 mm. long, stellately mealy outside, devided about 1/3 the way down; lobes ovate-oblong, subacute. Male flowers: Stamens about level with the top of the corolla- tube; fillaments 2 mm. long, glabrous; antherrs 3-4 mm. long. Ovary ovoid, without style or stigma. Female flowers: Stamens scarcely reaching ½ way up the corolla-tube; filaments about 0.85 mm. long; anthers smaller than in the male flowers, sterile. Ovary ovoid, glabrous; style glabrous; stigma mushroom- shaped, 2-lamellate. **Fruits** : Berry 6-8 mm. diam., globose,smooth, closely girt by the enlarged membranous calyx which is scurfy-pubescent outside. Seeds 2.5-3 mm. diam., somewhat ear-shaped, glabrous. **Seeds** : 2.5-3mm diam., dark brown, ear-shaped, glabrous; **Flowering period:** from January to April and berries ripen during January to May. The natural regeneration is from seed[3].

**Chemical constituents :** The berries contain the milk-coagulating enzyme, two esterases, free amino acids, fatty oil, an essential oil and alkaloids. The amino acids present are proline, hydroxyproline, valine, tyrosine, aspartic acid, glycine asparagin, cysteine and glutamic acid. Fourteen alkaloidal fractions have been isolated from the alcoholic extract of the fruits. The seeds on petroleum ether extraction, give a yellow fatty oil and unsaponifiable matter. Fatty acid composition are oleic, linoleic, palmitic, stearic and arachidonic acid. The unsaponifiable matter consist of triacontain, three sterols including dihydrostigmasterol and β-sitosterol. The defatted meal from the seeds contains free sugar consisting of D-galactose and D-arabinose and traces of

maltose. The leaves contain four steroidal lactones called Withanolides, viz Withaferin-A, 5, 20α(R)-dihydroxy-6α,7α-epoxy-1-oxo-(5α)-with a-2,24-dienolide and two minor withanolides, of which one is probably 5α, 17α-dihydroxy-1-oxo-6α, 7α-epoxy-22R-witha-2,24-dienolide (the so called withanone).[4]

Withaferin A is the most important of the withanolides isolated so far. It has good antibiotic and anti tumor activities. Withaferin A in concentration of 10μml. inhibited the growth of various gram-positive bacteria, acid fast bacilli, aerobic bacilli and pathogenic fungi. It was active against Micrococcus pyogenes var. aureus and Bacillus subtilis glucose-6-phosphate-dehydrogenase. Withaferin A has marked tumor-inhibitory property when studied *in vitro* against cells derived from human carcinoma of nasopharynx (KB). It also act as mitotic poison arresting the division of cultured human larynx carcinoma cells at metaphase. The studies also showed growth inhibitory and radio sensitizing effects in vivo on mouse Ehrlich ascites carcinoma. It also caused mitotic arrest in embryonal chicken fibroblast cells. Withaferin A exhibits positively potent anti-arthritic and anti-inflammatory effect. It suppress effectively arthritic syndrome without any toxic effect. In contrast to hydrocortisone treated animals which shows weight loss, the animal treated with withaferin A showed weight gain in arthritic syndrome[4].

Withaferin A inhibits angiogenesis (Mohan et al., 2002)[5]. It has been reported that some of the withanolide affescts events in the cholinergic signal transduction cascade of the cortical and the basal forebrain, indicating their promising role in the treatment of Alzheimer's disease (Kuboyama et al., 2005)[6].

**Therapeutic uses :** The fruits is sweet; applied to wounds; used in asthma, biliousness stranguary. The seeds are emmenagogue, diuretic; useful in lumbago, opthalmia; lessen the inflamation of piles. The ripe fruits are supposed to possess anodyne or sedative properties. They are alterative, diuretic and believed to be useful in chronic liver complaints. They are used as an emetic. The dried fruits, sold as Punir-ja- fota in Sind, are employed in dyspepsia and flatulent colic, and other intestinal affections. They are prescribed in infusion, either alone or conjoined with the leaves and twigs of *Rhazya stricta*, an excellent bitter tonic. Honigberger says that the bitter leaves are given as febrifuge by the Luhanees. In Bombay, the berries have a reputation as blood purifiers. In Las Bella, the fruit is pounded and used as a cure for colic; the wood is used for cleaning the teeth. In the Ormera Hills, the smoke is applied to aching teeth 'to destroy the worm' (Hughes Buller). The twigs are chewed for cleaning teeth, and the smokes of the plant is inhaled for relief in toothache.[3&4] In Nothern India traditional healers use dry fruits for the treatment of Diabetes mellitus. It has also antimicrobial, anthelmintic, antifungal, hepatoprotective, hypoglycemic, hypolipidemic, cardiovascular, free radical scavenging, anti-inflammatory, antitumor, immunosuppressive, depressant property.

Round capsular fruit and the leaves have the peculiar property of coagulating or curdling milk; a small portion is rubbed with a little water or milk and is added to the milk to be coagulate. Dried capsules also retain the coagulating property in an equal degree. The active principle named "withanin" residing in the numerous small seeds contained within the capsules is a ferment closely allied to the animal rennet.[7]

## Experimental studies done on *Withania coagulans Dunal:*

**Antihyperglycaemic Activity:** The drug Withania coagulans exhibited hypoglycaemic activity which is an effective and safe alternative treatment for diabetes ( Budhiraja et al 1977)[8]. Hypoglycemic activity of Withania coagulans was exhibited in streptozotocin induced rats (Hemalatha et al 2004)[9]. Significant improvements in symptoms and signs were observed and euglycemia was attained in diabetes mellitus type 2 (Jaiswal et al 2009)[10]. A withanolide, named coagulanolide isilated from Withania coagulans fruits has antihyperglycemic activity in rats (Maurya et al 2008)[11]. The median effective dose of isolated coagulanolide from fruits of Withania coagulans was determined about 25 mg/kg in streptozotocin-induced

diabetic rats, which is comparable to the standard antidiabetic drug metformin (Maurya et al 2008)[11]. The 4-week treatment with Withania coagulans dried fruit extract significantly reversed hyperglycemia in streptozotocin-induced diabetic rats that was comparable to glipizide[12].

**Antihyperlipidemic activity** The aqueous extract of Withania coagulans fruits in high fat diet induced hyperlipidemic rats, significantly reduced elevated serum cholesterol, triglycerides, lipoprotein and the LPO levels. The hypolipidemic effect of Withania coagulans fruits were found to be comparable with ayurvedic product containing Commiphora mukkul (Hemalatha et al 2006)[13]. The coagulanolide isolated from fruits of Withania coagulans has antidyslipidemic effect on mice (Maurya et al 2008)[11]. The hydroalcoholic extract of Withania coagulans dried fruits was effective and comparable to atorvastatin in controlling the high cholesterol diet-induced hyperlipidemia in rats.

**Anti-inflammatory activity:** The alcoholic extract of Withania coagulans showed significant anti-inflammatory effect in acute inflammation induced with egg albumin (Budhiraja et al 1977)[8]. A withanolide from Withania coagulans showed significant anti-inflammatory effects in acute inflammation (Budhiraja et al 1984)[14]. The hydro alcoholic extract of Withania coagulans fruits showed significant anti-inflammatory activity in carragenin induced rat paw oedema model (Rajurkar et al 2001)[15].

**Antifungal and Antibacterial Effects**: The essential oil obtained by steam distillation of the petroleum ether extract of the fruits was active against Micrococcus pyogens var. aureus and vibrio cholerae (Gaind & Budhiraja 1967)[16]. The volatile oil from the fruits of Withania coagulans showed antibacterial activity against Staphylococcus aureus and Vibrio cholerae (Khan et al 1993 Choudhary et al 1995)[17&18]. Two withanolides (14,15β-epoxywithanolide I [(20S,22R) 17β,20β-dihydroxy -14β, 15β-epoxy-1-oxo-witha-3,5,24-trienolide] and 17β- hy- droxywithanolide K (20S,22R) 14α,17β,20β-trihydroxy- 1-oxo-witha-2,5,24-trien-olide]) have been isolated from the Withania coagulans. The second compound was found to be active against a number of potentially pathogenic fungi (Choudhary et al 1995). The antifungal activity of the crude extract, 17β-hydroxy withanoloied k and withanolide F were tested against nine highly pathogenic fungi. These compounds also showed activity against gram positive bacteria (Atta-ur-Rahman and Choudhary 1998).

**Cardiovascular Effects:** A steroidal lactone, Withanolide isolated from the aqueous extract of fruits of *Withania coagulans*, has cardiovascular effect. A new withanolide, with a unique chemical structure similar to the aglycones of the cardiac glycoside, isolated from the fruits of Withania coagulans. This withanolide produced a moderate fall of blood pressure in dogs which has blocked by atropine and not 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)[19].

**Immunosuppressive Effects:** Withaferin A and withanolide E were reported to have specific immunosuppressive effects on human B and T lymphocytes as well as on mice thymocytes (Shohat et al 1978)[20]. 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)[21].

**Another Activity:**

**i**.Moreover, The hepatoprotective effect of 3F-hydroxy-2, 3 dihydro-withanolide F obtained from fruit of Withania coagulans was studied against the CCl4 induced hepatotoxicity in adult albino rats. (Budhiraja et al 1986)[22] showed that the hepatoprotective effect of withanolide F was more active than hydrocortisone.

**ii**. Withania coagulans has wound healing activities in streptozotocin-induced diabetic rats. The hydroalcoholic fraction of the methanolic extract (standardized by withaferin A) of Withania coagulans in both topical and oral form showed a significant increase in the rate of wound contraction. The withaferin-A is responsible for significant increase in the collagen levels, protein, DNA, SOD, CAT and decreased level of hexosamine (Prasad et al 2010)[23].

**iii**. The aqueous extract of Withania coagulans also exhibited free radical scavenging activity in an *in vitro* system using DPPH (Budhiraja et al 1986)[22] and (Hemalatha et al 2004)[9]. Aqueous extract of fruits of Withania coagulans have antioxidant potential against several diseases such as ageing, artherosclerosis etc. which caused due to ROS. ( Mathur et al. 2011)[24]

**iv**. The essential oil obtained by steam distillation of the petroleum ether extract of the fruits of Withania coagulans has shown anthelmintic activity (Gaind and Budhiraja 1967)[16]. The aerial parts of Withania coagulans have anthelmintic activity in ruminants (Jabbar et al 2006)[25]. Also Khare reported an anthelmintic activity for Withania coagulans (Khare et al 2007)[26].

**v**.Using the aqueous extract of Withania coagulans fruits in experimental rats have a diuretic potential. Withanolides from Withania coagulans are more polar in nature compared to the other Withania species. The diuretic effects may be associated with the presence of the active principles of polar nature where withanolides are the main chemical protagonist of this activity. Dabheliya et al (2010)[27] investigation's supports using Withania coagulans as the diuretic agent in traditional folklore medicine.

**vi.**The extract of Withania coagulans have hypotensive, respiratory stimulant and muscular relaxant activity in experimental animals Siddiqui et al (1963)[28]

**Conclusion:** The different part i.e. berries, leaves, root etc. of Withania coagulans posses variety of biological activity. It is an important medicinal herb as large numbers of phytochemicals (esterases, free amino acids, fatty oil, an essential oil, alkaloids and withanolides) have been isolated from this plant. Withanolides are steroidal lactones having significant pharmacological activities. In various studies it has been seen that the *Withania coagulans* posses several medicinal properties such as hepatoprotective, anti-inflammatory, antihyperglycaemic, free radical scavenging, hypolipidaemic, antimicrobial, cardiovascular, central nervous system depressant, immunomodulating, antitumour and cytotoxic activities. In Further study on this plant to elucidate its effect on other diseases and mechanism of action in depth is need of hour. In the coming era, it could be consider as noble ayurvedic drug for the treatment of various ailments.

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