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Therapeutic Potential of *Withania coagulans* Dunal. (*Rishyagandha*) on Diabetes Mellitus Type- II: A Review

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Abstract-

In *Ayurveda* there are many classical herbs frequently used in the treatment of diabetes mellitus type-II. In recent years, some new herbs have showed potential for the management of DM-II. One of such herbs is *Withania coagulans* Dunal. (*Doda Paneer*) which has profound hypoglycemic activity. *W. coagulans* has been acclaimed *Rishyagandha* in Ayurveda and used for nervine tonic, debility, insomnia, aphrodisiac, and rejuvenator. *Rishyagandha* (W. coagulans) is described in *Charaka Samhita* in "*Brihaniya Mahakashaya"*and "*Madhur Skandha Dravya*". *Acharya Charaka* has described two types of therapies for *Prameha*, *Brihana* for *krish* and *dourbala pramehi* and *Samshodhana* for *sthula* and *balvan pramehi*. So in *krisha* and *dourbala* patient, *Rishyagandha* improves the

quality of *Dhatu* production, promotes the *Ojas* formation by its *Brimhana* properties. The active compound withanolide isolated from the plant are considered to have hypoglycemic activity. Aqueous extract of the fruit significantly lower the blood glucose level. A 30 days study of Aqueous extracts on streptozotocin induced Swiss albino mice showed reduction of 48.5 and 52.6% in fasting blood glucose and postprandial glucose levels, respectively and prove to be better alternative for Hypoglycemic agents.

Keywords: Diabetes mellitus type-II, Withania coagulans, hypoglycemic agents, Withanolides.

INTRODUCTION

Among several health problems, *Prameha* is considered as one of arch enemy of the mankind. *Prameha* comprises of a number of disease with various physical and chemical change in urine. The manifestations of the disease are described as "*Prabhutavilmutrata*" which means frequent and copious urine with terbidity[1]. It is also believed that, if not cured or treated properly in due course of time, *Prameha* change to *Madhumeha*, which is similar to diabetes mellitus, the most debilitating disease[2]. Although the introduction of many oral hypoglycemic agents and insulin in modern science have great importance in the management of diabetes, the hazardous effects of these drugs after long term use are incurable or many times prove fatal. Ayurvedic management of diabetes aims not only to achieve a euglycemic state but also treat the root cause of disease. There are many medicinal plants mentioned in Ayurvedic texts, Particularly in *Nighantus* having *Pramehahara* properties. In the present paper, therapeutic potential of "*Rishygandha*" (*Withania coagulans* Dunal) in the management of *prameha* has been reviewed. The shrub is important for the property of coagulating milk possessed by its berries. The milk coagulating activity is due to the presence of enzyme. It is also known as "*Doda Paneer*" Which can 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. It is also used in Dyspepsia, flatulent colic and other intestinal infections. It is common throughout Pakistan. It is also found in North - West India and Afghanistan. *Withania coagulans* Duanl. belongs to family Solanaceae. Its fruits are used for liver complaints, *asthama*, and biliousness. Flowers are used in the treatment of diabetes. Antimicrobial, anti inflammatory, antitumor, hepatoprotective, anti-hyperglycemic, cardiovascular, immunosuppressive**,** free radical scavenging and central nervous system depressant activities of the plant have been reported. *Withania coagulans* is an important medicinal herb as large number of phytochemical have been isolated from this, which are in use in different herbal formulation and pharmaceutical products[3].

TAXONOMICAL DISCRIPTION[4]-

Order-Solanales

Family-Solanaceae
Subfamily-Solanoideae
Tribe-Physaleae
Subtribe-Withanine
Genus-Withania
Species-W.cougulans
Sanskrita name-Rishygandha[5]
Hindi name - Punir, Akri, Punir Bandh, Binputakah, Paneer doda.
English name- Indian Cheese maker, Indian rennet, Vegetable rennet.
Trade Name-Paneer dodi, Doda, Panir bed.

Distribution- The shrub is common in East India, Nepal, and Afghanisthan. In India it occurs in Panjab, Rajasthan, Shimla, Kumaun and Garhwal.

Morphological Identification - A rigid grey- tomentose undershrub 0.3-0.9 m. Leaves: 2.5-5.7 X 1-2.2cm. Lanceolate-oblong, obtuse, entire, uniform colour on both sides, thick, more or less rugose. Flowers: Dioceous, in axillary clusters; Fruits: Berry 6-8 mm, globose, smooth; Seeds: 2.5-3 mm, dark brown, ear shaped, glabrous. Flowering period: From January to April and berries ripen during January to May. The natural regeneration is from seed.[6]
Useful Part- Whole plant, roots, leaves, stem, green barriers, fruit seed and bark.

In Classics
1. B*rihaniya Mahakashaya*[7]
2. *Madhura Skandha dravya*[8]

In Northern India, its fruits are used in the treatment of Prameha.[9] This plant has the property of coagulating milk, and has been used for preparing vegetable rennet ferment for making cheese.

Classics References

The plant of *Rishygandha* (*W.coagulans* Dunal) is described in *Charaka Samhita* in *"Brihaniya Mahakashaya*" (A collection of drugs, which increase body mass) and "*Madhura Skandha Dravya"*

THERAPEUTIC USES-

- The fruit is sweet applied to wound, asthma, biliousness strangury.
- The berries are also used as blood purifier. The twigs are chewed for cleaning of teeth and smoke of the plant is inhaled for relief in toothache.
- The seeds are emmenagogue, diuretic, useful in opthalmia, lessens the inflammation of piles[11].
- In Nothern India traditional healers use dry fruit for treatment of Diabetes mellitus.
- It has also antimicrobial, antihelmenthic, antifungal, hepatoprotective, hypoglycemic, hypolipidimic, Cardiovascular, free radical scavenging, antitumor, immunosuppressive**,**
- Round capsular fruit and the leaves have the peculiar property of coagulating milk, a small portion is rubbed with a little water and added to the milk to be coagulate. Dried capsules also retain the coagulating property in an equal degree. The active principal name "withanin"

residing in the numerous small seeds contained within the capsules is a ferment closely allied to the animal rennet[12].

- 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.

- *Charaka* has described two types of therapies for *premeha*, that is *Sambrinhan* (process which increase body mass) for *krisha* and *durbala pramehi* and *samshodhana* (a type of therapy which eliminates impurities from body) for *sthula* and *balvan pramehi*.[10] So in *krisha* and *durbala* patient, *Rishyagandha* improves the quality of *Dhatu* production, promotes the oja formation, and cures the *prameha* by its *brimhana* property. In *sthula pramehi* (obese diabetic), trial drugs acts by virtue of *Dravya prabhava* (effect of drug). By *Dravya prabhava*, its act on the pathogenesis of *Madhumeha* and breaks down the continuity of *premeha*.

Phytochemistry-

Different phytochemistry studies have been done on *W. coagulans* and various compounds have been isolated from plant. The most important constitution of *W. coagulans* is Withanolides which can be chemically classified in the following groups[13].

a. Withanolide glycoside.
b. Withaphysalin
c. Physalin
d. Nicandrenons or ring D Aromatic Withanolides.
e. Jaborols or ring D Aromatic Withanoides.
f. Acnistins.
g. Perculactones.
h. Withajardines

The berries contain the milk coagulating enzyme, two esterases, free amino acids, fatty oils, an essential oil, and alkaloids. The amino acids present are proline, hydroxyproline, valine, tyrosine, aspartic acid, glycine, asparagine, cysteine and glutamic acid. Fourteen alkaloidal fractions have been isolated from the alcoholic extract of the fruits.

The leaves contain four steroidal lactones called withanolides, viz Withaferin-A,5,20 alpha (R) dihydroxy – 6 - alpha, 7-alpha-epoxy-1-oxo- (5 alpha) -1- oxo – with a 2 ,24 - dienolide and minor withanolides of which one is probably 5-alpha,17-alpha-dihydroxy-1-oxo-6-alpha,7-alpha-epoxy-22-R-with a-2,24-dienolide (the so-called withanone).[14]

PHARMACOLOGICAL STUDIES ON WITHANIA COAGULANS DUNAL-

1. **Antihyperglycaemic activity –** *W. coagulans* exhibited the hypoglycemic activity which is an effective and safe alternative treatment for diabetes (Budhraja et al 1977)[15]. Hypoglycemic activity of *W. coagulans* was exhibited in streptozotocin-induced rats (Hemalatha et al 2004)[16]

2. **Antihyperlipidemic activity** - The aqueous extract of *W. coagulans* fruits in

high-fat diet induced hyperlipidemic rats, Significantly reduced elevated serum cholesterol, triglycerides, lipoprotein. The hypolipidemic effect of *Withania* fruit was found to be comparable with an ayurvedic product containing *Commiphora mukkul* (Hemlatha et al 2006)17. The hydroalcoholic extract of *W. coagulans* dried fruits was effective and comparable to atorvastatin in controlling the cholesterol diet-induced hyperlipidemia in rats (Maurya et al 2008)[18].

3. **Antibacterial and antihelmintic activities -** The volatile oil obtained from alcoholic extract of fruits of *W. coagulans* has antibacterial activity against *S. aureus* and *Vibrio cholera*, and it is also found to have antihelmintic activity[19].

4. **Hepatoprotective effects -** Protective effect of 3-β-hydroxy-2,3-dihydrowithanolide F isolated from *W. coagulans* was tested against CCl4 - induced hepatotoxicity and the compound was found to possess marked protective effect. A comparison of the protective properties showed that it is more active than hydrocortisone on a weight basis[20].

5. **Immuno-suppressive effects -** Six new withanolides, withacoagulins A-F (1-6, resp.), together with ten known withanolides, 7-16, were isolated from the aerial parts of Withania coagulans. These compounds, including the crude extracts of this herb, exhibited strong inhibitory activities on the T- and B-cell proliferation[21].

6. **Diuretic effect -** The diuretic activity of the aqueous extract of fruits of *W. coagulans* was studied by in vivo Lipschitz test model with slight modifications using furosemide as a standard. The results indicated a significant increase in the urine volume by 79.12 % and 71.02 % at 500 mg/kg and 750 mg/kg body weight doses respectively compared to controls. Urinary electrolyte excretions were increased at both the doses compared to controls[22].

7. **Antimutagenic and anticarcinogenic effects -** The genotoxic nature of any herbal drug is determined on the basis of the presence of phytoconstituents. *W. coagulans* contains withanolides, which are reported for antitumor activity, and flavonoids which have been shown to possess antimutagenic and anticarcinogenic activities. The underlying mechanism behind the anti-mutagenic action of *W. coagulans* is still unknown. The antimutagenic activity of *W. coagulans* fruit extracts was investigated on cyclophosphamide-induced micronucleus formation in mouse bone marrow cells. The results confirmed that a single i.p administration of *W. coagulans* fruit extract at the doses of 500, 1000 and 1500 mg/kg body weight prior to 24 h significantly prevented the micronucleus formation in a dose-dependent manner in bone

marrow cells of mice as compared to cyclophosphamide group[23].

8. Wound healing activity - The hydroalcoholic fraction of the methanolic extract of W. *coagulans* was administered in the form of 10% w/w ointment topically and at a dose of 500 mg/kg body weight orally to streptozotocin-induced diabetic rats. The hydroalcoholic fraction in both the forms, i.e., topical (10% w/w ointment) and oral (500 mg/kg body weight,p.o.) showed a significant increase in the rate of wound contraction compared to diabetic controls[24].

CONCLUSION:

Medicinal plants are part and parcel of human society to combat diseases from the dawn of civilization. *W. coagulans* has been found to contain a vast array of biologically active compounds, which are chemically diverse and have got an enormous therapeutic potential. It has been proved that the *W. coagulans* possess several medicinal properties such as hepatic-protective, antimicrobial, cardiovascular, central nervous system depressant, immuno-modulating, anti-hyperglycemic activity. It not only lowers the blood sugar level but also minimizes the future complications of diabetes such as neuropathy, retinopathy, cardiovascular pathologies. It can be concluded from the present study that *Rishyagandha* fruit powder can be used effectively for a long-term therapy in the treatment of *Prameha* (type II Diabetes mellitus) without any side effect.

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