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"BRIEF REVIEW ON MEDICINAL ASPECTS OF *WITHANIA COAGULANS DUNAL*"

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ABSTRACT
Withania coagulans belonging to the family Solanaceae plays an important role in ayurvedic system of medicine. Apart from its medicinal value it is regarded as Indian Cheese maker due to its excellent quality of coagulating milk. The extracts of the plants reported the presence of alkaloids, steroids, Phenolic compounds, tannins, saponins, carbohydrates, proteins, amino acids and organic acids. Flower of the plant are used for treating Diabetes. For cleaning teeth twigs of the plants are also used while smoke of the plant if inhaled relief toothache. It acts as a multiple purpose medicine and renowned for its anti-inflammatory, antifungal activity, immunosuppressive effects, antibacterial, antihelmenthic, wounding healing activity, diuretic, Antihyperglycaemic and antihyperlipidemic, hepatoprotective activity, cardiovascular activities and anticarcinogenic effects.

KEYWORDS: Indian Cheese Maker, Phenolic compounds, Tannins, Immunosuppressive, Antiglycemic, Anticarcinogenic.

INTRODUCTION
Withania coagulans is an important medicinal plant belonging to the family Solanaceae. The plant is known as "Rishyagandha" in Sanskrit. This is also known as "Vegetable rennet" or "Indian Cheese maker" due to its milk coagulating property. The berries contain rennet like protease that can be used to clot milk for cheese production. The milk-coagulating activity is due to the presence of an enzyme, which can 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 then dried at low temperature and the enzyme is obtained as a brownish white powder. Milk coagulating property is due to the presence of an enzyme Withanin. A decoction prepared by mixing 1 ounce of its fruits to 1 quarts of boiling water. 1 tablespoon of this decoction is useful to coagulate near about 1 gallon of milk within hours.[1]

Figure showing the Flowering Plant of *Withania coagulans*

Medicinal plants play an important role in the development of herbal drugs. It is used as a traditional medicine and recommended for the treatment of various disorders including Dyspepsia, Flatulent colic, as blood purifier and other intestinal infections. The fruits of the plants are sweet are also used for liver complaints, asthma and biliousness. Plant is also used in treating nervous exhaustion, insomnia, failure to thrive in children and impotence. Flower of the plant are used for treating Diabetes. For cleaning teeth twigs of the plants are also used while smoke of the plant if inhaled relief toothache. The plant has many other properties including antimicrobial, anti-inflammatory, anti-tumor, hepatoprotective, anti-hyperglycemic, cardiovascular, immune-suppressive, free radical scavenging and central nervous system depressant activities. [2]

The plant is native of western Asia-Afghanistan and Indian Subcontinents and Nepal regions. In India is occurs in Punjab, Rajasthan, Shimla, Kumaun and Garhwal. The leaves showed the presence of 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 ithanolides, of which one is probably 5, 17-dihydroxy-1-oxo-6, 7-epoxy-22R-witha-2,24-dienolide (the so called withanone). The extracts of the plants reported the presence of alkaloids, steroids, Phenolic compounds, tannins, saponins, carbohydrates, proteins, amino acids and organic acids.[3]

Vernacular Name of *W. coagulans*

The plant is known by different names in different languages. Some of these include:
Bengal: Asvagandha
Mumbai: Kaknaj
Gwalior: Asgandha
Panjab: Khamjaria, Khamjira, Panir
Sindhi: Punir ja fota, Punirband
Persian: Kaknajehindi, Punirbad
Arabic: Javzulmizaja, Kaknajehindi
Canares: Asvagandhi
Telgu: Panneru-gadda
Urdu: Hab kaknaj

MORPHOLOGICAL DESCRIPTION

Withania coagulans belonging to the family Solanaceae is a small shrub about 60-120cm tall. The leaves are lanceolate oblong while sometimes appears to be slightly ovate or obtuse with very short stalked. The flowers are usually yellowish in color positioned in axillary cymose clusters. They are dioecious and polygamous in nature. Calyx is long (6mm), campanulate triangular teeth. The corolla is 8mm long with lobes that are ovate-oblong, subacute. The male flowers have stamens approximately 0.85mm long, the anthers smaller than in the male flowers and sterile.

Figure showing the Seed of *Withania coagulans*

The ovary is ovoid, glabrous, the style glabrous, and the stigma mushroom-shaped, 2-lamellate. The berries usually 6-8mm in diameter are red in color, smooth to touch enclosed in leathery calyx.

The seeds are dark brown in color, glabrous and ear shaped with a sharp fruity smell.[1] Flowering is observed January to April and berries ripen during January to May. The natural regeneration is through seeds.

TAXONOMY

Kingdom : Plantae
Unranked: Angiosperms
Unranked: Eudicots
Unranked : Asterids
Order : Solanales
Family: Solanaceae
Genus: *Withania*
Species: c*oagulans*

MEDICINAL USES

Antihyperglycaemic and Antihyperlipidemic Effects:

The extracts of *W. coagulans* (both aqueous and chloroform extracts) have showed its positive effects in reducing blood glucose level, total cholesterol, triglyceride, LDL, VLDL while its helps in increasing HDL.[4,5] Aqueous extract of fruits is also found to be important in lowering serum LPO and hepatic LPO levels streptozotocin induced diabetic rats.[6,7] Hemakatha et al in 2006 reported the hypolipidemic effect of *W. coagulans* fruits.[8] The coagulanoside isolated from their fruits has antidyslipidemic effect on mice as reported by Maurya et al in 2008.[9]

Antimutagenic and Anticarcinogenic Effects

The withanolide content in *W. coagulans* has been showed to possess Antimutagenic and anti carcinogenic activities while the reason is still unknown. Withaferin A has marked tumor inhibitory property when studied *in vitro* against cells derived from human carcinoma of nasopharynx (KB). It also acts 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 arcinoma. It also caused mitotic arrest in

embryonal chicken fibroblast cells. Single doses of intraperitoneal administration of the fruit extracts at the doses of 500, 1000 and 1500mg/kg body weight prior to 24hrs significantly prevents the micronucleus formation in dose dependent manner in bone marrow cells of mice as reported by Mathur et al., 2011.[10]

Immune-suppressive Effects

Shobat et al reported Withaferin A and Withanolide E to have specific immunosuppressive effects on human B and T lymphocytes as well as on mice thymocytes.[11] Coagulin-H, a well known Withanolide was estimated for its effect on various cellular functions related to lymphocyte proliferation, interleukin 2 and cytokine expression. Coagulin-H was found to have a powerful inhibitory effect on lymphocyte proliferation and the Th-1 Cytokine production. The inhibition of the phytohaeagglutinin (PHA) activated T-cell proliferation by Coagulin –H.[12]

Hepatoprotective Effects

3β –hydroxyl-2, 3-dihydrowithanolide F found in the extract of *W. coagulans* was tested against CCl_4 induced hepatotoxicity showed to have more active regarding protective properties than hydrocortisone on a weight basis as reported by Budhiraja R.D. et al in 1986. The protective effect was assessed by observing pentobarbitone induced hypnosis, the determination of serum glutamic oxaloacetic transaminase as well as serum glutamic pyruvic transaminase levels. Withanolide secreted observed to have protected the liver significantly.

Diuretic Effect

The treatment with aqueous extracts at 500 and 750mg/Kg showed Dose-independent Diuretic effect. The extract at 500mg/kg showed a significance increase in Na^+, K^+ and Cl^- by 94.64%, 97.76 % and 92.72% respectively. At 750mg/kg the volume of urine was increased by 71.02 % as compared to control while the extract possess increase amount of Na^+, K^+ and Cl^- by 80.57%, 90.29% and 75.79% respectively. The aqueous extract of fruits of *W. coagulans* has diuretic activity showed significant increase in urine volume by 79.12% at 500mg/kg of body weight doses as compared to controls as reported by Dabheliya J et. al.[13]

Antibacterial and Antihelmenthic Activities

Withaferin A is the most important of the withanolides isolated till date. It has good antibiotic property. 10µml quantity has the potency to inhibit the growth of various gram-positive bacteria, acid fast bacilli and aerobic bacilli. It was active against *Micrococcus pyogenes ar. aureus* and *Bacillus subtilis glucose-6-phosphate-dehydrogenase*. The alcoholic extract of fruit has antibacterial and activity against *S. aureus* and *V. cholera*. It also possess antihelmenthic activity.[14,15]

Wound Healing Activity

The hydroalcoholic fraction of the methanolic extract of W.coagulans was used in the form of 10% w/w ointment topically and at a dose of 500mg/kg body weight orally to streptozotocin- induced diabetic rats. The hydroalcoholic fraction in both in both forms the form, i.e., topical and oral showed a showed a significant increase in the rate of wound contraction compared to diabetic control.[16]

Anti –inflammatory and Anti-arthritic Activity

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. Extracts from fruits shown to possess anti-inflammatory properties. Budhiraja et al., in 1977 reported that the alcoholic extract showed significant anti-inflammatory effect in acute inflammation with egg albumin.[7]

Antifungal Activity

The ethanolic extracts of the whole plant contains withanolide, 14,15β-epoxywithanolide I [(20*S*,22*R*) 17*β*,20*β*-dihydroxy-14*β*,15*β*-epoxy-1 oxowitha- 3,5,24-trienolide] and 17β-hydroxywithanolide K (20*S*,22*R*) 14*α*, 17*β*, 20*β*-trihydroxy-1-oxo-witha-2,5,24- trien-olide] which has been found to be active against a number of pathogenic fungi.[17] The antifungal activity of the crude extract, 17β-hydroxy Withanolide k and withanolide F were tested against nine highly pathogenic fungi. These compounds also showed activity against gram positive bacteria has been reported by Atta-ur-Rahman and Choudhary in 1995.[18]

Cardiovascular Effects

Withanolide extracted from the fruits of the plant showed to have similar structure to that of aglycones of cardiac glycosides and was screened for cardiovascular effects. 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 has been reported by Budhiraja et al in 1983.[19]

CONCLUSION

The use of herbal drugs is increasing worldwide. This is due to presence of having fewer or no side effects as compared to synthetic drugs. It is an important medicinal herb as large number of withanolide has been isolated from the plant. These withanolide are steroidal lactones which is having pharmacological activities. Isolation of these withanolide will surely enhance their pharmacological value. Coagulans L are present in major amount in *W. coagulans*. Withanolides containing a 14, 20–epoxide bridge are specific to *W. coagulans.* Several medicinal properties include anti-inflammatory,

antifungal activity, immunosuppressive effects, antibacterial, antihelmenthic, wounding healing activity, diuretic, Antihyperglycaemic and antihyperlipidemic, hepatoprotective activity, cardiovascular activities and anticarcinogenic effects. The variety of activities reported for the extracts, fractions and withanolides isolated from *W. coagulans.*

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