



Review on *Withania coagulans* (Paneer Phool)- for the treatment of diabetes

Miss. Nandini Shimpi¹, Mr. Hemant Bhosle², Miss. Swati Gutte³, Miss. Monika Vishe⁴.

Institute of Pharmaceutical Sciences and Research (for girls) (College Code - 6914) Pune-Solapur Highway, Swami Chincholi (Bhigwan), Tal-Daund, Dist-Pune, 413 130.

Abstract:

Diabetes mellitus (DM) is one of the serious long-term health problems. In ancient India, it was called "Madhumeha". Diabetes is a common metabolic disease that causes an increase in blood sugar levels. Ayurvedic drugs are widely used in the treatment of many diseases. Paneer Dodi (*Withania coagulans* Dunal) is a small South Asian bush that belongs to the Solanaceae family. The seeds, the emetics, the alteration, and the diuretic properties of the plants were described. They are also beneficial for liver problems, asthma, and biliary illnesses. This plant, commonly known as an Indian cheese maker, is used for the fermentation and production of vegetables and cheese, due to the enzyme activity of Paneer Dodi fruit. A large number of botanical compounds have been isolated from *Withania coagulans*, which are responsible for various pharmacological effects of this plant. The aim of the paper is to project a detailed review of platforms, chemical components, and pharmaceutical properties. It also included therapeutic effects of the whole plant and its extracts and isolated analogues.

Keywords: Madhumeha, Paneer Dodi, Asianbush, biliary illnesses, analogues.

Introduction:

In the Indian Medical system, many herbal and herbal medicines have long been used for various diseases of humans (Brekhman and Dardimov 1969). Traditional medicine is increasingly sought by traditional practitioners and herbalists for the treatment of various diseases. At present, more than 80% of the world's population depends on health products derived from plants for daily intake because of their absence of side effects (Hassan 2009; Gangadhar 2012). *Withania coagulans* Dunal (Solanaceae) is commonly known as "vegetable rennet" or "Indian Cheese Manufacturer" and is well known for its medicinal and ethno-pharmacological applications. *W. coagulans* (Solanaceae) is often referred to in Hindi as "Panir ke phool" and is widely and regularly used in India and other tropical countries. *W. coagulans* dunal is known for its ethnopharmacological activity. In Punjab, the fruits of *W. coagulans* are used as the source of the coagulation enzymes to clot milk called paneer. Diabetes mellitus is a chronic metabolic disorder that is increasingly prevalent worldwide and is the most common type of diabetes characterized by hyperglycemia, insulin resistance, and relative insulin deficiency. Type 2 diabetes suffers from various short and long-term complications and is often fatal. *W. coagulans* is used in chronic liver disease. A combined Hepatoprotective medicine of Ayurvedic herbs "Liv-52" contains extracts from *W. coagulans* and *W. Somnifera*. They are also used to treat diabetes, dysplasia, flatulent colic, and other

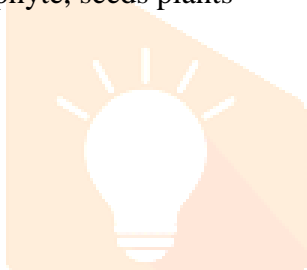
intestinal infections. In parts of the Pakistani-Indian subcontinent, strawberries are used as blood purifiers. The Leaves Are chewed for teeth cleaning and the smoke of the plant is inhaled to alleviate tooth pain 5-8.

Botanical description of Withania coagulans:

- Botanical Name: Withania coagulans Dunal ● Family: Solanaces
- Subfamily: Solanoideae.
- Tribe: Physaleae.
- Subtribe: Withaninae.
- Sanskrit Name: Rishyagandha 1&2
- Hindi Name: Punir, Punir bandh, Akri, Binputakah, Paneer Doda.
- English Name: Indian Cheesemaker, Indian Rennet, Vegetable Rennet.
- Trade Name : Paneer dodi, Panner, doda, Panir bed, Paneer dhodi.

Taxonomical classification:

- Kingdom: Plantae, plants
- Subkingdom: Tracheobionta, vascular plants
- Superdivision: Spermatophyte, seeds plants
- Division: Angiosperm
- Class: Dicotyledons
- Order: Tubiflorae
- Family: Solanaceae
- Genus: Withania
- Species: Coagulans



Vernacular Name of Withania coagulans:

The plant is known by different names in different local languages such as;

Language	Vernacular Names
Bengal	Asvagandha
Bombay	Kaknaj
Gwalior	Asgandha
Panjab	Khamjaria, Khamjira
Sindhi	Punirjafota, Punirband
Persian	Kaknajehindi, Punirbd
Arabic	Kaknajehindi
Telgu	Panneru-gadda
Urdu	Hab kaknaj

Geographical sources:

It is found in the Eastern Mediterranean and extends to North Africa and Southeast Asia. It is growing throughout India In Dry areas such as Punjab, Gujarat, Rajasthan, Shimla, Kumaon, and Gujarat.

Morphological characteristics:**Seeds:**

Seeds of Dodipaneer 2.5-3.0 mm in diameter, dark brown, slightly pear-shaped, pale. Natural regeneration occurs from seeds.



Fig No.1 Seeds of Paneer Dodi

Leaves:

The Leaves of the Paneer Dodi 2.5-5.7 by 1-2.2cm long, lanceolate-oblong, complete, obtuse, uniform color on both sides, thick, small, or more rugose with acute base.



Fig No.2 Leaves Of Paneer Dodi

Flowers:

The flowers of the Paneer Dodi are long, campanulate, clothed with fine stellate grey hair, triangular teeth, 2.5 mm long dioecious, in axillary clusters, 0.6mm long, inflexible, slender, calyx 6mm long. The flower's corolla length is 8mm, is vertically measured outside and divided by about a third down; the lobes are oval and subacute [1]. The stem is about the same width as the base of the corolla tube; the filament is 2mm long and glabrous; the anthers are 3 mm long. Ovary ovoid, without style or stigma; female flowers stamens about the same size as the upper tube of the corolla; filaments 2 mm long, glabrous; anthers 3-4 mm long. Female flowers: Stamens

reach just the 12th height of the corolla tube; filaments about 0.85mm long; the thersin male flowers are small and sterile. Within The Flowers the ovaries are ovoid, glabrous; style glabrous; mushroom-shaped stigma, and 2-lamellat. The Plants bloom from November to April and the fruits from January to May.



Fig No.3 Flowers Of Paneer Dodi

Fruits:

Berry 6-8 mm.Globose, smooth, closely curved by the enlarged membrane calyx, the outside-pubescent scurfy-pubescent.



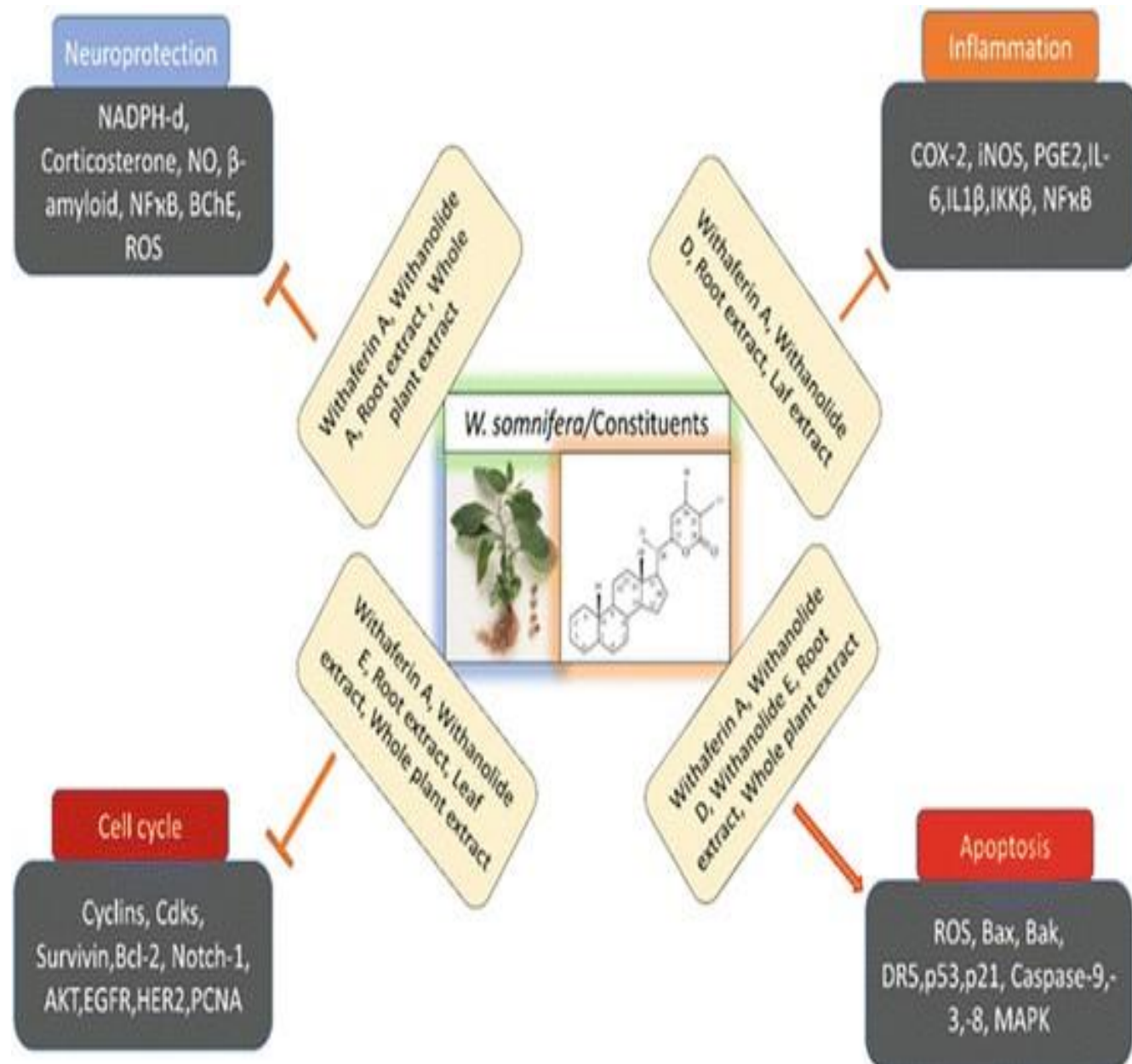
Fig No.4 Fruit Of Paneer Dodi

Chemical constituents:

Chemical and Spectral methods identified

3,14,20F,27-tetrahydroxy-1-oxo-20R,22R-with-5,24-dienolide. The structure is correlated with comparative studies of closely related withanolides. Withania coagulans is a sterile lactone-rich in sterile lactone called withanolides, naturally occurring polyhydroxy 28 sterile lactones [14,48,50]. The structure of the withanolide is characterized by six or five lactones and lactone rings glued to an intact or rearranged Ergosten skeleton. The Fruits Contain Milk coagulation enzymes, two esterases, free amino acids, fatty acids, essential oils, and alkaloids [51]. The protein contains five amino acids: proline, hydroxyproline, valine, tricolorine, aspartate, glycol, aspartate, tricoloride, and glutamine. Fourteen Alkaline parts have been isolated from fruit alcoholic extracts, while seeds obtained from oil ether produce lipids and unprofitable substances. Contains ergosta-5,25-diene-3-D-glucoside and withanolide from W.coagulans. Five withanolides were isolated from the roots of the

plant. There are two types of side chains in the 17 and 17 directions of withanolides. Essential oils have antimicrobial and antihelminthic properties compared to *Micrococcus pyogenes* var. *Aureus*.



Therapeutic effects:

Diabetes mellitus: is a chronic disease that affects all groups of people from different parts of society. Modern Hectic Lifestyles contribute to an increase in diabetes patients, some of whom are between 30 and 40 years old. The causes include increased tension, unhealthy eating habits, and increased dependency on junk food. Smoking, increased tobacco use, pollution, and genetics are also factors that increase diabetes in young people. Although oral hypoglycemic agents such as sulfonylurea and biguanide continue to be the main protagonists in disease treatment, there is increasing interest in herbal medicine due to the side effects associated with oral hypoglycemic agents¹⁹. It has been found that *Withania coagulans* Dunal has profound hypoglycemic activity. *Withania coagulans* Dunal showed hypoglycemic activity, which is an effective and safe alternative treatment for diabetes^{20, 21, 22}. Isolated alkaloids and steroids from plant sources are responsible for the hypoglycemia of these sources²³. Paneer Doda not only blood glucose but also repairs the beta cells of the pancreas to provide insulin to the body²⁴. *Withania coagulans* affect various locations in different ways to effectively control the factors and pathways that lead to diabetes. Synthetic antidiabetics only work in one place. It attacks various factors that precipitate the condition of diabetes and corrects the degenerative complications caused by diabetes. It is a safe and effective dietary supplement to synthetic anti-diabetic drugs, as a single agent for the treatment of diabetes.

Inflammation: inflammation is a complex biological response of vascular tissue to harmful stimulants such as pathogens, damaged cells, or stimulating substances. The alcohol extracted from *Vaccinium coagulans* Dunal has shown significant anti-inflammatory effects in acute inflammation caused by egg albumin. Subacute Inflammation induced by formalin and granulated tissue is formed by the cotton pellet method 21. Budhiraja et al. 26 reported the anti-inflammatory activity of ethanol from *Withania coagulans* Dunal. Hydroalcoholic extracts from *Withania coagulans* Dunalberry have demonstrated significant anti-inflammatory activity in carrageenan-induced rat paw edema models 27. Budhiraja et al. (1984)28 showed that water extracts of the fruit of *Withania coagulans* Dunal Have a significant anti-inflammatory activity of 10 mg kg⁻¹ in subacute inflammation models such as granuloma formation and formalin-induced arthritis in rats.

Cancer: Cancer, known from a medical point of view as a malignant neoplasm, is a wide range of diseases that involve uncontrolled cell growth. In cancer, cells divide and grow uncontrollably and form malignant tumors. Invading parts of the nearby body. Cancer can also spread to more distant parts of the body through the lymph system and blood. Not all tumors are cancerous; benign tumors do not invade jacent tissues or spread throughout the body. The anticancer effect of *Withania* has been extensively studied, and its effectiveness has been proven to reduce tumor size. *Withania coagulans* Dunal contains anecdotes, which have been reported to have antitumor effects, and flavonoids, which have shown antimutagenic and anticarcinogenic effects. The treatment of *withania coagulans* Dunal's root extract on induced skin cancer in mice significantly reduced the incidence and average number of skin injuries compared to the control group. Withaferin Ademons treated the inhibition of tumors against cells derived from nasopharyngeal human carcinoma, while Shohat et al. (1967)30 and Shohat and Joshua 31 Discovered the effect of tumor chemotherapy and immune stimulation mice with tumors.

It also showed anti-proliferative activity against head adenosquamous carcinoma by reducing cells ur vivalin invitro cells 32. The Mechanism is part of the result of the inhibition of the G2/M cell cycle and induction of apoptosis in HNSCC cells. In another study, *Withania coagulans* Dunal was evaluated for the antitumor effect of lung cancer in male albino mice caused by urethane. *Withania coagulans* Dunal fruit extract administered in doses of 500, 1000, and 1500 mg/kg prior to 24 h significantly prevents the formation of micronuclei in bone marrow cells based on doses compared to the group of cyclophosphamide 33. Water extracts from *Withania coagulans* Dunal have been used to inhibit the cytotoxic effects of chicken lymphocytes, and the enzyme inhibition activity induced by dimethyl sulfide (DMSO) is observed to reduce the production of TNF-G34.

Cardiovascular disease: a type of disease involving the heart, blood vessels (arteries, capillaries, veins), or both 35. Cardiovascular Diseases refer to all diseases that affect the cardiovascular system, mainly heart disease, brain and kidney vascular diseases, and peripheral arteries 36. Cardiovascular diseases have many causes, but atherosclerosis and/or high blood pressure are the most common. In high-fat diets, *Withania coagulans* Dunal fruit extracts induced hyperlipidemia in rats, significantly reducing serum cholesterol, triglycerides, lipoproteins, and LPO levels. This drug also showed low-lipid activity Triton hypercholesterolemia. The hypolipidemic effect of Paneer Doda fruits was found to be comparable to that of Ayurvedic products 37. Cocaolinolide Isolated from fruits of *Withania coagulans* Dunal hasanti-distribution effectinmice 38. Water extracts of dried fruit from *Withania coagulans* Dunal (1g/kg per oral)also reported hyperlipid activity in hypercholesterolemia caused by Triton in albino rats 37. Antihyperlipidemic and antiatherosclerotic effects of extracts of fruit from *Withania coagulans* Dunal have also been reported in diabetic rats caused by streptozotocin 39. Hypolipid activity can be caused by interference in the synthesis, metabolism, and excretion of lipids. Studying the active principle of this action is underway. *Withania coagulans* Dunal fruit extracts contain many withanolides and lactones, which have been reported to be beneficial for the cardiovascular system in dyslipidemia 40,41,42 and 43.

Hypertension: is a chronic disease in which blood pressure in the arteries is elevated (HTN). (2010) 45 revealed that the water extract of *Withania coagulans* Dunalhas demonstrated and powerful diuretic potential. Fruits had diuretic activity 46,47.

Alzheimer's Disease: is a neurological disease that causes cognitive decline by killing brain cells. Neurodegenerative dementia, the disease starts soft and progressively worse 48. It has also been reported that withanolides inhibit metastatic activity and quinone reductase. Some of them have been shown to have a preferred effect on events in the cascade of cholinergic signal transmission in the cortical and basal forebrain, indicating their promise to treat Alzheimer's disease 49.

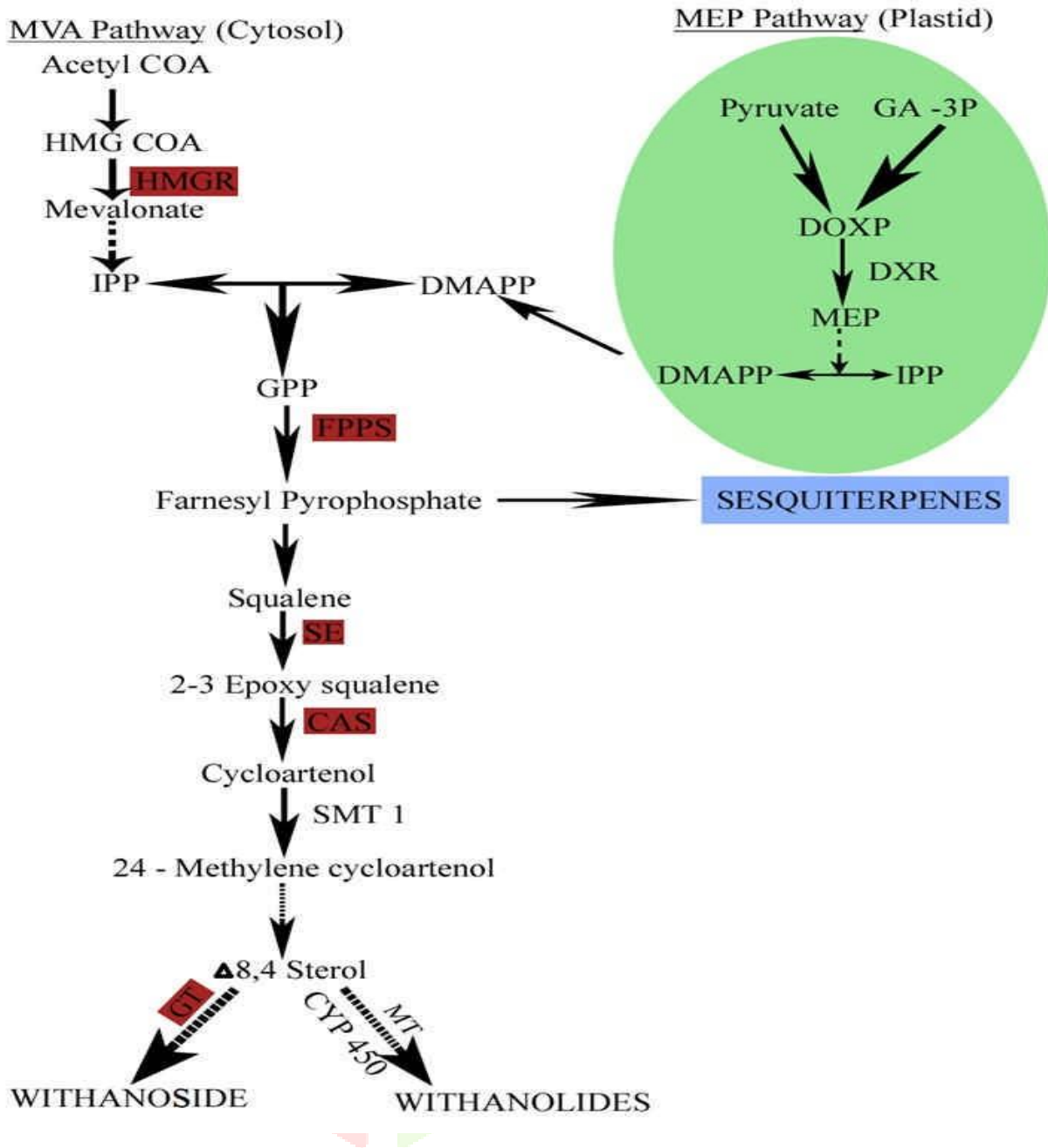
central nervous system: Diseases of the central nervous system It has been found that the isolated bioactive metabolites of the withania help alleviate many disorders of the central nervous system, such as epilepsy, anxiety, depression, catalepsy, and sleep. In mice, rabbits, and dogs, the total extract of *Sania coagulans* Dunal contains a central nervous system (CNS)inhibitor activity 56, 21, and 57.

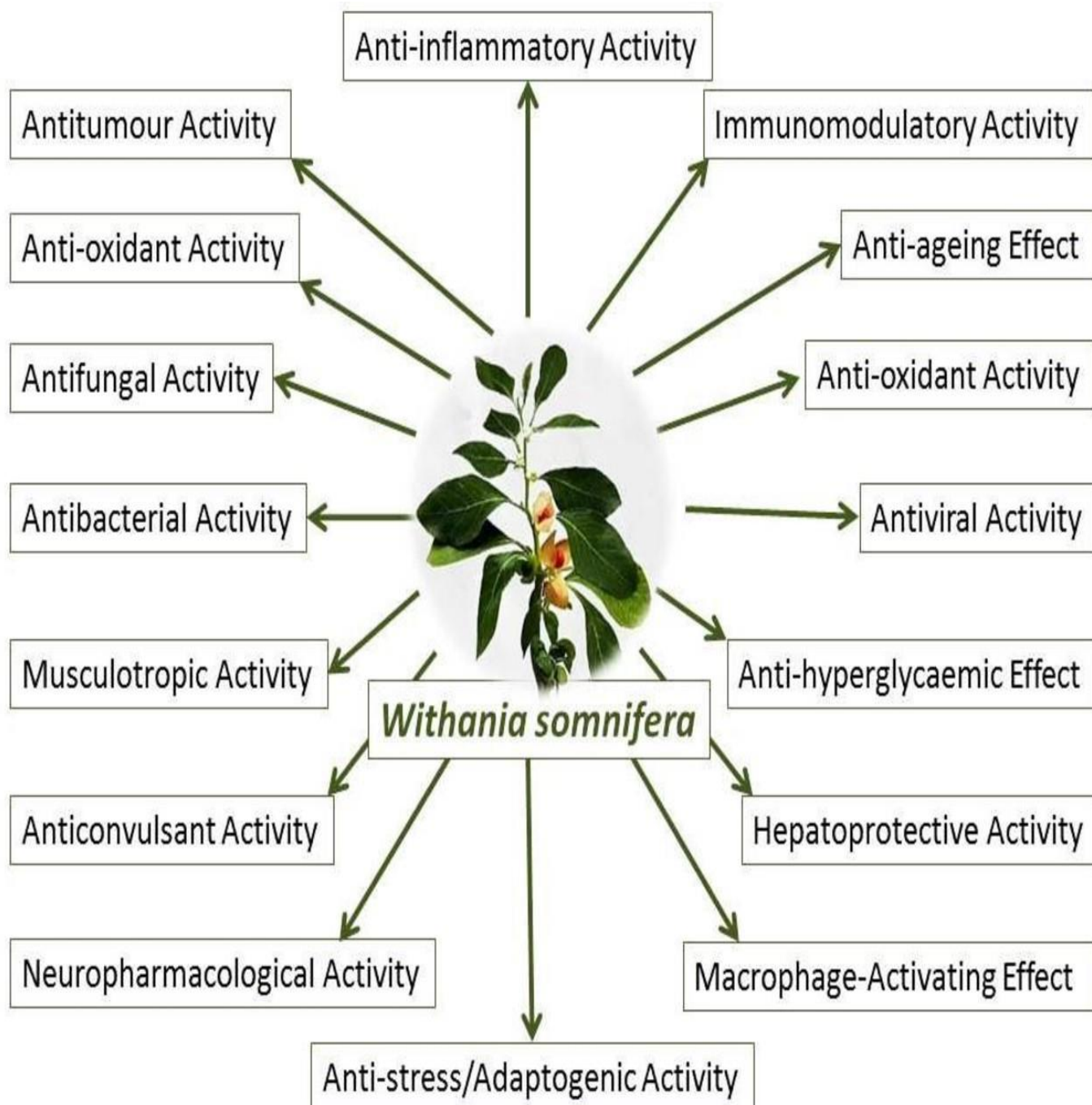
The symptomatic activity: the hydrolysis alcohol fraction of *Sania coagulans* Dunal methanol extract is administered to diabetic rats caused by streptozotocin and injected with 10% w/w topically and 500 mg/kg body weight orally. The hydroalcoholic fraction was significantly increased by 10 percent in topical and oral alcohols (500 mg/kg body weight) compared to diabetic control 58;

Miscellaneous: protective effect of 3-hydroxy-2,3-dihydro withanolide F isolated from *Withania coagulans* Dunal was tested against CCl₄-induced hepatotoxicity and the compounds showed a significant protective effect 26. The essential oil obtained by steam distillation of the oil ethyl extract from the fruits of *Withania coagulans* Dunal Showed anthelmintic activity. The aerial parts of the *Withania coagulans* Dunal have anthelmintic activity in ruminants. Khan also reported anti-helmintic activity for *Withania coagulans* 50,59,60. *Withania coagulans* Dunal root extract significantly (P0.05) reduced morphine withdrawal steps and reduced morphine dependence so that it can be successfully used to treat addiction.

Bacterial and fungi activity: Essential oils extracted by steam distillation of fruits of oil have been active against *Micrococcus pyogenes*, *Aureus* And *Vibrio cholerae* 50. Two Aromatics (14, 15 Ethanol I [(20S,22R)]) 17, 20 hydroxyls 14, 15 epoxy ls1 Ozols with 3,25 trienols) and 17 hydroxyls K (20S, 22R) 14, 17, 20 trihydroxy 1 oxo 2,5 trienols)) were isolated from *withania coagulans* Dunal. It was found that the second compound was active against some potentially pathogenic fungi 51. (2010) 52 concluded that methanol extracts from *Heliotropism Sterigosum* had synergistic effects with *Withania coagulans* Dunal against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*.

Biosynthesis of withania coagulans:



Pharmacological action:**Conclusion:**

The review article summarizes botanical names, taxonomic classification, morphology, phytochemistry, biosynthesis of withanolides, traditional uses, and pharmacological effects of *Withania coagulans*. *Withania Coagulans*, known by the name "Panner Dodi", is the most important multi-purpose Ayurvedic herb, widely used in herbal formulations. Panner Dodi is chemically rich in steroidal lactone, known as an anolide with significant pharmacological activity. In this study, we reviewed the literature on *Withania Coagulans* and pharmacological activities such as anti-inflammatory activity, anti-inflammatory activity, cardiovascular effect, antimicrobial activity, hepatoprotective activity, antifungal activity, antioxidant activity, wound healing activity, antitumor properties, hyperlipid activity. However, more clinical trials are needed to support its therapeutic use. As a result, there is still ample room for growth. Further scientific exploration of *Withania coagulans* to determine their therapeutic efficacy as well as commercial potential.

Reference:

1. World Health Organization (WHO) (2002), The World Health Report 2002, Geneva, Switzerland, World Health Organization (<http://www.oecd.org/els/healthsystems/40324263.pdf>)
2. <http://www.mrc.ac.za/chronic/cdloverview.pdf>
3. <http://umm.edu/health/medical/altmed/treatment/herbal-medicine>
4. M. Eddouks, De Feo V. Chattopadhyay & W.C. Cho, Medicinal plants in the prevention and treatment of chronic diseases. Evid Based Complement Alternat Med. 2012, 458274
5. W. Dymock, C. J. H. Waden and D. Hopper, Pharmacographia Indica, Reprinted by Institute of Health and Tibbi Research, 1972, Karachi, pp-306
6. Y. R. Chadha, The Wealth of India Publication and Information Directorate CSIR, 1976.
7. V. Gupta and B. B. Keshri, *Withania coagulans* Dunal (Paneer Doda): A Review. International Journal of Ayurvedic and Herbal Medicine, 2013 3(5):1330–1336.
8. Illustrated Dravyaguna Vijnan, Vol. 5, by Prof. P.V. Sharma, Chaukhamba Bharati Academy, Reprint 2006.
9. S. Mishra, Studies on Madhumeহারাকarma of Rishyagandha (*Withania coagulans*) and Amalaki (*Emblica officinale*). Ph.D. research work in the department of Dravyaguna, Faculty of Ayurveda, IMS, BHU, 2008.
10. <http://www.flickr.com/photos/atropanthe/2863887183/>
11. http://www.herbalveda.co.uk/index.php?dispatch=products.view&product_id=30157
12. D. Mathur, R. C. Agrawal and V. Shrivastava, Phytochemical screening and determination of the antioxidant potential of fruits extracts of *Withania coagulans*. Recent Research in Science and Technology, 2011, 3(11): 26-29.
13. W. Kreis and F. Muller-Uri, Biochemistry of sterols, cardiac glycosides, brassinosteroids, phytoecdysteroids, and steroid saponins. In: Michael W (ed), Annual Plant Reviews, 2010, Vol 40. Wiley-Blackwell, Singapore, pp 304–363.
14. D. Lavie, E. Glotter and Y. Shvo, Constituents of *Withania somnifera*. III. The side chain of withaferin A. J Org Chem., 1965 a, 30:1774–1778.
15. D. Lavie, E. Glotter and Y. Shvo, Constituents of *Withania somnifera*. IV. The structure of withaferin A. J. Chem. Soc., 1965 b, IV: 7517–7531.
16. M. Khodaei, M. Jafari, M and Noori, Remedial use of withanolides from *Withania coagulans* (Stocks) Dunal. Advances in Life Sciences, 2012, 2(1): 6-1920) Budhiraja RD, Sudhir S, Garg KN. Cardiovascular effects of a withanolide from *Withaniacoagulans*, dunalfruits. Indian journal of physiology and pharmacology. 1983 Apr 1;27(2):129-34.

17. Mir SR, Ali M, Waris M, Sultana S. Chemical constituents from the fruits of *Withaniacoagulans* (Stocks) Dunal. *Trends in Phytochemical Research*. 2020 Jun 1;4(2):45-58.
18. Neelam-Bare B, Pratima-Jadhav S. Pharmaceutical importance of *Withaniacoagulans* in health and diseases. *International Journal of Advances in Science Engineering and Technology*. 2017;5(3).
19. Mirjalili HM, Fakhr-Tabatabaei SM, Bonfill M, Alizadeh H, Cusido RM, Ghassempour A, Palazon J. Morphology and withanolide production of *Withaniacoagulans* hairy root cultures. *Engineering in Life Sciences*. 2009 Jun;9(3):197-204.
20. Gupta S, Sidhu MC, Ahluwalia AS. Plant-based remedies for the management of diabetes. *Current Botany*. 2017 Mar 21; 8:34-40.
21. Budhiraja RD, Bala S, Garg KN. Pharmacological investigations on fruits of *Withaniacoagulans*, Dunal. *Planta Medica*. 1977 Sep;32(06):154-7.
22. Ramaiah PA, Lavie D, Budhiraja RD, Sudhir S, Garg KN. Spectroscopic studies on a withanolide from *Withaniacoagulans*. *Phytochemistry*. 1984 Jan 1;23(1):143-9.
23. Gupta PC. *Withaniacoagulans*Dunal-an overview. *International Journal of Pharmaceutical Sciences Review and Research*. 2012;12(2):68-71.
24. Liu Q, Meng X, Li Y, Zhao CN, Tang GY, Li HB. Antibacterial and antifungal activities of spices. *International journal of molecular sciences*. 2017 Jun;18(6):1283.
25. Sudhir S, Budhiraja RD, Miglani GP, Arora B, Gupta LC, Garg KN. Pharmacological studies on leaves of *Withaniasomnifera*. *Planta Medica*. 1986 Feb;52(01):61-3.
26. Budhiraja RD, Sudhir S. Review of biological activity of withanolides. *Journal of Scientific and Industrial Research*. 1987.
27. Mughal T, Shahid S, Qureshi S. Antifungal studies of *Withaniacoagulans* and *Tamarixaphylla*. *J. Appl. Pharm*. 2011;3(3):289-94.
28. Jaiswal D, Rai PK, Watal G. Antidiabetic effect of *Withaniacoagulans* in experimental rats. *Indian Journal of Clinical Biochemistry*. 2009 Jan 1;24(1):88-93.
29. Salwaan C, Singh A, Mittal A, Singh P. Investigation of the pharmacognostical, phytochemical and antioxidant studies of plant *Withaniacoagulans*dunal. *Journal of Pharmacognosy and Phytochemistry*. 2012 Sep 1;1(3):32-9.
30. Mathur D, Agrawal RC, Shrivastava V. Phytochemical screening and determination of the antioxidant potential of fruits extracts of *Withaniacoagulans*. *Rec Res SciTech*. 2011 Jun 2; 3:26-9.
31. Ojha S, Alkaabi J, Amir N, Sheikh A, Agil A, Fahim MA, Adem A. *Withaniacoagulans* fruit extract reduces oxidative stress and inflammation in kidneys of streptozotocin-induced diabetic rats. *Oxidative medicine and cellular longevity*. 2014 Sep 14;2014.
32. Sharma S, Joshi A, Hemalatha S. Protective effect of *Withaniacoagulans* fruit extract on cisplatin-induced nephrotoxicity in rats. *Pharmacognosy research*. 2017 Oct;9(4):354.

33. Mathur D, Agrawal RC. Evaluation of in vivo antimutagenic potential of fruit extracts of Withaniacoagulans. *Der Pharma Chemica*. 2011;3(4):373-6.
34. Maher S, Choudhary MI, Saleem F, Rasheed S, Waheed I, Halim SA, Azeem M, Abdullah IB, Froeyen M, Mirza MU, Ahmad S. Isolation of antidiabetic withanolides from WithaniacoagulansDunal and their in vitro and in silico validation. *Biology*. 2020 Aug;9(8):197.
35. Ahmad R, Fatima A, Srivastava AN, Khan MA. Evaluation of apoptotic activity of Withaniacoagulans methanolic extract against human breast cancer and Vero cell lines. *Journal of Ayurveda and integrative medicine*. 2017 Jul 1;8(3):177-83.
36. Ahmadi S, Salehi M, Ausi S. Kinetic and thermodynamic study of aspartic protease extracted from Withaniacoagulans. *International Dairy Journal*. 2021 May 1; 116:104960.
37. Hemalatha S, Wahi AK, Singh PN, Chansouria JP. Hypolipidemic activity of aqueous extract of WithaniacoagulansDunal in albino rats. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*. 2006 Jul;20(7):614-7.
38. Budhiraja RD, Sudhir S. Review of biological activity of withanolides. *Journal of Scientific and Industrial Research*. 1987.

