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Review Article

Withania coagulans: Bridging tradition and therapeutic

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Abstract

Withania coagulans have significant medicinal properties, well-proven therapeutic effects and a lack of side effects. It is commonly known as an Indian cheese maker, Indian rennet, Panir ke phool, or Panner Doda.It is a member of the Solanaceae family. *Withania coagulans* is a gray-whitish shrub east of the Mediterranean region extending to South Asia. *Withania coagulans* are geographically distributed in the various areas of India, Iran, Afghanistan, Pakistan, and Nepal. *Withania coagulans* are mainly used in multiple Ayurvedic preparations. The main chemical constituent of *Withaniac oagulans* is Withanolide. Withanolide is primarily classified into seven groups that is Withanolide glycoside, Withathysalin, Thysalin, Nicadrenons, Withajardine, Terculactones, and Acnistins. *Withania coagulans* exhibit Hypoglycemic, Hypolipidemic, Anti-Inflammatory, Anti-microbial, Anti-Bacterial, Immunosuppressive, Hepatoprotective, Anti-Tumour, Anti-oxidant, and diuretic properties. The leaves of *Withania coagulans* consist of Withaferin that possesses Anti-cancer activity. Various marketed preparations of *Withania coagulans* are available. The fruits of *Withaniacoagulans* have sedative activity.

Keywords: *Withania coagulans*, Hypoglycemic activity, Hypolipidemic activity, Anti-inflammatory, Anti-microbial, Anti-tumor

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1. Introduction

A very well-quoted 'Nanaushadhi Bhootam Jagat Kinchit' means no plant in the world has no medicinal value. There are 26 species of Withania, but only two of them, i.e. Withania coagulans (Rishyagandha) (**Table 2**) and *Withania somnifera* (Ashwagandha) are economically important. Withania has been used for centuries to conserve food, treat health disorders, and prevent epidemics. *Withania coagulans dunal* is commonly called 'Indian cheese maker' or 'Vegetable rennet'.[1-2] It is a well-known ethno-pharmacological plant used for various purposes in the Indian Ayurveda system of medicine. A survey of the literature has shown that in different traditional systems of medicine, the plant has been recommended for the treatment of various disorders.[3] It is one of India's most well-known genera of medicinal plants.[1]

1.1. Synonyms

Rishyagandha (Sanskrit), Paneerphool/Paneerdodi (Hindi), Amukkra (Tamil).

1.2. Microscopy

The transverse section of the pedicel shows a single layer of epidermis composed of tabular cells, covered with many branched and unbranched trichomes, followed by a cortex composed of 5-10 layers of collenchymatous cells. The pericycle shows the presence of pericyclic fibres with intervening parenchymatous cells.[1,8] The central region consists of a narrow band of phloem encircling the xylem beneath a ring of intra-xylary phloem. The centremost region is a hollow pith surrounded by parenchymatous cells with a few thick-walled lignified fibres towards the phloem.

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The transverse section of the calyx exhibits a single layer of thin-walled cells in both the upper and lower epidermis with a few branched and unicellular covering trichomes present in the upper epidermis (**Table 3**). The mesophyll is represented by spongy parenchyma traversed by several small veins covered with bundle sheath cells composed of thin-walled parenchymatous cells.[1]

The transverse section of the pericarp (fruit wall) shows the presence of an exocarp which consists of a single layer of cells while the mesocarp shows a wide zone of parenchymatous cells with strong cellulosic thickening. The endocarp consists of a single layer of cells.

The transverse section of the seed shows a single layer of epidermis followed by a layer of flattened thin-walled sub-epidermal cells. Beneath the sub-epidermis, there is a layer of highly lignified sclerenchyma cells with narrow lumen. The inner epidermis of the seed coat comprises 1-3 layers of thin-walled parenchymatous cells which at places are collapsed. The endosperm is represented by cells showing strong cellulosic thickening filled with aleurone grains. The cotyledon shows thin-walled radially elongated cells enclosing a wide zone of round to oval to polyhedral parenchymatous cells.[8]

2. Geographic Distribution, Collection and Cultivation

Withania coagulans is a rigid grey undershrub with a 60-120 cm height. Geographically, the plant is distributed in the East of the Mediterranean region extending to South Asia that is Iran, Afghanistan, Pakistan, Nepal, and India.[9] It is distributed in dried areas. In India, two species of Withania are available, *Withania somnifera* or Indian ginseng and *Withania coagulans*, the morphology of both species is quite similar (**Figure 5**).[10] *Withiana coagulans* is a subshrub native to Asia and also known as Rishyagandha, especially growing in tropical and temperate regions.[11] The species of *Withania* has been reduced due to several factors like the polygamous nature of the flower, self-incompatibility, challenges in domestication, low seed germination and biological constraints, etc [In India, *Withania coagulans* is commercially cultivated in various parts of Punjab, and Haryana.[9] Naturally, *Withania coagulans* is distributed in South Asia but it has been introduced and cultivated in other Western countries including the United States, Australia, and Europe. It is adapted to grow in Arid and semi-arid environments.[9] It is cultivated by seed propagation; seeds are directly sown in the soil. It is sown in moist soil at an early stage but needs less water. At the initial stage of plant growth, mulching helps to suppress weeds and conserve soil moisture. *Withiana coagulans* is pest and disease-resistant but susceptible to microbes like aphids, spider mites, and powdery mildew.

The important cultivation areas for *Withania coagulans* include:

1. **India:** In India, it is extensively cultivated in arid and semi-arid regions of Rajasthan, Gujarat, Punjab, and Haryana, these regions are suitable for its growth.
2. **Pakistan:** In Pakistan, it is cultivated primarily in regions like the Thar Desert and the arid part of the country.
3. **Afghanistan:** It is cultivated particularly in areas with dry and arid conditions.[9]

India is a major cultivator of *Withiana coagulans* and it is due to its suitable plant growth requirements and its traditional use in ayurvedic preparations.(**Figure 3**) The plant species get the required conditions such as and warm climate, well-drained soil, and limited rainfall for growth. India is meeting both domestic demand and supply of other foreign countries for its medicinal and therapeutic effects. The farmers in India who recognize the traditional and medicinal value of the *Withania coagulans* grow it as a Cash crop.

Collection of *Withiana coagulans* is carried out from various ecological regions like along roadside, hilly regions, and barren land. The collection is done by the following steps:

1. Identification
2. Harvesting
3. Processing

1. **Identification:** For the collection of the plant, one should identify the location and the season of cultivation of the plant. The flowers and fruits are collected usually in the warmer months like the end of April and the beginning of May. It consists of yellow-green flowers and red berries enclosed in a paper calyx.
2. **Harvesting:** The plant should be harvested in a specific period because if it is harvested before time or behind time then the root and berries may lose their medicinal value.
3. **Processing:** After harvesting, the collected product should be cleaned gently with water to remove excess waste like soil. The harvested product should be dried and the sunlight must be avoided because it can degrade the beneficial compounds in the plant. It is stored in an airtight container.

3. Phytoconstituents

The seeds of *Withania coagulansdunal* contain 17.8% free sugar consisting of D-galactose and D-arabinose in the ratio of 1:1; with some traces of maltose. The seeds of *Withania coagulans* consist of 12-14% of fatty oils. The oils were found to contain high percentages of Linoleic acid and d-sitosterol which is responsible for the hypocholesterolemic effect. *Withania coagulans* is a rich reservoir of pharmaceutically active steroidal lactones known as 'Withanolides' (**Figure 6**). The most important constituent of *Withania coagulans* is Withanolide which can be chemically classified into seven groups and are as follows:

1. Withanolide glycoside

2. Withathysalin
3. Thysalin
4. Nicadrenons
5. Withajardines
6. Terculactones
7. Acnistins

Figure 1: Fruits of *W. coagulans*[3]

Figure 2: Leaves of *W. coagulans*[3]

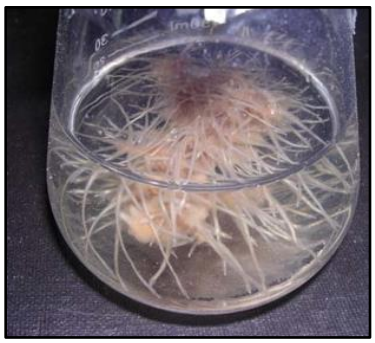

Figure 3: Roots of *W. coagulans*[4]

Figure 4: Stems of *W. coagulans*[5]

Figure 5: Geographical distribution of *W. coagulans* [2,11]

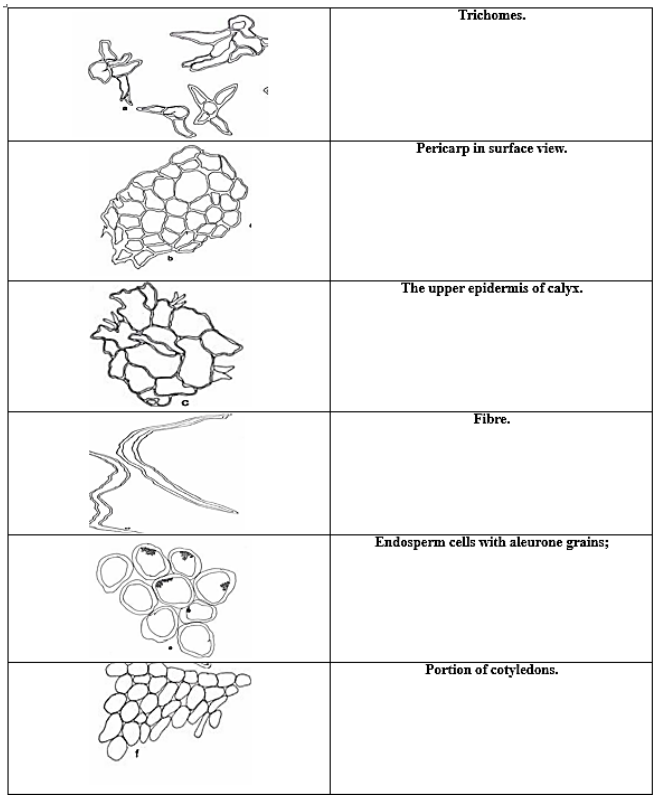

Figure 6: W. coagulansdunal: Powder characteristics of fruits[1]

Table 1: Biological source of *W. coagulans*.[6-8]

Botanical name	*Withaniacoagulans Dunal*
Part of plant	Flowers, leaves, roots, stems (**Figure 4**) and fruits.
Family	Solanaceae

Table 2: Taxonomical hierarchy of *W. coagulans*.[6-7]

Species	Coagulance
Genus	Withania
Family	Solanaceace
Order	Tubiflorae
Class	Dicotyledons
Division	Angiosperma
Subkingdom	Tracheobionta
Kingdom	Plantae

Table 3: Phyto constituents of *Withania coagulan*[2,8]

Sr. no.	Name of Compound	Plant part	Medicinal Activity
1.	D-arabinose	Seed	Hypoglycemic agent
2.	D-galactose	Seed	Hypoglycemic agent
3.	Withanolide F	Fruits	Hypoglycemic agent
4.	Withaferin A	Root	Anti-microbial, Immunomodulating, Anti-tumor and Cytotoxic agent
5.	Withacoagulin	Whole plant	Anti-tumor
6.	Coagulin	Whole plant	Hypoglycemic
7.	14,15 β Epoxywithanolide I	Whole plant	Anti-microbial and hypoglycemic
8.	17 β-hydroxywithanolide K	Whole plants and fruits	Anti-microbial and hypoglycemic
9.	Coagulin B,C,D,E,F,G	Whole plant	Hypoglycemic
10.	Coagulin H,L	Whole plant	Immunosuppressive
11.	3β, 14α, 17β, 20αF,tetrahydroxy-1-oxo-20S,22R-witha-5,24dienolide	Fruits	Hepato protective, Anti-inflammatory, Blood pressure lowering, Central nervous system depressant
12.	Coagulin J ((14R,17R,20R,22R)-3β,27-dihydroxy-14,20-epoxy-1-oxowitha-5,24-dienolide)	Whole plant	Anti-inflammatory, Anti-cancer, Neuro-protective, Anti-microbia, Anti-oxidant
13.	Coagulin K ((14R,17R,20R,22R)-14,20-epoxy-3β-(O-β-D-glucopyranosyl)-1-oxowitha-5,24-dienolide)	Whole plant	Anti-inflammatory Activity, Anticancer Effects, Anti-microbial Activity, Antioxidant Effects
14.	Coagulin L ((14R,17S,20S,22R)-14,17,20-trihydroxy-3β-(O-β-D-glucopyranosyl)-1-oxowitha-5,24-dienolide)	Whole plants and fruits	Anti hyperglycemic
15.	Coagulin M ((14R,17R,20R,22R)-5α,6β,27-trihydroxy-14,20-epoxy-1-oxowitha-24-enolide)	Whole Plant	Anti-inflammatory Activity, Anticancer Effects, Anti-microbial Activity, Antioxidant Effects
16.	Coagulin N ((14R,17S,20R,22R) -15α,17-dihydroxy-14,20-epoxy-3β-(O-β-D-glucopyranosyl)-1-oxowitha-5,24-dienolide)	Whole Plant	Anti-inflammatory Activity, Anticancer Effects, Anti-microbial Activity, Antioxidant Effects
17.	Coagulin O ((14R,20S,22R)-14, 20-dihydroxy-3β-(O-β-D-glucopyranosyl)-1-oxowitha-5,24-dienolide)	Whole plant	Anti-inflammatory Activity, Anticancer Effects, Anti-microbial Activity, Antioxidant Effects
18.	Coagulin P (20,27-dihydroxy-3β-(O-β-D-glucopyranosyl)-1-oxo-(20S,22R)-witha-5,14,24-trienolide)	Whole plant	Anti-inflammatory Activity, Anticancer Effects, Anti-microbial Activity, Antioxidant Effects

19.	Coagulin Q (1α,20-dihydroxy-3β-(O-β-D-glucopyranosyl)-(20S,22R)-witha-5,24-dienolide)	Whole plant	Anti-inflammatory Activity, Anticancer Effects, *Antimicrobial* Activity, Antioxidant Effects
20.	Coagulin R (3β,17β-dihydroxy-14,20-epoxy 1-oxo-(22R)-witha-5,24-dienolide)	Whole plant	Anti-inflammatory Activity, Anticancer Effects, *Antimicrobial* Activity, Antioxidant Effects
21.	20β-Hydroxy-1-oxo-(22R)-witha-2,5,24-trienolide	Whole plant	Anti-inflammatory Activity, Anticancer Effects, *Antimicrobial* Activity, Antioxidant Effects
22.	With a coagulin	Whole plant	Adapt genic Properties, Cardio protective Action
23.	17β-Hydroxy-14α, 20α-epoxy-1-oxo-(22R)-witha-3,5,24-trienolide	Whole plant	Adapt genic Properties, Cardio protective Effects
24.	Coagulin	Whole plant	Anti-inflammatory, anticancer, antioxidant, neuroprotective, Anti-microbial, and cardio protective effects.
25.	Bispicropodophyllinglucoside	Whole plant	Anti-cancer, Anti-viral, Anti-oxidant
26.	3β,14α,17β,20αF-Tetrahydroxy-1-oxo-20S,22R-witha-5,24-dienolide(or 3β-hydroxy-2,3-dihydrowithanolide F)	Fruits	Hepato protective, Anti-inflammatory, blood pressure lowering, central nervous system depressant
27.	Ergosta-5,25-diene-3β,24ξ-diol	Fruits	anti-fungal effect, cholesterol-lowering effects
28.	3β,14α,20αF,27-Tetrahydroxy-1-oxo-20R,22R-witha-5,24-dienolide(or 3β-hydroxy-2,3-dihydrowithanolide H)	Fruits	Neuroprotective properties, adaptogenic effects
29.	Sit sterol-β-D-glucoside	Fruits	Gastro protective activity, Cardiovascular protection
30.	Coagulanolide ((17S,20S,22R)-14α,15α,17β,20β-tetrahydroxy-1-oxowitha-2,5,24-trienolide)	Fruits	Anti-hyperglycaemic
31.	Withanolide F	Fruits	Ant hyperglycaemic
32.	Withaferin A	Root	Anti-microbial, immunomodulation, Anti-tumor, cytotoxic
33.	5,27-Dihydroxy-6α,7α-epoxy-1-oxo-(5α)-witha-2,24-dienolide	Root	Immunomodulatory action
34.	With acoagin ((20R,22R)-5α,20-dihydroxy-1-oxowitha-2,6,24-trienolide)	Root	Neuroprotective activity, Adapt genic activity
35.	(20R,22R)-6α,7α-Epoxy-5α-20-hydroxy-1-oxowitha-2,24-dienolide	Root	Anti diabeticactivitiy
36.	36 (20S,22R)-6α,7α-Epoxy-5α-dihydroxy-1-oxowitha-2,24-Dienolide	Root	Immunosuppressant

4. Uses

The fruit of this plant is sweet and is used in treating wounds, asthma, digestive issues, and conditions like biliousness and stranguary (difficulty urinating). The seeds are helpful for menstrual issues, act as a diuretic, and are used to treat conditions like lumbago (back pain) and eye inflammation. They also help reduce inflammation in piles (haemorrhoids). Ripe fruits are thought to have pain-relieving or calming effects and are beneficial for liver problems. They can be used to induce vomiting. Dried fruits, sold as "Punir-ja-fota" in Sind, are used for indigestion and gas problems.[16]These fruits are often brewed as tea, sometimes combined with the leaves and twigs of Rhazyastricta, a plant known for its bitter tonic properties.In some regions, the bitter leaves are used to reduce fever, and in Bombay, the berries are seen as blood purifiers. In Las Bella, the fruit is mashed and used to treat colic (stomach pain), and the wood is used to clean teeth. In the Ormera Hills, the smoke from the plant is inhaled for toothache relief. In Northern India, traditional healers use dried fruits to help manage diabetes.[16] The plant also has Anti-microbial, anti-fungal, Anti-inflammatory, and other health benefits, such as protecting the liver, lowering blood

sugar and cholesterol, and supporting the immune system. It also has properties that may help in fighting tumours, reducing inflammation, and fighting harmful microorganisms.[16]

5. Pharmacological Actions

5.1. Hypoglycemic activity

The fruit of *Withania coagulan* is utilized in traditional Indian medicine since it has been demonstrated to have anti-hyperglycemic qualities.(**Figure 1** and **Figure 2**) Research in this area has also demonstrated that the medication *Withania coagulan* demonstrates hypoglycemic activity, which is a safe and efficient substitute therapy for diabetes. It is the isolated alkaloids and steroids derived from plants that cause hypoglycemic action. Rats exhibit anti-hyperglycemic effects from the coagulin L that is isolated from *Withania coagulan* fruits.[17] A factor that helps enhance hypoglycemic activity is minerals. The lower blood glucose level and improved glucose tolerance test results demonstrated that *Withania coagulan* have greater Mg and Ca content that plays a major role in the management of diabetes.[21] Higher magnesium concentrations and lower potassium concentrations have previously been linked to important roles in the management of diabetes.[16] The substantial anti diabetic potential of *Withania coagulan* may result from the high Mg and Ca^{2+} concentrations. The exocytosis of stored insulin is facilitated by the Ca2+ ion, which also promotes insulin gene expression through CREB (Calcium Responsive Element Binding Protein).[2,16]

5.2. Hypolipidemic activity

Lipid profile and blood insulin levels are correlated indirectly. Insulin is recognized to function as a down-regulator of apoprotein B (apoB) through the PI3K pathway. Insulin regulates the metabolism of fats and carbohydrates in muscle, adipose tissue, and the liver.[16] Insulin controls the oxidation of hepatic fatty acids, lipogenesis, and protein synthesis. Insulin regulates the export of fatty acids into lipoproteins from the liver to the extrahepatic organs as well as the synthesis of lipids from glucose in the liver and adipose tissue. A series of processes cause some of these effects to be applied at the transcriptional level (Nowak et al.). Insulin stimulates the promoter, fatty acid synthase (FAS), an enzyme involved in lipogenesis.[2]

5.3. Anti-Inflammatory activity

The COX-2 receptors are competitively bound by withanaloides, which then change the receptors to render them unsuitable for attachment (Alternative Molecular Review, monograph, 2010). Analoideglycans and withnaloides exhibited preferential interaction with COX-2 better than COX-1, as compared to NSAIDs, according to molecular docking studies of cyclooxygenase with a set of ligands.[16] Thus, withanaloide glycans and with analoides may represent the next generation of NSAID replacements.[2]

5.4. Anti –microbial activity

The volatile oil found in *Withania coagulan* fruits has been shown to have antibacterial activity against Vibrio cholera and Staphylococcus aureus. Withanolides were extracted from the ethanolic leaf extract and were discovered to possess antibacterial qualities. It was discovered that the entire plant's 17β-hydroxywithanolide K (20S, 22R) and the 14α, 17β, and 20β-trihydroxy-1-oxo-witha-2,5,24-trien-olide were effective against a variety of potentially harmful fungus.[16] Nine highly pathogenic isolated fungi, namely Nigrospora oryzae, Aspergillus niger, Curvularia lunata, Pleurotus ostreatus, Stachybotrys atra, Allescheria boydii, Drechslera rostrata, Microsporum canis, and Epidermo-phytonfloccosum, were used to test the anti-fungal activity of the crude extract, 17β-hydroxywithanolide K, and withanolide F. Moreover, the chemical exhibited efficacy against gram-positive bacteria (S. aureus).The essential oil had anti-Micrococcus properties.[2,15]

5.5. Anti-bacterial activity

Some pure cultures of bacteria like Salmonella typhii, E.coli, etc, and the cultivation of bacteria was carried in 0.8% Nutrient broth medium. To scrutinize antibacterial activity, the agar well diffusion method was adopted.[16] The different test organism was poured separately in different nutrient agar plates and 20 microlitres of test solution was poured separately. Plates are kept in the refrigerator for cooling for at least 30 minutes and then incubatedat 37°C for 24 hours. After 24 hours zone of inhibition is measured and the activity index is calculated.[12]

5.6. Anti-Tumour activity

Withacoagulin A, withacoagulin C, withacoagulin D, withacoagulin E, withanolide L, withanolide J, Δ3 iso withanolide F, withanolide F, withacoagulin and (22R)-14α15α17β-20 β, tetrahydroxy-1-oxowitha-2,5,24-trien-26,22-withanolide compounds (**Figure 6**) relatively show anti-tumor activity. *Withania coagulan*also inhibit the DNA nucleotide base that is Thymidine. The chemical constituent Withaferin-A that is obtained from leaves of *Withania coagulan* also inhibits cancerous cell growth and thus *possesses* Anti-cancer activity.[13] Methanolic extract of *Withania coagulan* showed cytotoxicity against human breast cancer cells with less effect on normal cells.[14]

5.7. Anti-oxidant activity

Free radicals, also known as Reactive Oxygen Species (ROS), are harmful molecules that can damage cells and tissues in the body. Antioxidants are substances that can neutralize or "scavenge" these harmful free radicals, helping to prevent damage. Medicinal plants contain natural antioxidants that can boost the body's ability to fight these free radicals. These plant-based antioxidants have been shown to help in healing wounds by reducing the damage caused by free radicals and oxidative stress (an imbalance between free radicals and antioxidants in the body). In simple terms, antioxidants from plants can help repair damage to the body, including wounds, by protecting cells from harmful

substances.[18] The aqueous extract of *Withania coagulan* and phytochemical extracts like glycolwithanaloides possess Anti-oxidant activity. Thus, *Withania coagulan* is utilized to formulate natural Anti-oxidant that can be used in several disease conditions like atherosclerosis and ageing.[13]

5.8. Diuretic Activity

The aqueous extract of *Withania coagulan* possesses potent diuretic activity. The treatment with aqueous extracts at 500 and 750 mg/kg showed dose dose-independent diuretic effect. At 500 mg/kg, the volume of urine was increased by 79.49 %.[13] *Withania coagulan* is unlikely to act as a Thiazide diuretic, as Thiazide diuretics typically increase urinary potassium levels and affect the Na+/K+ ratio. In this study, although the sodium (Na+) level was increased, there was no significant change in the Na+/K+ ratio. However, the diuretic effect of *Withania coagulan* extract at a 500 mg/kg dose was strong, with an intensity similar to that of furosemide, and was accompanied by a significant rise in both urinary sodium and potassium levels.[19]

5.9. Hepatoprotective activity

The hepatoprotective activity is obtained by 3F-hydroxy2,3-dihydro-withanaloide. It was found that *Withania coagulans* have more potent hepatoprotective activity than hydrocortisone. It is used in hepatitis and liver cirrhosis.[13] Administration of fruit extract of *Withania coagulans* showed remarkable recovery of enzymes and liver texture.Low and high doses of *Withania coagulans* both fruit extracts have an equal hepatoprotective effect.[20]

5.10. Immunosuppressive activity

Six novel withanolides (Withanolides A–F, 1–6) and ten known withanolides (7–16) were isolated from the aerial parts of *Withania coagulans*. These compounds exhibited significant inhibitory effects on T- and B-cell proliferation. Among them, Coagulin-H demonstrated potent immunosuppressive activity by inhibiting Th1 cytokine production and lymphocyte proliferation. Specifically, Coagulin-H effectively suppressed phyto hemagglutinin (PHA)-induced T-cell proliferation.[16] Additionally, withaferin A and withanolide E have been reported to exert selective immunosuppressive effects on human B and T lymphocytes, as well as on mouse thymocytes. The cell-mediated immune response is primarily driven by different sub populations of T lymphocytes.[12]

5.11. Angiogenesis Inhibitor

Human umbilical vein endothelial cells (HUVECs) were shown to be inhibited by withaferin A in a three-dimensional collagen-I matrix during an endothelial cell-sprouting experiment, at levels that correspond to NF-κ inhibitory activity.[12] Through a mechanism linked to the suppression of cyclin D1 expression, withaferin A suppresses cell proliferation in HUVECs (IC50 = 12 nM) at levels far lower than those needed for tumour cell lines.[12] The higher amounts of poly-ubiquitinated proteins were thought to indicate that withaferin A's suppression of NF-κB in HUVECs is due to interference with the ubiquitin-mediated proteasome pathway.[12] It was demonstrated that withaferin exhibited strong anti-angiogenic action in vivo at doses 500 times lower than those previously documented to have anti-tumor activity in vivo.[12]

5.12. Neuroprotective Activity

Researchers found multiple active ingredients in a study where they examined herbal medications for neurite outgrowth activity.[12] Neurite outgrowth activity in each drug was examined in the context of amyloid-beta-induced neuritic atrophy.[12] In mice with Alzheimer's disease model, the majority of the substances exhibiting neurite regeneration activity also showed memory enhancement activity. In both healthy and injured cortical neurons, withanolide derivatives (Withanolide A, withanoside IV, and withanoside VI) demonstrated neurite extension.[12]

5.13 Adverse effects

Withania coagulans generally do not cause any side effects/adverse effects when consumed in recommended doses. But fruits have sedative activity so it is mentioned to consume in the recommended dose and with caution. The recommended dose of Panner phool powder is 4-5 gm twice a day.[22-23]

5.14. Reported folk uses

The best time to consume Panner dodi for diabetes is just before the meal. One can consume it in the morning before breakfast and after lunch.[24] The various home remedies are as follows:

1. Soak 10 to 15 dried Panner dodi in 300 ml of water overnight. In the morning, squeeze the paneer dodi to ensure you get all the ingredients, and further filter it off and consume it.
2. Soak 7 to 10 dried paneer dodi in 300ml of water for 2 hours, then boil for about 10 mins. Filter the mixture before drinking.
3. Mix about 10 to 15 panner dodi powder in 250ml water. Boil it to make half the quantity of it. Let it cool and then consume.
4. Six fruits of *Withania coagulans* (paneer phool) (**Figure 1**) were soaked overnight in 100 ml of water. In the morning, the fruits were squeezed into the water. The extract was filtered, and to this, 1 ml of tamarind extract was added and administered.[6]

6. Conclusion

Withania coagulans has emerged as a promising natural source of a potent and generally safe chemotherapy drug, based on current research. The aqueous and methanolic extracts of its fruit, leaves, and roots contain various bioactive compounds, including esterases, free amino acids, fatty oils, essential oils, and withanolides. These compounds contribute to the plant's diverse pharmacological properties, such as Anti-inflammatory, anticancer, antidiabetic,

cardioprotective, neuroprotective, and Anti-microbial activities. The potential of *Withania coagulans* in preventing and managing conditions like cancer, Alzheimer's disease, diabetes, and cardiovascular disorders underscores the need for further exploration. In particular, withanolides, the primary bioactive constituents of *Withania coagulans*, exhibit a wide range of therapeutic benefits, with strong antioxidant and anti-diabetic properties. These compounds play a crucial role in lowering blood sugar and cholesterol levels, making the plant a valuable natural remedy for diabetes management. The qualitative and quantitative phytochemical analysis has confirmed the presence of significant amounts of essential phytochemicals in the fruits of *Withania coagulans*, further supporting its therapeutic potential. To fully harness the medicinal value of *Withania coagulans*, further studies focusing on the structure-activity relationship (SAR) and molecular docking of withanolides are essential. Such research could help in identifying specific molecular interactions responsible for their pharmacological effects, paving the way for drug development.

Overall, *Withania coagulans* offer significant potential as a natural therapeutic agent. Its broad spectrum of pharmacological activities and bioactive composition make it an important candidate for further research and development in the field of natural medicine.

7. Source of Funding

None.

8. Conflict of Interest

None.

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