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A Comprehensive Review on *Withania coagulans* (Paneer Dodi)

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ABSTRACT

This pioneering attempt aims to provide detailed information of *Withania coagulans* Dunal, also called Paneer dodi belongs to the family Solanaceae is a well-known plant in herbal medicinal systems for its great potential against various diseases. This plant particularly leaves, fruits, and roots are known to have biological as well as pharmacological activities including hypoglycaemic, hypolipidemic, free radical scavenging, cardiovascular, central nervous system depressant, anti-inflammatory, wound healing, antitumor, immune-suppressive, cytotoxic, antifungal, antibacterial, sedative, emetic, diuretic, antidiabetic, antimicrobial, antitumor and hepatoprotective properties. The present review article highlights the significance of species, botanical name, taxonomical classification, morphology, chemical constituents, biosynthesis of withanolides, phytochemistry, and pharmacological action. This extensive information will be of great value for future researchers.

INTRODUCTION:

Herbal medicines have a growing demand in the world market and they are a valuable gift of nature. Since ancient times, a wide range of herbal medicines has been used in Indian systems of medicine to treat various types of diseases. World Health Organization (WHO) estimated that more than 80% of the world's population uses plant-derived health care products for their daily regimes because of their good activity and comparatively fewer side effects as compared to synthetic drugs [16]. *Withania coagulans* Dunal belongs to the family Solanaceae is one of the important ayurvedic medicinal plants commonly known as vegetable rennet, Indian cheesemaker, Indian rennet, Paneer ke phool, Paneer band or Paneer dodiis widely used over 3,000 years in India[1,11]. It is found in the Eastern Mediterranean region and extends into South Asia. Across India, it grows in drier regions such as Punjab, Gujarat, and Rajasthan [16,46]. *Withania coagulans* is commonly known as paneer in Punjab because fruits and leaves have properties to coagulate milk. The milk coagulating properties of the fruit is attributed to the pulp and husk of berries which possess enzyme which has milk coagulating activity [27]. One ounce fruit and a quart of boiling water make a decoction, one tablespoonful of which coagulate a gallon of warm milk in about an hour. Buffalo or sheep milk is warmed to about 100^0F and crushed berries of the plant, tied in a cloth, are dipped in it. The milk takes 30-40 minutes to curdle. In folk medicine, different parts of the plant, especially fruits are considered magic healers [27]. Fruits of *Withania coagulans* exhibit sedative, emetic as well as diuretic properties. They help treat diabetes, nervous exhaustion, disability, insomnia, wasting diseases, failure to thrive in children, impotence. chronic liver disease, dyspepsia, flatulent coli asthma, biliousness, and other gastrointestinal infections [21]. The berries are used to purify the blood. Chewing the twigs of the plant is used to clean teeth and inhaling the smoke relieves toothaches. [22,27]. In parts of India's northwestern region, traditional practitioners use dry fruits of this species to treat diabetic patients, although their antihyperglycemic activity has not been systematically evaluated. A highly valued ethnomedicinal plant of the drier part of the country, skill-less and unscientific uprooting of the whole plant is being practiced with upcoming threats [16]. Therefore, shortly these plants will need to be protected through ex-situ and in situ conservation.

Botanical description: [1,10]

Botanical name: *Withania coagulans*

Family: Solanaceae

Subfamily: Solenoidal

Tribe: Physaleae

Subtribe: Withaninae

Sanskrit Name: Rishyagandha

Hindi Name: Paneer doda

English Name: Indian cheesemaker, Indian rennet, vegetable rennet

Trade Name: Paneer dodi, Paneer doda, Paneer bed, Paneer dhodi

Taxonomical classification: [27].

Kingdom: Plantae, plants

Subkingdom: Tracheobionta, vascular plants

Superdivision: Spermatophyte, seeds plants

Division: Angiosperma

Class: Dicotyledons

Order: Tubiflorae

Family: Solanaceae

Genus: Withania

Species: Coagulans

Synonyms: [1,3,7,27]

Sanskrita Name: Rishyagandha

Hindi Name: Punir, Punir bandh, Akri, Binputakah, Paneer doda

English Name: Indian Cheesemaker, Indian Rennet, Vegetable Rennet

Arabic: Javzuhnizaja, Kaknajehindi;

Bengali: Ashvagandha; Bombay-Kaknaj; Decca Handikaknaj;

Trade Name: Paneer dodi, Panner, doda, Panir bed, Paneer dhodi.

Telugu: Panneru-gadda

Urdu: Habkaknaj

Kannada: Amakiregadday

Malayalam: Amukiram

Tamil: Amukara, Amukkura

Punjabi: Kharmjaria, Khumazare, Kutilana, Makhazura, Panir, Shapiang, Spinbajia

Sindhi: Punirband, Punirjafota

Geographical description:[2]

It is found in the Eastern Mediterranean region and extends northern Africa to Southwest Asia. Across India, it grows in drier regions such as Punjab, Gujarat, Rajasthan, Shimla, Kumaon, and Garhwal.

Morphological Description:

Withania coagulans Dunal is a rigid, grey undershrub, 60-120 cm high [53].

Seeds: Seeds of the paneer Dodi 2.5-3.0 mm diameter, dark brown, somewhat ear-shaped, glabrous. Natural regeneration occurs from the seed [1].

Fig No. 1: Seeds of Paneer Dodi

Leaves: The Paneer Dodi's leaves are 2.5-5.7 by 1-2.2 cm, lanceolate-oblong, entire, obtuse, clothed with a persistent not easily detachable greyish tomentum, of uniform colour on each side, thick, small or more rugose with base acute [1].

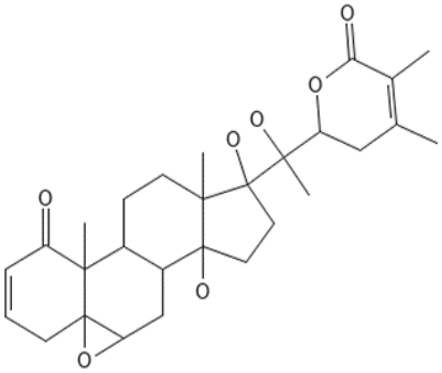
Fig No.2: Leaves of Paneer Dodi

Flowers: The flowers of the paneer Dodi are long, campanulate, clothed with fine stellate grey tomentum; teeth triangular, 2.5 mm long dioecious, in axillary clusters; pedicles 0.6 mm. long, deflexed, slender, Calyx 6 long. Corolla of the flower is8mm long, stellatelymealy outside, divided about one-third the way down; lobes ovate-oblong and subacute [1]. Stamens about level with the very best of the corolla- tube; filaments 2 mm. long, glabrous; anthers 3-4 mm. long. Ovary ovoid, without style or stigma.Male flowers stamens about level with the top of the corolla tube; filament 2 mm long, glabrous; anthers 3-4 mm long. Female flowers: Stamens scarcely reaching ½high the corolla-tube; filaments about 0.85 mm. long; anthers are small within the male flowers, sterile. Within flowers the Ovary ovoid, glabrous; style glabrous; stigma mushroom-shaped, 2-lamellat. The plant flowers from November to April and the berries ripen from January to May [10].

Fig No. 3: Flower of Paneer Dodi

Fruits: Berry 6-8 mm. globose, smooth, closely girt by the enlarged membranous calyx which is scurfy-pubescent outside [53].

Fig No.4: Fruits of paneer Dodi



Chemical Constituents: With chemical and spectroscopic methods, 3β,14α,20αF,27-tetrahydroxy-1-oxo-20R,22R-with-5,24-dienolide were identified. The structure correlates with comparative studies of closely related withanolides. The *Withania coagulansis* rich in steroidal lactone, known as withanolides, which are naturally occurring polyhydroxy C28 steroidal lactones [14,48,50]. The structure of withanolides is characterized by a six or five-membered lactone or lactol ring attached to an intact or rearranged ergostane skeleton. The berries contain the milk-coagulating enzyme, two esterases, free aminoalkanoic acid, fatty oil, essential oil, and alkaloids [51]. There are five amino acids present in the protein are proline, hydroxyproline, valine, tyrosine, aspartic acid, glycine, asparagine, cysteine, and glutamic acid. Fourteen alkaloidal fractions have been isolated from the alcoholic extracts of the fruits, whereas seeds on petroleum ether extraction yield lipid and unsaponifiable

material. From W. coagulans, including ergosta-5,25-diene-3β-D-glucoside and withanolide. From the roots of the plant, five withanolides have been isolated. There have been two types of side chains found in withanolides both 17-α-oriented and 17-β-oriented. The essential oil shows antimicrobial and antihelminthic properties against Micrococcus pyogenes var. aureus [33].

Withanolide A

Correlation between traditional use and modern pharmacological property:

In Indian Ayurveda, *Withania coagulans* play an important role in promoting good physical and mental health [8]. Most of the plant's parts contain withanolides, which have antibacterial and antifungal properties [2]. Various crude extracts of the plants, as well as an essential oil extract, have been determined to possess antimicrobial properties [3]. Staphylococcus aureus, Vibrio cholera, Micrococcus pyogenes, Pseudomonas aeruginosa, Klebsiella pneumonia, Proteus vulgaris, Enterobacter aerogenes are some bacterial species that shows well known antibacterial activity [28,49]. Herbs have antifungal activity against fungi as diverse as Nigrosporaoryzae, Aspergillus niger, Curvularialanata, Microsporumcanis, and Epidermophyton floccosum [2]. Fruit is applied to wounds, used for asthma biliousness, and strangury. Seeds of the plant are also diuretic and used to decreases inflammation of piles. The ripe fruits are also known to possess anodyne or sedative properties [55]. The root is harvested in autumn and dried for later use [37]. Withanin is commonly used to coagulate milk [39]. Fruits of *Withania coagulans* show glucose-lowering effect [17]. Besides coagulin L, other alkaloids and steroids obtained from plants have antihyperglycemic properties [11]. The presence of a considerable amount of calcium and magnesium in *Withania coagulans*is responsible for its role in Diabetes [32]. The administration of aqueous and hydroalcoholic extract of plants appear to reduce blood glucose levels, cholesterol levels and triglycerides in test animal. Dyslipidemia is a well-known complication associated with diabetes mellitus, elevated by the immature risk of premature atherosclerosis [41]. An aqueous extract of the herb was used to study its effect on the level of lipid in diabetic induced rats, revealing that repeated oral administration of herb *Withania coagulans* possesses significant antihyperlipidemic activity [2].

Table No. 1: Medicinal use of different parts of *Withania coagulans*

Sr. No.	Pharmacological Activity	Part of Plant	Description	References
1.	Antihyperglycemic activity	Fruits and Flowers	Pharmacological effect on blood glucose, lipid profile.Soak about 10-15 pods of paneer dodi in glass of water overnight.	[14]
2.	Cardiovascular effect	Fruits	The Withanolides produces moderate fall in blood pressure.	[26]
3.	Immunosuppressive effect	The aerial part of the plant/root	Withaferin A has a specific immunosuppressive effect on human B and T-lymphocytes.	[43]
4.	Anti-inflammatory activity	Fruits	Its external application prescribes for inflammatory conditions.	[9]
5.	Antifungal activity	Whole Plant	Used in the treatment of antifungal disease.	[9]
6.	Antibacterial and Antihelmintic	Fruits	It is protective against microbial infections.	[19]
7.	Hepatoprotective activity	Fruits	It helps in protecting the liver and maintain its general well-being.	[11]
8.	Anti-tumor activity	Root	It shows the remarkable inhibitory activity of DMSO induced cytotoxicity and decrease TNFα production.	[53]
9.	Wound healing activity	Whole plant	Both topical and oral forms showed a big increase in the rate of wound contraction.	[3]
10.	Diuretic activity	Seeds	It works as a diuretic because they increase urinary K^+ level and alter Na^+/K^+output.	[7]
11.	Antimicrobial activity	Root	It has inhibited the growth of various Gram +ve micro tumor activities.	[9]
12.	CNS Depressants	Fruits	It is used in Alzheimer's disease.	[19]
13.	Antimutagenic and Anticarcinogenic effect	Fruits	Ability to reduce the tumor size.	[10]
14.	Antihyperlipidemic activity	Fruits	Reduce the serum cholesterol, Triglycerides, Lipoprotein, and LPU levels.	[1]

Biosynthesis of Withanolide [2]:

Withanolides are steroidal lactones of the C28 structure. Withanolide consists of six or five-membered lactone rings arrange on the ergostane skeleton [51]. The biosynthesis of withanolides begins with the synthesis of cholesterol which is converted to 24-methylene cholesterol which is believed to be the actual precursor of withanolides. Cholesterol is synthesized by two molecules of acetyl CoA which then condenses with another molecule of acetyl CoA to form 3-hydroxy-3-methylglutaryl CoA which upon reduction forms mevalonic acid [2]. Squalene is formed when six molecules of mevalonic acid are combined. Mevalonic acid is converted to squalene via a series of phosphorylation reactions catalyzed by respective enzymes. When molecular oxygen is incorporated into leads squalene and 2, 3-epoxysqualene is formed. Through cyclization of the squalene chain and series of 1, 2 Transmigration of hydrogen atoms and methyl groups lanosterol is formed. A methyl group is removed from one ring of lanosterol, and the double bonds in another ring are rearranged to form 24-methyl cholesterol, which on reduction yields 24-methylenecholesterol, which is a precursor of steroidal lactones [2]. It is an extraordinary feature of withanolide-producing plants that they can introduce oxygen function almost anywhere in the carbocyclic skeleton or in a side chain[11].

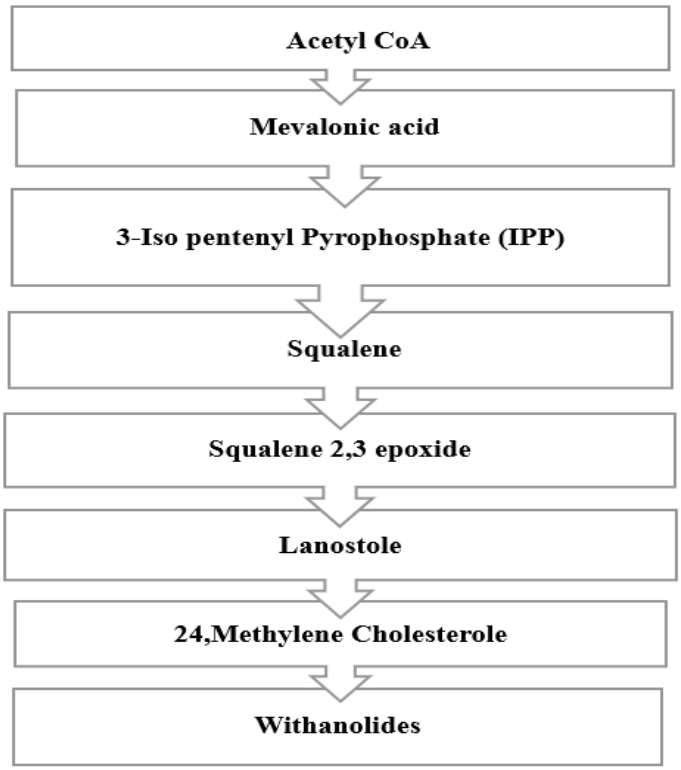


Fig No. 5: Biosynthesis of *Withania coagulans*

Phytochemistry [4-6]:

Table No.2: Isolated compounds from *Withania coagulans* and the reported biological activity

Sr. no.	Name of compound	Chemical formula	Molecular weight	Plant parts	Biological activity	Reference
1.	Coagulin (17β,27-dihydroxy-14,20-epoxide-1-oxo-(22*R*)-witha-3,5,24-trienolide)	$C_{28}H_{38}O_6$	470.6	whole plant	Antihyperglycemic and Antimicrobial	[4,11,38,45,47]
2.	14,15β-Epoxywithanolide I ((20*S*,22*R*) 17β,20β-dihydroxy-14β,15β-epoxy-1- oxowitha-3,5,24-trienolide)	$C_{28}H_{38}O_6$	470.6	whole plant	Antihyperglycemic and Antimicrobial	[4,11,38,45,47]
3.	17β-Hydroxywithanolide K ((20*S*,22*R*) 14α,7β,20β-trihydroxy-1-oxowitha-2,5,24-trienolide)	$C_{28}H_{38}O_6$	470.6	Whole plant and fruit	Antihyperglycemic and Antimicrobial	[4,10,11,43,45]
4.	Coagulin B	$C_{28}H_{36}O_5$	452.6	Whole plant	Antihyperglycemic and Antimicrobial	[4,10,11,43,45]
5.	Coagulin C	$C_{28}H_{36}O_5$	452.6	Whole plant and fruit	Antihyperglycemic	[4,10,11,43,45]
6.	Coagulin D	$C_{28}H_{36}O_4$	436.6	Whole plant	Antihyperglycemic	[4,10,11,43,45]
7.	Coagulin E	$C_{28}H_{36}O_4$	436.6	Whole	Antihyperglycemic	[4,10,11,4

				plant		3,45]
8.	Coagulin F (27-hydroxy-14,20-epoxy-1-oxo-(22*R*)-witha-3,5,24-trienolide)	$C_{28}H_{36}O_5$	452.6	Whole plant	Antihyperglycemic	[4,10,11,43,45]
9.	Coagulin G (17β,27-dihydroxy-14,20-epoxy-1-oxo-(22*R*)-witha-2,5,24-trienolide)	$C_{28}H_{38}O_6$	468.6	Whole plant	Antihyperglycemic	[4,10,11,43,45]
10.	Coagulin H ((17*S*,20*S*,22*R*)-5α,6β,14α,15α,17,20-hexahydroxy-1-oxowitha-2,24-dienolide)	$C_{28}H_{40}O_9$	520.6	Whole plant	Immunosuppressive	[4,10,11,43,45]
11.	Coagulin I ((14*R*,17*S*,20*S*,22*R*)-5α,6β,17-trihydroxy-14,20-epoxy-1-oxowitha-2,24-dienolide)	$C_{28}H_{38}O_7$	486.6	Whole plant	Immunosuppressive	[4,10,11,43,45]
12.	Coagulin J ((14*R*,17*R*,20*R*,22*R*)-3β,27-dihydroxy-14,20-epoxy-1-oxowitha-5,24-dienolide)	$C_{28}H_{38}O_6$	470.6	Whole plant	Immunosuppressive	[4,10,11,43,45]
13.	Coagulin K ((14*R*,17*R*,20*R*,22*R*)-14,20-epoxy-3β-(*O*-β-D-	$C_{34}H_{48}O_{10}$	616.7	Whole plant	Immunosuppressive	[4,10,11,43,45]

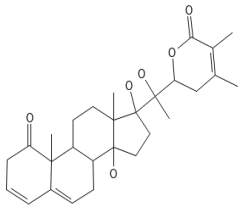
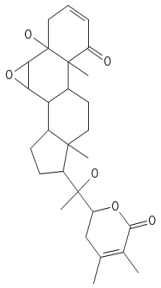
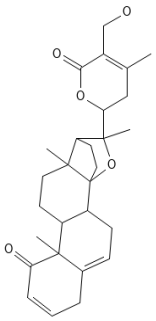
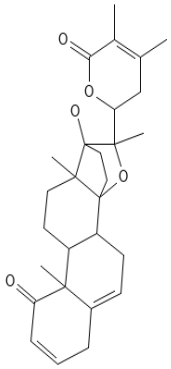
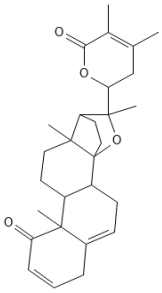
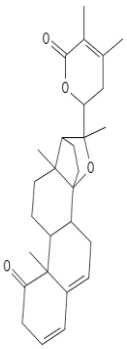
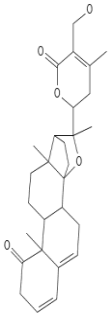
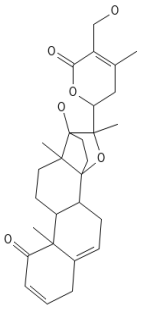
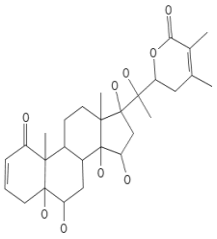
	glucopyranosyl)-1-oxowitha-5,24-dienolide)					
14.	Coagulin L ((14*R*,17*S*,20*S*,22*R*)-14,17,20-trihydroxy-3β-(*O*-β-D-glucopyranosyl)-1-oxowitha-5,24-dienolide)	$C_{34}H_{50}O_{12}$	650.8	Whole plant and fruit	Antihyperglycemic	[4,10,11,43,45]
15.	Coagulin M ((14*R*,17*R*,20*R*,22*R*)-5α,6β,27-trihydroxy-14,20-epoxy-1-oxowitha-24-enolide)	$C_{28}H_{40}O_{7}$	488.6	Whole plant	Antihyperglycemic	[4,6,10,11,43,45]
16.	Coagulin N ((14R,17S,20*R*,22R)-15α,17-dihydroxy-14,20-epoxy-3β- (*O*-β-D-glucopyranosyl)-1-oxowitha-5,24-dienolide)	$C_{34}H_{48}O_{12}$	648.7	Whole plant	Antihyperglycemic	[4,6,10,11,43,45]
17.	Coagulin O ((14*R*,20*S*,22*R*)-14,20-dihydroxy-3β-(*O*-β-D-glucopyranosyl)-1-oxowitha-5,24-dienolide)	$C_{34}H_{50}O_{11}$	634.8	Whole plant	Antihyperglycemic	[4,6,10,11,43,45]
18.	Coagulin P (20,27-dihydroxy-3β-(*O*-β-	$C_{34}H_{48}O_{11}$	632.7	Whole plant	Antihyperglycemic	[4,6,10,11,43,45,50]

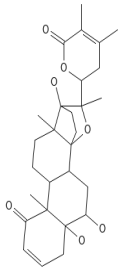
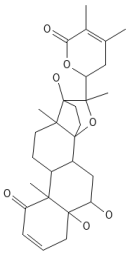
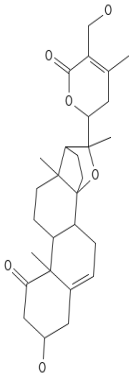
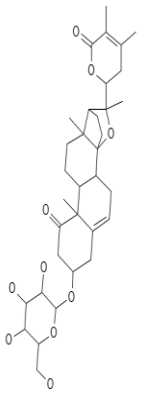
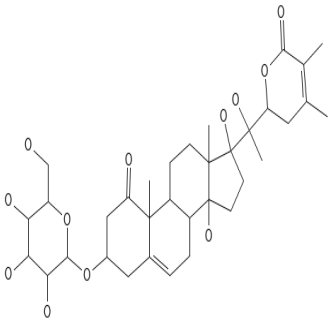
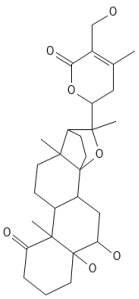
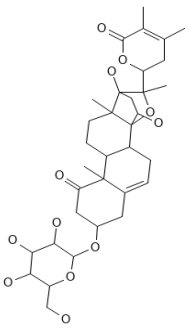
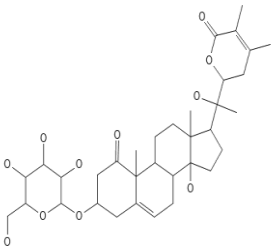
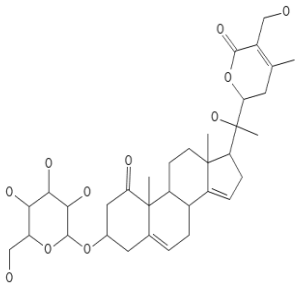
	D-glucopyranosyl)-1-oxo-(20*S*,22*R*)-witha-5,14,24-trienolide)					
19.	CoagulinQ(1α,20-dihydroxy-3β-(*O*-β-D-glucopyranosyl)-(20*S*,22*R*)-witha-5,24-dienolide)	$C_{34}H_{52}O_{10}$	620.8	Whole plant	Antihyperglycemic	[4,6,10,11,43,45,50]
20.	CoagulinR(3β,17β-dihydrox-14,20-epoxy-1-oxo-(22*R*)-witha-5,24-dienolide)	$C_{28}H_{38}O_6$	470.6	Whole plant	Antihyperglycemic	[4,6,10,11,43,45,50]
21.	20β-Hydroxy-1-oxo-(22*R*)-witha-2,5,24-trienolide	$C_{28}H_{36}O_5$	452.6	Whole plant	Antihyperglycemic	[4,6,10,11,43,45,50]
22.	Withacoagulin	$C_{28}H_{36}O_5$	452.6	Whole plant	Antihyperglycemic	[4,6,10,11,38,43,45,50]
23.	17β-Hydroxy-14α,20α-epoxy-1-oxo-(22*R*)-witha-3,5,24-trienolide	$C_{28}H_{38}O_6$	470.6	Whole plant	Antihyperglycemic	[4,6,10,11,38,43,45,50]
24.	Coagulin S	$C_{28}H_{40}O_8$	504.6	Whole plant	Antihyperglycemic	[4,6,10,11,38,43,45,50]
25.	Bispicropodophyllin glucoside			Whole plant	Antihyperglycemic	[4,6,10,11,38,43,45,50]
26.	3β,14α,17β,20α_F-Tetrahydroxy-1-oxo-20S,22*R*-witha-5,24-	$C_{28}H_{40}O_7$	488.6	Fruit	Hepatoprotective, Anti-inflammatory, Bloodpressure	[4,6,10,11,38,43,45,50]

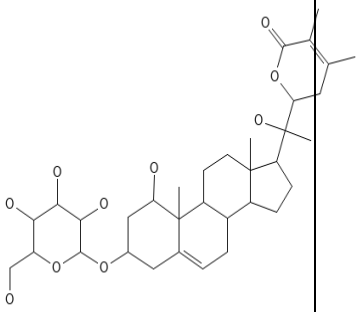
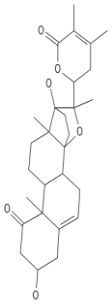
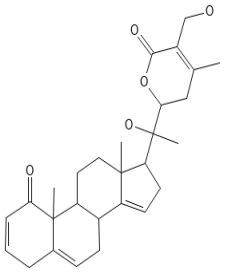
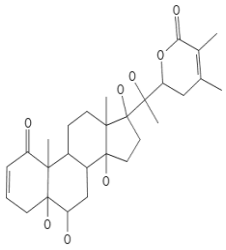
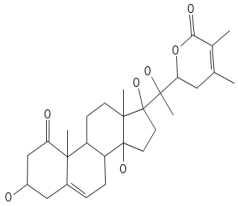
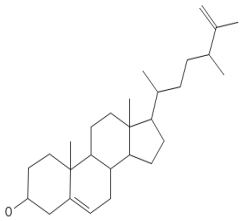
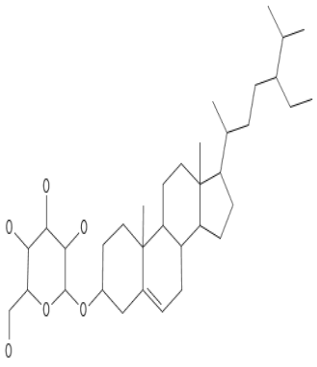
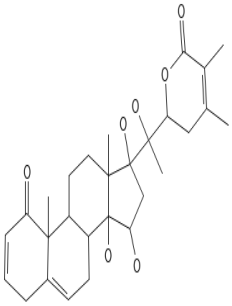
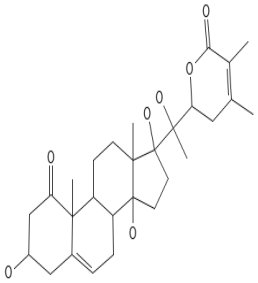
	dienolide (or 3β-hydroxy-2,3-dihydrowithanolide F)				lowering, Central nervous system depressant	
27.	Ergosta-5,25-diene-3β,24ξ-diol	$C_{28}H_{46}O$	398.7	Fruit	Hepatoprotective, Anti-inflammatory, Bloodpressure lowering, Central nervous system depressant	[4,6,10,11,38,43,45,50]
28.	3β,14α,20α_F,27-Tetrahydroxy-1-oxo-20*R*,22R-witha-5,24-dienolide (or 3β-hydroxy-2,3-dihydrowithanolide H)	$C_{28}H_{40}O_7$	488.6	Fruit	Hepatoprotective, Anti-inflammatory, Bloodpressure lowering, Central nervous system depressant	[4,6,10,11,38,43,45,50]
29.	Sitosterol-β-D-glucoside	$C_{28}H_{46}O$	576.8	Fruit	Hepatoprotective, Anti-inflammatory, Bloodpressure lowering, Central nervous system depressant	[4,6,10,11,38,43,45,50]
30.	Coagulanolide ((17*S*,20*S*,22*R*)-14α,15α,17β,20β-tetrahydroxy-1-oxowitha-2,5,24-trienolide)	$C_{28}H_{38}O_7$	486.6	Fruit	Hepatoprotective, Anti-inflammatory, Bloodpressure lowering, Central nervous system depressant	[4,6,10,11,38,43,45,50]
31.	Withanolide F	$C_{28}H_{40}O_7$	488.6	Fruit	Antihyperglycemic	[4,6,10,11,38,43,45,50]
32.	Withaferin A	$C_{28}H_{38}O_6$	470.6	Root	Antimicrobial,	[4,6,10,11

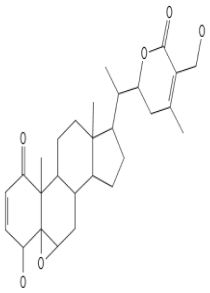
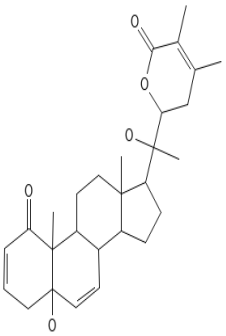
					Immunomodulating, Antitumour, Cytotoxic	,38,43,45, 50]
33.	5,27-Dihydroxy-6α,7α-epoxy-1-oxo-(5α)-witha-2,24-dienolide	$C_{28}H_{38}O_5$	454.6	Root	Antimicrobial, Immunomodulating, Antitumour, Cytotoxic	[4,6,10,11 ,38,43,45, 50]
34.	Withacoagin ((20*R*,22*R*)-5α,20-dihydroxy-1-oxowitha-2,6,24-trienolide)	$C_{28}H_{38}O_5$	454.6	Root	Antimicrobial, Immunomodulating, Antitumour, Cytotoxic	[4,6,10,11 ,38,43,45, 50]
35.	(20*R*,22*R*)-6α,7α-Epoxy-5α-20-hydroxy-1-oxowitha-2,24-dienolide	$C_{28}H_{38}O_7$	486.6	Root	Antimicrobial, Immunomodulating, antitumor, cytotoxic	[4,6,10,11 ,38,43,45, 50]
36.	(20*S*,22*R*)-6α,7α-Epoxy-5α-dihydroxy-1-oxowitha-2,24-dienolide	$C_{28}H_{38}O_6$	470.6	Root	Immunosuppressive	[4,6,10,11 ,38,43,45, 50]

Table No. 3: Structures of isolated compound:

1.Coagulin 	**2.Epoxywithanolide-I** 	**4.Coagulin-B** 
5.Coagulin-C 	**6.Coagulin-D** 	**7.Coagulin-E** 
8.Coagulin-F 	**9.coagulin-G** 	**10.Coagulin-H** 

11.Coagulin-I 	**12.Coagulin-J** 	**13.Cogulin-K** 
14.Coagulin-L 	**15.Coagulin-M** 	**16.Coagulin-N** 
17.Coagulin-O 	**18.Coagulin-P** 	**19.Coagulin-Q** 

20.Coagulin-R 	**21.20β-Hydroxy-1-oxo-with a-2,5,24-trienolide** 	**22.Withacoagulin** 
24.Coagulin-S 	**26.** 	**27.Ergosta-5,25-diene-3β,24ξ-diol** 
29.Sitosterol-β-D-glucoside 	**30.Coagulanolide** 	**31.Withanolide-F** 

32.Withaferin-A	34.Withacoagin	
		

Pharmacological actions:

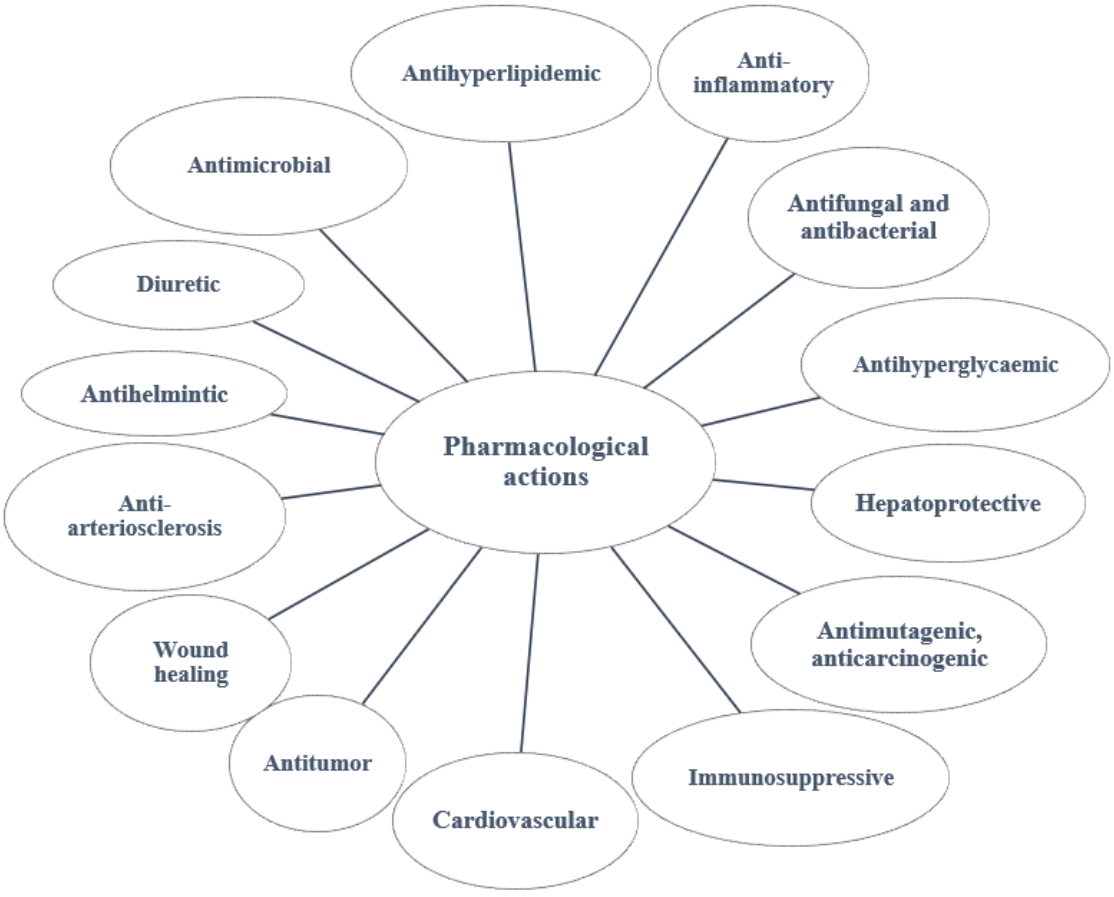


Fig No. 6: Pharmacological actions

Withania coagulans possess the following activities:

1. Antihyperglycemic activities:

Diabetes can be effectively managed with *Withania coagulans* since it exhibits hypoglycemic properties, which is a safe and effective alternative treatment option [32]. An aqueous extract of *Withania coagulans* berries (1gm/kg; P.O.) significantly lowers vital signs, serum glucose, and lipid peroxide. It promotes the correct amount of insulin secretion. *Withania coagulans* improve glucose utilization and carbohydrate metabolism, thereby depleting blood glucose. Hyperglycaemia is reduced due to it [35]. Treatment with coagulanolide alongside four known withanolides 1-3 and 5 isolated from four fruits of *W. coagulans*, shows significant inhibition on the postprandial rise in hyperglycemia post sucrose load in normoglycemic rats also as streptozotocin-induced diabetic rats [11]. Hence, *Withania coagulans* is considered an antihyperglycemic and antidyslipidemic agent [14]. *Withania coagulans* are commonly used in the management of type-2 diabetes mellitus [15].

2. Antihyperlipidemic activities:

In high-fat diet-induced hyperlipidemic rats, extracts of *Withania coagulans* fruits significantly reduced levels of elevated serum cholesterol, triglyceride, lipoprotein, and therefore LPO levels. Ayurvedic products containing Commiphora Mukul are analogous to the hypolipidemic effect of fruits of *Withania coagulans*[41].

3. Anti-inflammatory activities:

Withania coagulans alcoholic extract has a significant anti-inflammatory effect in acute inflammation induced by egg albumin [25,11]. Withanolides from *Withania coagulans* are effective in reducing inflammation in acute inflammation [4]. The hydroalcoholic extract of *Withania coagulans* berries exhibits significant anti-inflammatory activity in a carrageenin-induced rat paw edema model [38].

4. Antifungal and antibacterial effects:

Micrococcus pyrogens var. aureus vibrio cholera is inhibited by the volatile oil produced by steam distillation of the petroleum ether extract of the fruits.Two new withanolides 14,15β-epoxywithanolides I [(20S, 22R) 17ẟ,20ẟ-dihydroxy-14ẟ,15ẟ-epoxy-1-oxo-with a-3,5,24-trienolides] and 17β-hydroxy withanolides K[(20S,22R)14α,17ẟ,20ẟ-trihydroxy-1-oxo-with

a-2,5,24-trien-olide],isolated from ethanolic extract of whole plant *Withania coagulans* found to move against a variety of potentially pathogenic fungi [38].

5. Cardiovascular Effects:

Withanolide, a steroidal lactone derived from the aqueous extract of Paneer Dodi fruits, has a cardiovascular effect[18,52]. This withanolide replacement, isolated from the fruits of *Withania coagulans,* has a similar chemical structure to the aglycones of cardiac glycosides [29]. Withanolide produced a moderate fall in blood pressure in dogs (34 +/- 2.1, mm Hg), which was blocked by atropine and not by mepyramine or propranolol at doses of 5 mg/kg body weight. It produces a myocardial depressant effect in rabbit Langendorff or preparation of ECG studies but produces mild positive ionotropic and chronotropic effects in perfused dogs' hearts [1].

6. Immunosuppressive Effects:

Withanolide E and Ashwagandha possess specific immunosuppressive properties on human B and T lymphocytes as well as mice thymocytes[45]. Withanolides, such as coagulin-H, acts on several cellular functions involved in immune responses, including lymphocyte proliferation and interleukin-2 (IL-2) cytokine expression [17]. It is comparable to the effects of prednisolone. The coagulin-H possesses a strong inhibitory effect on lymphocyte proliferation, and therefore, cytokine production by Th-1 cells. Coagulin-H inhibits phytohaemagglutinin (PHA)-induced T-cell motivation[7].

7. Antimutagenic and anticarcinogenic effects:

The genotoxicity of herbal drugs is determined by their phytoconstituents. *Withania coagulans* contain withanolides, which have antitumor properties, as well as flavonoids that exert antimutagenic and anticancer effects [27]. The antimutagenic properties of *Withania coagulans* remain unknown. *Withania coagulans* extract cyclophosphamide-induces micronucleus formation in mice bone marrow cells. The results show that a single i.p. injection of *Withania coagulans* fruits extracts at doses of 500,1000,1500 mg/kg weight before 24 hours effectively reduces micronucleus development in bone marrow cells of mice in a dose department manner as compared to the cyclophosphamide group [36]. The plant is ethnobotanically reported in cancer treatment [12].

8. Hepatoprotective Activity:

In adult albino rats, 3-hydroxy-2, 3-dihydro-withanolide F derived from a fruit of *Withania coagulans* has been shown to have hepatoprotective effects against CCl4-induced hepatotoxicity. A weight-based comparison revealed that it is more active than hydrocortisone and exhibits a marked protective effect [14].

9. Antitumor properties:

Withaferin (3β-hydroxy-2, 3-dihydro-withanolide F) exhibits antitumor effects. *Withania coagulans* aqueous extract has anticyto toxic properties. The extract shows the remarkable inhibitory activity of DMSO-induced cytotoxicity and decreases in TNF-α production in chicken Lymphocytes [53].

10. Wound healing activity:

A study suggests the wound healing activity of *Withania coagulans* in streptozotocin-induced diabetic rats. In both topical and oral forms, hydro-alcoholic fractions of the methanolic extract (standardized by withaferin A) of *Withania coagulans* increase the rate of wound contraction. Withaferin-A enhances collagen, protein, DNA, SOD, and CAT levels, and decreases the levels of hexosamine [6]. Hydroalcoholic fractions of *Withania coagulans* methanolic extract sort of 10 %w/w ointment were applied topically and orally at a dose of 500mg/kg weight to streptozotocin-induced diabetic rats [13]. In models of open and incised wounds, the aqueous-methanolic phase of the methanolic extract of *Withania coagulans* has shown significant wound healing activity. It accelerates collagen, mucopolysaccharides, DNA, and protein synthesis [35].

11. Anti-arteriosclerosis Activity:

The aqueous extract of *Withania coagulans* also exhibits radical scavenging activity in an in vitro system using DPPH and. Aqueous extract of fruits of *Withania coagulans* has antioxidant potential against several diseases like aging, atherosclerosis, etc[36].

12. Anthelmintic activity:

In the steam distillation of the petroleum ether extract of *Withania coagulans* fruits, essential oil appears to possess anthelmintic properties. The upper parts of *Withania coagulans* have anthelmintic activity in ruminants [31].

13. Diuretic activity:

Withania coagulans fruits exhibit diuretic potential in an aqueous extract when studied in rats. When compared with other Withania species, *Withania coagulans* have more polar Withanolides[19]. Using furosemide as a standard, the diuretic activity of the aqueous extract of paneer Dodi roots can be studied in the Lipschitz test model. The results showed significant increases in urine volume by 71.02% and 79.12% at 500mg/kg and 75mg/kg weight dosages, respectively, when compared to regulate. Urinary electrolyte excretion where increases in both the dosage compared to regulate. The diuretic effect is due to the presence of the active principles of polar nature, of which withanolides are the chemical protagonists. Research supports the use of *Withania coagulans* as a diuretic agent in folk medicine [34]. *Withania coagulans* extract has hypotensive, respiratory stimulant, and muscle relaxing properties [11].

Toxicology:

When the body is exposed to medications or poisons, nephrotoxicity is a common adverse outcome. It leads to uremia due to a failure of the kidneys to filter excess urea, nitrogenous substances, and creatinine. There is no specific treatment for acute renal failure; only supportive care is required to restore renal function. This condition can only be avoided by avoiding nephrotoxic substances and maintaining adequate hydration and perfusion.

CONCLUSION:

The review article summarised the botanical name, taxonomical classification, morphology, phytochemistry, biosynthesis of withanolides, traditional uses, and pharmacological action of *Withania coagulans. Withania coagulans* was known by the name ‘Panner Dodi’ is the most important multipurpose ayurvedic medicinal plant, extensively used in herbal formulations. Paneer Dodi, chemically rich in steroidal lactone, which is known as withanolides having significant pharmacological activity. In this study, we have reviewed literature about *WithaniaCoagulans* and their pharmacological activities such as anti-inflammatory activity, antidiabetic activity, cardiovascular effect, antimicrobial, hepatoprotective activity, anthelmintic activity, antifungal activity, antioxidant activity, wound healing activity, antitumor properties, hypolipidemic activity. More clinical trials, however, are needed to support its therapeutic uses. Therefore, there remains ample scope for

further scientific exploration of *Withania coagulans* to determine their therapeutic efficacy as well as commercial potential.

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