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PHYTOCHEMICAL AND PHARMACOLOGICAL OVERVIEW OF *WITHANIA COAGULANS*

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Keywords:

Withania coagulans, Solanaceae,
Withacoagulins, Coagulonides,
Antidiabetic, Neuroprotective

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ABSTRACT: *Withania coagulans*, commonly known as *Rishyagandha* in Sanskrit and *Paneer phool* in Hindi, is a plant in the Solanaceae or nightshade family, native to Afghanistan, Pakistan and the Indian subcontinent. Within the genus *Withania*, *W. somnifera* and *W. coagulans* are economically significant and are cultivated in several regions for their use in Ayurveda. Roots of *W. somnifera* have been known since ancient times for their use as Rasayana for the overall wellbeing of humanity. *Withania coagulans* fruit, though not as popular, has earned its medicinal importance because of its recently claimed use in diabetes. The antidiabetic activity of the plant is attributed to several reported phytoconstituents ranging from steroidal lactones like withanolides and withaferins to coagulonides and withacoagulins etc. The plant has also been reported to possess a wide range of pharmacological activities like antidiabetic, anticancer, immunomodulatory, hepatoprotective, neuroprotective, anti-inflammatory and many more. Though from the well-appreciated *Withania* family, the plant *Withania coagulans*, could attract less attention from the researchers. Hence, this review article aims to highlight the recent findings on the chemical and pharmacological potential of *Withania coagulans*, aiming to explore and enhance the plant's therapeutic benefits with a curative and preventive approach.

INTRODUCTION: The science of life is known as Ayurveda. In Ayurveda, plants are the primary source of medicine for treating and preventing diseases and maintaining a healthy lifestyle¹. Many plants in the natural system of medicine must have a wide range of biological activities. *Withania* is a minor genus in the Solanaceae family of shrubs (which has about 2000–3000 species divided around 90 families)².

Withania species, from the East Mediterranean to South Asia, may be found worldwide. *Withania coagulans* and *Withania somnifera* are two species found in Pakistan². *Withania* is a flowering plant of the Solanaceae family with roughly 23 species endemic to North Africa, the Middle East and the Canary Islands³. In various sections of Afghanistan, Pakistan, India, and Nepal, *W. coagulans* is prevalent. It may be found in Punjab, Rajasthan, Simla, Kumaun and Garhwal in India⁴.

This plant carries different local names, such as Akri, Punir bandh, Paneer Dodi, or Puni-ke-Bij (Hindi), Khamjira (Panjabi), Tukhmekaknaje-Hindi (Persian), Spiubajja (Afghanistan), Punirband or Punir-ja-fota (Sindhi), Indian Cheesemaker, Indian Rennet, Vegetable Rennet (English), Asvagandha

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(Urdu) *Withania coagulans*⁵, often known as paneerdodi or pannerdoda, is a type of vegetable

rennet. The shrub's berries are used to coagulate milk⁶.



FIG. 1: FRESH PLANT OF *W. COAGULANS*



FIG. 2: DRY FRUITS OF *W. COAGULANS*

Taxonomical Classification:

Kingdom: Plantae

Division: Magnoliophyta

Order: Solanales

Family: Solanaceae

Genus: *Withania*⁶

Withania coagulans is a coagulant plant (Stocks) Dunal is used to treat nervous tiredness, disability, insomnia, wasting disorders, children's failure to thrive, and impotence. Externally administered to treat inflammatory diseases, ulcers, and scabies, *W. coagulans* is a great stress-relieving, blood purifier, and anti-cancer medicine⁵.

The fruits of this plant are used to treat liver problems, asthma, and biliousness. Dunal flowers of coagulans (Stocks) are used to cure diabetes (Bowm D., 1995). The plant has been shown to have antimicrobial, anti-inflammatory, anticancer, hepatoprotective, antihyperglycemic, cardiovascular, immunosuppressive, free radical scavenging and central nervous system depressant properties (Maurya R., et al. 2010). The antimutagenic potential of *Withania coagulans* fruit extracts has been documented by (Mathur D. and Agrawal R., 2011)

Withania coagulans (Paneer Doda) have been used in Indian Ayurvedic treatment since immemorial. The procedure for using it is pretty straightforward. 10 of those seed-like flowers should be placed in a glass of water overnight. Drink the water in the morning after filtering it with a sieve. Paneer Doda may be purchased for roughly 50 cents per 100 gm from any good Ayurvedic specialized shop. In a

fortnight, if you stick to this medication, you'll be able to control your blood sugar. *Withania coagulans* are used to treat chronic liver problems. Extracts of *Withania coagulans* and *Withania somnifera* are used in the Ayurvedic herbal hepatoprotective medication 'Liv-52.' Dyspepsia, flatulent colic, and other intestinal illnesses are also treated with them. The berries are used to purify the blood⁶.

Unfortunately, many plant species' populations decrease and are dispersed in the wild, which can be linked to low rates of natural regeneration. It has been found that *Withania* seed germination is poor and seedling mortality is high under field circumstances⁵.

Botanical Description: Shrub with ridges and furrows, 2-3m in length, slightly hairy stem cylindrical, 0.5-0.16cm length, hair curving. Sepals cover the fruit and end in a crown-like structure. Fruit berries and globose are 1.5-1 cm long and 0.7-1 cm wide. Seeds are yellowish-brown, oblong to rounded, 41-59 in number, 0.1-0.3cm long, 0.2-0.3cm broad, and dotted. From January to April, the plant blooms⁶.

Chemical Profile:

3 β -hydroxy-2,3-dihydrowithanolide F⁷: **Fig. 3.**

- ❖ IUPAC Name: (2R)-2-[(1S)-1-hydroxy-1-[(3R, 8R, 9S, 10R, 13S, 14R, 17R)-3, 14, 17-trihydroxy - 10, 13-dimethyl - 1-oxo-2, 3, 4, 7, 8, 9, 11, 12, 15, 16-decahydrocyclopenta[a]

phenanthren-17-yl]ethyl]-4,5-dimethyl-2,3-dihydropyran-6-one

- ❖ InChI: 1S/C₂₈H₄₀O₇/c1-15-12-22(35-23(31)16(15)2)26(5,32)28(34)11-10-27(33)20-7-6-17-13-18(29)14-21(30)25(17,4)19(20)8-9-24(27,28)3/h6,18-20,22,29,32-34H,7-14H2,1-5H3/t18-,19+,20-,22-,24+,25+,26+,27-,28-/m1/s1.

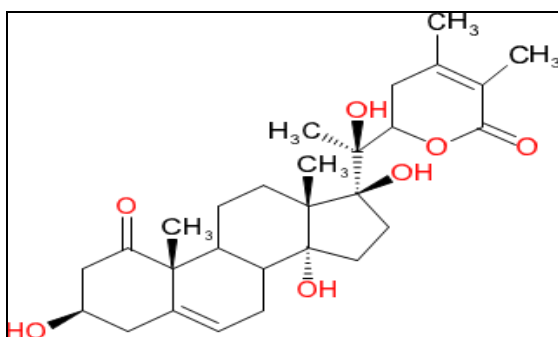


FIG. 3: 3B-HYDROXY-2,3-DIHYDROWITHANOLIDE

- ❖ InChI Key: BQRGHHNBIPOTTJ-DVKLICRISA-N.

- ❖ Molecular Formula: C₂₈H₄₀O₇.
- ❖ This compound is isolated from the fruit part.
- ❖ Biological Activity: Anti-inflammatory activity.

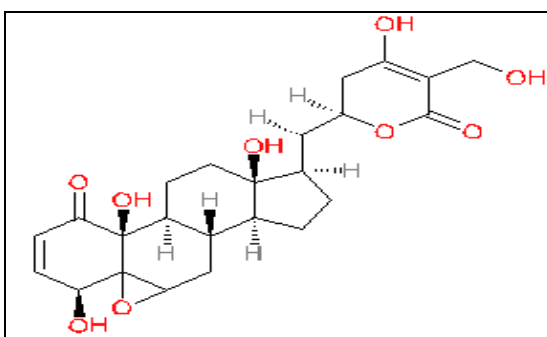


FIG. 4: WITHAFERIN A

Withaferin A⁸:- Fig. 4.

- ❖ IUPAC Name: (1S, 2R, 6S, 7R, 9R, 11S, 12S, 15R, 16S)-6-hydroxy-15-[(1S)-1-[(2R)-5-(hydroxymethyl) - 4-methyl - 6-oxo-2, 3-dihydropyran- 2 -yl]ethyl] - 2, 16-dimethyl-8-oxapentacyclo [9.7.0.02,7.07,9.012,16]octadec-4-en-3-one
- ❖ InChI: 1S/C₂₈H₃₈O₆/c1-14-11-21(33-25(32)17(14)13-29)15(2)18-5-6-19-16-12-24-28(34-24)23(31)8-7-22(30)27(28,4)20(16)9-10-26(18,19)3/h7-8,15-16,18-21,23-24,29,31H,5-6,9-13H2,1-4H3/t15-,16-,18+,19-,20-,21+,23-,24+,26+,27-,28+/m0/s1

- ❖ InChI Key: DBRXOUCRJQVYJQ-CKNDUULBSA-N

- ❖ Molecular Formula: C₂₈H₃₈O₆
- ❖ This compound is isolated from the root part.
- ❖ Biological Activity: Antimicrobial, immunomodulating, antitumour, cytotoxic activity

Withanolide F⁷:- Fig. 5.

- ❖ IUPAC Name: (2R)-2-[(1S)-1-hydroxy-1-[(3R, 8R, 9S, 10R, 13S, 14R, 17R)-3, 14,17-trihydroxy-10,13-dimethyl-1-oxo-2, 3, 4, 7, 8, 9, 11, 12, 15, 16-decahydrocyclopenta[a]

phenanthren-17-yl]ethyl]-4,5-dimethyl-2,3-dihydropyran-6-one

- ❖ InChI: 1S/C₂₈H₄₀O₇/c1-15-12-22(35-23(31)16(15)2)26(5,32)28(34)11-10-27(33)20-7-6-17-13-18(29) 14-21(30) 25(17,4) 19(20)8-9-24(27,28)3/h6,18-20,22,29,32-34H,7-14H2,1-5H3/t18-,19+,20-,22-,24+,25+,26+,27-,28-/m1/s1

- ❖ InChI Key: BQRGHHNBIPOTTJ-DVKLICRISA-N

- ❖ Molecular Formula: C₂₈H₄₀O₇
- ❖ This compound is isolated from the part of the aerial part.
- ❖ Biological Activity: Anti-hyperglycemic, Anti-Inflammatory, Anti-Cancer activity.

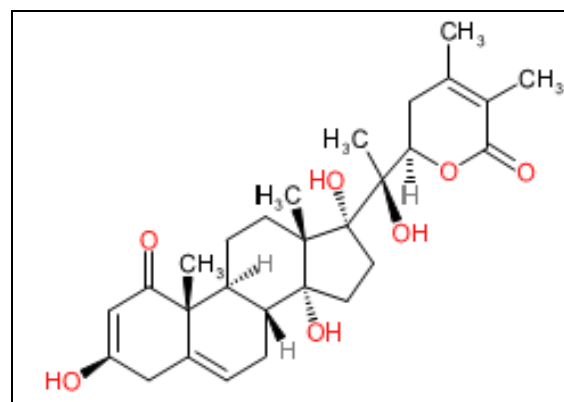


FIG. 5: WITHANOLIDE F

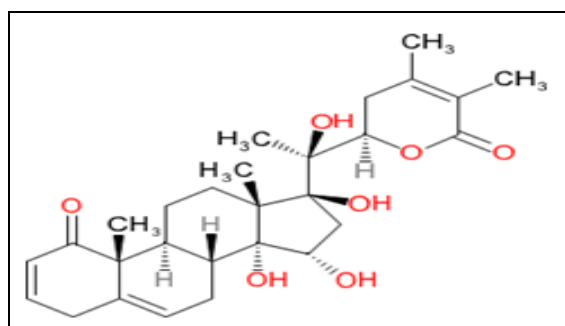


FIG. 6: COAGULANOLIDE 7

Coagulanolide 7:- Fig. 6

- ❖ IUPAC Name: (2R)-2-[(1S)-1-hydroxy-1-[(8R, 9S, 10R, 13S, 14R, 15S, 17S)-14, 15, 17-trihydroxy-10, 13-dimethyl-1-oxo-4, 7, 8, 9, 11, 12, 15, 16-octahydrocyclopenta[a]phenanthren-17-yl]ethyl]-4,5-dimethyl-2,3-dihydropyran-6-one
- ❖ InChI: 1S/C₂₈H₃₈O₇/c1-15-13-22(35-23(31)16(15)2) 26(5,32) 27(33)14-21(30) 28(34) 19-10-9-17-7-6-8-20(29) 25(17,4) 18(19)11-12-24(27,28) 3/h6,8-9,18-19,21-22,30,32-34H,7,10-14H2,1-5H3/t18-,19+,21-,22+,24+,25-,26-,27-,28-/m0/s1
- ❖ InChI Key: XAEUKOBJPRGERY-VLXOZLMSA-N

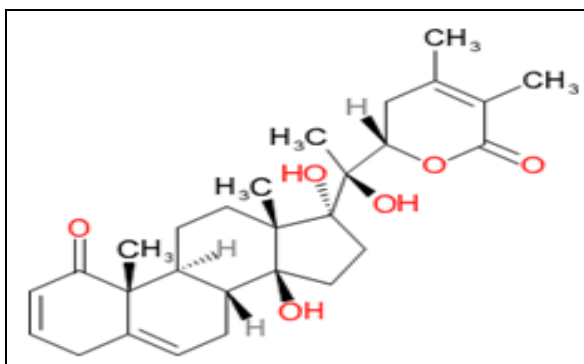


FIG. 7: WITHACOAGULIN 7

Withanolide D¹⁰:-Fig. 8.

- ❖ IUPAC Name: (1S, 2R, 6S, 7R, 9R,11S, 12S,15S, 16S)-15-[(1R)-1-[(2R)-4,5-dimethyl-6-oxo-2,3-dihydropyran-2-yl]-1-hydroxyethyl]-6-hydroxy-2,16-dimethyl-8-oxapentacyclo[9.7.0.02, 7.07, 9.012,16] octadec-4-en-3-one
- ❖ InChI: 1S/C₂₈H₃₈O₆/c1-14-12-22(33-24(31) 15(14)2)27(5,32)19-7-6-17-16-13-23-28(34-23)21(30)9-8-20(29)26(28,4)18(16)10-11-

- ❖ Molecular Formula: C₂₈H₃₈O₇
- ❖ This compound is isolated from the fruit part.
- ❖ Biological Activity: Antihyperglycemic activity

Withacoagulin 7:-Fig.7.

- ❖ IUPAC Name: (2R)-2-[(1R)-1-[(8R, 9S, 10R, 13R, 17S)-10,13-dimethyl-1-oxo-4,7, 8, 9, 11, 12, 16,17-octahydrocyclopenta[a] phenanthren-17-yl]-1-hydroxyethyl]-5-(hydroxymethyl)-4-methyl-2, 3-dihydropyran – 6 - one
- ❖ InChI: 1S/C₂₈H₃₆O₅/c1-16-14-24(33-25(31) 19(16)15-29)28(4,32)22-11-10-20-18-9-8-17-6-5-7-23(30) 27(17,3) 21(18)12-13-26(20, 22)2/h5, 7-8, 10, 18, 21-22, 24,29,32H,6,9,11-15H2,1-4H3/t18-,21-,22-,24-,26-,27-,28+/m0/s1
- ❖ InChI Key: ZKTNOURYQAESEW-WSLQVVCNSA-N
- ❖ Molecular Formula: C₂₈H₃₆O₅
- ❖ This compound is isolated from the fruit part.
- ❖ Biological Activity: Cardioprotective activity

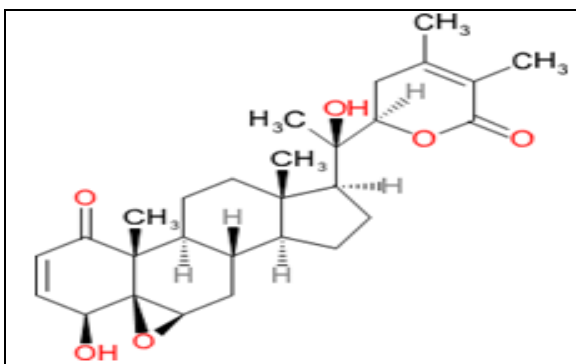


FIG. 8: WITHANOLIDE D

25(17,19)3/h8-9,16-19,21-23,30,32H,6-7,10-13H2,1-5H3/t16-,17-,18-,19-,21-,22+,23+,25-,26-,27+,28+/m0/s1

- ❖ InChI Key: SASUFNRGCZMRFD-JCUIIOWSA-N
- ❖ Molecular Formula: C₂₈H₃₈O₆
- ❖ This compound is isolated from the fruit part.
- ❖ Biological Activity: Antitumor activity.

Withanolide H⁷:-Fig. 9.

- IUPAC Name: 14 α , 20 α F, 27-trihydroxy-1-oxo-20R, 22R-with a-2,5,24- trienolide
- InChI: 1S/C₂₈H₃₈O₆/c1-16-14-23(34-24(31)18(16)15-29)27(4,32)21-11-13-28(33)20-9-8-17-6-5-7-22(30)26(17,3)19(20)10-12-25(21,28)2/h5,7-8,19-21,23,29,32-33H,6,9-15H2,1-4H3/t19?,20?,21?,23?,25-,26+,27-,28-/m1/s1.

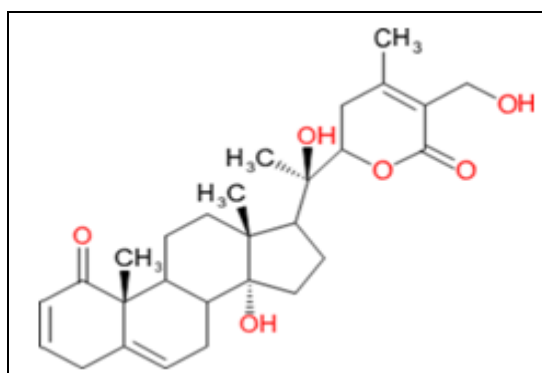


FIG. 9: WITHANOLIDE H

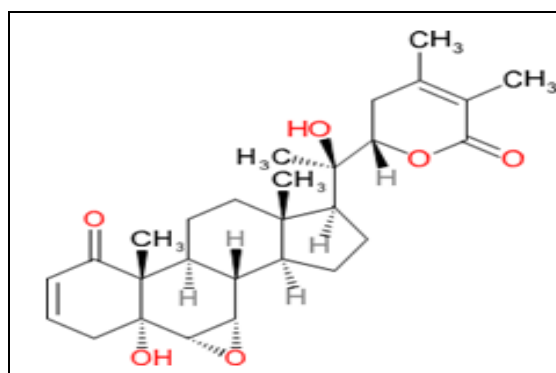


FIG. 10: WITHANOLIDE A

Withanolide A⁸:-Fig.10.

- ✓ IUPAC Name: (1S, 2S, 4S, 5R, 10R, 11S, 14S, 15S, 18S)-15-[(1R)-1-[(2S)-4,5-dimethyl-6-oxo-2,3-dihydropyran-2-yl]-1-hydroxyethyl]-5-hydroxy-10, 14-dimethyl - 3 - oxapentacyclo [9.7.0.02,4.05,10.014,18] octadec-7-en-9-one
- ✓ InChI: 1S/C₂₈H₃₈O₆/c1-14-13-20(33-24(30)15(14)2)27(5,31)18-9-8-16-21-17(10-12-25(16,18)3)26(4)19(29)7-6-11-28(26,32)23-22(21)34-23/h6-7,16-18,20-23,31-32H,8-13H2,1-5H3/t16-,17-,18-,20-,21-,22-,23-,25-,26-,27+,28-/m0/s1
- ✓ InChI Key: DXWHOKCXBGLTMQ-AWROWWNASA-N
- ✓ Molecular Formula: C₂₈H₃₈O₆
- ✓ This compound is isolated from the fruit part.
- ✓ Biological Activity: Immunosuppression activity.

Withanolide B⁹:-Fig. 11.

- ❖ IUPAC Name: (1S, 2S, 4S, 5R, 10R, 11S, 14R, 15R, 18S)-15-[(1S)-1-[(2R)-4, 5-dimethyl-6-oxo-2, 3-dihydropyran-2-yl]ethyl]-5-hydroxy-10,14-dimethyl-3-

- InChI Key: SZVJDQSFFAIGDR-LWGVTTDVSA-N
- Molecular Formula: C₂₈H₃₆O₆
- This compound is isolated from the fruit part.
- Biological Activity: Anti-inflammatory activity.

oxapentacyclo[9.7.0.02,4.05,10.014,18]
octadec-7-en-9-one.

- ❖ InChI: 1S/C₂₈H₃₈O₅/c1-14-13-20(32-25(30)15(14)2)16(3)17-8-9-18-22-19(10-12-26(17,18)4)27(5)21(29)7-6-11-28(27,31)24-23(22)33-24/h6-7,16-20,22-24,31H,8-13H2,1-5H3/t16-,17+,18-,19-,20+,22-,23-,24-,26+,27-,28-/m0/s1
- ❖ InChI Key: ZTEVDTFJUJBLP-MBMSZCMESA-N
- ❖ Molecular Formula: C₂₈H₃₈O₅
- ❖ This compound is isolated from the fruit part.
- ❖ Biological Activity: Immunosuppression activity.

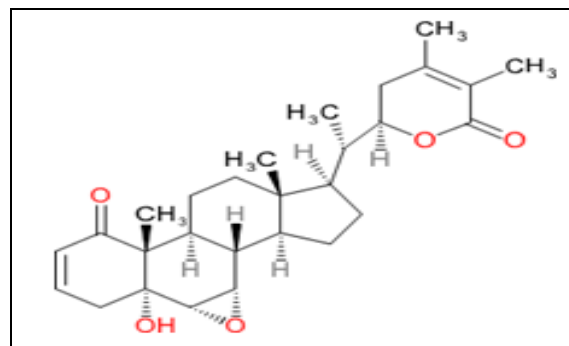


FIG. 11: WITHANOLIDE B

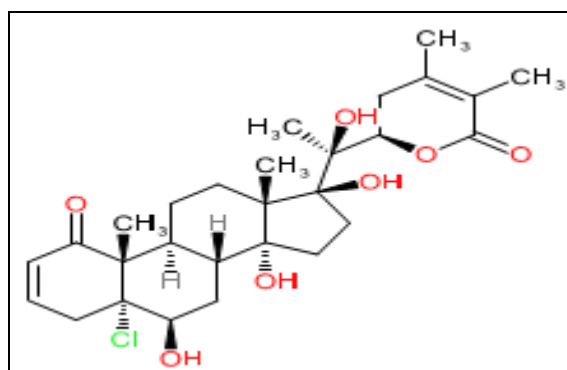


FIG. 12: WITHANOLIDE C

Withanolide C⁹:-Fig. 12.

- ✓ IUPAC Name: (2R)-2-[(1S)-1-[(5R,6R,8R,9S,10S,13S,14R,17S)-5-chloro-6,14,17-trihydroxy-10,13-dimethyl-1-oxo-6,7,8,9,11,12,15,16-octahydro-4H-cyclopenta[a]phenanthren-17-yl]-1-hydroxyethyl]-4,5-dimethyl-2,3-dihydropyran-6-one
- ✓ InChI: 1S/C₂₈H₃₉C₁O₇/c1-15-13-21(36-22(32)16(15)2)25(5,33)28(35)12-11-27(34)18-14-20(31)26(29)9-6-7-19(30)24(26,4)17(18)8-10-23(27,28)3/h6-7,17-18,20-21,31,33-35H,8-14H2,1-5H3/t17-,18+,20+,21+,23-,24-,25-,26-,27+,28-/m0/s1
- ✓ InChI Key: JEJZNYLQNCIUEG-DEMKEYSCBSA-N

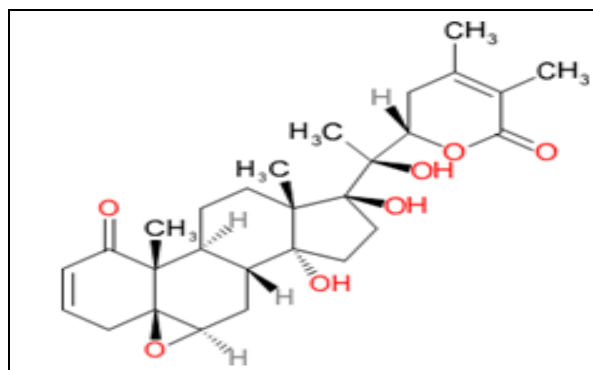


FIG. 13: WITHANOLIDE E

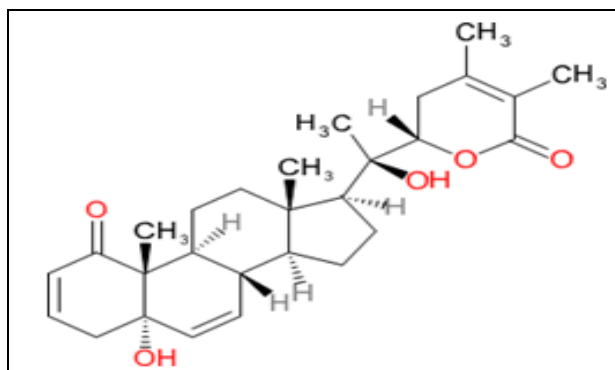


FIG. 14: WITHACOAGIN

Withacoagin¹¹:- Fig. 14.

- ❖ IUPAC Name: (2R)-2-[(1R)-1-hydroxy-1-[(5S,8S,9S,10R,13S,14S,17S)-5-hydroxy-10,13-dimethyl-1-oxo-8,9,11,12,14,15,16,17-octahydro-4H-cyclopenta[a]phenanthren-17-yl]ethyl]-4,5-dimethyl-2,3-dihydropyran-6-one
- ❖ InChI: 1S/C₂₈H₃₈O₅/c1-16-15-22(34-23(30)17(16)2)26(5,31)28(33)14-10-19-18-8-13-27(32)11-6-7-21(29)25(27,4)20(18)9-12-24(19,28)3/h6-8,13,18-20,22,31-33H,9-12,14-15H2,1-5H3/t18-,19-,20-,22-,24-,25-,26-,27-,28+/m0/s1
- ❖ InChI Key: CNPITZCWPQTGB-SZJVKPFRSA-N
- ❖ Molecular Formula: C₂₈H₃₈O₅

- ✓ Molecular Formula: C₂₈H₃₉C₁O₇
- ✓ This compound is isolated from the fruit part.
- ✓ Biological Activity: Immunosuppression activity.

Withanolide E¹⁰:- Fig. 13.

- IUPAC Name: (1S,2R,7S,9R,11R,12R,15S,16S)-15-[(1S)-1-[(2S)-4,5-dimethyl-6-oxo-2,3-dihydropyran-2-yl]-1-hydroxyethyl]-12,15-dihydroxy-2,16-dimethyl-8-oxapentacyclo[9.7.0.02,7.07,9.012,16]octadec-4-en-3-one
- InChI: 1S/C₂₈H₃₈O₇/c1-15-13-20(34-22(30)16(15)2)25(5,31)28(33)12-11-26(32)18-14-21-27(35-21)9-6-7-19(29)24(27,4)17(18)8-10-23(26,28)3/h6-7,17-18,20-21,31-33H,8-14H2,1-5H3/t17-,18+,20-,21+,23-,24-,25-,26+,27+,28-/m0/s1
- InChI Key: RUVPNJSJTWTANE-UZKJPURASA-N
- Molecular Formula: C₂₈H₃₈O₇
- This compound is isolated from the fruit part.
- Biological Activity: Immunosuppression activity.

- ❖ This compound is isolated from the root part.
- ❖ Biological Activity: Anti-lipido activity.

17β-hydroxywithanolide K¹³: -Fig. 15.

- ✓ IUPAC Name: 2-[(1S)-1-[(8R, 9S, 10R, 13S,14R,17S)-14,17-dihydroxy-10,13-dimethyl-1-oxo-2, 7, 8, 9, 11, 12, 15,16-octahydrocyclopenta[a]phenanthren-17-yl]-1-hydroxyethyl]-4,5-dimethyl-2,3-dihydropyran-6-one
- ✓ InChI: 1S/C₂₈H₃₈O₆/c1-16-15-22(34-23(30)17(16)2)26(5,31)28(33)14-13-27(32) 20-10-9-18-7-6-8-21(29) 25(18,4) 19(20)11-12-24(27,28) 3/h6-7,9,19-20,22,31-33H,8,10-15H2,1-5H3/t19-,20+, 22?,24-,25-,26-,27+,28-/m0/s1
- ✓ InChI Key: HYSIDFWCYWFQMQ-AXKKPADPSA-N

- ✓ Molecular Formula: C₂₈H₃₈O₆
- ✓ This compound is isolated from the whole plant.
- ✓ Biological Activity: Antihyperglycemic, Antimicrobial activity.

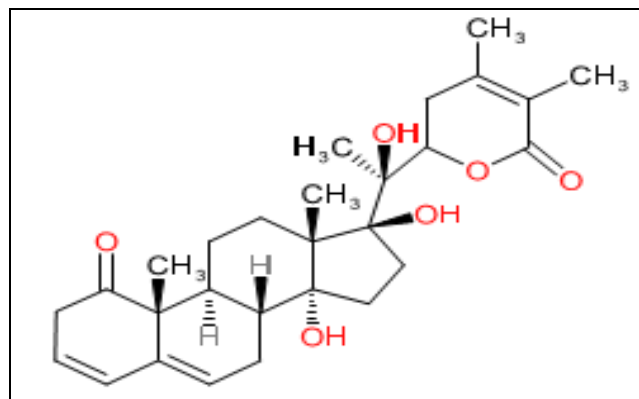


FIG. 15:

Pharmacological Profile:

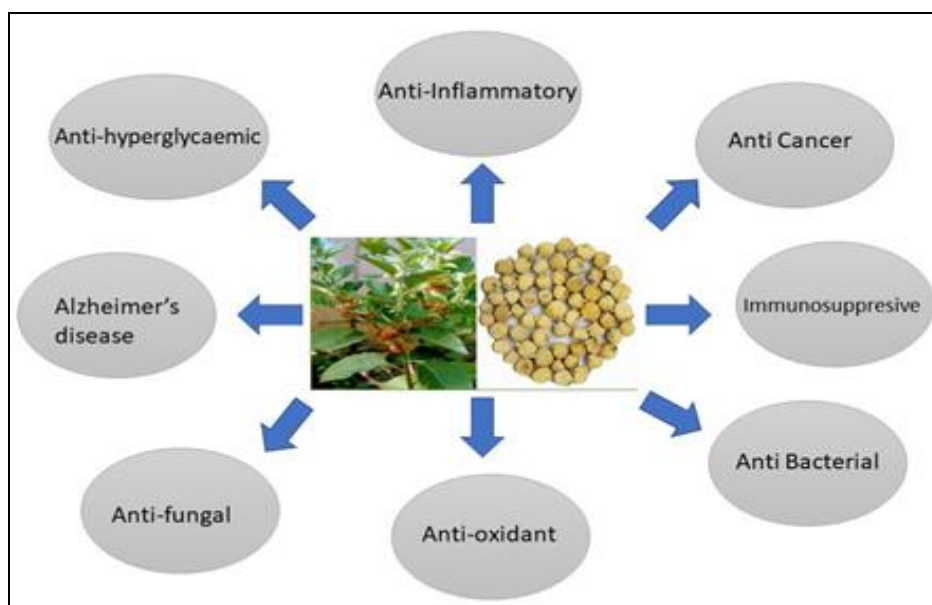


FIG. 16: PHARMACOLOGICAL ACTIVITIES

Pharmacological Activities:

Anti-Inflammatory: Inflammation in the human body is caused by several ways. Cyclooxygenase – 1 (COX-1) and Cyclooxygenase – 2 (COX-2) are two enzymes that make prostaglandins, thromboxane, from arachidonic acid and these prostaglandins can cause inflammation in the body. *Withania coagulans* fruit extract includes 3-hydroxy-2,3-dihydro withanolides F Fig. 3, which has the highest anti-inflammatory activity by inhibiting COX-2 as opposed to COX-1^{14, 15, 16}.

The anti-inflammatory activities of *W. coagulans* have been studied by several researchers. Budhiraja *et al.* (1984) found that a 10 mg kg⁻¹ dose of the aqueous extract of *W. coagulans* fruits has a significant anti-inflammatory effect in subacute inflammation models such as granuloma formation and formalin-induced arthritis in rats¹⁷.

Anti Cancer: *Withania coagulans* have been shown to have anti-cancer properties in numerous

research. Compared to other constituents, withaferin A Fig. 4 and withanolide F Fig. 5, key constituents derived from the aerial part and fruit of *Withania coagulans*, have the most anti-cancer action. Withaferin A suppresses the G2 and M phases of the cell cycle, causing growth inhibition and cytotoxicity in human lung cancer cell lines^{18, 19}.

In another study, aqueous extract of *W. coagulans* was used to suppress cytotoxicity in chicken lymphocytes. Significant inhibitory activity of DMSO-induced cytotoxicity was reported, as well as a decrease in TNF- α production. It has been discovered to be the most effective agent for lowering tumour size and preventing cancer.²⁰

Hypercholesterolemic: The fruit's aqueous extract contains Withanolide F Fig. 5, Coagulanolide Fig. 6, Withacoagulin Fig. 7, Withanolide D Fig. 8 and Withanolide H Fig. 9, all of which have antihypercholesterolemic properties. These *Withania coagulans* compounds improved HDL-cholesterol levels in plasma while reducing LDL, VLDL, and triglyceride levels^{18, 22}.

An aqueous extract of *W. coagulans* fruits has been demonstrated to decrease total lipid, cholesterol, and triglycerides in hypercholesterolemic rats (Andallu and Radhika, 2000; Hemalatha et al., 2006). *W. coagulans* was also shown to have hypocholesterolemic characteristics by Hemalatha et al. An aqueous extract of *W. coagulans* fruits administered to hyperlipidemic rats on a high-fat diet for 7 weeks significantly reduced serum cholesterol, triglycerides and lipoprotein levels. Furthermore, this extract displayed hypolipidemic activity in triton-induced hypercholesterolemia (Hemalatha et al., 2006)^{24, 35}.

Immunosuppression: Withanolide A Fig. 10, Withanolide B Fig. 11, Withanolide C Fig. 12, Withanolide D Fig. 8, Withanolide E Fig. 13, and Withanolide F Fig. 5, which show immunosuppressive activity by inhibiting B- and T-cell proliferation, are present in the crude extract of the aerial part of *Withania coagulans*²¹.

Sexual Behaviour: *Withania coagulans* are used in Ayurveda to treat male libido and penile erectile dysfunction. Withacoagulin Fig. 14 and Withaferin A Fig. 4 are two compounds found in the root extract

of *Withania coagulans* that have anti-lipido action and promote sexual energy and performance. These ingredients directly raise GABAergic and serotonergic levels rather than testosterone levels^{23, 27}.

Antidiabetic: *Withania coagulans* contains Alkaloids, steroidal lactone and saponin along with some metal ions such as Cadmium, Mercury, Magnesium, and calcium. The higher concentration of calcium and magnesium ions shows antihyperglycaemic activity, as calcium is the main cofactor that increases the expression of a gene required to produce insulin through Calcium Responsive Element Binding Protein (CREB)²².

Kirtikar Shukla et al. studies show that the aqueous extract of *Withania coagulans* Fruit reverses the Nicotinamide and Streptozotocin-induced Diabetes in Rats by increasing the glucokinase and phosphofructokinase while significantly decreasing the glucose-6-phosphatase activity³³.

Effects on Heart: Compared to the alcoholic extract, the aqueous extract of *Withania coagulans* fruit contains 3b-hydroxy-2,3-dihydro withanolides F Fig. 3, which has a stronger cardiovascular effect. It demonstrates a drop in blood pressure while raising contraction force and heart rate²⁶.

Antifungal and Antibacterial: The extract of *Withania coagulans* fruit contains 17 β -hydroxy withanolide k Fig. 15, withanolide F Fig. 5 and volatile oil which shows a wide spectrum of Antifungal activity on Human fungus. While the root contains Withaferin A which shows significant Antibacterial activity against Gram-positive as well as Gram-negative bacteria.

Wardah Shahid et al. performed a study of antibacterial activity of Withaferin A by using nutrient agar culture against *B. subtilis*, *E. coli* and *S. aureus* and concluded that after 2 days, there is inhibition of bacteria on culture with the help of the Inhibition zone method^{28, 30}.

Neuroprotective: The root extract contains Withaferin A Fig. 4 and Withanolide A Fig. 10, both of which have neuroprotective properties by enhancing the strength of dendritic and axon regeneration, as well as the ability to re-establish synapses in neurons³¹.

Tomoharu Kuboyama *et al.* experiment using a cell culture model of rat cortical neurons to study the activity of Withanolide A **Fig. 10** as a neurodegenerative drug. Withanolide A is a water extract product of *Withania coagulans* roots. They treated these cultures with Withanolide A for 7 consecutive days and found 70% of dendritic and axon regeneration and the ability to re-establish synapses in neurons³⁴.

Diuretic: The diuretic activity is calculated based on the excretion of electrolytes from the body. Withaferin A **Fig. 4** has the potential to show maximum diuretic activity by exerting action on the Proximal tubule and ascending loop of the henle as a result of a high number of Sodium and Potassium ions get excreted from the body.²⁷

Hepatoprotective: The extract of *Withania coagulans* fruit contains the steroidal glycoside 3-b-hydroxy-2,3 dihydro withanolides F **Fig. 3** which shows the hepatoprotective activity against the CCl₄-induced Hepatotoxicity.

R. D. Budhiraja *et al.* compares the effect of hydrocortisone, a hepatoprotective drug with 3-b-hydroxy-2,3 dihydro withanolides F and conclude their the study by stating that the 3-b-hydroxy-2,3 dihydro withanolides F is much more effective than Hydrocortisone in Hepatotoxicity^{21, 23, 34}.

Novel Drug Delivery Systems for *Withania coagulans*: The extract was encapsulated in nature-derived polymers in the Kaarunya Sampathkumar et al. investigation to improve bioavailability. The aqueous extract of the plant *W. coagulans* was discovered to have a glucose-lowering effect by increasing insulin production from pancreatic cells. When compared to untreated cells, cells treated with the extract secreted roughly twice as much insulin. A delivery mechanism for the extract was created based on electrospray chitosan nanoparticles coated with food-based starch. The enteric starch coating delayed the release of the extract in the stomach (by 2.5 times). The encapsulated extract's bioactivity was then examined in vitro on mouse-derived pancreatic cells, and the delivery mechanism was found to enhance insulin secretion. Finally, the extract-encapsulated oral delivery method was evaluated

on diabetic mice and demonstrated a 60% reduction in blood glucose levels³². Deepika Tripathi *et al.* generated AgNPs by reducing a silver nitrate solution using *in-vitro*-grown leaf extract of the anti-diabetic medicinal herb *Withania coagulans* Dunal. When compared to *W. coagulans* leaf extract, the antioxidative potential of synthesized *Withania coagulans*-reduced gold nanoparticles was higher. The antibacterial potential of *Withania coagulans*-reduced gold nanoparticles is strong, and they inhibit the growth of both gram-positive and gram-negative bacteria³³.

CONCLUSION: Two species of the genus *Withania*, namely, *W. somnifera* and *W. coagulans* are found prevalently in India and are known to possess good therapeutic benefits. Though withanolides are the principal compounds found in both species, there is variation in the nature and content of some withanolides specific to each of them. Withaferin A is a major compound found in *W. somnifera*, whereas withacoagulin has been found in major amounts in *W. coagulans*. Withanolides containing a 14, 20-epoxide bridge are specific to *W. coagulans* alone. *W. coagulans* had a greater therapeutic value overall, and has been reported to possess Hepatoprotective, anti-inflammatory, antihyperglycaemic, hypolipidaemic, free radical scavenging, antimicrobial, cardiovascular, central nervous system depressant, immunomodulating, antitumour, and cytotoxic activities. The variety of activities reported for the extracts, fractions, and withanolides isolated from *W. coagulans* may provide promising evidence for future research.

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