

A REVIEW ON PHARMACOLOGICAL ACTIVITY OF WITHANIA COAGULANS IN TREATMENT OF DIABETES

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ABSTRACT

Withania coagulans, also known as Indian Rennet or Paneer Doda, is a significant medicinal plant from the Solanaceae family, valued for its extensive therapeutic applications in traditional medicine. This review explores the phytochemical composition, pharmacological activities, and medicinal potential of *W. coagulans*, focusing on its role in managing diabetes and related metabolic disorders. The plant is rich in bioactive compounds, including withanolides, flavonoids, saponins, and phenolic compounds, which contribute to its antioxidant, anti-inflammatory, antihyperglycemic, and hepatoprotective properties. Research indicates that *W. coagulans* effectively reduces blood glucose levels, improves insulin sensitivity, and normalizes lipid profiles in diabetic models. Its compounds, such as withanolide J and coagulin E, have shown significant inhibitory effects on key enzymes involved in glucose metabolism. Furthermore, the plant exhibits wound healing, cardiovascular protective, and diuretic activities, making it a versatile therapeutic agent. Its traditional applications range from treating gastrointestinal disorders and toothaches to being used as a blood purifier. However, habitat loss and overexploitation have endangered its natural populations, emphasizing the need for conservation and sustainable use. Future studies should focus on elucidating its mechanisms of action, optimizing its bioavailability, and validating its therapeutic efficacy in clinical settings. *W. coagulans* represents a cost-effective, natural alternative to synthetic drugs, with minimal side effects and broad medicinal potential. This review underscores the significance of *W. coagulans* as a promising candidate for integrative and modern medical practices, particularly in the management of diabetes and associated health conditions.

Keywords: Withania Coagulans, Antidiabetic Activity, Phytochemicals, Metabolic Disorders, Traditional Medicine.

I. INTRODUCTION

In ancient medicinal practices, numerous plants have been identified as beneficial for treating various health issues and ailments. Herbalism refers to the use of plants and plant extracts in traditional or folk medicine. The Charaka Samhita and Sushruta Samhita provide detailed accounts of different medicinal plants. Medicinal plants are vital for the creation of new herbal medications. Currently, about 25% of prescriptions filled in the United States include at least one ingredient derived from plants[1]. Diabetes mellitus is a long-lasting condition that has affected the global population significantly, with over 300 million individuals suffering from it, and the numbers are rising rapidly as modern medicine offers no definitive cure for the illness.[2] This disorder is complex and varied, as managing blood sugar levels also necessitates control over lipid levels, blood pressure, and thrombotic factors. Treating diabetes is both challenging and cumbersome; it is often costly and beyond the means of a large portion of the population.[3] Insulin and synthetic medications are currently used to treat diabetes mellitus. Long-term use of contemporary medications can result in a number of adverse consequences and complications for various body organs, which can ultimately cause weight gain, liver and kidney disease, and cardiovascular issues. These synthetic medications are useful, but they are limited by their adverse effects, which include diarrhea, lactic acidosis, liver damage, hypoglycemia, stomach pain, weight loss, and appetite loss. [3,4].

Many diabetics turn to natural plant-based alternative medicines that are meant to help glycemic control because of the issues with the present treatments. Therefore, more medicinal plants with hypoglycemic action that are safe, affordable, biodegradable, and have fewer adverse effects need to be screened. [4].

One of the biggest worldwide challenges, according to the World Health Organization, is preventing diabetes and its complications. As a result, finding plants with antidiabetic properties that could be consumed by humans has received a lot of attention in recent years. [5]One such source is *Withania coagulans*, sometimes

known as paneer poo, where all parts of the plant have medicinal qualities. Its pharmacological and biological effects are caused by a variety of bioactive substances. Its main bioactive ingredients, withanolides, are phenols, flavonoids, tannins, saponins, and alkaloids. These compounds have antibacterial, anti-inflammatory, anticancer, hepatoprotective, antihyperglycemic, cardiovascular, immunosuppressive, and free radical scavenging qualities. It is widely accessible in herbal stores, less costly, and has no known toxicity or adverse effects. [6,7].

Thus, the purpose of this study was to assess the fruit of *W. coagulans*'s potential as an auxiliary hypoglycemic agent, which should help to clarify its potential application as a safe, affordable, and natural therapeutic option for the treatment of type 2 diabetes mellitus. [7].

One of the significant medicinal plants is *Withania coagulans* (*W. coagulans*), which is a member of the Solanaceae family. *W. somnifera* and *W. coagulans* are the two species of *Withania* that are found in the eastern Mediterranean region that stretches into South Asia. It can be found throughout India and Pakistan..[8]

Almost 23 species of *Withania*, a significant flowering plant in the Solanaceae family, are endemic to portions of North Africa, the Middle East, the Mediterranean, the Canary Islands, and South West Asia. The genus has the name of Henry Withania, a well-known paleobotanist and geologist. *Withania coagulans*, often known as vegetable rennet or Indian rennet, is a medicinal plant that is endangered but has enormous therapeutic potential. Doda Paneer (Hindi), Khamjira (Punjabi), Punir Band (Sindi), or Spiubajja (Persian) are the native names for it in India. The species' berries, which are used as a coagulating agent in milk, are vital to the economy. The components in berries have the enzymatic ability to cause milk to coagulate. As a result, this plant has been utilized for decades to produce cheese. *W. coagulans* has amazing therapeutic qualities and is used to treat intestinal infections, wasting illnesses, impotence, insomania, nervous weariness, dyspepsia, and flatulent colic. Plant flowers have been shown to have antidiabetic properties, and berries are employed as blood purifiers. The plant's twigs are eaten to clean teeth, and the smoke is inhaled to relieve toothaches. The plant is known to have a number of pharmaceutical actions in addition to these therapeutic benefits, including antibacterial, anti-inflammatory, anti-tumor, hepatoprotective, antihyperglycemic, cardiovascular, immune-suppressive, free radical scavenging, and central nervous system depressive effects. [9]

II. PLANT DESCRIPTION

Propagation:- *Withania coagulans* is regarded as an underused plant that is found in South Asia in small, dispersed populations. Iran, Afghanistan, Pakistan, East India, and Nepal are among its locations. The drier regions of Rajasthan, Punjab, Gujarat, Simla, and Kumaon are home to the plant in India. It can be found up to 1700 meters above sea level in arid, hot, stony areas (Khodaei et al., 2012; Pezeshki et al., 2011; Gilani et al., 2009; Negi et al., 2006). Traditionally, seeds and stem cuttings are used to grow the plant. Overuse of the plant, whether for traditional applications like animal feed or medicinal purposes, has put it in danger of extinction. Another factor contributing to the plant's current endangered status is habitat destruction. Another obstacle to the plant's extensive propagation is its low germination rate and reproductive failure brought on by its dioecious character.[10]

Plant Authentication:

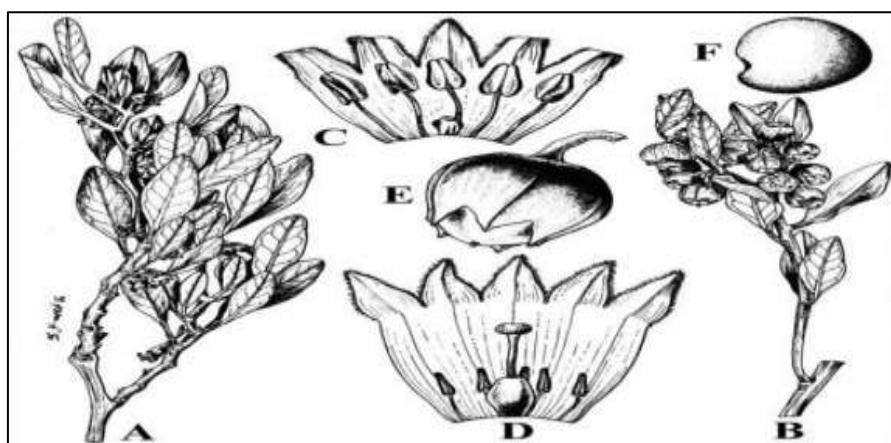


Fig 1: Floral diagram of *Withania coagulans* Dunal

- A- Flowering Shoot
- B- Fruiting Shoot
- C- Male Flower with corolla opened
- D- Female flower with corolla opened
- E- Berry Partially enclosed in calyx
- F- Seed

Withania coagulans Dunal (Flower bud):

The dried flower buds of *Withania coagulans* Dunal was collected.



Fig 2: Plant showing flowers of *Withania coagulans* Dunal



Fig 3: Dried flowers of *Withania coagulans* Dunal

Taxonomical classification of *Withania coagulans* Dunal:

Table 1: Taxonomical classification of *Withania coagulans* Dunal[11]

Rank	Scientific Name and Common Name
Kingdom	Plantae – Plants
Subkingdom	Tracheobionta – Vascular plants
Superdivision	Spermatophyta – Seed plants
Division	Magnoliophyta – Flowering plants
Class	Magnoliopsida – Dicotyledons
Subclass	Asteridae
Order	Solanales
Family	Solanaceae
Genus	<i>Withania</i>

Species	coagulans (L.) Dunal
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Morphological Characters:

The whole plant is an upright, grayish shrub that grows to a height of 60 to 120 cm. The leaves are 25-75 mm long and 1500 mm wide, with a tendency to narrow at the base. The branches are densely packed and either grey or yellow-white. The 7–12 cm yellowish flowers are polygamous and dioecious. The stamen's filament is 2 mm long, and its anther is 3–5 mm long. The corolla tube and the stamen are level.[17, 18] The ovary is round in form and lacks a stigma. It is glabrous all around, with a glabrous style and a mushroom-shaped, 2-lamellate stigma. The berry is smooth and globose, with a diameter of 6 to 8 mm. The glabrous seeds, which measure 2.5-3 mm in diameter, resemble ears.[7,19] Superior indehiscent berries with many seeds are the fruits. As seen in Figure 1, it is pedicellate, 4-6 mm in diameter, round to globular in shape, and yellow to brown in color. The fruits taste a little off-putting and have a slight scent.[12]

III. CHEMICAL CONSTITUENTS

The milk-coagulating enzyme, protein, phenolic substance, tannins, saponins, carbohydrate organic acid, two types of esterases, free amino acids, fatty oil, an essential oil, and alkaloids are all present in *Withania coagulans* berries. Proline, hydroxyproline, valine, tyrosine, aspartic acid, glycine, asparagin, cysteine, and glutamic acid are among the different types of amino acids that are present. From the fruit's alcoholic extract, fourteen alkaloidal fractions have been identified. 17.8% of the free sugars in *Withania coagulans* Dunal are made up of D-galactose and D-arabinose in a 1:1 ratio, with trace amounts of maltose. Enzymatic analysis revealed that the polysaccharide lacked a B-galactosidic bond. It has been reported that 12–14% of the seeds of *Withania coagulans* contain fatty oil.

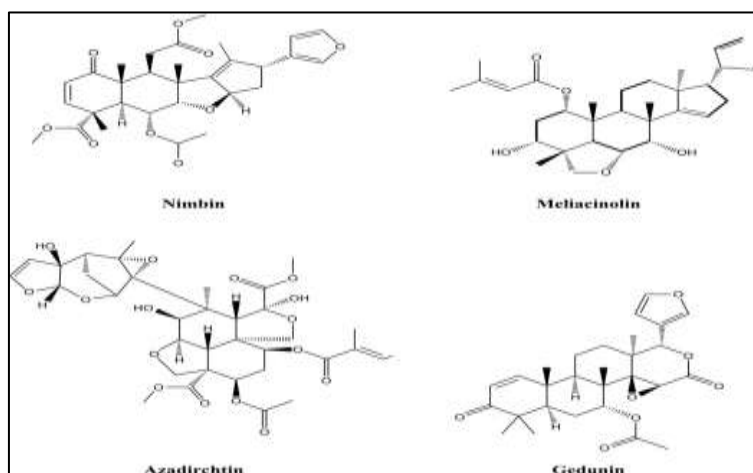


Fig 4: Chemicals Structure Of *Withania Coagulans* Constituents

IV. PHARMACOLOGICAL ACTIVITIES

The scientific community has always been very interested in the chemical components of *withania*. The plant's berries are used to coagulate milk. It has long held a significant position in the ancient Indian, Unani, and Ayurvedic medical systems. They exhibit a range of biological characteristics.

• **Antidiabetic Effect:**

In order to create a safe and efficient alternative treatment for diabetes mellitus, the current study outlines the methodical assessment of the glycemic potential of an aqueous extract of *Withania coagulans* fruits as well as the role of minerals in this process. Glycemic element detection was done using laser-induced breakdown spectroscopy. The study is predicated on the findings of lowering blood glucose levels in rats with normal, sub-, mild, and severe diabetes as determined by glucose tolerance testing, postprandial glucose studies, and fasting blood glucose levels.[13]

• **Diabetes treatment:**

When Streptozotocin (STZ), a chemical that causes diabetes, is introduced to male albino wistar rats, this plant will be more effective at the right dose for diabetes (Shukla et al. 2012; Hemalatha et al. 2004). The rats' body

weight and serum insulin levels decreased, while their catabolic responses, plasma glucose level, and kidney weight all dramatically increased as a result of STZ (Kitukale and Chandewar 2017). According to the aforementioned trial, a dose of roughly 10 grams per day per person is necessary to cure diabetes (Jaiswal et al. 2009). If taken consistently for 14 days, the aqueous extract of *W. coagulans* helps to reduce blood plasma glucose levels (Khodaei et al. 2012). When diabetics consume fruit aqueous extract in addition to allopathic medication for approximately one month, it works wonders. Blood sugar levels can be controlled with a continuous treatment for at least two months (Bharti et al. 2012). Sampathkumar et al. (2019) delivered *W. coagulans* extract using enteric coated nanoparticles based on polysaccharides. It enhanced the extract's bioavailability by a factor of 2.5. Maher et al. (2020) used NMR, mass spectrometry, FTIR, and UV-Vis to detect the presence of antidiabetic withanolides in the chloroform and n-butanol plant extract. Antidiabetic substances such as withanolide J, 27-hydroxywithanolide I, coagulin E, ajugin E, and withaperuvin C are present in the extract.[14] People of all races and socioeconomic backgrounds are equally affected by chronic diabetes mellitus. A more hectic, modern lifestyle is to blame for the rising incidence of diabetes; some people with the condition are even in their 30s or 40s.46 Among the contributing reasons include elevated stress levels and unhealthy eating patterns, including a growing reliance on junk food. Smoking and increased tobacco use are other factors that are contributing to the growth in diabetes cases, in addition to pollution and heredity. in youth. The primary rivals are still oral hypoglycemia medications called biguanides and sulphonylureas. The possible negative effects of oral hypoglycemic drugs on the management of the condition have led to a rise in interest in herbal remedies.48 *Withania coagulans* Dunal has been found to have deep hypoglycemic effect. Hypoglycemic efficacy was demonstrated by *Withania coagulans* Dunal, a safe and effective substitute drug for diabetes.49 *Withania coagulans* Dunal has been found to have deep hypoglycemic effect. Hypoglycemic efficacy was demonstrated by *Withania coagulans* Dunal, a safe and effective substitute drug for diabetes.[15][16][17]

OTHER PHARMACOLOGICAL ACTIVITIES:**• Antihyperglycemic Activity:**

Coagulin L from *W. coagulans* fruits has antihyperglycemic action, and the fruits demonstrated hypoglycaemic activity, a safe and effective alternative treatment for diabetes. In type II diabetic rats, it demonstrated pharmacological effects on body weight, lipid profile, and blood glucose, resulting in a notable drop in total cholesterol and blood glucose levels. [18]

• Cardiovascular Effects:

The aqueous extract of Paneer Dodi fruits yields a steroidal lactone called withanolide, which has cardiovascular effects[19][20]. This withanolide substitute, which was extracted from *Withania coagulans* fruits, was examined for cardiovascular effects because it shares a chemical structure with the aglycones of cardiac glycosides.[20]

• Wound Healing Activity:

Streptozotocin-induced diabetic rats were given the hydroalcoholic fraction of the methanolic extract of *Withania coagulans* orally at a dose of 500 mg/kg body weight and topically as a 10% w/w ointment. [21] In models of open and incised wounds, *W. coagulans* demonstrated notable wound healing activity. When compared to diabetic controls, the hydroalcoholic fraction in both topical (10% w/w ointment) and oral (500 mg/kg body weight, p.o.) form significantly increased the rate of wound contraction. [22]

• Anti-Inflammatory Activity :

Alcoholic extract from *Withania coagulans* significantly reduces acute inflammation brought on by egg albumin. [24]. In cases of acute inflammation, withanolides derived from *Withania coagulans* effectively reduce inflammation. [25]. In a rat paw edema model caused by carrageenin, the hydroalcoholic extract of *Withania coagulans* berries has strong anti-inflammatory activity.[26]

• Anti-Hyperlipidemic Activity:

Fruit extracts from *Withania coagulans* considerably decreased increased serum cholesterol, triglyceride, lipoprotein, and consequently LPO levels in rats with hyperlipidemia brought on by a high-fat diet. The hypolipidemic impact of *Withania coagulans* fruits is comparable to that of *Commiphora mukul*-containing Ayurvedic medicines. [27]

• **Diuretic Activity:**

Rats are used to study the diuretic capacity of *Withania coagulans* fruits in an aqueous extract. There are more polar withanolides in *Withania coagulans* than in other *Withania* species. The Lipschitz test paradigm can be used to examine the diuretic action of the powdered Dodi root aqueous extract using furosemide as a reference. Withanolides are the main chemical protagonists of the polar active principles that cause the diuretic action. The use of *Withania coagulans* as a diuretic in traditional medicine is supported by research. The extract from *Withania coagulans* has the ability to relax muscles, stimulate the respiratory system, and lower blood pressure. [28].

• **Hepatoprotective effects:**

It has been demonstrated that 3-hydroxy-2, 3-dihydro-withanolide F, which is extracted from a fruit of *Withania coagulans*, exhibits hepatoprotective properties against CCl₄-induced hepatotoxicity in adult albino rats. It has a noticeable protective effect and is more active than hydrocortisone, according to a weight-based comparison. [29]

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V. THERAPEUTIC SIGNIFICANCE

Free radical scavenging, anti-inflammatory, anticancer, immunosuppressive, depressant, hepato protective, hypoglycemic, hypolipidemic, cardiovascular, antimicrobial, anthelmintic, and antifungal properties are among its many attributes. Traditional healers in Northern India cure diabetes mellitus with dry fruits. The leaves and round, capsular fruit have the unusual ability to curdle or coagulate milk; a small amount is added to the milk to coagulate it after being rubbed with a small amount of water or milk. Additionally, dried capsules maintain their coagulating ability to the same extent. In Las Bella, the wood is used to clean teeth, while the fruit is mashed and used as a remedy for colic. According to Hughes Buller, smoke is applied to sore teeth in the Ormera Hills "to destroy the worm." The plant's smoke is inhaled to relieve toothaches, and the twigs are chewed to clean teeth. The sweet fruits are applied to wounds and used to treat biliousness and asthma. The seeds reduce pile inflammation, have diuretic properties, and are helpful in lumbago and ophthalmia. It is believed that the ripe fruits have sedative or anodyne qualities. They are thought to help with chronic liver problems and are diuretics and alteratives.[31]

VI. CONCLUSION

Withania coagulans, an underutilized medicinal plant, demonstrates significant potential as a therapeutic agent for managing diabetes and related metabolic disorders. Its rich phytochemical profile, including withanolides, saponins, and phenolic compounds, contributes to its diverse pharmacological activities such as hypoglycemic, anti-inflammatory, antioxidant, and hepatoprotective effects. Studies confirm its effectiveness in improving glycemic control, lipid profiles, and insulin sensitivity while minimizing the side effects associated with conventional antidiabetic drugs. Additionally, *W. coagulans* exhibits promising benefits in wound healing, cardiovascular protection, and as a natural diuretic, reinforcing its versatility in traditional and modern medicine. However, the plant's endangered status due to habitat destruction and overharvesting necessitates sustainable cultivation and conservation strategies. Further research is essential to better understand its mechanisms of action, optimize its bioavailability, and validate its therapeutic efficacy in clinical trials. *W. coagulans* stands out as a cost-effective and safe alternative for diabetes management, offering a promising future in integrative medicine for addressing modern healthcare challenges.

VII. REFERENCE

- [1] Anesini C and Perez C. Screening of plants used in Argentine folk medicine for antimicrobial activity. *J Ethnopharmacol*, 39: 1993, 119 – 128
- [2] Dimple, Kumar A, Kumar V, Vidisha T. Traditional medicinal systems for treatment of diabetes mellitus: A review. *Int J Pharm Pharm Sci* 2018;10:7-17.

- [3] Mohammed A, Kumar D, Rizvi SI. Antidiabetic potential of some less commonly used plants in traditional medicinal systems of India and Nigeria. *J Intercult Ethnopharmacol* 2015;4:78-85.
- [4] Kalsi A, Singh S, Taneja N, Kukal S, Mani S. Current treatments for Type 2 diabetes, their side effects and possible complementary treatments. *Int J Pharm Pharm Sci* 2014;7:13-8.
- [5] Demain AL, Sanchez S. Microbial drug discovery: 80 years of progress. *J Antibiot (Tokyo)* 2009;62:5-16.
- [6] World Health Organization. Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycaemia: Report of a WHO/IDF Consultation. Geneva: World Health Organization; 2006.
- [7] Gupta PC. *Withania coagulans* dunal-an overview. *Int J Pharm Sci Rev Res* 2012;12:68.
- [8] Jaiswal D, Rai PK, Watal G. Antidiabetic effect of *Withania coagulans* in experimental rats. *Indian J Clin Biochem* 2009;24:88-93.
- [9] A Review On The Biological properties and conservation of critically endangered plant *Withania coagulans* - Indian Renet Nishesh Sharma¹, Durgesh¹, Varnika, Eapen P Koshy Manjul Dhiman.
- [10] A Review On The Biological properties and conservation of critically endangered plant *Withania coagulans* - Indian Renet Nishesh Sharma¹, Durgesh¹, Varnika, Eapen P Koshy Manjul Dhiman.
- [11] International Journal of Novel Research and Development(IJNRD) Research On phytochemistry and pharmacology of *withania coagulans*.
- [12] Prasad SK, Singh PN, Wahi AK, Hemalatha S. Pharmacognostical standardization of *Withania coagulans* Dunal. *Pharmacogn J [Internet]* 2010;2(11):386-94. Available from: [http://dx.doi.org/10.1016/S0975-3575\(10\)80020-3](http://dx.doi.org/10.1016/S0975-3575(10)80020-3)
- [13] Dolly Jaiswal et al Jan "Antidiabetic effect of *Withania coagulans* in experimental rats" *Indian J Clin Biochem*, 2009. 3:4
- [14] An overview on pharmaceutical properties *withania coagulans* on the world journal of pharmaceutical Gurson CT, Saner G. Effect of chromium on glucose utilization in marasmic protein-calorie malnutrition. *American Journal of Clinical Nutrition*. 1971;24(11):1313-9.
- [15] Jaiswal D, Rai PK, Watal G. Antidiabetic effect of *Withania coagulans* in experimental rats. *Indian Journal of Clinical Biochemistry*. 2009 Jan;24:88-93.
- [16] Hemalatha S, Wahi AK, Singh PN, Chansouria JP. Hypoglycemic activity of *Withania coagulans* Dunal in streptozotocin induced diabetic rats. *Journal of Ethnopharmacology*. 2004 Aug 1;93(2-3):261-4.
- [17] Remedial Use of Withanolides from *Withania Coagulans* (Stocks) Dunal. Maryam Khodaei , Mehrana Jafari , Mitra Noori
- [18] Antidiabetic Activity of Fruits of *Withania Coagulanus* Dunal In Streptozocin Induces Diabetic: A Review. Bhuvanesh Baniya
- [19] Antidiabetic and antihyperlipidemic activity of hydroalcoholic extract of *Withania coagulans* Dunal dried fruit in experimental rat models. Ankur Datta, Chiranjib Bagchi, Saibal Das, Achintya Mitra , Anuradha De Patil , Santanu Kumar Tripathi.
- [20] *Withania Coagulans* Dunal- An Overview. Prakash Chandra Gupta. Jan(2012)
- [21] Pharmaceutical Importance of *Withania Coagulans* In Health and Diseases. Neelam B. Bare, Pratima S. Jadhav.
- [22] Remedial Use of Withanolides from *Withania Coagulans* (Stocks) Dunal. Maryam Khodaei , Mehrana Jafari , Mitra Noori.
- [23] Chemistry and pharmacology of *Withania coagulans*: an Ayurvedic remedy. Rakesh Maurya, Akanksha and Jayendra.
- [24] Isolation of Antidiabetic Withanolides from *Withania coagulans* Dunal and Their In Vitro and In Silico Validation. Saima Maher, M. Iqbal Choudhary, Farooq Saleem, Saima Rasheed, Imran Waheed, Sobia Ahsan Halim, Muhammad Azeem, Iskandar Bin Abdullah, Matheus Froeyen, Muhammad Usman Mirza and Sarfraz Ahmad. (2020)
- [25] Phytochemical, Pharmacological and Beneficial Effects of *Withania coagulans* Dunal. (Paneer Doda): A Review Ashwini Bankar, Aishwarya Supekar, Manoj Jograna, Sachin Kotwal