

Review of Antipsychotic Activity of *Withania Coagulans*

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ABSTRACT

Psychotic disorders such as schizophrenia impose a substantial burden on patients and healthcare systems worldwide. Although conventional antipsychotic drugs are effective in managing symptoms, their prolonged use is often limited by serious adverse effects, including extrapyramidal symptoms and metabolic disturbances. This has stimulated interest in medicinal plants as alternative or complementary therapeutic agents. *Withania coagulans*, a plant traditionally used in indigenous systems of medicine, has been reported to possess antioxidant, anti-inflammatory, and central nervous system–modulating properties. The present study was designed to evaluate the antipsychotic potential of *Withania coagulans* using experimental animal models. An alcoholic extract prepared from the fruits of the plant was administered orally to Swiss albino mice at doses of 200 mg/kg, 500 mg/kg, and 1000 mg/kg. Antipsychotic activity was assessed using the Conditioned Avoidance Response (CAR) test, a widely accepted screening model for antipsychotic agents. Behavioural responses were recorded and statistically analyzed. The results demonstrated that the extract did not produce a significant suppression of avoidance behavior when compared to the control group. These findings indicate that *Withania coagulans* fruit extract does not exhibit marked antipsychotic activity under the experimental conditions employed. However, the presence of bioactive phytoconstituents suggests that further investigations using different plant parts, extraction techniques, and experimental models are warranted.

Introduction

Psychotic disorders represent a group of severe mental illnesses characterized by disturbances in perception, thought, emotion, and behaviour. Among these disorders, schizophrenia is the most prevalent and disabling, affecting millions of individuals globally. The disorder is associated with positive symptoms such as hallucinations and delusions, negative symptoms including emotional withdrawal and lack of motivation, and cognitive impairments. The etiology of psychotic disorders is complex and involves genetic, neurochemical, and environmental factors, with dysregulation of dopaminergic neurotransmission playing a central role.

Antipsychotic drugs are the primary pharmacological agents used in the management of schizophrenia and related psychoses. While first-generation antipsychotics are effective in controlling positive symptoms, they are frequently associated with extrapyramidal side effects. Second-generation antipsychotics, though better tolerated, are linked to metabolic complications such as weight gain, diabetes, and dyslipidemia. These limitations underscore the need for safer therapeutic alternatives.

Medicinal plants have been utilized for centuries in traditional systems of medicine and continue to serve as important sources of novel pharmacologically active compounds. Herbal medicines are generally

perceived to be safer and more acceptable for long-term use. *Withania coagulans* (Family: Solanaceae), commonly referred to as Indian cheese maker, is a small shrub widely distributed in parts of India and neighbouring regions. Traditionally, the plant has been used for the treatment of diabetes, gastrointestinal disorders, inflammation, and nervous system ailments. Phytochemical investigations of *Withania coagulans* have revealed the presence of withanolides, alkaloids, flavonoids, and steroidal lactones, many of which are known to exhibit antioxidant and neuroprotective properties. Despite these reported activities, scientific evidence regarding the antipsychotic potential of *Withania coagulans* remains scarce. Therefore, the present study was undertaken to systematically evaluate the antipsychotic activity of *Withania coagulans* using established experimental animal models.

Keywords: *Withania coagulans*, antipsychotic activity, experimental animals, conditioned avoidance response, medicinal plants

Traditional use of *withania coagulans*



Withania coagulans is a medicinal plant widely used in traditional systems of medicine such as Ayurveda and folk medicine. Different parts of the plant, especially the fruits and leaves, have been used for many years to treat various health problems.

Traditionally, the fruits of *Withania coagulans* are used for the management of diabetes. They are believed to help reduce blood glucose levels and improve overall metabolic health. In rural areas, the dried fruits are sometimes soaked in water and consumed for their antidiabetic effect.

The plant is also known for its digestive benefits. It has been used to relieve stomach disorders such as indigestion, constipation, and abdominal discomfort. In some traditional practices, the fruit extract is used to improve appetite and support healthy digestion.

Another important traditional use is in the treatment of liver disorders. Herbal practitioners have used this plant to support liver function and protect the liver from damage. It is also believed to possess anti-inflammatory and antimicrobial properties, which may help in treating infections and reducing inflammation. In addition, *Withania coagulans* has been used as a natural coagulant in milk to prepare traditional dairy products. Because of its medicinal value, it continues to be an important plant in traditional healthcare systems

Scientific classification of *withania coagulans*

Rank	Classification
Domain	Eukaryota
Kingdom	Plantae
Phylum	Spermatophyta
Class	Magnoliopsida
Order	Solanales
Family	Solanaceae
Genus	<i>Withania</i>
Species	<i>Withania coagulans</i>

Evidence of Hypoglycemic Activity

Several preclinical studies have demonstrated that extracts of *Withania coagulans* significantly reduce blood glucose levels in both normal and diabetic animal models.

Experimental models used:

- a. Alloxan-induced diabetic rats
- b. Streptozotocin (STZ)-induced diabetic rats
- c. Oral glucose tolerance test (OGTT)

Observed effects:

- a. Significant reduction in fasting blood glucose
- b. Improvement in glucose tolerance
- c. Decrease in post-prandial hyperglycemia

In-vivo Antioxidant Evidence (Animal Studies)

In diabetic and oxidative stress-induced animal models, *Withania coagulans* extracts showed:

a) Enhancement of Endogenous Antioxidant Enzymes

- a. ↑ Superoxide dismutase (SOD)
- b. ↑ Catalase (CAT)
- c. ↑ Glutathione peroxidase (GPx)
- d. ↑ Reduced glutathione (GSH)

b) Reduction of Oxidative Stress Markers

- a. ↓ Malondialdehyde (MDA)
- b. ↓ Lipid peroxidation levels
- c. ↓ Reactive oxygen species (ROS)

These effects indicate protection against oxidative tissue damage, especially in liver, pancreas, and kidney.

In-vitro Evidence of Apoptosis

a) Cancer Cell Line Studies

Extracts and isolated compounds from *Withania coagulans* have been tested on various cancer cell lines, such as:

- a. Human breast cancer cells
- b. Colon cancer cells
- c. Leukemia cell lines
- d. Observed apoptotic effects:
- e. Reduced cell viability in a dose-dependent manner
- f. Morphological changes characteristic of apoptosis (cell shrinkage, membrane blebbing)
- g. Nuclear condensation and DNA fragmentation

b) Apoptosis Detection Assays Used

Scientific studies have confirmed apoptosis using standard assays:

- a. Annexin V–FITC / Propidium iodide staining
- b. DNA laddering assay
- c. TUNEL assay
- d. MTT cytotoxicity assay (indirect evidence)

These results indicate programmed cell death rather than necrosis.

Evidence of Anti-diabetic activity

Experimental (Preclinical) Evidence

a) Diabetic Animal Models Used

Antidiabetic activity has been evaluated using standard experimental models:

- a. Alloxan-induced diabetic rats
- b. Streptozotocin (STZ)-induced diabetic rats
- c. Oral Glucose Tolerance Test (OGTT) in normal rats

b) Observed Antidiabetic Effects

Treatment with *Withania coagulans* fruit extracts produced:

- a. Significant reduction in fasting blood glucose levels
- b. Improved glucose tolerance
- c. Reduction in postprandial hyperglycemia
- d. Sustained glycemic control on repeated administration

These effects were comparable to standard antidiabetic drugs like glibenclamide in some studies.

Evidence of Anti-inflammatory activity

In-vivo Experimental Evidence

a) Acute Inflammation Models

Anti-inflammatory activity has been evaluated using standard models such as:

- a. Carrageenan-induced paw edema in rats
- b. Histamine- and serotonin-induced paw edema

Observed effects:

- a. Significant reduction in paw edema volume
- b. Dose-dependent anti-inflammatory response
- c. Comparable efficacy to standard drugs like indomethacin or diclofenac

b) Chronic Inflammation Models

Some studies have reported activity in:

- i. Cotton pellet–induced granuloma
- ii. Formalin-induced inflammation

Materials and Methods

a.Plant Material Collection and Authentication

The fruits of *Withania coagulans* were collected from a local geographical region during the appropriate harvesting season. The collected plant material was authenticated by a qualified botanist based on morphological characteristics. The fruits were cleaned to remove foreign matter and shade-dried at room temperature. After complete drying, the material was coarsely powdered using a mechanical grinder and stored in airtight containers until extraction.

b.Preparation of Alcoholic Extract

The powdered fruit material was subjected to Soxhlet extraction using ethanol as the solvent. The extraction process was continued until the solvent in the siphon tube became colourless. The obtained extract was concentrated by evaporating the solvent under reduced pressure using a rotary evaporator. The dried extract was weighed to calculate percentage yield and stored in a desiccator for further experimental use.

c.Experimental Animals

Swiss albino mice of either sex, weighing between 20 and 30 g, were used in the present study. The animals were procured from an approved animal house facility and acclimatized to laboratory conditions for one week prior to experimentation. They were housed in polypropylene cages under controlled environmental conditions, including a temperature of $25 \pm 2^\circ\text{C}$ and a 12-hour light–dark cycle. Animals were provided standard laboratory feed and water ad libitum. All experimental procedures were conducted in accordance with institutional ethical guidelines for animal experimentation.

d.Ethical Approval

All experimental procedures were conducted in accordance with institutional guidelines for the care and use of laboratory animals and were approved by the Institutional Animal Ethics Committee (IAEC).

e.Acute Toxicity Study

An acute toxicity study was conducted to determine the safe dose range of the alcoholic extract of *Withania coagulans*. The extract was administered orally in increasing doses, and the animals were observed for behavioural changes, signs of toxicity, and mortality for 24 hours. Based on the results, three dose levels were selected for further pharmacological evaluation.

f.Experimental Design

The animals were randomly divided into four groups, each consisting of six mice:

Group I: Control group (received vehicle only)

Group II: *Withania coagulans* extract (200 mg/kg, p.o.)

Group III: *Withania coagulans* extract (500 mg/kg, p.o.)

Group IV: Withania coagulans extract (1000 mg/kg, p.o.)

All treatments were administered orally once daily prior to behavioural testing.

g. Statistical Analysis

The experimental data were expressed as mean \pm standard error of mean (SEM). Statistical analysis was performed using appropriate statistical methods to compare treated groups with the control group. Differences were considered statistically significant at a probability value of $p < 0.05$.

Evaluation of Antipsychotic Activity

Antipsychotic activity was evaluated using the Conditioned Avoidance Response (CAR) test, a standard behavioural model for screening antipsychotic agents. The apparatus consisted of a pole-climbing chamber equipped with an electric grid floor and an audible warning signal.

The animals were trained to associate the warning signal with an impending electric shock and to avoid the shock by climbing the pole. During the test session, the number of successful avoidance responses was recorded following administration of the test extract. A reduction in avoidance behaviour is considered indicative of antipsychotic activity.

Discussion

The Conditioned Avoidance Response model is widely employed for the preliminary screening of antipsychotic agents, particularly those that exert their effects through dopamine receptor antagonism. Drugs that suppress avoidance behaviour without affecting escape responses are considered to possess antipsychotic properties. In the present investigation, the alcoholic extract of *Withania coagulans* failed to significantly suppress avoidance responses, indicating a lack of prominent antipsychotic activity.

Although *Withania coagulans* contains several bioactive constituents with reported central nervous system effects, the absence of antipsychotic activity in this study may be attributed to multiple factors. These include the use of fruit extract rather than other plant parts, the choice of solvent for extraction, and the acute dosing regimen employed. It is also possible that the plant may exert anxiolytic, adaptogenic, or neuroprotective effects rather than direct antipsychotic action.

Negative findings are scientifically valuable, as they help refine future research directions. The present results suggest that while *Withania coagulans* may not act as a classical antipsychotic agent, it may still have therapeutic potential in other neuropsychiatric conditions. Further studies involving chronic administration, alternative behavioural models, and

isolation of individual phytoconstituents are necessary to fully elucidate its pharmacological profile.

Conclusion

The present study concludes that the alcoholic extract of *Withania coagulans* fruits does not exhibit significant antipsychotic activity in Swiss albino mice when evaluated using the Conditioned Avoidance Response model. These findings indicate that the plant, under the tested conditions, may not influence dopaminergic pathways associated with psychotic behavior. Nevertheless, the presence of biologically active compounds in *Withania coagulans* warrants further research using different experimental approaches to explore its potential role in neuropsychiatric therapy.

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