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# PHYTOCHEMISTRY, BOTANY, AND THERAPEUTIC POTENTIALS OF *WITHANIA COAGULANS*: A COMPREHENSIVE REVIEW

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## ABSTRACT

Herbal plants have long been used to manage and treat a wide range of health conditions. Ayurvedic medicine, in particular, remains important due to its minimal side effects and extensive therapeutic benefits. *Withania coagulans* (Family: Solanaceae), a highly valued medicinal plant, has traditionally been employed to treat abnormal cell growth, wasting disorders, neurological and physical ailments, diabetes mellitus, insomnia, and both acute and chronic liver diseases. This review offers a comprehensive overview of the phytochemistry, pharmacognosy, and biological activities of *W. coagulans*. The plant exhibits notable diuretic, anti-inflammatory, antibacterial, antifungal, cardioprotective, hepatoprotective, hypoglycemic, antioxidant, and antimutagenic effects, largely attributed to its rich content of withanolides. In addition, *W. coagulans* contains other important phytoconstituents such as flavonoids, tannins, and β-sterols. Evidence from multiple studies suggests that various plant parts and their bioactive compounds possess significant pharmacological and therapeutic potential, supporting the use of *W. coagulans* as a promising candidate for developing new treatments for diverse diseases.

**Keywords:** Ayurvedic properties; diuretic; phytochemistry; pharmacognostic properties.

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## INTRODUCTION

Plants have long served as valuable sources of medicinal compounds and have been integral to traditional healing systems since antiquity. Many medicinal plants are rich in diverse bioactive constituents that contribute to the prevention and treatment of various disorders, thereby supporting overall health. Within the genus *Withania*, *Withania coagulans* holds particular importance in Ayurvedic medicine due to its notable nutraceutical and pharmaceutical properties. This species is cultivated across a broad geographic range, including the Mediterranean region and areas extending from North Africa to South Asia [1]. Of the twenty-three recognized *Withania* species, only *W. coagulans* and *W. somnifera* possess significant economic value [2]. *W. coagulans* is traditionally employed as a milk-coagulating agent because its berries contain an enzyme that functions as a natural rennet, earning it the common name "Indian cheesemaker" [3]. Figure 1 illustrates the morphological features of the plant, including its leaves, stems, and fruits. Various plant parts—particularly the fruits, roots, and leaves—exhibit a wide range of therapeutic activities. The berries contain several key constituents, such as essential oils, esterases, amino acids, and alkaloids [4]. The plant's medicinal properties are largely attributed to steroidal lactones known as withanolides. Numerous withanolides have been identified throughout the plant, including coagulin F, coagulanolide, withacoagulin, and coagulin G [3].

The ripe fruit is sweet in taste and traditionally used for wound healing, asthma, dyspepsia, and as a sedative. In several countries, dried fruits are commonly utilized in folk medicine for the management of diabetes [5] and have been reported to possess antibacterial [6], antimicrobial [7], hepatoprotective [8], hypolipidemic [9], antioxidant [10], antitumor [11], antidepressant [12], immunosuppressive [13], and anti-inflammatory properties [14]. The seeds are valued for their anti-inflammatory, diuretic, and ophthalmic applications, whereas the flower buds exhibit anthelmintic activity [15–17]. Additionally, the twigs are traditionally used for dental hygiene, toothache relief, and blood purification in various South Asian communities [3].

Given the increasing reliance on medicinal plants within traditional and contemporary healthcare practices, this review aims to provide a comprehensive and updated overview of the phytochemistry, food applications, and therapeutic potential of *W. coagulans*.

### Botanical Description

The plant is a rigid, grey-whitish small shrub that grows 60–120 cm tall. Its leaves are 2.5–7.5 cm long and about 1.5 cm broad, lanceolate-oblong or sometimes ovate, obtuse, and narrow at the base [18]. The flowers, which appear from January to April, are yellowish, 7–12 mm across, and exhibit dioecious as well as polygamous characteristics. In female flowers, the stamens reach halfway up the corolla tube, with filaments about 0.85 mm long and smaller sterile anthers compared to male flowers [19,20]. The ovary is ovoid and glabrous, with a smooth style and a mushroom-shaped, 2-lamellate stigma. The resulting berry is globose, smooth, and 6–8 mm (sometimes 7–12 mm) in diameter, turning red when

mature. Seeds are 2.5–3 mm in diameter, dark brown, ear-shaped, and glabrous with a sharp fruity smell. The plant's pharmacological activities are largely attributed to withanolides—steroidal lactones possessing an ergostane skeleton. The fruits are known to exhibit diuretic and hypolipidemic properties [21].

**(a)** **(b)**

**Figure 1: (a) *Withania coagulans dunal* plant (b)*Withania coagulans dunal* fruits.**

**Taxonomical Classification**

The taxonomical classification of *Withania coagulans* is as follows: it belongs to the Kingdom Plantae and the Subkingdom Tracheobionta, comprising vascular plants. It falls under the Superdivision Spermatophyta (seed plants) and the Division Angiosperma. The species is classified within the Class Dicotyledons, Order Tubiflorae, and Family Solanaceae. Within this family, it is placed in the Genus *Withania*, with the specific species identified as *Withania coagulans* [22,23].

**Table 1. Taxonomical Classification**

| | |
|---|---|
| Kingdom | Plantae |
| Subkingdom | Tracheobionta |
| Super division | Spermatophyte |
| Division | Angiosperma |
| Class | Dicotyledons |
| Order | Tubiflorae. |

| | |
|---|---|
| Family | Solanaceae |
| Genus | Withania |
| Species | coagulans. |

**Phytochemistry**

A variety of bioactive compounds have been identified in different parts of *W. coagulans*, reflecting its rich phytochemical profile. Choudhary et al. [24] reported the presence of 17β-hydroxywithanolide K [(20S,22R)-14α,17β,20β-trihydroxy-1-oxo-witha-2,5,24-trienolide] and 17β,20β-dihydroxy-1-oxo-witha-2,5,24-trienolide in the whole plant. Similarly, Shahwar [25,26] identified withahejarin, withasomniferine-A, and coagulin A. Additionally, thirteen coagulins—Coagulin F, G, H, I, J, K, L, M, N, O, P, Q, and R—have been isolated from the entire plant [27–29].

Other metabolites detected in *W. coagulans* include coagulin U, methyl-4-benzoate, and phytosterols such as β-sitosterol and β-sitosterol glycoside. Important withanolides such as (22R),20β-hydroxy-1-oxowitha-2,5,24-trienolide and (22R)-14,20-epoxy-17β-hydroxy-1-oxowitha-3,5,25-trienolide have also been reported [30]. Further studies have identified 17β,27-dihydroxy-14,20-epoxy-1-oxo-22R-witha-3,5,24-trienolide and 17β-hydroxy-14α,20α-epoxy-1-oxo-(22R)-witha-3,5,24-trienolide [31]. Coagulin S has likewise been isolated and structurally characterized using spectroscopic methods [32].

Additional metabolites include coagulansin B and coagulanolide [33,34]. Withacoagulin J has been isolated alongside the previously known withanolide H [35]. A more recently identified withanolide, (20R,22R)-14α,17,20β,27-trihydroxy-1-oxowitha-5,24-dienolide-27β-(O-β-d-glucopyranoside), has also been reported [36]. Furthermore, withacogulanoside-B, together with five other known withanolides, has been isolated [37]. The distribution of these compounds across various plant parts is summarized in Table 2, and representative structures of selected withanolides are shown in Figure 2.

**Table 2. Distribution of these compounds across various plant parts**

| Plant Part | Compound name | Ref. |
|---|---|---|
| Root | Withaferin A | [38] |
| Root | (20R,22R)-6α,7α-epoxy-5α,20-dihydroxy-1-oxo-witha-2,24-dienolide) | [39] |
| Root | (20R,22R)-6α,7α-epoxy-5α,20-dihydroxy-1-oxo-witha-2,24-dienolide) | [40] |
| whole plant | Coagulin B, Coagulin C, Coagulin D, Coagulin E, Coagulin R | [41] |
| Aerial parts | Amyrin | [42] |

| | | |
|---|---|---|
| Aerial parts | Withacoagulin A: (¼(20S,22R)-17β,20β-dihydroxy-1-oxowitha-3,5,14,24-tetraenolide) | [43] |
| Fruit | (Ergosta-5,25-diene-3β,24ξ-diol) | [44] |
| Fruit | Ajugin E | [45] |
| Fruit | Ajugin A | [46] |
| Fruit | Coagulanolide (17S,20S,22R)-14α,15α,17β,20β-tetrahydroxy-1-oxowitha-2,5,24-trienolide) | [47] |
| Fruit | (20R,22R)-14,20α,27-trihydroxy-1-oxowitha-3,5,24-trienolide | [48] |

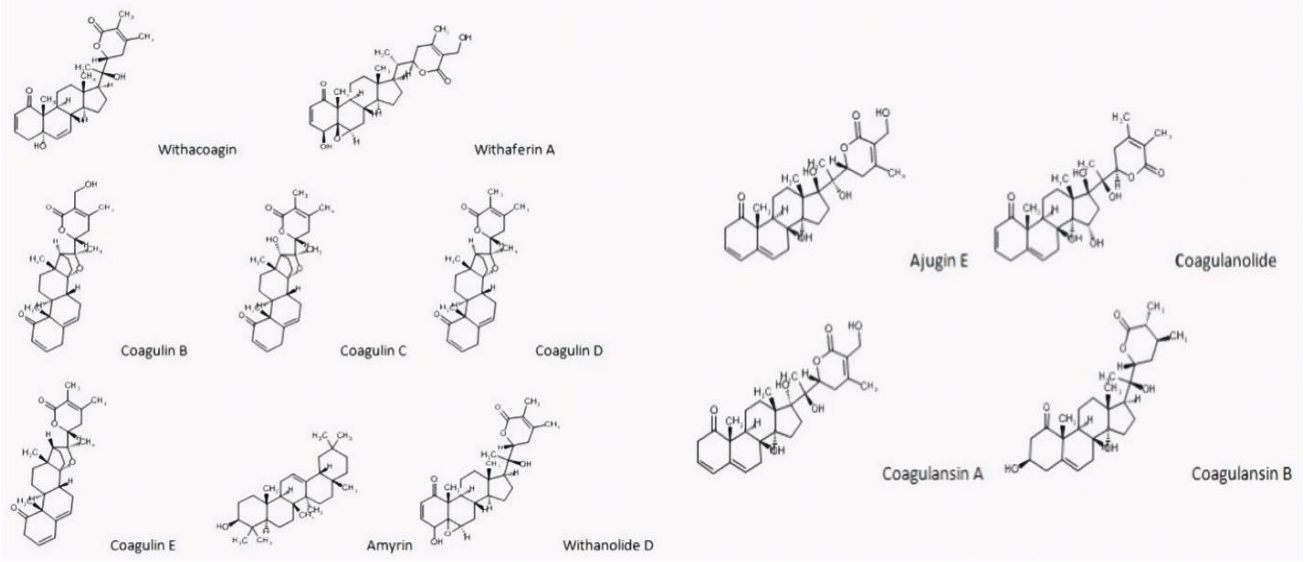


**Figure 2. Structures of Chemical Constituents**

**Pharmacological Activities**

*Withania coagulans* exhibits a wide spectrum of medicinal properties, including antifungal, anti-cytotoxic, antidiabetic, hypolipidemic, neuroprotective, anti-inflammatory, anticancer, anthelmintic, antioxidant, and wound-healing activities [49]. These pharmacological and therapeutic effects are associated with various plant parts—particularly the roots, leaves, and fruits—as illustrated in Figure 3. The anti-inflammatory mechanism of action of coagulin L, a withanolide isolated from *W. coagulans*, is depicted in Figure 4. A comprehensive summary of the therapeutic roles of *W. coagulans* and its withanolide constituents is provided in Table 3.

**Neuroprotective Activity**

Gosavi D, et al studied on *Withania coagulans* fruits have significant neuropharmacological activities. The alcoholic extract showed antidepressant-like effects in Swiss albino mice, evidenced by reduced immobility time in the Tail Suspension Test. Further investigations revealed CNS depressant and

analgesic activities, along with a dose-dependent improvement in motor coordination in the rotarod test. These findings suggest that *W. coagulans* fruit extracts possess potential antidepressant, neuroprotective, and neuromuscular-enhancing properties, warranting further mechanistic and clinical evaluation [50,51].

**Anti-arthritic activity**

Shendkar A. K. et al investigatigated methanolic and hydroalcoholic extracts have shown anti-arthritic activity by protein denaturation method, membrane stabilization method and protein inhibitory method. The finding of study suggested that *Withania coagulans dunal* fruit could be a potential natural source of anti-arthritic activity. From the above investigation WCHAE possess anti-arthritic effect. WCHAE show more significant anti-arthritic activity then WCME [52].

**Analgesic Activity**

Archana K. et al conducted this study was assessing the central analgesic activity of *Withania Coagulans* Dunal fruit extract in Swiss albino mice. Hot plate method and tail immersion method is generally used *in vivo* model for estimation of central analgesic activity. Methanolic and hydro-alcoholic extract of WC was used. In both cases Diclofenac Sodium was used as standard drug. Both the extracts at doses of 100 mg/kg and 200 mg/kg have significant analgesic activity in dose defendant manner by using Hot plate method and Tail immersion method. But hydro-alcoholic extract of WC at 200 mg/kg showed more significant activity than other extracts. Both methanolic and hydro-alcoholic extract of WC fruits have potent analgesic activity against different stimuli due to significant increase in reaction time [53,54].

**Anti-diabetic Activity**

Roshni B. et al. compared *Withania coagulans* and *Psidium guajava* for their antidiabetic potential in the treatment of diabetes mellitus. Both plants were collected, authenticated, and subjected to successive solvent extraction. Phytochemical screening revealed steroids, saponins, alkaloids, flavonoids, glycosides, and tannins in their extracts. In vivo oral glucose tolerance tests showed that the aqueous extract of *W. coagulans* produced a significantly greater reduction in blood glucose levels compared to *P. guajava*, indicating stronger antidiabetic activity [55,56].

In vivo antidiabetic activity was assessed in streptozotocin-induced diabetic rats. A 10 mg dose of glipizide produced a 70% reduction in blood glucose levels. Comparable reductions were achieved with 1106 mg of aqueous *Withania coagulans* extract and 1193 mg of aqueous *Psidium guajava* extract. These findings indicate that *W. coagulans* is more potent, as a lower dose is required to match the effect of glipizide. Overall, *W. coagulans* demonstrated greater efficacy than *P. guajava* in reducing blood sugar levels [57].

**Anti-inflammatory Activity**

Jhansee M. et al. studied the genus *Withania*, a small group of shrubs whose berries are traditionally used for milk coagulation — the species *W. coagulans* is popularly known as the "Indian cheese maker." In their study, the authors highlighted that *W. coagulans* serves as a source of coagulating enzyme for clotting milk to make "paneer." They reported that "doda paneer," derived from this plant, is an effective treatment for diabetes mellitus: it not only lowers blood sugar levels, but — owing to its strong antioxidant activity — may also reduce the risk of future diabetic complications such as neuropathy, retinopathy, nephropathy, and cardiovascular disease. Furthermore, their work noted that *W. coagulans* exhibits significant hepatoprotective, antitumor, anti-angiogenic, chemopreventive, and anti-inflammatory properties [58,59].

**Anti-hyperlipidaemic Activity**

Ankur D. et al. evaluated the hyperlipidemic activity of the hydroalcoholic *Withania coagulans* dried fruit extract (WCDF) in high-cholesterol diet–induced hyperlipidemic albino rats. The WCDF extract significantly improved the lipid profile by reducing elevated cholesterol and triglyceride levels. Its effect was found to be effective and comparable to atorvastatin, a standard lipid-lowering drug. These findings suggest that WCDF possesses strong lipid-modulating properties. Overall, the extract shows promising potential as a natural agent for managing hyperlipidaemia [60].

**Anti- oxidant Activity**

Chetan S. et al. evaluated the antioxidant activity of *Withania coagulans* using DPPH and nitric oxide radical scavenging assays. The plant extract exhibited moderate antioxidant activity in the DPPH method but showed relatively low activity in the nitric oxide inhibition assay. Overall, the extract was more effective in the DPPH test, and its activity was compared against the standard antioxidant, ascorbic acid [61].

**Diuretic Activity**

Janak D. et al. evaluated the diuretic activity of aqueous *Withania coagulans* fruit extract using the in vivo Lipchitz test with furosemide as the standard. The extract significantly increased urine output by 79.12% at 500 mg/kg and 71.02% at 750 mg/kg compared to the control. Both doses also enhanced the excretion of sodium, potassium, and chloride ions. Notably, the 500 mg/kg dose showed more significant diuretic and electrolyte excretion effects than the higher dose. The study confirms that *W. coagulans* possesses potent and demonstrable diuretic activity [62].

**Anti-ulcer (Gastroprotective) Activity**

Recent studies demonstrate that *Withania coagulans* fruit extract exhibits potent anti-ulcer activity by reducing gastric acid secretion and enhancing mucosal defense. It increases protective factors such as prostaglandins (PGE2), nitric oxide, and antioxidant enzymes (SOD, CAT), while decreasing inflammatory cytokines (TNF-α, IL-6). The effect was found comparable to standard drugs like ranitidine, indicating strong gastroprotective potential [63].

**Anti-hyperuricemic Activity**

A recent pharmacological study revealed that *Withania coagulans* exerts anti-hyperuricemic effects primarily through inhibition of xanthine oxidase (XOD), thereby reducing uric acid synthesis. This mechanism is complemented by improved uric acid clearance when combined with other plant agents. This highlights its potential as a natural therapeutic option for gout and metabolic disorders [64].

**Nanoparticle-mediated Antioxidant & Antimicrobial Activity**

Recent advancements show that *Withania coagulans* extracts are used in green synthesis of silver nanoparticles (AgNPs), which significantly enhance antioxidant and antimicrobial activity. These nanoparticles exhibit strong free radical scavenging (DPPH, $H_2O_2$ assays) and cytotoxic effects against pathogens, indicating improved pharmacological efficacy compared to crude extracts and opening avenues in nanomedicine [65].

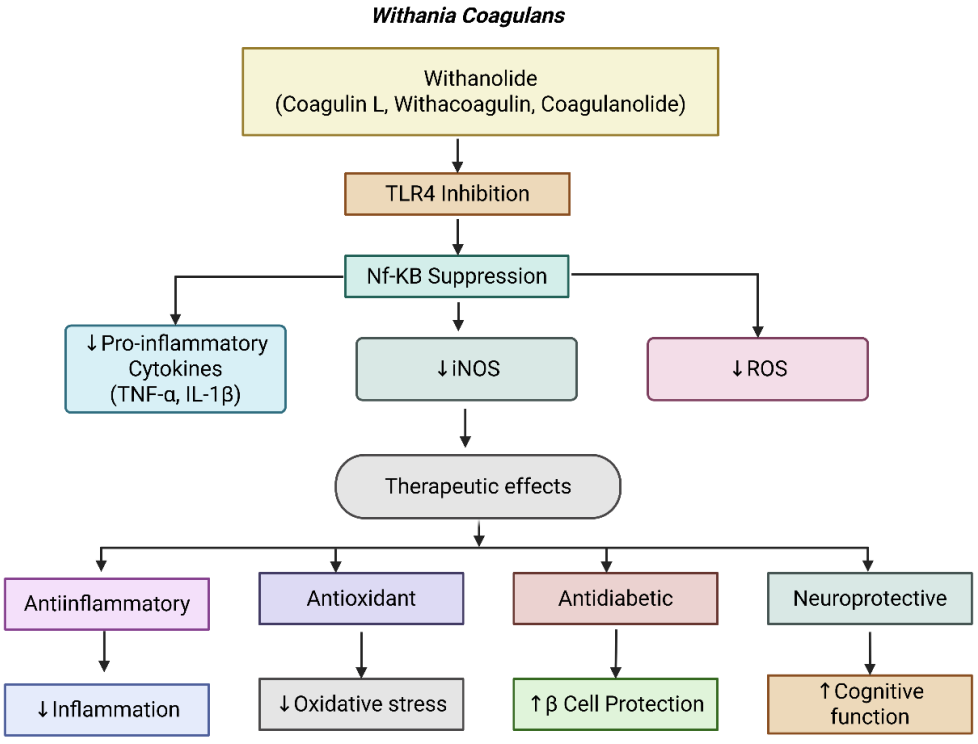

**Figure 1: Therapeutic effects of *Withania Coagulans***

**Table 3. A comprehensive summary of the therapeutic roles of *W. coagulans* and its withanolide constituents**

| Plant Part | Extract | Animal Model | Dose | Result | References |
|---|---|---|---|---|---|
| Fruit | Methanolic | Rabbits (1–1.5 kg weight) | 200 and 600 mg/kg BW | Enhances lipid profile, enzyme function, and antioxidant activity. | [66] |
| Fruit | Withacoagulin and coagulin C | Female Albino rats (100–120 g) | 25 and 50 mg/kg BW | Antihypertensive impact in a dose-dependent manner | [67] |
| Fruit | Withacoagulin | Male Albino rats (120–150 g) | 25 mg/kg BW | Superoxide dismutase, catalase, CPK, and LDH levels were markedly reduced. | [68] |
| Fruit | Coagulin L | Human murine cells, mice model (male Swiss Albino mice) | 1, 3, 10 µM (In vitro) 10, 25, and 50 mg/kg BW | It inhibits NF-κB by blocking TLR4 signaling, lowering iNOS and pro-inflammatory cytokines. | [69] |
| Aerial parts | Crude extract (methanol and chloroform in 1:1) | Sprague Dawley rats (180–220 g) | 200, 100 and 50 mg/kg BW | Anti-inflammatory | [70] |
| Plant | Methanolic extract | Wistar rats (150–200 g) | 250 and 500 mg/kg BW | Antioxidant activity | [71] |
| Roots and leaves | Chloroform, ethyl acetate, and aqueous extract | Bacterial strains | 0.5, 1, 1.5, and 2 mg/mL | Anti-bacterial activity | [72] |
| Fruit | Methanolic extract | Male Charles Foster Albino rats (150–200 g) | 400 mg/kg BW | Decrease the level of free radicals | [73] |

| | | | | | |
|---|---|---|---|---|---|
| Leaves | Silver nanoparticles (leaf extract) | Bacterial strains | 5, 10, 15, and | Growth of both gram-positive and negative bacteria reduced | [74] |
| Fruit | Ethanolic extract | Wistar rats and in vitro | 400 mg/kg BW | *W. coagulans* reduced DPP-4 levels by 63.2% in vitro at 14 µg/mL. | [75] |
| Whole plant | Aqueous extract | Male SD rat | 1000 mg/kg BW | Reduce postprandial glucose level | [76] |
| Whole plant | Hydro-methanolic extract | Forty male Wistar rats (200–250 g) | 1000 mg/kg BW | *W. coagulans* extract triggered cell apoptosis in the prostate. | [77] |
| Fruit | Methanolic extract | Human breast cancer and normal kidney epithelial cell lines | 20–200 µg/mL | Methanolic fruit extract showed substantial anticancer activity | [78] |
| Leaves | Methanol and chloroform extract | Methanol and chloroform extract | 10–250 µg/mL | The extract induced apoptosis and reduced cancer cell viability and invasion. | [79] |
| Whole plant | Water and methanol extract | Wistar rats (200–250 g) | 250, 500, and 1000 mg/kg BW | *W. coagulans* extract lowered malondialdehyde and raised total antioxidant capacity. | [80] |
| Whole plant | Hydroalcoholic extract | Male Wistar rats | 250, 500, and 1000 mg/kg BW/day | Sperm count, GSI, and viability were significantly reduced. | [80] |
| Whole plant | Ethanolic extracts | Vermicidal activity against the earthworm *Pheretima posthuma*. | 75 and 100 mg/mL | *W. coagulans* extract showed strong anti-helminthic activity against *P. posthuma*. | [81] |

## CONCLUSION

*W. coagulans* exhibits substantial therapeutic potential and has long been used to treat a variety of disorders due to its rich content of withanolides. It also contains esterases, free amino acids, fatty oils,

and essential oils. Numerous pharmacological studies have demonstrated its hepatoprotective, anti-inflammatory, hypoglycaemic, cardioprotective, free radical–scavenging, antimicrobial, CNS-depressant, immunomodulatory, antitumor, and cytotoxic properties. Nevertheless, further research is required to elucidate the mechanisms of action of its bioactive compounds in higher animal models to validate their efficacy and safety. Crude extracts particularly from the fruit show considerable medicinal value. With comprehensive investigation into their mechanisms, bioactivities, toxicity, and pharmacotherapeutic potential, alongside clinical trials and proper standardization, plant-derived compounds from *W. coagulans* may lead to the development of modern therapeutics.

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