



Therapeutic usefulness of *Withania coagulans* (*Tukhm-e-Hayat*): An update

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Abstract: *Withania coagulans* (L.) Dunal (*Tukhm-e-Hayat*) is a novel drug that belongs to the family Solanaceae. It is grown in Eastern parts of the Mediterranean regions and extends up to South Asia. In the Unani system of medicine, it is known as *tukhm-e-hayat*, which means fruit of life. It is also called Indian cheese maker because of its milk coagulation property. In classical literatures, it has been recommended for managing various disorders like strangury, chronic liver diseases, ulcers, indigestion, and dropsy, as well as in managing wasting diseases. The drug possesses *nāfi' dhayābīṭus* (antidiabetic), *muqawwī-i-mi'da* (stomachic), *muḥallil-i-waram* (anti-inflammatory), *muqawwī-i-qalb* (cardiotonic), *muqawwī-i-a'ṣāb* (nervine tonic), *muṣaffī-i-dam* (blood purifier) and *mudirr-i-bawl* (diuretic) properties among others. Numerous studies have documented its hypolipidemic, antioxidant, and diuretic activity. Studies have also reported the hypoglycaemic effect of aqueous and ethanolic extract of *tukhm-e-hayat* in diabetes Mellitus. This paper aims to review the effect of *tukhm-e-hayat* in reference to the Unani literature and modern pharmacological research.

Keywords: *Tukhm-e-Hayat*, *Withania coagulans*, *Hypoglycemic activity*, *Unani*

INTRODUCTION

Withania coagulans (L.) Dunal (*Tukhm-e-Hayat*) is a valuable herb that has been extensively used in traditional medicine for almost three millenia¹. It is described in ancient literature as a cure for a plethora of diseases and conditions². It is commonly known as '*Tukhm-e-hayat*', which means fruit of life^{3,4}. In the English language, it is known as "Indian cheese maker" because in North West India and adjoining countries, people used its fruits/berries for milk coagulation^{1,5}. A large genus of plant is distributed in the Eastern parts of Mediterranean regions and extends up to South Asia. It belongs to the family Solanaceae (Night shade)^{1,6,7,8,9}. In the Unani literature it is described as undershrub plant having seeds as a type of *Asgandh*. Its seeds resemble the seeds of *Lepidium sativum*^{10,11}. Some of its vernacular names are *javzulmizaja*, *panirbad*, *pitabhreege*,^{1,5,10,11,12,13} *akri*,^{1,5,10,11,12,13,14} Indian rennet, *panir ke phool*⁵. Its fruits and seeds are mainly used for medicinal purposes^{10,12}. The fruits/ berries are used as single or in various compound formulations in Unani and Ayurveda to reduce hyperglycemic conditions.

Taxonomical Classification^{15,17}

Kingdom: Plantae; **Class:** Magnoliopsida; **Subclass:** Asteridae; **Order:** Solanales

Family: Solanaceae/nightshade; **Genus:** *Withania*; **Species:** *coagulans* (L.) Dunal

Morphology

Macroscopic Examination

The fruits are superior, indehiscent, 4–6 mm in diameter, pedicellate, and round to glabrous in shape. It is red when fresh but yellowish to chaffy in colour when dry; the outer surface is smooth and encapsulated in the leathery calyx. **(Figure 1)** Fruits filled with dark brown seeds are reniform-shaped and, have a fruity odour. The fruits have an indistinct odour with a slightly bitter taste^{5,17}.

Microscopic Examination

The microscopically transverse section of fruits/berries shows the presence of an exocarp, which contains a single layer, while the mesocarp contains a wide zone of parenchymatous cells with strong cellulosic thickening. The endocarp is somewhat similar to the exocarp in some places, and it contains flattened and collapsed cells. The transverse section of the seed is observed as a single layer of epidermis followed by sub-epidermal cells. There is a layer of highly lignified palisade-like cells with a narrow lumen under the sub-epidermal layer. The composition of the inner epidermis of the seed is 1–2 layers of thin-walled parenchymatous cells⁵.

Geographical Distribution

The plants of *Withania coagulans* (L.) Dunal grows widely in the East Mediterranean to South Asian regions upto 1700 metre, mainly in Iran, Afghanistan, Nepal, India and Pakistan (Sind, Sutlej valley and Baluchistan)⁹.

It has a natural occurrence in dry, hot, and stony places⁵. In India, it is found in the North-West parts such as Punjab, Shimla, Kumaun, Garhwal, and Gujarat^{5,18,19,20,21,22}, Himachal Pradesh, Uttarakhand and Rajasthan⁹.

Parts Used: Fruits^{1,18, 23, 24, 25, 26, 27}

Seeds^{12,18,23}

Toxic: No adverse effect has been reported so far²⁸.

Temperament: Hot 2° and dry 2°^{10,11}

Taste: Bitter^{10,11}

Dose: Fruit: 9-12 in quantity²⁹; 10 in quantity³⁰, in the form of infusion (*Khaisanda*) orally.

Preservation and Storage:

The drugs are dried under shade, and repeatedly brushed during, and after drying to remove the soil. After that, fruits are stored in air-tight containers in a cool and dry place.

Cultivation:

It is conventionally propagated through stem cutting and seeds. Stem cutting method is used for the propagation of plants instead of the seeds germination method due to the poor viability of seeds³¹. The plants' flower and berries ripen during November to April and January to May, respectively¹.

Phytochemical constituents:

The phytochemical constituents in *Withania coagulans* are two esterase, free amino acids, fatty oil, an essential oil, and alkaloids. The amino acids are proline, hydroxyproline, valine, tyrosine, aspartic acid, glycine, cysteine, asparagine, and glutamic acid¹. The principal component of *Withania coagulans* are lactone steroids known as Withanolides^{32,33}.

Other phytochemicals isolated from fruits, seeds and whole plants are Withaferin, Withacoagulin, 20 β , Hydroxy-1-oxo-(22R)-witha-2,5,24-trienolide; 5 α , 20 α (R) Dihydroxy-6 α ,7 α -epoxy-1-oxo witha-2, 24dienolide; 5 α , 17 α Dihydroxy-1-oxo-6 α , 7 α -epoxy-22 R- witha-2, 24-dienolide; 5 α , 27-Dihydroxy-6 α ,7 α -epoxy-1-oxo witha-2, 24-dienolide; 3 β -hydroxy-2,3-dihydrowithanolide F; Ergosta-5,25-dien-3 β , 24- ϵ diol; β -Sitosterol-3- β -D- glucoside; 3 α , 14 α , 17 β , 20 α -Tetrahydroxy-1-oxo-20 S, 22R-with-5, 24-dienolide^{1,34, 35,36,37}, Linoleic acid; β -Sitosterol; D-Galactose; D-Arabinose; fatty acid¹, 17 β , 27 Dihydroxy-14, 20-epoxy-1-oxo-22R-witha-3, 5, 24-trienolide; 14 β , 15 β -epoxywithanolide I; 17 β , 20 β -Dihydroxy-1-oxo-with a-2,5,24-trienolid; Coagulin B,C,D,E,F,G,H,I,J,K,L,M,N,O,P,Q,R,S, respectively^{37,38,39}. Chlorogenic acid, Withaferin A, Withacoagin were also isolated from *Withania coagulans*^{5,35,40}.

Pharmacological Actions

The fruits of *Withania coagulans* have various pharmacological actions. These include:

Muqawwī-i-mi'da (stomachic)^{10,11,14}, *nāfi'dhayābītus* (antidiabetic)^{5,10,11,14,23,27,29}, *mudirr-i-bawl* (diuretic)^{15,18,41,42}, *mudirr-i-ḥayḍ* (emmenagogue)⁵, *muḥallil-i-waram* (anti-inflammatory)^{5,14,43,44}, *qātil-i-dīdān-i-am'ā'* (anthelmintic)^{1,5}, *muqawwī-i-qalb* (cardiotonic)^{34,43}, *muqawwī-i-a'ṣāb* (nervine tonic)¹⁴, anodyne/ sedative^{5,16}, lipid-lowering agent²⁷, milk coagulant^{1,5,10,11,14}, *muṣaffī-i-dam* (blood purifier)^{1,5,14}, *mughalliz-i-manī* (semen inspissant)^{10,11}, and *mudammil qurūḥ* (wound healing)².

Therapeutic Uses

Fruits/berries of *Withania coagulans* are used to treat various disease conditions like:

Dhayābīṭus shakri (diabetes mellitus)^{5,10,11,14,18,27,29,43}, dyspepsia^{5,10,14,45}, *dard-mi'da* (stomach pain)^{10,11}, *tukhma* (indigestion)^{10,11}, *zakhm* (wound)^{5,45}, *amrāḍ-i-kabid* muzmin (chronic liver diseases)^{1,5,13,14}, *waja' al-asnān* (toothache)^{5,45}, *dīdān-i-am'ā'* (helminthiasis)⁵, *jiryān-i-manī* (spermatorrhoea)^{10,11}, *amrāḍ-i-qalb* (cardiac disorders)⁴⁶, nervous exhaustion^{47,48}, strangury^{1,12}, milk coagulation^{5,10,11,14,43}, and diabetic nephropathy⁴.

Pharmacological Activities:

Hypoglycaemic activity

Hoda Q et al., 2010, and Hemalatha S et al., 2006, observed that the *tukhm-e-hayat* fruits extract (aqueous and chloroform) showed significant decrease in blood glucose level in diabetic induced rats^{45,49}.

Hemalatha S et al., 2004 evaluated that the administration of an aqueous extract of fruits of *tukhm-e-hayat* significantly lowered the elevated blood sugar levels in streptozotocin-induced diabetic rats after seven days of treatment⁵⁰.

Maurya R et al., 2008 evaluated the hypoglycaemic potency of aqueous extract of fruits against streptozotocin (STZ) induced diabetes in rats. It was found that coagulanolide, along with four known Withanolides showed significant improvement inof elevated postprandial sugar⁵¹.

Upadhyay BN et al., 2011 clinically assessed the hypoglycaemic potency of *tukhm-e-hayat* in the management of Prameha (type 2 Diabetes Mellitus) and showed encouraging results⁵².

Hypolipidemic Activity

Saxena B et al., 2010 investigated the hypolipidemic activity of the aqueous extract of *tukhm-e-hayat* in hyperlipidaemic rats, and it was concluded that repeated oral administration of aqueous extract possesses significant hypolipidemic activity⁵³.

S. Hemalatha et al., 2006 assessed the antihyperlipidemic activity of aqueous extract of fruits of *tukhm-e-hayat* in high-fat diet-induced hyperlipidaemic rats for seven weeks. A significant reduction in elevated serum cholesterol, triglycerides, lipoprotein, and lipid peroxide level was found⁴⁵.

Antioxidant activity

Dhuley et al.,1998 investigated the antioxidant activity of aqueous extracts of *tukhm-e-hayat* in stress-induced rabbits and mice. It was found that the oral administration of extract lowered the elevated lipid peroxidation due to free radical scavenging properties⁵⁴.

Hemalatha et al., 2004 evaluated that *tukhm-e-hayat* has free radical scavenging properties and concluded that its aqueous extract significantly lowered the liver and serum lipid peroxidation⁵⁰.

Anti-inflammatory activity

Budhiraja et al., 1984, and Rajurkar et al., 2001 investigated the anti-inflammatory effect of hydroalcoholic extract on experimental inflammatory conditions. *Tukhm-e-Hayat* extract showed significant anti-inflammatory activity in the carrageenan-induced paw oedema model^{55,56}.

Budhiraja et al., 1984 investigated the anti-inflammatory activity of *tukhm-e-hayat* aqueous extract in sub-acute inflammation in experimental rats, such as granuloma formation and formalin-induced arthritis. It has a significant anti-inflammatory effect at 10mg/kg, due to the presence of withanolide⁵⁵.

Antimicrobial activity

Owais et al., 2005 evaluated the antimicrobial activity of aqueous fruit extracts of *tukhm-e-hayat*. It successfully obliterated *Salmonella* infection in mice, as revealed by increased survival rate, and the animal treated with aqueous extract had less bacterial load⁵⁷.

Sudhanshu et al., 2012 assessed the antimicrobial activity of methanol, aqueous, petroleum ether, chloroform, benzene, and ethyl acetate extract of fruits of *tukhm-e-hayat*. It was testified against *Shigella flexneri*, *Staphylococcus aureus*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Proteus vulgaris*, *Enterobacter aerogenes*, *Aspergillus niger*, *Candida albicans* and *Trichophyton rubrum*⁵⁸.

Anticarcinogenic activity

Mathur D et al., 2011 investigated that *tukhm-e-hayat* fruit extract shows an inhibitory effect of micronucleus formation in a dose-dependent manner in cyclophosphamide-induced micronucleus formation in bone marrow cells of mice⁵⁹.

Chattopadhyay et al., 2007 investigated the protective efficacy of aqueous extract of *tukhm-e-hayat* in chicken lymphocytes and dimethyl sulfoxide (DMSO) induced cytotoxicity. Aqueous extract-treated chicken showed a decrease in TNF-G production⁶⁰.

Antiobesity Activity

Muheeb Beg et al., 2014 observed body weight reduction in in-vitro models of adipocyte differentiation, including 3T3-L1 pre-adipocyte, stromal mesenchymal C3H10T1/2 cells of mice after the administration of Coagulanolides, particularly coagulin-L, isolated from *tukhm-e-hayat*⁶¹.

Hepatoprotective activity

Rohit Jain et al., 2012 investigated the hepatoprotective efficacy of *tukhm-e-hayat* extract against carbon tetrachloride (CCL4) induced hepatotoxicity in adult albino rats of either sex. This hepatoprotective effect was due to the presence of withanolide F⁶².

Budhiraja et al., 1984 evaluated the hepatoprotective activity of fruit extract of *tukhm-e-hayat* in CCL4-induced hepatotoxicity in animals⁵⁵.

Cardioprotective activity

Budhiraja R.D et al.,1983 assessed the cardioprotective effect of withanolide isolated from the fruits of *tukhm-e-hayat*, and showed a drop in blood pressure in dogs, which was blocked by atropine and not by mepyramine or propranolol³⁴.

Diuretic activity

Dabheliya J et al., 2010 investigated the diuretic activity of the aqueous extract of *tukhm-e-hayat* fruits in in-vivo Lipschitz test model with furosemide as the standard drug. A significant increase in the volume of urine was observed⁶³.

Immunosuppressive activity

Isha Pandey et al., 2015 observed that the crude fruit extract of *tukhm-e-hayat* showed significant inhibitory activities on the T- and B-cell proliferation⁶⁴.

Wound healing activity: Prasad S K et al., 2010 evaluated those herbal formulations consisting of 10% w/w hydroalcoholic extracts of *tukhm-e-hayat* showed wound healing properties in streptozotocin-induced diabetic rats⁶⁵.



Fig 1: Fruit sample of *Withania Coagulans*

Conclusion

Withania coagulans (L.) Dunal (*Tukhm-e-Hayat*) is widely mentioned in the Unani literature and conventional texts for its therapeutic applications in various health conditions. This comprehensive review summarizes the properties mentioned in classical Unani literature and recent pharmacological studies. Various preliminary investigations and scientific studies showed promising results in hyperglycemic states. Further investigations are needed to determine the mechanism of action, active ingredients, and usage in clinical trials to establish it as a standard drug in hyperglycemic states.

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