

PHCOG REV.: Plant Review

Withania coagulans Dunal: A Review

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ABSTRACT

The *withania coagulans* belonging to family Solonaceae and distributed mainly in East of the Mediterranean region, extending to South Asia. This plant is rich in withanolide. The *Withania coagulans* possess a number of medicinally important activities such as antifungal activity, anthelmintic, antimicrobial, hypolipidemic, antioxidant, anti-cytotoxic, anti-fungal activity, Hypoglycemic activity etc. Fruits of *Withania coagulans* gaining popularity as a antidiabetic. The present review explores its economical importance, distribution, chemical composition, pharmacological activity and traditional uses of *Withania coagulans*.

KEY WORDS: Antidiabetic, hypolipidemic, wound healing, anti-inflammatory, *Withania coagulans*, Withanolide.

INTRODUCTION

Plants have a long therapeutic history over thousands of years and still considered to be promising source of medicine in the traditional health care system. The efficacy and safety of herbal medicine have turned the major pharmaceutical population towards medicinal plant's research. In view of the widespread interest on using medicinal plants the present review on *Withania coagulans* is to provide up to date information, in references to botanical, commercial, ethnopharmacological, phytochemical and pharmacological studies that appears in the literature (1). *W. coagulans* Dunal belongs to family Solanaceae. It is distributed in the East of the Mediterranean region and extends to South Asia (2). Different parts of this plant have been reported to possess a variety of biological activities. The fruit, berries are use for commercial purposes for milk coagulation. Literature surveys on this plant revealed the presence of esterases, lignan, alkaloids, free amino acids, fatty oils, essential oils and withanolides.

TAXONOMICAL CLASSIFICATION

Kingdom	: Plantae, Plants;
Subkingdom	: Tracheobionta, Vascular plants;
Super division	: Spermatophyta, Seeds plants;
Division	: Angiosperms
Class	: Dicotyledons
Order	: Tubiflorae
Family	: Solanaceae
Genus	: <i>Withania</i>
Species	: <i>Withania coagulans</i> Dunal.

Botanical description:

W. Coagulans Dunal is a rigid, grey under shrub, 60-120 cm high, occurring in drier parts of the Punjab. It has also been recorded from the region around Simla, Garhwal, and Kumaun. The plant flowers during November-April and the berries ripen during January-May. The natural regeneration is from the seed. The flowers dioceous, in auxiliary clusters; pedicils 0.6 mm long, Deflexed, slender. Calyx 6 mm long, campanulate, clothed with fine stellate gray tomentum; teeth triangular, 2.5 mm long. Corolla 8 mm long stellately mealy outside, divided about 1/3 the way down; lobes ovate-

oblong, sub acute. Male flowers stamens about level with the top of the corolla-tube; filament 2 mm long, glabrous; anthers 3-4 mm long. Ovary ovoid, without style or stigma. Female flowers stamens scarcely reaching 1/2 way up the corolla-tube; filaments about 0.85 mm long; anther smaller than in the male flowers, sterile. Ovary ovoid, style glabrous; stigma mushroom-shaped, 2-lamellate. Berry 6-8 mm globose, smooth, closely girt by the enlarged membranous calyx, which is scurfy-pubescent out side. Seeds 2.5-3.0 mm diameter, somewhat ear shaped, glabrous.

Synonyms:

Arabic-Javzuhnizaja, Kaknajehindi; Bengali: Ashvagandha; Bombay-Kaknaj; Decca Handikaknaj; English- Cheese maker, Indian Rennet, Vegetable Rennet; Hindi-Akri, Binputakah, Punir; Punjabi-Kharmjaria, Khumazare, Kutilana, Makhazura, Panir, Shapiang, Spinbajia; Sindhi-Punirband, Punirjafota; Tamil- Amukkra; Telgu-Pennerugadda; Urdu-Kakanaj.

Economical importance:

W. coagulans is commonly known as paneer in Punjab (Pakistan), 'The cheese maker' or 'vegetable rennet' because fruits and leaves have properties to coagulate milk. The milk coagulating properties of the fruit is attributed to the pulp and husk of berries which possess an enzyme which has milk coagulating activity. One ounce fruit of *W. coagulans* and quart of boiling water make a decoction, one table spoonful of which coagulate a gallon of warm milk in about an hour. In Punjab, the berries of *W. coagulans* are used as the source of coagulating enzyme for clotting the milk is called 'paneer'. Buffalo or sheep milk is warmed to about 100^o F and crushed berries of plant, tied in a cloth, are dipped in it. The milk takes 30-40 minutes to curdle (2,3).

Ethnomedical uses:

The fruits are reported to posses sedative, emetic alterative and diuretic. They are useful in dyspepsia, flatulent colic and other intestinal infections. They are employed for the treatment of asthma, biliousness and stranguary. In some parts of the sub-continent, the berries are used as a blood purifier. It is well known in the indigenous system of medicine for the treatment of ulcers, rheumatism, dropsy, consumption and sensile debility. The twigs are chewed for cleaning teeth

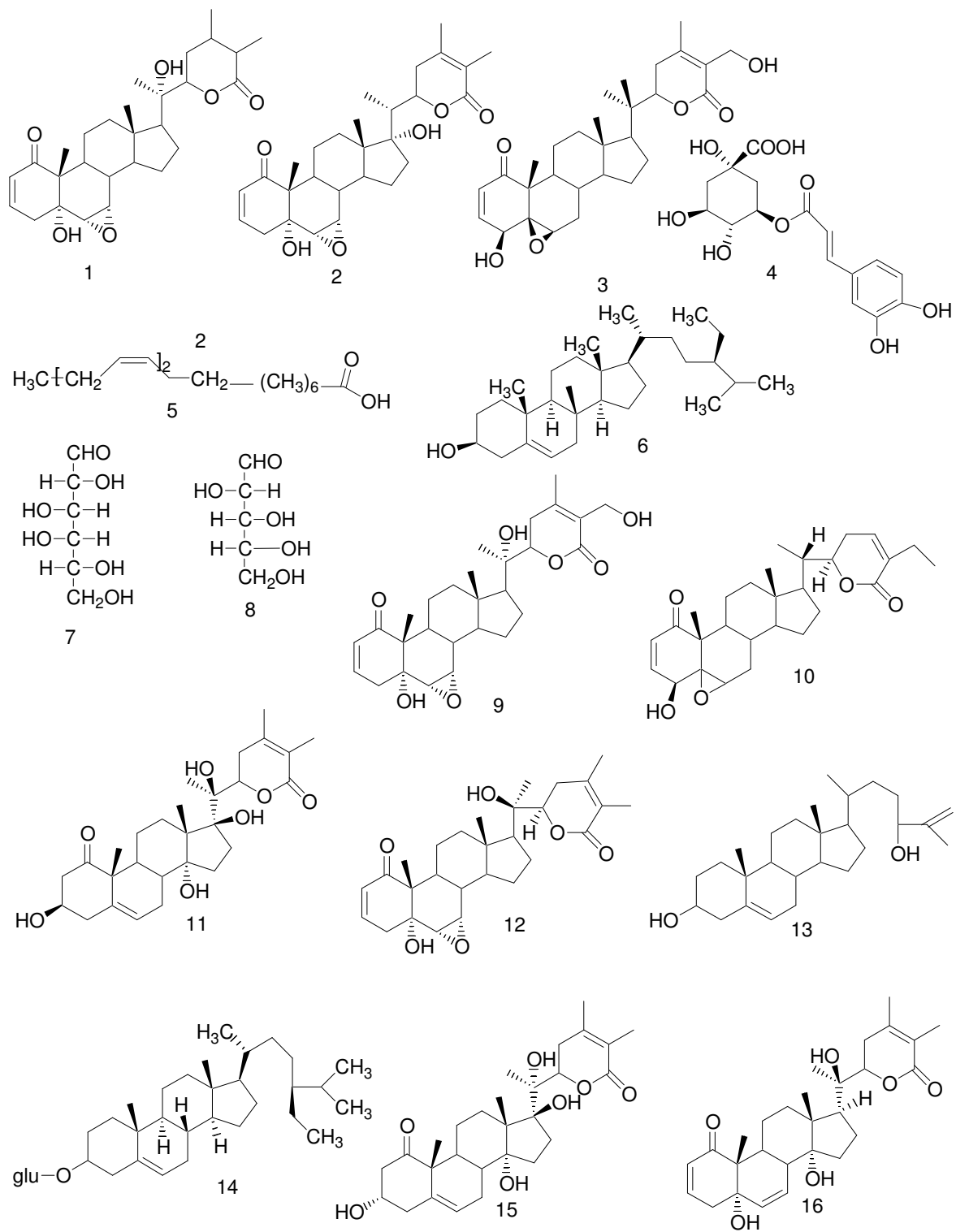
and the smoke of the plant is inhaled for relief in toothache. The leaves are used in Pakistan as vegetable, and as fodder for camel and sheep. The fruit is applied to wound. They are useful in chronic complaints of liver. The leaves are employed as febrifuge. The seeds are useful in lumbago, ophthalmia, and lessen the inflammation of piles (2, 4).

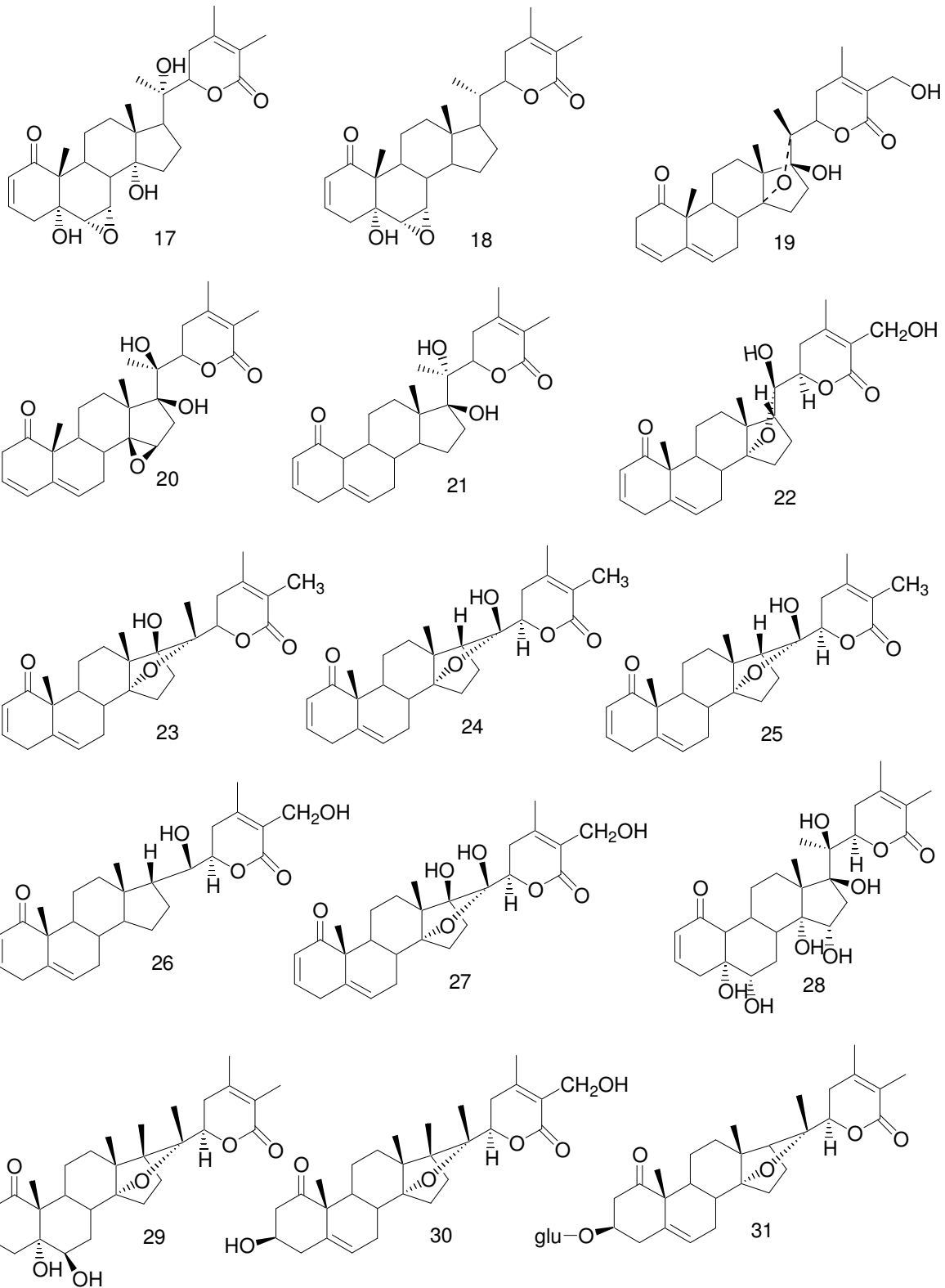
Phytochemical investigation on plant *W. coagulans* up to year 2007 reported number of phytoconstituents. Various types of withanolides and others types of chemical constituents isolated from this plant. Structure of most of isolated compound from this plant is shown below with common name and there references.

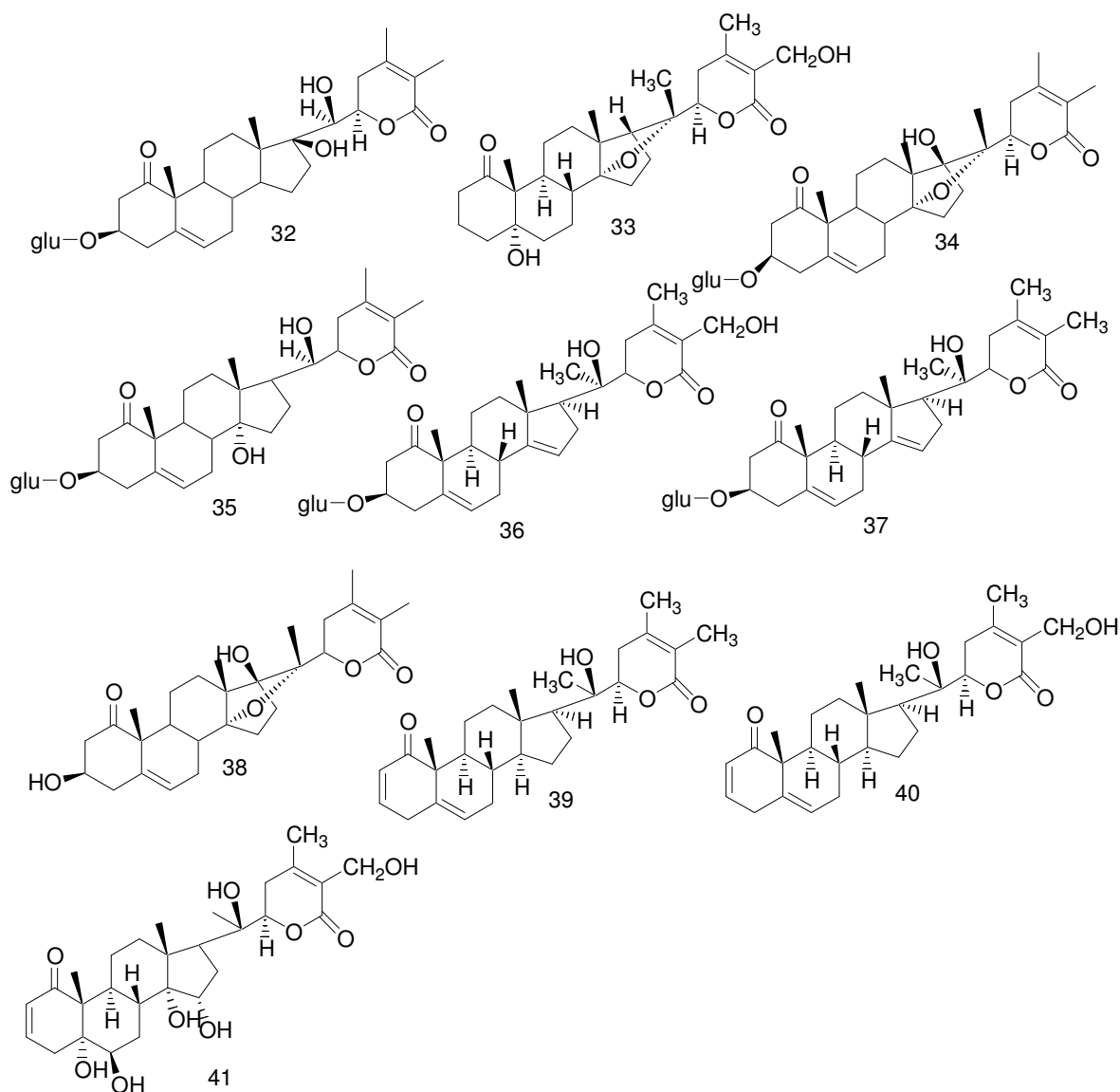
PHYTOCHEMISTRY

Constituents	Structure	Isolated from part of plant/extract	References	Ref. No.
5 α , 20 α (R) Dihydroxy-6 α ,7 α -epoxy-1-oxo witha-2, 24-dienolide	1	Fruit	Anonymous (1966)	5
5 α , 17 α Dihydroxy-1-oxo-6 α , 7 α -epoxy-22 R- witha-2, 24-dienolide	2	Fruit	Anonymous (1966)	5
Withaferin	3	Fruit	Neogi, et al. (1988)	6
Chlorogenic acid	4	Leaves	Karthikar & Basu (1918)	2
Linoleic acid	5	Seed	Anonymous (1966)	5
β -Sitosterol	6	Seed	Anonymous (1966)	5
D-Galactose	7	Seed	Anonymous (1966)	5
D-Arabinose	8	Seed	Anonymous (1966)	5
5 α , 27-Dihydroxy-6 α ,7 α -epoxy-1-oxo witha-2, 24-dienolide	9	Fruit	Anonymous (1966)	5
Withaferin A	10	Root	Subramanian, et al. (1969)	7
3 β -hydroxy-2,3-dihydrowithanolide F	11	Fruit	Budhiraja et al., (1983)	8
5,20 α (R)-dihydroxy-6 α ,7 α -epoxy-1-oxo-(5 α)-witha-2,24-dienolide	12	Dry leaves	Subramanian et al., (1971)	9
Ergosta-5,25-dien-3 β , 24- ϵ diol	13	Fruit	Vandavelde et al. (1983)	10
β -Sitosterol-3- β -D- glucoside	14	Fruit	Vandavelde et al. (1983)	10
3 α , 14 α , 17 β , 20 α -Tetrahydroxy-1-oxo-20 S, 22R-with-5, 24-dienolide	15	Fruit	Vandavelde et al. (1983)	10
Fatty acid	-	Seed	Sattar at al. (1988)	11
Withacoagin	16	Root	Neogi, et al. (1988)	12
(20 R, 22R) 6 α , 7 α -epoxy-5 α ,20-dihydroxy-1-oxo- witha-2, 24-dienolide	17	Root	Neogi, et al. (1988)	12
(20 S, 22R) 6 α , 7 α -epoxy-5 α -hydroxy-1-oxo- witha-2, 24-dienolide	18	Root	Neogi, et al. (1988)	12
17 β , 27 Dihydroxy-14, 20-epoxy-1-oxo-22R-witha-3, 5, 24-trienolide	19	Whole plant	Atta-ur-Rahman et al. (1993)	13
14 β , 15 β -epoxywithanolide I	20	Whole plant	Chaudhary et al. (1995)	13
17 β , 20 β - Dihydroxy-1-oxo-witha-2,5,24-trienolide	21	Whole plant	Chaudhary et al. (1995)	14
Enzymes-esterase, Amino acids	-	Fruit	Anonymous (1966)	5
Coagulin B	22	Aerial parts of plant	Atta-ur-Rahman et al. (1998)	16
Coagulin C	23	Aerial parts of plant	Atta-ur-Rahman et al. (1998)	15
Coagulin D	24	Aerial parts of plant	Atta-ur-Rahman et al. (1998)	15
Coagulin E	25	Aerial parts of plant	Atta-ur-Rahman et al. (1998)	15
Coagulin F	26	Whole plant	Atta-ur-Rahman et al. (1998)	16
27-hydroxy-14,20-epoxy-1-oxo-(22R)-witha-3,5,24-trienolide				
Coagulin G	27	Whole plant	Atta-ur-Rahman et al. (1998)	16
17 β ,27-dihydroxy-14,20-epoxy-1-oxo-(22R)-witha-2,5,24-trienolide				
Coagulin H	28	Whole plant	Atta-ur-Rahman et al. (1998)	17
5 α ,6 β ,14 α ,15 α ,17,20-hexahydroxy-1-oxowitha-2,24-dienolide				

Constituents	Structure	Isolated from part of plant/extract	References	Ref. No.
Coagulin J 3 β , 27-dihydroxy-14,20-epoxy-1-oxowitha-5,24-dienolide	30	Whole plant	Atta-ur-Rahman et al. (1998)	17
Coagulin K 14,20-epoxy-3 β -(O- β -D-glucopyranosyl)-1-oxowitha-5,24-dienolide	31	Whole plant	Atta-ur-Rahman et al. (1998)	17
Coagulin L 14,17,20-trihydroxy-3 β -(O- β -D-glucopyranosyl)-1-oxowitha-5,24-dienolide	32	Whole plant	Atta-ur-Rahman et al. (1998)	17
Coagulin M 5 α , 6 β , 27-trihydroxy-14,20-epoxy-1-oxo-witha-24-enolide	33	Whole plant	Atta-ur-Rahman et al. (1998)	18
Coagulin N 15 α , 17-dihydroxy-14,20-epoxy-3 β -(O- β -D-glucopyranosyl)-1-oxo-witha-5,24-dienolide	34	Whole plant	Atta-ur-Rahman et al. (1998)	18
Coagulin O 14,20-dihydroxy-3 β -(O- β -D-glucopyranosyl)-1-oxo-witha-5,24-dienolide	35	Whole plant	Atta-ur-Rahman et al. (1998)	18
Coagulin P 20,27-dihydroxy-3 β -(O-b-D-glucopyranosyl)-1-oxo-(20S,22R)-witha-5,14,24-trienolide,	36	Whole plant	Atta-ur-Rahman et al. (1999)	19
Coagulin Q 1 α , 20-dihydroxy-3 β -(O- β -D-glucopyranosyl)-(20S,22R)-witha-5,24-dienolide	37	Whole plant	Atta-ur-Rahman et al. (1999)	19
Coagulin R 3 β , 17 β -dihydroxy-14,20-epoxy-1-oxo-(22R)-witha-5,24-dienolide	38	Whole plant	Atta-ur-Rahman et al. (1999)	19
20 β , Hydroxy-1-oxo-(22R)-witha-2,5,24-trienolide	39	Fruit	Atta-ur-Rahman et al. (2003)	20
Withacoagulin	40	Fruit	Atta-ur-Rahman et al. (2003)	20
Coagulin S (20S*,22R*)-5 α , 6 β , 14 α , 15 α , 17 β , 20,27-heptahydroxy-1-oxowith-24-enolide	41	Ethanollic Ext. of <i>W. Coagulans</i>	Nur-E-Alam et al., 2003	21







Structure of isolated compounds

PHARMACOLOGY

The *W. coagulans* possess a number of medicinally important activities such as anthelmintic, antimicrobial, hypolipidemic, antioxidant, anti-cytotoxic, anti-fungal activity, hypoglycemic activity etc. In present review briefly each activity appears in literature is discussed.

Antidiabetic activity & Anti-oxidant activity

Aqueous extract of the fruits of *W. coagulans* (1g/kg; po; 7 days) reported to possess hypoglycemic activity in normal and streptozotocin induced diabetic rats. The aqueous extract significantly reduced the elevated blood glucose, cholesterol and lipid peroxidation (LPO) levels in diabetic rats. It was

also exhibited free radical scavenging activity in an *in-vitro* system using DPPH (22). It is well known that insulin promotes glucose uptake by peripheral cells and tissues. The aqueous extract of fruits of this plant had shown significant glucose utilization in isolated rat hemidiaphragm (23).

Antimicrobial & Anthelmintic activity

The essential oil obtained by the stem distillation of petroleum ether extract of the fruit was active against *Micrococcus pyrogenes* var *aureus* and *Vibrio cholerae*. Various extracts of the whole fruit of *W. coagulans* were tested for antibacterial activity against *Staphylococcus*

aureus, *Escherichia coli*, and *Vibrio cholerae*. It was also reported to have anthelmintic activity. The ethanolic extract of leaves and stem of *W. coagulans* exhibited antibacterial activity. Withaferin, 3 β -hydroxy-2, 3 dihydro-withanolide F was reported to possess antibacterial activity (24-26).

Anti-fungal activity

A steroidal lactone 17 β -hydroxywithanolide K (20S, 22R) 14 α , 17 β , 20 β -trihydroxy-1-oxo-witha-2,5, 24-trienolide isolated from the ethanolic extract of whole plant of *W. coagulans* was found to be active against a number of potentially pathogenic fungi. (14).

Anti-inflammatory activity

Anti-inflammatory activity of a withanolide from *W. coagulans* was reported by Budhiraja et al. it showed marked effects in sub-acute inflammation in experimental rats. The withanolide did not exhibit any effect on CNS. The hydro alcoholic extract of the berries of *W. coagulans* showed significant anti-inflammatory activity in carragenin induce rat paw oedema model. (27-28).

Antitumor properties

Withaferin (3 β -hydroxy-2, 3 dihydro-withanolide F) was reported to possess anti tumor activity. Aqueous extract of *W. coagulans* was studied for anti-cytotoxic effect. The extract showed remarkable inhibitory activity of DMSO induced cytotoxicity and decrease in TNF- α production in chicken Lymphocyte (26, 29).

Cardiovascular effect

A withanolide isolated from fruits of *W. coagulans* had been reported to possess cardiovascular effects. At dose of 5 mg/kg body weight the withanolide produced a moderate fall of blood pressure in dogs (34 \pm 2.1 mm Hg), which was blocked by atropine and not by mepyrmine or propranolol. In rabbit Langendorff preparation and ECG studies, it produced myocardial depressant effects but in perfused frog heart it produced mild positive inotropic and chronotropic effects (30).

Effect on withdrawal syndrome

Root extract of *W. coagulans* had shown significant effect on the withdrawal syndrome on mice. It shows the significant suppression in morphine induce withdrawal jump, induced by naloxone and decreases development of morphine dependence (31).

Hepatoprotective activity

The protective effect of 3 β -hydroxy-2, 3 dihydro-withanolide F obtained from fruits of *W. coagulans* against CCl₄ induced hepatotoxicity was assessed and the compound was found to possess marked protective effect. A comparison of the protective effect showed that it was more active than hydrocortisone on wt. basis. (27).

Hypolipidemic activity

Administration of an aqueous extract of fruits of *W. coagulans* (1 g/kg; p.o.) to high fat diet induced hyperlipidemic rats for 7 weeks, significantly reduced elevated serum cholesterol, triglycerides, lipoprotein and LPO levels. This drug also showed hypolipidemic activity in triton induced hypercholesterolemia. The histopathological examination of liver tissues of treated hyperlipidemic rats showed comparatively lesser degenerative changes compared with

hyperlipidemic controls. The hypolipidemic effect of *W. coagulans* fruits was found to be comparable to that of an Ayurvedic product containing *Commiphora mukul* (32).

Wound healing activity

Aqueous-methanolic phase of methanolic extract of *W. coagulans* showed significant wound healing activity in open and incised wound model. It was also found to accelerated collagen, mucopolysaccharides, DNA and protein synthesis (33).

CONCLUSION

Plant is utilized as medicine since time immorial. The extensive survey of literature revealed that *W. coagulans* is an important source of many withanolide and plant possess variety of pharmacological activities like Antidiabetic activity, Antimicrobial & Anthelmintic activity, Anti-fungal activity, Anti-inflammatory activity, Anti-oxidant activity, Antitumor properties, Cardiovascular effect, Effect on withdrawal syndrome, Hepatoprotective activity, Hypolipidemic activity, Wound healing activity. This plant gaining popularity as an antidiabetic activity in Northern parts of India. It has been used in one of formulation for anti diabetic in USA. Further studies on activity guided fractions of the fruit of *W. coagulans* will explore a new lead bio active molecule for human welfare which is the global need.

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