

ASHWAGANDHA – *Withania somnifera* A SHEET ANCHOR IN AYURVEDIC THERAPY.

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Overview

Withania somnifera Dunal, is commonly known as "Ashwagandha" which in Sanskrit means the odour of horses. Curious though this may, be the roots of this plant which are the main parts used in therapy, happen to simulate the sweat odor of horses. It is a plant which belongs to the family SOLANACEAE which also produces such commonly known food plants such as the tomato, the aubergene or brinjal, and another similarly popular vegetable well known in Sri Lanka as Batu or Elabatu. Like the tomato, Ashwagandha bears yellow flowers and a red fruit which is berry-like in shape. It is also called the "Winter Cherry" a name which amply suits its appearance. In Sri Lanka and Malaysia, and also in Tamil Nadu in India, it is known as "Ammukkara" or "Ammukkarana". This name may also apply in the Indonesian region.

In the North American region it is available as an OTC (Over The Counter) supplement and is recommended for stress conditions and as a rejuvenative agent.

Ashwagandha grows prolifically in the Indian subcontinent and in Sri Lanka and is used in the Ayurvedic system of medicine as treatment for a wide variety of musculoskeletal conditions such as: rheumatoid arthritis, and as a constituent of general tonics. The Latin name for the species, *somnifera*, means "sleep inducing" which indicates that it was considered a sedative in some parts where it was used. Herbalists refer to Ashwagandha as "Indian ginseng" possibly on account of the multiple curative properties attributed to the plant. Legend has it that during the conquests of the Greek general Alexander the Great, it was found that the plant had been used to prepare wine. It had been also recorded that in the Old English Herbarium it was called "apollinaris" and also "glofwyrt",

and that according to legend it was first discovered by Apollo who gave it to the healer Aesculaptus.



Its wide and varied use in therapy is such, that today it has been extensively domesticated from the spontaneous flora, and in India five different improved cultivars have been developed for enhanced size of root, and adaptation to different climatic conditions. The appeal of the plant is manifest in the fact that several companies from the USA and Japan have filed patents for formulations containing extracts of the herb for uses such as skin conditions, promoting reproductive fertility, and arthritis.

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Uses in Ayurvedic Medicine

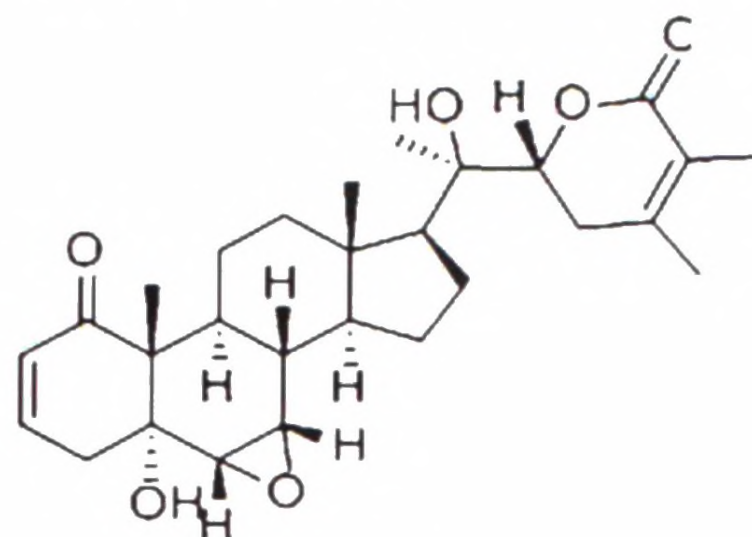
Ashwagandha is one of the most valuable medicinal plants in the Ayurvedic pharmacopoeia. It is primarily employed in preparations prescribed for conditions of stress, anxiety, depression, insomnia and also in the treatment for rheumatoid arthritis and related conditions. In arthritic conditions it is the concept in Ayurveda that the pains in the joints that are characteristic of this disease, are the result of the body's degenerative process. Ashwagandha is prescribed as a long term treatment for the process of ageing and is regarded as a rejuvenating agent. A popular Ayurvedic preparation is the herbal wine or Arishta known as Ashwagandha arishta which is prescribed for regular use as a rejuvenating agent to counter the effects of the body's degenerative process with time. The plant is also considered useful in boosting the body's resistance to infections.

Chemical studies

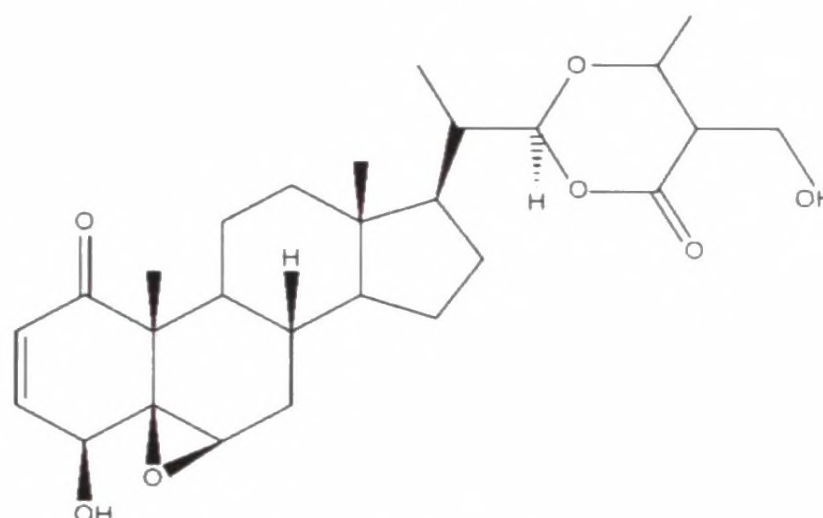
In the half century following the World War II there was considerable worldwide interest in the medicinal plants used in Ayurvedic therapy; and Ashwagandha was one of the primary candidates for chemical examination. During that period phyto-chemists conducted their researches primarily to isolate new chemical entities with interesting chemical structures and interest in biological activity was merely the shadow behind the exercise. As a consequence many of Ashwagandha's biological effects have not been completely scientifically searched. This may have given rise, understandably, to skepticism when considering a herb with so many claims to usefulness. During this period the term "Adaptogen" was used to describe such herbs that cause adaptive positive reactions to disease and had proved useful in cases of many unrelated illnesses. Ashwagandha was such a case that showed itself, (in terms of western concepts), as being able to produce "a state on non-specific increased resistance." Since then the chemistry of *Withania somnifera* had been studied extensively. Now well over 45 constituents have been isolated and characterized in terms of their chemical structures. The biologically active chemical entities are:

- Twelve Alkaloids - including: tropanol, isopelletierine, anaferine.
- Thirty five Steroidal lactones (Now called Withanolides, and Withaferins)

- Withanosides, ie. Withanolides with a sugar attachment.
- Saponins, containing an additional acyl entity, (Sitoindosides),



Withanolide



Withaferin A

Current scientific research has been able to corroborate some of the biological activities that have been attributed to the plant Ashwagandha.

Pharmacological studies

Antiinflammatory activity

Ashwagandha has proved itself to be effective in a number of conditions related to arthritis and rheumatism. There is ample clinical evidence for this. Researchers attribute this in part to the anti-inflammatory properties of the extracts which have been studied recently in animal models. They have recorded considerable reduction in inflammation, and found it was more effective than phenylbutazone under comparative conditions.

A double blind placebo controlled clinical trial has supported the possible use of Ashwagandha as therapy for arthritis. The study involved 42

osteoarthritis patients who were randomized, to receive a preparation of Ashwagandha or a placebo over a period of three months. The usual precautions and conditions for such a study were observed. It was found finally that the herbal formula, which contained about 70% Ashwagandha together with turmeric, an oleo gum resin of Boswellia, with a zinc complex, significantly reduced the pain levels.

Anti-tumour properties

Anti-tumour effects of extracts of Ashwagandha, have been observed in a variety of animal studies by different laboratories but no clear mechanisms have been postulated. A growth inhibitory effect has been recorded in sarcoma S-180, a transplantable mouse tumour. Other studies with promising indications have been recorded with some of the isolated constituents of Ashwagandha like Withaferin A, and the studies were promisingly suggestive of anti-tumour activity.

Anti-stress effects

Experiments on the anti-stress effects of the extracts of Ashwagandha, as well as the isolated individual compounds abound, but apart from positive indications which point to the need for further studies, no mechanistic postulates are available as yet. The extracts as well as the Sitoindosides displayed considerable effects in tests with mice and rat models. With mice in a swimming performance test in water the extracts approximately doubled the time in comparison with controls. The Sitoindosides exhibited significant anti-stress activity in mice and also displayed other positive responses. The inevitable conclusion is that if the effects recorded in animal models could be reproduced in humans, Ashwagandha would be an effective therapy in the treatment of a variety of stress conditions.

Anti-oxidative effects

It is believed that free radical damage of nervous tissue contributes to neuronal loss in cerebral ischemia, and also contributes towards neurodegenerative diseases and ageing. Examples are Alzheimer's disease, Parkinsonian syndrome etc. The traditional usage of Ashwagandha seems to be associated with diseases resulting from free radical oxidative damage, and it is likely that its beneficial effects may

be due to a degree of anti-oxidant activity. The active constituents such as Sitoindosides and Withaferin A, have indicated in experiments on animal models, that the plant has an effect on the brain which may account for its diverse pharmacological properties.

Immunomodulation

Experiments conducted with preparations of Ashwagandha on animal models leads to the conclusion that there is more than substance in the contention that it boosts the immune system. It produced significant anti-stress activity in mice and rats and augmented learning acquisition and memory retention in both young as well as old specimens. Researchers have recorded significant increases in hemolytic antibody responses towards human erythrocytes which indicated immunostimulatory activity.

Clinical studies on male volunteers gave reason to infer that Ashwagandha was a useful tonic for both young and old. All subjects in the study aged 50-59 displayed significantly increased haemoglobin and RBC counts, and improvements in hair melanin and seated stature. Over 70% reported increased libido.

Similar trials enhanced the reputation of the drug as a relaxant. Ashwagandha seems to produce many effects. They include anti-inflammatory, antitumour, and immunomodulatory properties as well as exerting an influence on the endocrine, nervous and cardiopulmonary systems. Accordingly the experimental evidence indicates that the plant may be effective in the treatment of ailments such as arthritis and similar musculoskeletal disorders, stress-induced nervous disorders, and hypertension.

New water-soluble analogue of the anti-cancer drug Withaferin A.

Researchers of the University of Arizona, headed by Leslie Gunatilaka, have found many other virtues of Ashwagandha. Besides developing a new quick-growing method to produce Ashwagandha in bulk and hence substantial quantities of its major chemical constituent Withaferin A in a water soluble form (Withaferin A sulfate), they have found that this compound and Withaferin A have potent anti-cancer activity against pancreatic cancer and brain tumors. The research has been con-

ducted at the Southwest Centre for Natural Products Research and Commercialization of the University of Arizona. (Presentation made by Prof. Gunatilaka at Link Natural Products Pvt. Ltd, Dompe, on 28 th September. 2011)

Agronomy



Ashwagandha cultivation

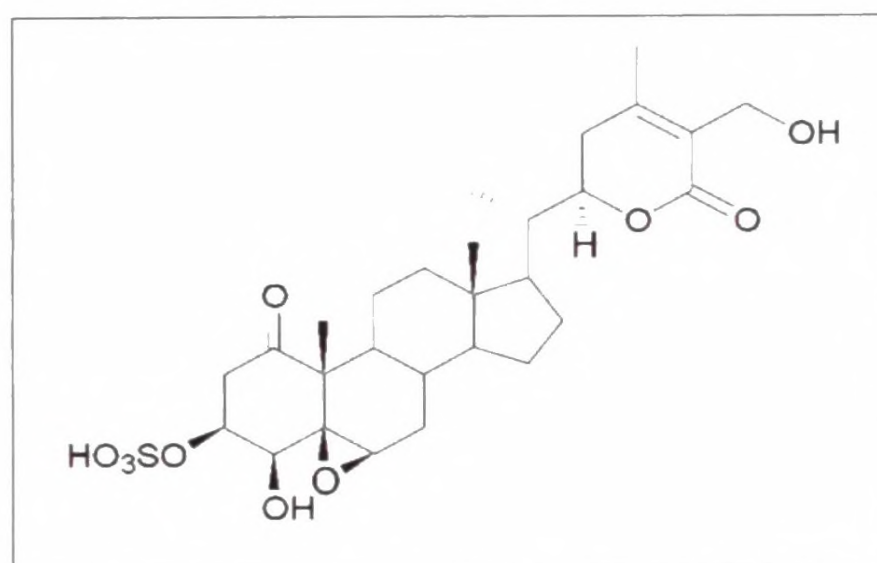
In the spontaneous state *Withania somnifera*, is a plant that grows profusely and occurs in the entire Indian sub-continent as well as in Sri Lanka. Planned cultivations are carried out mainly in India where it is a sheet anchor for therapy within the Ayurvedic system of Medicine. Fields with good water drainage and with a slightly basic soil are deemed ideal for such cultivations. Regions with around 500-700 mm of rainfall, and altitudes ranging from 600 - 1200 meters, and temperatures ranging from 20-32 degrees centigrade, are the climatic zones ideally suited for the crop. It can be a profitable cash crop in fields that are not well irrigated such as the marginal lands in arid areas of the island in the case of Sri Lanka. In the method developed in Arizona by the team led by Gunatilaka, the roots of the plants are artificially irrigated within an aeroponic chamber, and a profusion of root as well as foliage results, enabling the generation in turn, of comparatively large quantities of the active substance Withaferin A. This method represents a paradigm change in agro-technology of medicinal plants, and may come to be applied in other similar cases as well. It also represents maximizing the use of water now regarded as one of the crucially scarce commodities of the world.

Propagation from seeds

The seeds are first allowed to germinate in a nursery bed and then the seedlings are



Ashwagandha cultivation under an innovative aeroponic technique developed by Gunatilaka et al. at the University of Arizona



Water-soluble form (prodrug) of Withaferin A (Withaferin A sulfate) present as a major constituent of aeroponically grown *Withania somnifera*.

planted in rows in prepared field beds which have been well ploughed and aerated. The seedlings are generally about a month old when they are ready to be transplanted. Given the ultimate medicinal use of the plant there is a general reluctance to use artificial fertilizer. In extreme conditions where the soil is poor, the use of organic manure is recommended but in general the crop is managed without any addition of fertilizer. It is also a crop which can thrive in rain fed conditions only. Watering may be considered if conditions of severe drought prevail and the crop itself is endangered. Otherwise it is a crop that sustains itself where other food crops do not.

Harvesting

The crop can be harvested after about 40-48 weeks generally. By this time the red cherry-esque berries have begun to appear. The whole plant together with the roots is removed.

The berries are handpicked and separated. The whole plant is washed and the roots are cut off about 20-30mm. distance from where the aerial part commences. The roots and berries are dried. The roots which form the major drug are chopped to smaller dimensions and stored. The dried berries are used to generate the seeds for further propagation. About 350-400kg of Ashwagandha root can be expected from a single hectare.

Concluding Observations

The evidence is heavy in regard to the beneficial effects of Ashwagandha. Research into the mode of action of its chemical constituents is now the focus that is receiving worldwide scientific attention. Clarification of these and the effect of the multiple Ayurvedic prescriptions involving the plant will enlighten the scientific community in a manner that will focus even greater attention on the therapies of Ayurveda as a goldmine in reserve to combat the diseases that now dominate mankind.

Withania somnifera is written as "Ashwaganda" as well as "Ashwagandha" in English texts.

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