CHAPTER 1

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Withania somnifera Dunal (Ashwagandha) is an evergreen shrub belonging to the family Solanaceae. The leaves are 5-10 by 2-5 cm, ovate, acute, entire, pubescent, base acute, lateral nerves 6 pairs, petiole 1 cm long. Flowers are greenish yellow, in umbels of about 5, pedicels minute, calyx 0.5 cm long, tomentose, teeth linear, and acute. corolla 0.8 cm long, lobes acute and pubescent outside. The fruit of Withania somnifera is a berry which is 2.5 cm across and red when ripe. The flowering season is from August to September and the fruiting is observed in cold season (Patel, 1968). It grows in wild and under shrub stony places. It originates from Australia, East Asia and Africa. It is cultivated for the medicinal use in several parts of India. The constituents present in the roots of Withania somnifera are believed to be active and studied extensively (Bone, 1996).

Withania somnifera possesses katu, ticta and madhura rasa, ushna veerya and madhura vipaka (Dahanukar and Thatte, 1988). It acts as a potent deepana drug and increases agni bala and it causes amapachana. Owing to its katu and tikta rasa, it has vedana shamana (analgesic) and shothaharna (anti-inflammatory) properties. It alleviates aggravated vata and kaffa dosha and breaks the aetio-pathogenesis of disease process. The research has showed that withanolides which are similar to the body’s own steroid hormones are anti-inflammatory (Duke, 1985). It is considered to be tonic and rasayana which increases the vitality. Therefore, there is a feeling of general well-being and improvement in the patients due to its higher iron contents. It increases the haemoglobin and reduces the erythrocyte sedimentation rate by reducing the inflammatory disease
process due to its properties (Majumdar, 1995).

The roots of Ashwagandha contain various alkaloids viz. withanolides (Nittala and Lavie, 1981 and Atta et al., 1991), withanins and withaferins (Devi et al., 2000). The roots also contain flavonoides and reducing sugars (The Wealth of India, 1976). The active principles present in the roots of *Withania somnifera* bear resemblance, both in their action and appearance to the active constituents of Asian ginseng (*Panax ginseng*) called as ginsenosides. Due to its similarity with *Panax ginseng*, it is also called as Indian ginseng. Chinese medicine recommends the roots of *Withania somnifera* in cases of nervousness, insomnia, weakness, anemia, rheumatic pains, general debility, impotence and infertility among other conditions (Malhotra et al., 1965).

Ashwagandha always had a prominent place in the Ayurvedic and Unani medicines. This plant is endowed with curative properties against a number of diseases including cancer (Asthana and Raina, 1989) and finds mention in the ancient medical treatise of India (Charak Samhita, 1949).

Since many uses of Ashwagandha have been scientifically validated, skepticism can naturally be expected when presented as herb which is useful in so many preparations. In Ayurvedic medicines, there is a class of herbs, including *Withania somnifera* called as adaptogen or vitalizer. *Withania somnifera* acts as an adaptogenic herb with multiple nonspecific actions that counteract the effect of stress and promote wellness. The term adaptogen was first coined by a Russian scientist, Lazarev in 1947 while working on a synthetic compound, dibazol (2-benzyl-benzimidazole) which was found to
stimulate nonspecific resistance of organisms (Brekhman and Dardymov, 1969). An adaptogen is any substance that puts the organism into a state of non-specific heightened resistance against stress and extraordinary challenges. The idea of an adaptogen is that, it will lessen the reaction of the charm phase and delay the exhaustion phase. Adaptogens are known to prevent negative effects of radiation, toxins and prolonged cold exposure in animal studies. Adaptogen causes adaptogenic reactions and appears to produce a state of non-specific increased resistance (Singh et al., 1982 and Lazarev, 1969) to adverse effects of physical, chemical and biological agents. They are relatively innocuous, have no specific mechanism of action, normalize pathological effects and are usually glycosides or alkaloids of the plant (Rege et al., 1999). Although the Panax ginseng is considered a powerful adaptogen, several studies have shown Ashwagandha to be superior to Panax ginseng as an anti-stress adaptogen. The active principles of Withania somnifera are classified in Ayurveda as dravya rasayanas which form important constituents of the Ayurvedic concept of preventive medical care, aimed at improving the quality of life while promoting the longevity (Sharma et al., 1986). Rasayanas are claimed to improve physical and mental health, increase the resistance of body to the infection and other external factors tending to perturb the homeostasis of human system and promote the revival of physiological functions (Ghosal et al., 1989). The word rasayana, literally means the path that Rasa takes (Rasa: Primordial tissue/ plasma and ayana: path). It is believed in Ayurveda that the qualities of the rasa dhatu influence the health of other dhatus (tissues) of the body. Hence any medicine that acts as a rasayana should strengthen the health of all tissues of the body. The rasayana plants prevent aging, re-establish youth,
strengthen life and brain power and prevent disease, all of which imply that they increase the resistance of the body against the onslaught (Sharma, 1983 and Ghanekar, 1981). The major biochemical constituents of Ashwagandha from which its primary properties emanate are based upon the action of certain steroidal alkaloids and steroidal lactones in a class of constituents called as withanolides. These serve as important hormone precursors due to which the body is then able, as needed, to convert them into human physiological hormones. If there is an excess of certain hormone, the plant based hormone precursors occupy the hormone receptor sites. In this way, Ashwagandha, like other adaptogenic tonic herbs, is amphoteric and can serve to regulate important physiological processes, increasing or decreasing as needed. (Shwarting, 1963 and Rahman, 1993).

The roots of *Withania somnifera* are regarded as tonic, restorative, aphrodisiac, anti-tumor (Singh et al., 1986, Chopra et al., 1958, Suffness and Douros, 1982) and also prescribed for consumption and emaciation of children, rheumatism and as a narcotic and diuretic (Saraf and Bhide, 1983).

It is important to note that in approximately 60% of the medicinal plants used in the traditional systems of medicine, roots are the principal material for the drug preparation. It is estimated that more than 90% of the plant species used by the industry are collected from wild and more than 70% of the plant drugs involve destructive harvesting and very few are in cultivation (Sudha and Seeni, 2001).

Currently, pharmaceutical companies are manufacturing most of these compounds by cultivation of whole plants followed by
extraction and purification of desired bioactive compound. The continuous production of desired bioactive compounds requires repeated collection of plant material and consequently leads to the depletion of natural resources. Mass cultivation of medicinal plant species under natural conditions may not be possible due to environmental, ecological, or variable climatic conditions, duration of propagation or the need to use agricultural land to produce the primary food crops. Quality and quantity of the products are also affected by unforeseen environmental conditions (Fulzele, 2000). So, the development of biotechnological methods such as micropropagation, cell or root culture and hairy root culture are the major solutions to circumvent these problems. On these lines, development of fast growing root culture system offers unique opportunities for providing root drugs in laboratory, without resorting to field cultivation. Moreover, the development of root culture is highly advantageous, as it is an alternative method for the clonal propagation and germplasm conservation.

The present work is undertaken with the main aim to develop a system for the in vitro production of active principles from the root organ culture of *Withania somnifera*. 