

Abstract

Withania somnifera is a prevalent medicinal herb used all over the world as a domestic remedy for addressing several age-related ailments. The plant is also one of 32 medicinal plants that have been ranked as priority medicinal plants by the National Medicinal Plant Board (NMPB). Ayurveda refers the field grown *W. somnifera* roots as a *Rasayana* medication (Rejuvenator). It has been used as the major ingredient in a variety of formulations to help slow down the aging process, cope with stress, and be an excellent neuroprotectant. However, the quality and quantity of traditionally cultivated plants present a significant obstacle to their utilization in herbal formulations. This study aims to demonstrate that *in vitro* shoot tissues of *W. somnifera* could be used as an alternative and be as bioactive as roots grown in the field. The HPTLC quantification of major withanolides and GC-MS profiling of metabolites revealed that the pharmacological actives of IS (*in vitro* shoot) showed the overall similar metabolite profile as in FR (field grown roots). As measured by DPPH radical scavenging activity, the antioxidant potential of *in vitro* shoots (IS) was also higher than that of field grown tissues (FR & FS) and *in vitro* roots (IR). The animal model study in *Caenorhabditis elegans* presented numerous lines of evidence regarding the effectiveness of the IS on the health and life expectancy over the FR, IR and FS. Along with this, the study compares the molecular level mechanisms underlying the beneficial effects of FR, IR, FS and IS supplementation by using gene-specific mutants. The efficacy of *W. somnifera* extracts to prevent α -synuclein aggregation, its associated pathologies, and its capability for neuroprotection were studied in Parkinson's disease-modeled worms. The finding of this study highlighted that IS is equally bioactive as traditionally used FR. Moreover, the IS extracts efficiently prolongs the lifespan, health span and stress resistance via insulin/insulin-like growth factor-1 (IGF-1) signaling (IIS) and mitochondrial electron transport chain complexes (mETC). The IS extract is more effectual for suppressing oxidative stress, a remarkable neuroprotectant in Parkinson's disease modeled worms. As the first study to investigate the bioactivity of *W. somnifera* shoots cultivated *in vitro*, these results could contribute to the scaling up of IS culture systems and *in vitro* shoot tissues for treating neurological and age-related ailments, extending patients' lives, and improving their quality of life.