Abstract 3

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ASHWAGANDHA LEAF-DERIVED FACTORS FOR HEALTHY AGEING

Keywords: Ayurveda, Leaf extract, anti-stress

Ashwagandha (Withania somnifera) is a tropical herb that enjoys more than 5000 years of history of use in Indian home medicine 'Ayurveda'. It is extensively used to promote physical and mental health. However, laboratory evidence of its health promoting activities is lacking. We first identified anti-cancer activity in the alcoholic extract of Ashwagandha leaf extract (i-Extract) and found that only cancer cells were killed in response to i-Extract treatment; normal cells remained unaffected. In order to identify the anti-cancer components of i-Extract and its cellular targets in cancer cell killing, we used combined chemical and cell-based loss-of-function screenings using human siRNA and randomized ribozyme libraries. We found that the i-Extract and its component 'withanone' kills cancer cells by, at least, two mechanisms involving selective activation of (i) tumor suppressor protein p53 and (ii) ROS signaling in cancer cells. Biochemical and visual assays were conducted to validate the involvement of selected cellular targets. We further demonstrate that the i-Extract and withanone suppress tumor formation and metastasis in vivo. They also caused induction of proteins involved in cell differentiation and adhesion. Consistently, neuroblastoma and glioblastoma cells were seen to show neuronal differentiation and decrease in migration characteristic. Furthermore, we found that the i-Extract had protective effect in chemically induced models of Parkinson's Alzheimer's diseases. We propose Ashwagandha leaf extract and withanone as effective, cheap and safe reagents for interventions for age-related disorders including cancers and neuro-degeneration that largely affect quality of life in old age.