

# Active Ingredients Enriched Ashwagandha Leaves: Benefits, Bioactives, Biology and Biotechnology

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**Abstract**—Ashwagandha (*Withania somnifera*) has been in use in traditional Indian home medicine system, Ayurveda. Although popular for its use for a variety of preventive and therapeutic potentials the laboratory evidence and molecular mechanisms of action remain largely unknown. In contrast to the traditional use of roots, we have been exploring bioactivities in the leaves of Ashwagandha. We initially demonstrated that both alcoholic (i-Extract) and water extracts (WEX) of Ashwagandha leaves possess considerable anticancer activities. Using multiple experimental and bioinformatics approaches we demonstrated that the two kinds of extracts possess different bioactive constituents and work through independent pathways. Bioactives for anticancer activity were identified as Withanolides, Withanone (Wi-N) and Withaferin A (Wi-A) in the i-Extract, and Triethylene Glycol in the WEX. Molecular insights to understand the mechanism of action revealed that they cause activation of tumor suppressor genes and induction of oxidative stress. Of note, Wi-A showed cytotoxicity not only to the telomerase plus, but also to telomerase negative (ALT) cancer cells suggesting its potency and value as a powerful anticancer drug. Based on our studies, we have formulated a combination of Wi-N and Wi-A that exhibited potent anti-metastasis activity. Furthermore, combination of the extracts and active components were highly potent, endorsing the therapeutic merit of the combinational approach. In view of

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*these findings, we initiated to develop technologies to obtain Active Ingredients Enriched (AIE) Ashwagandha by manipulating its environmental conditions. We demonstrate, for the first time, (i) field raised i-Ashwagandha leaves with high proportion of active withanolides as compared to the roots, (ii) hydroponically raised i-Ashwagandha and characterization of its bioactives, and (iii) method of extraction with enriched bioactive components that may serve as cheap, and economic anticancer drug especially when modern medicine is either not available or limited by severe side effects.*

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