A Water-Soluble Prodrug for the Heat Shock-Inducing Compound Withaferin A

Background: Preparations of the dried root of Withania somnifera, known as ashwagandha, have been used for thousands of years in the Ayurvedic medical tradition; such preparations have been shown to have anti-inflammatory, immunomodulatory, cardioprotective, antioxidant, anti-angiogenic and anti-cancer activity.

University of Arizona investigators discovered that when grown aeroponically, w.somnifera produces a novel class of withanolides that, in vitro, readily convert to Withaferin A and exhibit the anti-proliferative and anti-tumorigenic activities of Withaferin A. Experiments have shown that the novel compounds activate the heat shock response in fibroblasts and inhibit cell proliferation/survival in breast cancer cell lines.

The newly discovered compounds, however, are more water soluble than Withaferin A and, thus, may be more amenable to formulation for in vivo administration.

UA investigators have developed an economically viable and environmentally friendly method for producing and isolating large quantities of both Withaferin A and the novel withanolides. Aeroponic cultivation is a significant achievement as acquiring an abundant supply of starting material is often a significant hurdle in the development of drugs derived from natural products.

Applications:
· Withaferin A analogs may be used to develop antitumor agents with high solubility and low toxicity.

Advantages:
· Large quantities of Withaferin A analogs can be produced cheaply with aeroponic cultivation of w.somnifera.
The compound can be delivered in a water soluble form that makes it an attractive potential cancer treatment. Work is ongoing to determine if this compound has any of the other attractive bioactivities of ashwaganda.

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