

Table of Contents

Speers, Alex - #5630 - Exploring human pharmacokinetics of withanolides, bioactive compounds from the botanical ashwagandha	1
Abstract submission for Institutional Repository	1



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Exploring human pharmacokinetics of withanolides, bioactive compounds from the botanical ashwagandha

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Abstract

Ashwagandha (*Withania somnifera*, WS) is a botanical commonly used in Ayurvedic medicine and other traditional medicine systems. In recent years, WS has gained mainstream popularity as a botanical dietary supplement for its reputed adaptogenic effects, particularly for the relief of insomnia and stress. Withanolides, a class of steroidal lactones that are relatively unique to WS, are thought to be its main bioactive compounds and have been the focus of much research. There is limited data, however, regarding which withanolides are present in human plasma, and at what concentration, following ingestion of WS products. One significant challenge is the lack of good quality reference standards. To address this challenge, our research team is developing liquid chromatography-mass spectrometry (LC-MS) based methods in collaboration with OHSU's Bioanalytical Shared Resource/Pharmacokinetics Core for analyzing withanolides in mouse and human plasma. The analytical methods are based on those initially developed by collaborators at Oregon State University, who have also assisted with verifying the product integrity of commercially available withanolide reference compounds. These LC-MS methods will be applied to future *in vivo* studies in mice and an upcoming trial at OHSU investigating the pharmacokinetics of withanolides from a commercial WS product in older adults. These projects will generate critical data for our understanding of a widely used botanical, while also supporting future studies investigating (a) herb-drug interactions, (b) whether compounds and concentrations showing activity in preclinical models are relevant for efficacy in humans, and (c) the oral absorption of potentially bioactive non-withanolide compounds.