

# Ashwagandha Extracts Protect Hepatocytes from Palmitate Acid Induced Lipid Accumulation and Oxidative Stress

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## ■ Introduction

Ashwagandha (*Withania Somnifera*) is an ayurvedic herb commonly used for a variety of health benefits in Indian traditional home medicine system. It is enriched in steroidal lactones that have been shown to be the bioactives. Among the active withanolides, Withaferin A (Wi-A) has been shown to possess good anticancer activity and Withanone (Wi-N) has been shown to possess antistress and antiaging potentials including improvement of memory and brain function<sup>1-3</sup>. In this study, we aim to investigate the effect of Ashwagandha extracts and some purified withanolides on steatosis, abnormal retention of fat within a cell or organ that often affects liver as non-alcoholic fatty liver disease (NAFLD)<sup>4</sup>.

## ■ Material & methods

Cytotoxicity of these extracts on human hepatocytes (Huh-7) was evaluated by cell viability assays. Nontoxic doses were used to treat the cells subjected to activated lipid accumulation by palmitic acid (PA). The lipolygenesis was evaluated by Oil Red O, triglyceride (TG) assays and Reactive oxygen species (ROS) assays, and the expression of molecules involved in this process.

## ■ Results & discussion

Wi-A and Wi-N have been demonstrated as major bioactive ingredients. Based on this, we engineered methods to obtain extracts from Ashwagandha leaves and stems. The four kinds of extracts; (i) high amount of total withanolides- (a) high ratio of Wi-A and (b) high ratio of Wi-N and (ii) low amount of total withanolides- (a) high ratio of Wi-A and (b) high ratio of Wi-N were selected. Cytotoxicity studies of these compounds showed higher cytotoxicity of (ia); the other three were mild.

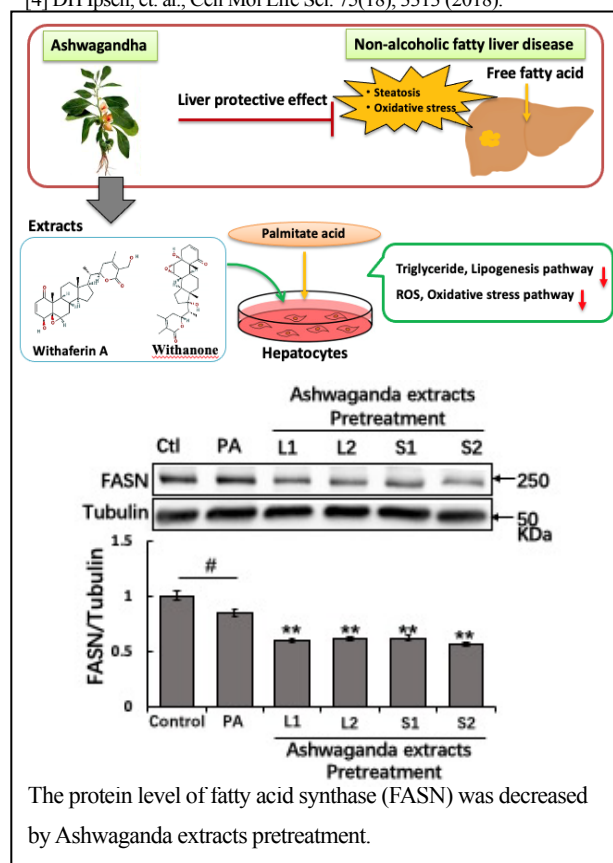
Cells were treated with PA to induce lipid accumulation. We found that in cells pre-treated with specific Ashwagandha extracts, TG and ROS accumulation were decreased. Of note, Sterol regulatory element-binding protein-1c (SREBP-1c), and its downstream effector-Fatty acid synthase (FASN), the key regulators of lipogenesis showed downregulation in specific extract-treated cells. Furthermore, the expression of Peroxisome

proliferator-activated receptor (PPAR) $\gamma$ , a key factor involved in hepatic lipogenesis, showed decrease in cells treated with some of these extracts. PPAR $\alpha$ , the transcription factor that upregulating fatty acid oxidation was induced by PA treatment related to a beneficial effect in preventing lipotoxicity and decreased in specific extract-treated cells.

Ashwagandha extracts may provide a useful natural resource with anti-steatosis and anti-oxidative stress activity, maintaining liver health and NAFLD prevention.

## ■ Reference

- [1] AN Sari, et. al., Cancers (Basel). 12(5), 1160 (2020).
- [2] S Garg, et. al., J Gerontol A Biol Sci Med Sci. 75(6), 1031 (2020).
- [3] S Garg, et. al., Ann. Neurosci. 25(4),201 (2018).
- [4] DH Ipsen, et. al., Cell Mol Life Sci. 75(18), 3313 (2018).



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 (2) Lipid accumulation  
 (3) Oxidative stress