

Milin Jacob George

**THE PHARMACOLOGICAL EFFECTS OF WITHANIA SOMNIFERA
(ASHWAGANDHA)**

Tutor: MD, PhD, associate professor Kotovich I.L.

Department of Pharmacology

Belarusian State Medical University, Minsk

Withania somnifera, commonly known as ‘Ashwagandha’ or ‘Indian winter cherry’ is a plant belonging to the Nightshade family known for its historic use in Ayurveda (a branch of Indian medicine using medications derived from natural sources) to treat diseases such as Parkinson’s disease, Huntington’s chorea, insomnia and many others. It has recently gained popularity due to its potent anxiolytic, anti-stress, anti-inflammatory and adaptogenic effects. There are many valid scientific studies performed on both humans and rats to support its use in modern evidence-based medicine, and it may be on the way to becoming FDA approved.

Typically, the roots of *Withania somnifera* are used, however its berries may also be utilised. The roots are dried and made into a powder referred to as ‘churna’. The powder is usually mixed with ghee (Indian clarified butter), honey or water and is given to the patient per os. Nowadays, the powder may be inserted into cellulose capsules or formed into tablets for oral consumption. According to studies, *Withania somnifera* has rather low oral bioavailability. LD50 is approximately 1750 mg/kg, comparable to Benzodiazepines which have an LD50 of 300-2000 mg/kg. Other pharmacokinetic parameters are not fully understood as of now. The most important chemicals produced by *Withania somnifera* are Withanolides, a group of naturally occurring steroids. The most active Withanolide claimed to produce the pharmacological effects of Ashwagandha is Withaferin A.

Studies have shown that Withaferin A acts on GABA-A receptors producing a strong anxiolytic and anti-stress effect similar to Lorazepam. It was shown that Ashwagandha also has effect on the hypothalamic-pituitary-adrenal axis and decreases the amount of Cortisol in the bloodstream. A study on the anti-stress and anxiolytic effects of Ashwagandha on humans, showed a massive decrease in the serum cortisol levels of all the participants (as compared to placebo) after 8 weeks of taking the preparation. All participants also showed decreased perceived stress scale and Hamilton anxiety scores at the end of the study. Studies in rats also showed a significant anxiolytic effect, confirmed by a decreased level of brain tribulin at the end of the study (tribulin is an endogenous MAO-A and benzodiazepine receptor inhibitor which is usually released in periods of extreme stress and anxiety). The studied rats also showed an astonishing increase in swimming endurance time, from 385 minutes (without Ashwagandha) to 740 minutes (with Ashwagandha). A 12-week study among COPD patients, proved that taking Ashwagandha along with the regular treatment for COPD greatly decreased the number of exacerbations and symptoms as compared to taking the generic treatment alone. Advanced mass spectrometry techniques revealed that the Withanolides present in Ashwagandha blocked angiotensin converting enzyme-2, myeloperoxidase and IL-6 receptors resulting in a profound anti-inflammatory effect. Significant anti-inflammatory effects were also observed in rats with collagen-induced arthritis, showing results similar to methotrexate. A study on the effects of Ashwagandha on stress-induced ulcers in rats showed positive anti-ulcer effects. Ashwagandha also showed satisfactory anti-malignancy effects on urethane-induced lung adenomas in mice and hamsters when combined with chemo- and radiotherapy, and showed mild leukocytosis which may help to maintain the immunity of patients undergoing cancer therapy.

The most common side-effects included increases in liver enzymes (AST, ALT, GGT) which may indicate liver damage, however this was only observed in patients with comorbid conditions. Other rarely occurring side effects include rhinitis, constipation, cough, drowsiness, and reduced appetite.

In conclusion, Ashwagandha has great potential for its use in modern medicine and further studies in both humans and rats are warranted.