Molecular insights to the dose-dependent activities of Ashwagandha extracts

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Background- Stress is an inevitable component of life. Several herbs are known for their health-supporting effects that range from treatment of stress, common cold to cancer. We investigated the dose-dependent effect of Ashwagandha (*Withania somnifera*) extracts on human normal and cancer cells, and have attempted to resolve the molecular mechanisms of their antistress activities.
Methods- Ashwagandha extracts were chemically profiled by HPLC. Cytotoxicity was determined by viability assays. Biochemical and immunoimaging assays were performed using specific antibodies.
Results- Human normal cells treated with low doses of the leaf extract or purified withanolides (Withaferin A or Withanone) showed no toxicity. Such non-toxic doses were selected for anti-stress, neurodifferentiation and neuroregenerative assays. We found that whereas normal cells exposed to oxidative and UV stresses showed poor viability/growth arrest/apoptosis, cells treated with low doses of Ashwagandha extracts were protected. Brain-derived cells exposed to glutamate and scopolamine stresses showed protection and strong differentiation as marked by expression of neurodifferentiation markers. Muscle-derived cells cultured in low doses of extract showed muscle differentiation as marked by expression of muscle differentiation markers. Most recently, using computational tools, we examined potential of Ashwagandha for anti-SARS-CoV-2 virus activity, and found that most of the Ashwagandha Withanolides have potential to block cell surface receptors (ACE2 and TMPRSS2) that are involved in entry of virus to human cells. Furthermore, Ashwagandha treated cells showed decrease in ACE2 and TMPRSS2 expression suggesting its potential in blocking virus infection.
Conclusion- Ashwagandha extracts and withanolides possess useful bioactivities.