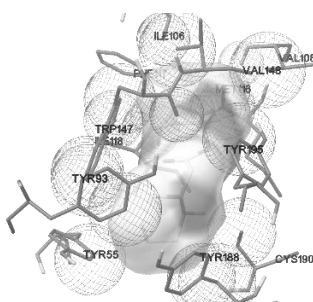


Molecular Docking Analysis to Elucidate the Potential Drug Action of Phytochemicals Present in Ashwagandharishta towards Memory Related Disorders

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Ashwagandharishta is an Ayurveda medicine that is used to treat psychiatric conditions, dullness, memory related diseases, sluggishness, epilepsy, depression, anxiety, schizophrenia. The main plant ingredient used to prepare this is *Withaniasomnifera*. It contains various classes of secondary metabolites such as steroidal lactones, phytosterols, sitoindosides and alkaloids. Memory-related disorders are closely associated with the defects in cholinergic neurotransmission. Repairing mechanisms for these defects provide promising treatment strategies for these kinds of disorders. The most abundant receptor found in cholinergic neurotransmission is nicotinic acetylcholine receptor. *Alpha-7* nicotinic acetylcholine receptor is a sub type of nicotinic acetylcholine receptor and has been identified as one of the most useful drug target for the treatment of nervous system related disorders. Potential agonists of *alpha-7* nicotinic acetylcholine receptor have shown to be enhancers of cognitive performance when memory related disorders are treated.

Molecular docking analyses have been carried out to identify any possible secondary metabolites present in Ashwagandharishta that could act as agonists of *alpha-7* nicotinic acetylcholine receptor using AutoDock4 software package. Four possible phytochemicals have been selected based on drug likeness, blood brain barrier penetrability and agonistic binding ability with the receptor. Their docked conformations, binding at correct binding site, binding energies and dissociation constants (kI) have been further investigated computationally



Based on the molecular docking studies it was revealed that anaferine and anahygrine possessed lower binding energies with compared to the binding energy of nicotine while cuscohygrine showed relatively higher energy in binding. When kI (dissociation constant) values were compared, anaferine and anahygrine possessed relatively higher values than that of nicotine. According to computational studies, cuscohygrine and palletierine showed some tendency to bind nonspecifically at other sites of the receptor. However, nonspecific bindings for anaferine and anahygrine were not energetically favorable. According this computational investigation, it has been found that two phytochemicals (anaferine and anahygrine) show promising agonistic activity towards the receptor. Thus anaferine and anahygrine have high possibility to serve as *alpha-7*nAChR agonists which show potential drug action towards memory related disorders.

Keywords: Ashwagandharishta, Phytochemicals, Anaferine, Anahygrine, *Alpha-7* Nicotinic Acetylcholine

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