**Notification No.: 593/2026**

**Date of Award: 26/12/2025**

**Name of the Scholar:** Sneh Prabha

**Name of the Supervisor:** Prof. Sonu Chand Thakur

**Name of the Co-Supervisor:** Prof. Md. Imtaiyaz Hassan

**Topic of Research:** Computational Approach for the Identification of Bioactive Compounds from *Berberis lycium* against Alzheimer's Disease

**Keywords:** Alzheimer's disease; Amyloid beta; *Berberis lycium;* Bioactive compounds; Differentially expressed genes; Feed Forward Loop; Gene set enrichment analysis; Kinases; Microarray analysis; Protein-Protein Interaction; Tau hyperphosphorylation

## Findings

Alzheimer's disease (AD) is a leading cause of dementia, affecting more than 24.3 million people worldwide in 2024. Understanding the risk factors and mechanisms underlying AD is crucial for developing effective treatments. Compared to synthetic drugs, natural products (NPs) are promising drug candidates due to their structural diversity, bioactivity, and lower toxicity. NPs derived from medicinal plants have reported neuroprotective properties and possess medicinal properties reported to modulate kinase activity with lower toxicity than synthetic drugs while reducing inflammation and improving neuronal health.

We selected the medicinal plant *Berberis lycium* (*B.ly.*), native to the Himalayan region of the northwest Indian subcontinent, to study its therapeutic effects on AD target proteins. B.ly. extracts exhibit anti-ulcer, antidiabetic, antimicrobial, and antioxidant properties and have been reported to attenuate chemotherapy induced toxicity and drug induced neuronal damage. Alkaloids present in B.ly. show strong free radical scavenging activity and promote autophagy, which may aid clearance of neurofibrillary tangles and amyloid plaques.

Microarray analysis of hippocampal gene expression datasets (GSE1297, GSE28146, GSE29378) identified 346 significant genes, including 103 upregulated and 243 downregulated genes. Network and pathway analyses revealed 47 key AD related genes. FFL analysis indicated upregulation of MYO1C and downregulation of RELA, SOCS3, TBP, AXIN1, CCND1, and YWHAZ associated with hyperactivation of tau kinases CDK5, GSK3β, MAPK14, Fyn, and MARK2. Virtual screening identified Canadine, THB, and N MTHB as potential Fyn inhibitors with favorable ADMET properties. Molecular dynamics and MM/PBSA analyses confirmed stable binding, with Fyn N MTHB showing the highest affinity. Apigenin-7-O-glucoside (A7OG) showed stable multitarget interactions with CDK5, Fyn, MAPK14, MARK2, and GSK3β. These findings suggest Canadine, THB, and A7OG as potential modulators of tau hyperphosphorylating kinases for AD therapy. These findings highlight the potential of *B.ly.* derived compounds as modulators of tau hyperphosphorylating kinases and support their further investigation as therapeutic candidates for Alzheimer's disease.