

# Molecular interaction studies of secondary metabolites of the lichen *Asahinea scholanderi* with acetylcholinesterase and butyrylcholinesterase



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## Introduction

Lichens, due to their symbiotic origin, have important properties for pharmacological research. This study focuses on the lichen *Asahinea scholanderi* (Llano) W.L. Culb. & C.F. Culb, which belongs to Parmeliaceae family and specifically to **Cetrarioid clade**.

According to its morphology, *Asahinea scholanderi* has a foliose growth form. These lichens are more widely distributed in **North America and Siberia**. This species grows over boulders and on humus in the tundras.



The etiology of Alzheimer's disease and other dementias is related with the degeneration of cholinergic neurons. Disruption in **cholinergic neurotransmission** affects to cognitive processes as memory and learning. The enzymes **acetylcholinesterase (AChE)** and **butyrylcholinesterase (BuChE)** degrade acetylcholine into the inactive metabolites. Therefore, inhibitors of cholinesterase enzymes are key in the prevention of Alzheimer's disease progression. Previous works with *Asahinea scholanderi* extracts showed IC<sub>50</sub> values 0.11 mg/mL for AChE and 0.29 mg/mL for BuChE inhibitory activities.

## Objectives

- ❖ Identification of the **major bioactive metabolites** of *Asahinea scholanderi*.
- ❖ Delve into the study of the **inhibition of the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE)** by the secondary metabolites from *Asahinea scholanderi*.

## Material and methods



**HPLC:** Agilent 1260 instrument. **Column:** reversed-phase Mediterranean Sea18 column (150 mm × 4.6 mm, 3 μm). **Phases:** (A)->1% orthophosphoric acid in milli-Q water, (B)->UHPLC-methanol. **Flow rate:** 0.6 ml/min. **UV spectrum** (190 and 400 nm)



### Docking studies

- Protein structures using Protein Preparation Wizard tool available in Schrödinger Suite.
- Chemical structures were built using Maestro Build Panel and processed with LigPrep.
- Molecular docking experiments using Glide 20-23 in the Extra Precision mode (XP) software.

## Results

### Phytochemical analysis and Docking studies

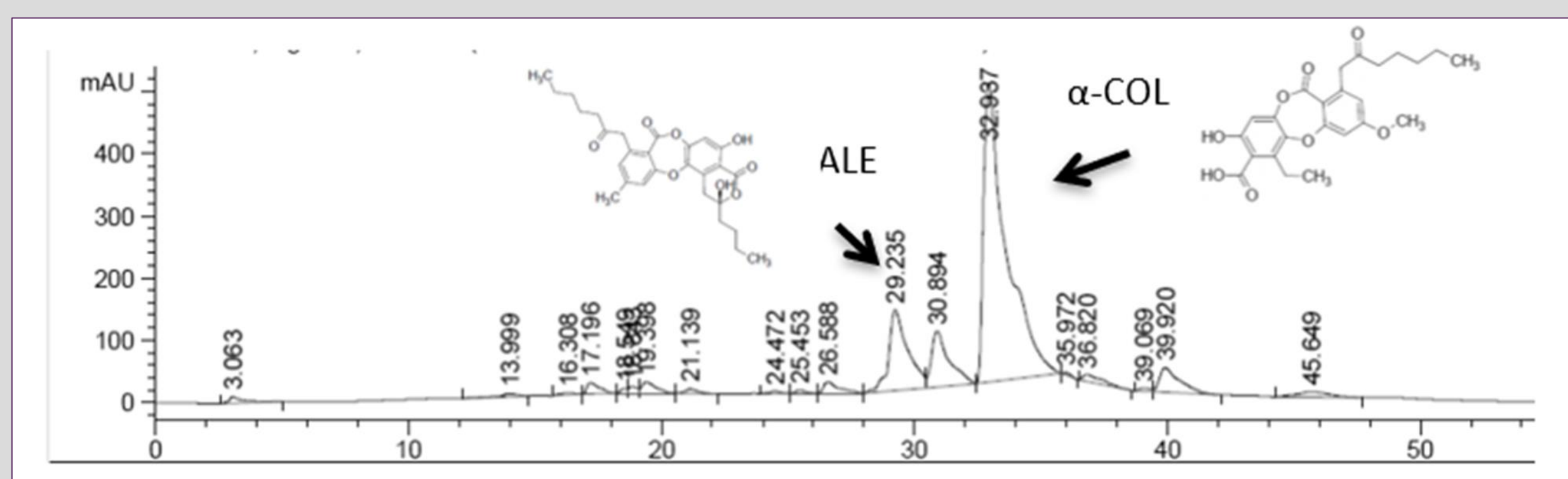
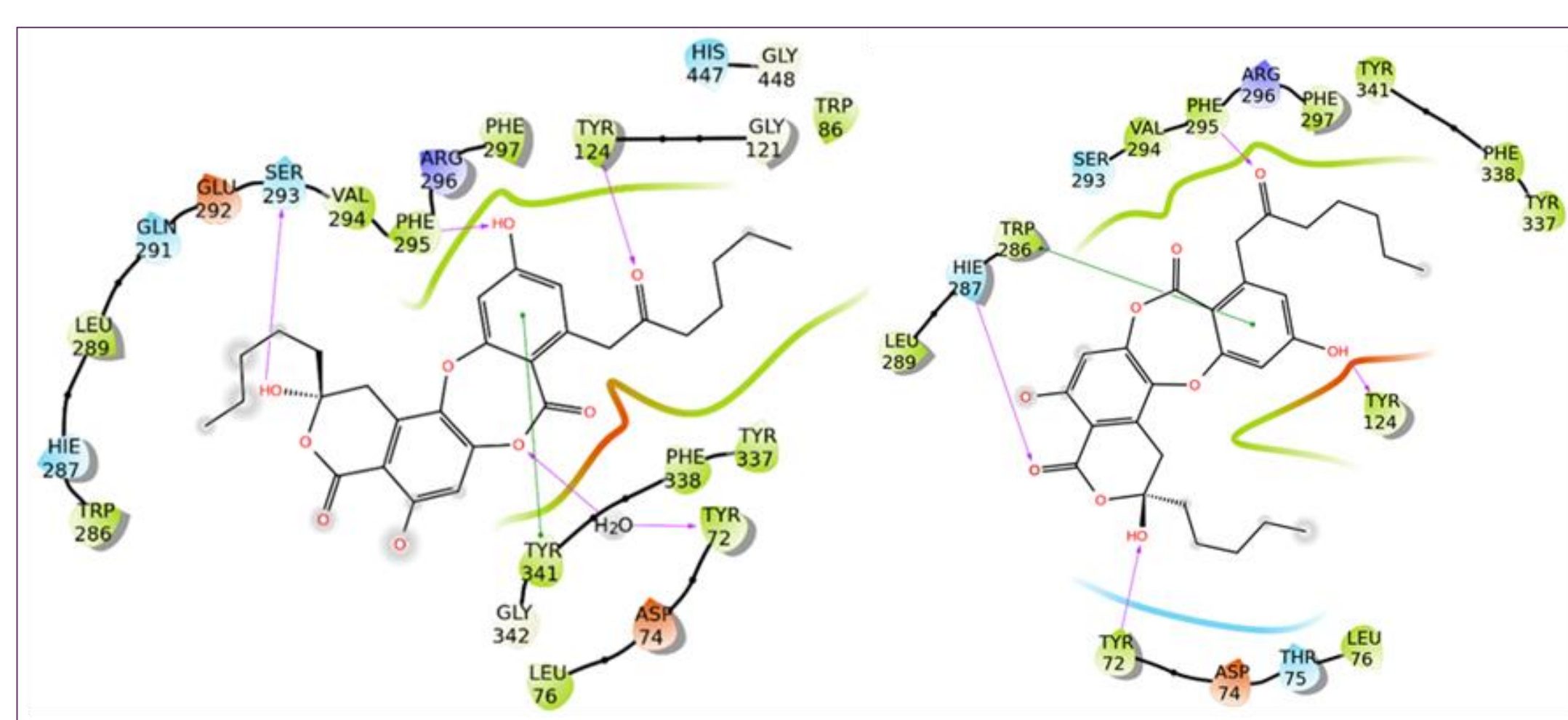


Figure 1. Representative HPLC chromatogram *Asahinea scholanderi* methanol extract at 254 nm.

Table 1. Predicted binding affinity between the compounds and enzymes (AChE and BuChE).

Compound	AChE		BuChE	
	With H <sub>2</sub> O	Without H <sub>2</sub> O	With H <sub>2</sub> O	Without H <sub>2</sub> O
Acetylcholine	-8.5	-7.4	-4.1	-5.1
Donepezil (AChE)	-18.5	-15.7	-15.9	-10.5
Naphthamide (BuChE)	-10.8	-11.1	-6.2	-6.6
Alpha-collatolic acid	-7.2	-9.9	-5.5	-6.7

A)



B)

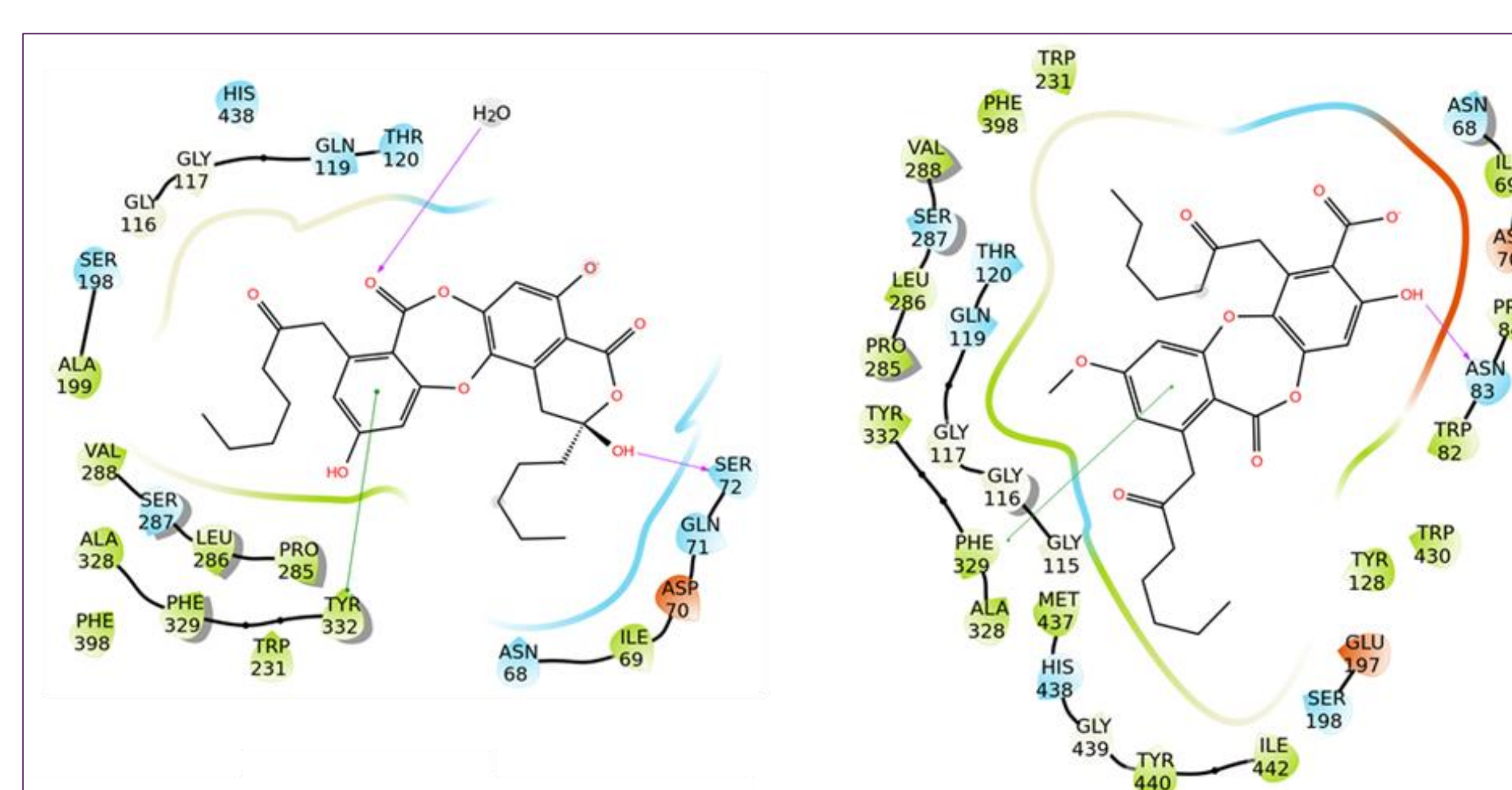


Figure 2. Protein-ligand interactions for alectoronic acid: A) with AChE B) with BuChE, with (left) and without (right) water molecules included in the binding site. Hydrogen bonds are represented by pink arrows and  $\pi$ - $\pi$  stackings are represented by green lines. Hydrophobic residues are in green, polar residues are in cyan, negatively charged residues are in red, positively charged ones are in blue, glycine residues and water molecules are in white.

## Conclusions

- The major compounds of *Asahinea scholanderi* identified by HPLC were **alectoronic acid** and **collatolic acid**.
- **Alectoronic acid** exhibited strong interactions with both AChE and BChE with and without water molecules in the binding site, even more than Ach.
- These molecules should be further investigated as **cholinesterase inhibitors** for the prevention and treatment of Alzheimer's disease.

## Bibliography

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