## Natural isoquinoline alkaloids as potential multi-target agents against Alzheimer's disease

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**Statement of the Problem:** Alzheimer's disease (AD) is the most prevalent neurodegenerative disorder and main form of dementia in elder people. AD is a multifactorial disorder with a complex pathogenesis, characterized by a progressive loss of memory and other cognitive abilities, associated with cholinergic detriment. Currently, cholinesterase inhibitors are the only approved drugs for treatment of AD; however, these only improve cognitive ability and have significant side effects. Consequently, the development for new therapeutically agents more effective and safety is necessary. Multi-target therapy is an innovative strategy focused on the treatment of complex diseases which arises to overcome lack of traditional paradigm "one molecule-one target". New generation of multi-target agents required not only to improve symptoms, but also to modify the disease.

**Methodology:** We achieved the AChEI-targeted isolation of isoquinoline alkaloids from *Ocotea discolor* (*Lauraceae*) and *Zanthoxylum schreberi* (*Rutcaeea*). Based on the amyloid hypothesis, was evaluated the multimodal potential. Thus, were assessed the anticholinergic activity against acetylcholinesterase (AchE) and butyrylchlolinesterase (BChE); antioxidant capacity (DPPH and β- carotene) and LXR agonists activity.

**Findings:** The studied species were selected from a previous screening of antioxidant and anticholinergic activity carried out in our laboratory. From the wood of *O. discolor* were isolated 3 aporphine alkaloids ocoxilonine, ocoteine and dicentrine. On the other hand, from the stem bark of *Z. schreberi* were isolated 2 protoberberines (berberine and columbamine) and a benzophenanthridine (chelerythrine). Four of the isolated alkaloids showed strong inhibition of AChE with IC50 lower than 50 µg/mL. Most of these were more active against AChE than BChE, nevertheless, columbamine and ocoxilonine were selective against BChE. The aporphine alkaloids presented highest antioxidant capacity. Additionally, the isolated alkaloids showed potential inhibition of LXR.

**Conclusion & Significance:** Isoquinoline alkaloids have multimodal prospective due to their activity against different AD targets, abundant distribution and few pharmacological studies.

### Speaker Biography

Erika Plazas G is a PhD student, Chemist with Master's in Science degree. Her experience in Natural Products Chemistry has been encouraging a growing interest in Medicinal Chemistry and Bioprospecting. Also, she has experience in research, evaluation, teaching and experimental work, specifically in Phytochemistry, Organic and Analytical Chemistry. Additionally, she has skills in natural products, biological activity assays, extraction, purification and identification techniques and management of instrumental (HPLC and GC) and spectroscopic (UV, IR, MS and NMR) methods, as well as, programs for multivariate statistical analysis (PCA, OPLS-DA) focused on metabolomic studies.

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