

UNIVERSIDAD DE LA FRONTERA

Facultad de Ingeniería y Ciencias

Doctorado en Ciencias de Recursos Naturales



**EVALUATION OF ACETYLCHOLINESTERASE
INHIBITORY ACTIVITY AND MODULATORY
EFFECT ON NICOTINIC ACETYLCHOLINE
RECEPTORS OF ALKALOIDS ISOLATED FROM
*Rhodolirium andicola***

**DOCTORAL THESIS IN FULFILLMENT OF
THE REQUIREMENTS FOR THE
DEGREE DOCTOR OF SCIENCES IN
NATURAL
RESOURCES**

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“Evaluation of acetylcholinesterase inhibitory activity and modulatory effect on nicotinic acetylcholine receptors of alkaloids isolated from *Rhodolirium andicola*”

Esta tesis fue realizada bajo la supervisión del director de Tesis Dra. ANA MUTIS TEJOS, y bajo la co-tutela del Dr. EMILIO HORMAZÁBAL URIBE, pertenecientes al Departamento de Ciencias Químicas y Recursos Naturales de la Universidad de La Frontera, y es presentada para su revisión por los miembros de la comisión examinadora.

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Thesis summary

"The conventional approach for neurodegenerative diseases like Alzheimer's involves using acetylcholinesterase (AChE) inhibitors to address deficits in the neurotransmitter acetylcholine. Various compounds, both synthetic and natural, have been FDA-approved as AChE inhibitors. While synthetic compounds like donepezil and rivastigmine effectively treat Alzheimer's, they often lead to side effects. Natural compounds such as galantamine and physostigmine exhibit fewer side effects. This study aims to investigate the alkaloid composition of the plant *Rhodolirium andicola*, a native Amaryllidaceae species in Chile, and its potential as an AChE inhibitor. The research also explores these compounds' effects on nicotinic acetylcholine receptors (nAChRs) as potential therapies. Alkaloids from plant bulb extracts, including galantamine, display inhibitory activity against AChE. In silico analysis identifies potential additional AChE inhibitors. Galantamine is found to inhibit nAChRs, particularly $\alpha 7$, suggesting that *R. andicola* could be a valuable source of AChE inhibitors for treating neurodegenerative diseases."