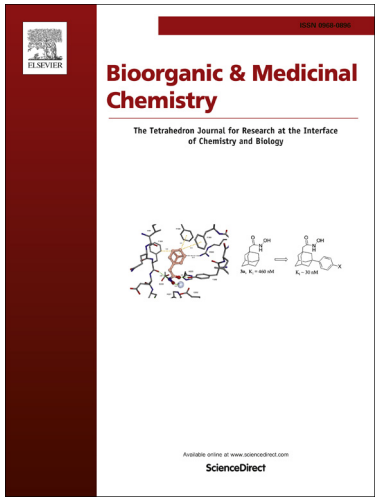

Preparation, anticholinesterase activity and molecular docking of new lupane derivatives

María Julia Castro, Victoria Richmond, Carmen Romero, Marta S. Maier, Ana Estévez-Braun, Ángel G. Ravelo, María Belén Faraoni, Ana Paula Murray

PII: S0968-0896(14)00315-0
DOI: http://dx.doi.org/10.1016/j.bmc.2014.04.050
Reference: BMC 11545

To appear in: *Bioorganic & Medicinal Chemistry*

Received Date: 12 March 2014
Revised Date: 16 April 2014
Accepted Date: 25 April 2014

Please cite this article as: Castro, M.J., Richmond, V., Romero, C., Maier, M.S., Estévez-Braun, A., Ravelo, Á., Faraoni, M.B., Murray, A.P., Preparation, anticholinesterase activity and molecular docking of new lupane derivatives, *Bioorganic & Medicinal Chemistry* (2014), doi: http://dx.doi.org/10.1016/j.bmc.2014.04.050

Preparation, anticholinesterase activity and molecular docking of new lupane derivatives

María Julia Castro[a], Victoria Richmond[b], Carmen Romero[c], Marta S. Maier[b], Ana Estévez-Braun[c], Ángel G. Ravelo[c], María Belén Faraoni[a], Ana Paula Murray[a,*]

[a] *INQUISUR-CONICET, Departamento de Química, Universidad Nacional del Sur, Av. Alem 1253, B8000CPB, Bahía Blanca, Argentina*

[b] *UMYMFOR (CONICET-UBA) and Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Ciudad Universitaria, Pabellón 2, 1428 Buenos Aires, Argentina*

[c] *Instituto Universitario de Bio-Orgánica (CIBICAN), Av. Astrofísico Francisco Sánchez 2, 38206, Departamento de Química Orgánica, Universidad de La Laguna, Tenerife, Spain*

* Corresponding author. Tel.: +54 291 4595101.

E-mail address *apmurray@uns.edu.ar*

ABSTRACT

A set of twenty one lupane derivatives (**2**-**22**) was prepared from the natural triterpenoid calenduladiol (**1**) by transformations on the hydroxyl groups at C-3 and C-16, and also on the isopropenyl moiety. The derivatives were tested for their inhibitory activity against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) and some structure-activity relationships were outlined with the aid of enzyme kinetic studies and docking modelization. The most active compound resulted to be 3,16,30-trioxolup-20(29)-ene (**22**), with an IC_{50} value of 21.5 μM for butyrylcholinesterase, which revealed a selective inhibitor profile towards this enzyme.

Keywords: Alzheimer's disease; cholinesterase inhibitors; lupane derivatives; triterpenoids; molecular modelling