

Strategies for the Generation of Triazolylpeptidyl Penicillin Analogs in the Search for New Antitumoral Compounds [†]

Nadia L. Martiren ¹, Sofia Bajicoff ², Yanina Bellizzi ², Elizabeth Barrionuevo ², Viviana C. Blank ², Leonor P. Roguin ², Ernesto G. Mata ^{1,*}, Patricia G. Cornier ^{1,*}

¹ Instituto de Química Rosario (CONICET-UNR) Facultad de Ciencias Bioquímicas y Farmacéuticas Universidad Nacional de Rosario, Suipacha 531, S2002LRK, Rosario, Argentina; martiren@iquir-conicet.gov.ar (N.M.)

² Departamento de Química Biológica, Instituto de Química y Fisicoquímica Biológicas (IQUIFIB), Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956, C1113AA, Buenos Aires, Argentina; sofibajicoff@gmail.com (S.B.); yaninabellizzi@gmail.com (Y.B.); arielely@hotmail.com (E.B.); vblank@qb.ffyb.uba.ar (V.C.B.); rvroguin@qb.ffyb.uba.ar (L.P.R.)

* Correspondence: mata@iquir-conicet.gov.ar (E.G.M.); cornier@iquir-conicet.gov.ar (P.G.C.);

[†] Presented at The Sixth International Meeting of Pharmaceutical Sciences (RICiFa), November 10-12, 2021, Córdoba, Argentina

Received: 26.04.2022; Revised: 4.05.2022; Accepted: 6.05.2022; Published: 8.05.2022

Abstract: Molecular hybridization methodology and solid-phase organic synthesis were employed by our research group to afford a library of compounds that conjugate a penicillin moiety with amino acids through a triazole group. These triazolyl peptidyl penicillins were evaluated as antiproliferative agents' *in vitro*, showing outstanding activity and selectivity. Motivated by these previous results, we designed three sets of peptoid analogs with strategic modifications aiming at different goals. One approach is based on *N*-substituted glycine to study the performance of these bioisosteres. Another strategy was the substitution of triazole moiety with a glycine monomer to assess the effect of this particular heterocycle on biological activity. And finally, we have developed a new approach to generate the triazole group to simplify the synthetic path. The desired compounds were synthesized using mainly a solid-phase approach. The cytotoxic effect was evaluated against the B16-F0 cell line and compared with the effects on normal murine mammary gland cells (NMuMG). A library of peptoid derivatives was obtained with good yields, and a preliminary structure-activity relationship was investigated.

Keywords: peptoid; solid-phase synthesis; antitumoral compounds.

© 2022 by the authors. This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Funding

This research was funded by CONICET (PUE-2016), ANPCyT (PICT 2017-2694), Agencia Santafesina de Ciencia, Técnica e Innovación (ASACTEI)(AC – 2015-00005), and Universidad Nacional de Rosario (BIO 514). We also acknowledge the support of CONICET (PIP 0154), ANPCyT (PICT 2017-1278), and Universidad de Buenos Aires (2018-2020, UBACYT 20020170100041BA).

Acknowledgments

N. Martiren thanks CONICET (PUE-2016) for the fellowship. CONICET, ANPCyT, UNR, UBA.

Conflicts of Interest

The authors declare no conflict of interest.