Chalcones and 4-hydroxy-2-quinolinone-triazole hybrid derivatives a, b and c as potential anti-inflammatory agents

Nikitas Georgiou[a], Andromachi Tzani[b], Ioanna Kostopoulou[b], Maria-Anna Karadendrou[b], Kyriaki Vavougyiou[a], Primoz Sket[c], Janez Plavec[c], Demeter Tzeli[d,e], Anastasia Detsi[b], Thomas Mavromoustakos[a]

[a]*Laboratory of Organic Chemistry, Department of Chemistry, National and Kapodistrian University of Athens, Panepistimioupolis Zografou, 11571 Athens, Greece*

[b]*Laboratoryof Organic Chemistry, Department of Chemical Sciences, School of Chemical Engineering, National Technical University of Athens, HeroonPolytechniou9, ZografouCampus, 15780 Athens, Greece*

[c]*SlovenianNMR Centre, National Institute of Chemistry, SI-1001 Ljubljana, Slovenia*
[d]*Laboratoryof Physical Chemistry, Department of Chemistry, National and Kapodistrian University of Athens, Panepistimioupolis Zografou, 11571 Athens, Greece*

[e]*Theoreticaland Physical Chemistry Institute, National Hellenic Research Foundation, 48 VassileosConstantinou Ave., 11635 Athens, Greece*

4-Hydroxy-2-quinolinones are heterocyclic compounds with various biological activities, including anti-inflammatory and antifungal effects. Their adaptable structure allows for modifications to enhance bioactivity. This study involved the synthesis of a hybrid molecule with an N-benzyl-triazole group added to the 4-hydroxyquinolinone framework to evaluate its impact on lipoxygenase inhibition. The compound 1,3-diphenylprop-2-en-1-one, commonly referred to as "chalcone" (a term introduced by Kostanecki and Tambor), is also known as benzalacetophenone or benzylidene acetophenone. Specifically, chalcone derivatives b and c were explored as potential drug candidates. Their structures were analyzed using 2D NMR spectroscopy and Density Functional Theory (DFT), while docking and molecular dynamics simulations assessed their binding affinity to the LOX-5 enzyme. *In silico* studies and DFT calculations indicated favorable binding, and in vitro experiments confirmed promising results against lipoxygenase

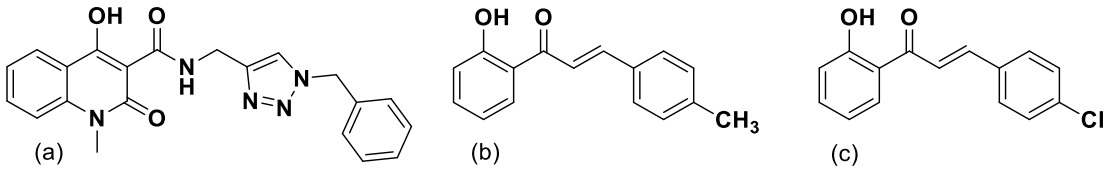

Figure 1: Structures of a 4-hydroxy-2-quinolinone-triazole (a) and chalcone hybrid derivatives (b,c).

References

1) Kostopoulou, I., Diassakou, A., Kavetsou, E., Kritsi, E., Zoumpoulakis, P., Pontiki, E., Hadjipavlou-Litina D., Detsi, A. *Molecular Diversity*, 25, (2020), 723-740.

2) Detsi, A**.**, Bouloumbasi, D., Prousis, K. C., Koufaki, M., Athanasellis, G., Melagraki, G., Afantitis, A., Igglessi-Markopoulou, O., Kontogiorgis, C., Hadjipavlou-Litina, D. J., 50, (2007)**,** 2450-2458.