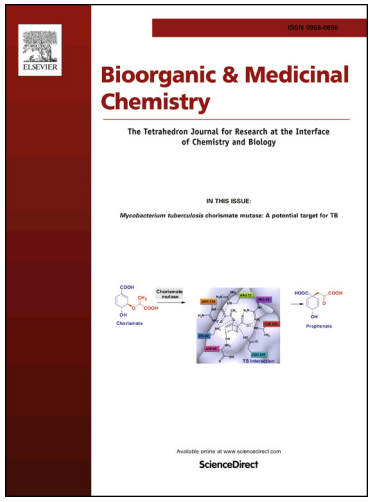
Accepted Manuscript



Inhibition of *Malassezia globosa* carbonic anhydrase with phenols

Yeganeh Entezari Heravi, Silvia Bua, Alessio Nocentini, Sonia Del Prete, Ali Akbar Saboury, Hassan Sereshti, Clemente Capasso, Paola Gratteri, Claudiu T. Supuran

PII: S0968-0896(17)30320-6
DOI: http://dx.doi.org/10.1016/j.bmc.2017.03.026
Reference: BMC 13624

To appear in: *Bioorganic & Medicinal Chemistry*

Received Date: 14 February 2017
Revised Date: 9 March 2017
Accepted Date: 15 March 2017

Please cite this article as: Heravi, Y.E., Bua, S., Nocentini, A., Del Prete, S., Saboury, A.A., Sereshti, H., Capasso, C., Gratteri, P., Supuran, C.T., Inhibition of *Malassezia globosa* carbonic anhydrase with phenols, *Bioorganic & Medicinal Chemistry* (2017), doi: http://dx.doi.org/10.1016/j.bmc.2017.03.026

Inhibition of *Malassezia globosa* carbonic anhydrase with phenols

Yeganeh Entezari Heravi,[1,2] Silvia Bua,[2] Alessio Nocentini,[2,3] Sonia Del Prete,[2,4] Ali Akbar Saboury,[5] Hassan Sereshti[1], Clemente Capasso,[4] Paola Gratteri,[3] Claudiu T. Supuran[2]*

[1]Department of Chemistry, Faculty of Science, University of Tehran, Tehran, Iran.

[2] Università degli Studi di Firenze, Department NEUROFARBA – Pharmaceutical and nutraceutical section, University of Firenze, via Ugo Schiff 6, I-50019 Sesto Fiorentino, Firenze, Italy.

[3] Università degli Studi di Firenze, Department NEUROFARBA – Pharmaceutical and nutraceutical section; Laboratory of Molecular Modeling Cheminformatics & QSAR, University of Firenze, via Ugo Schiff 6, I-50019 Sesto Fiorentino, Firenze, Italy.

[4] Istituto di Bioscienze e Biorisorse (IBBR)– CNR, Via P. Castellino 111, 80131 Napoli, Italy.

[5] Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran.

Abstract. A panel of 22 phenols was investigated as inhibitors of the β-class carbonic anhydrase (CAs, EC 4.2.1.1) from the fungal parasite *Malassezia globosa* (MgCA), a validated anti-dandruff drug target. The displayed inhibitory activities were compared to the ones previously reported against the off-target widely distributed human (h) isoforms hCA I and II. All tested phenols possessed a better efficacy in inhibiting MgCA than the clinically used sulfonamide acetazolamide, with K_Is in the range of 2.5 and 65.0 μM. A homology-built model of MgCA was also used for understanding the binding mode of phenols to the fungal enzyme. Indeed, a wide network of hydrogen bonds and hydrophobic interactions between the phenol and active site residues were evidenced. The OH moiety of the inhibitor was observed anchored to the zinc-coordinated water, also making hydrogen bonds with Ser48 and Asp49. The diverse substituents at the phenolic scaffold were observed to interact with different portions of the hydrophobic pocket according to their nature and position. Considering the effective MgCA inhibitory properties of phenols, beside to the rather low inhibition against the off-target hCA I and II, this class of compounds might be of considerable interest in the cosmetics field as potential anti-dandruff drugs.

Keywords: carbonic anhydrase; β-class enzyme; phenol; *Malassezia globosa,* docking