Synthesis of new 3-(2-mercapto-4-oxo-4H-quinazolin-3-yl)-benzenesulfonamides with strong inhibition properties against the tumor associated carbonic anhydrases IX and XII

By: Bozdag, M (Bozdag, Murat)[1,4]; Alafeefy, AM (Alafeefy, Ahmed Mahmoud)[2]; Altamimi, AM (Altamimi, Abdul Malik); Carta, F (Carta, Fabrizio)[1]; Supuran, CT (Supuran, Claudiu T.)[1]; Vullo, D (Vullo, Daniela)[4]

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Abstract

We report a series of novel metanilamide-based derivatives 3a-q bearing the 2-mercapto-4-oxo-4H-quinazolin-3-yl moiety as tail. All compounds were synthesized by means of straightforward condensation procedures and were investigated in vitro for their inhibition potency against the human (h) carbonic anhydrase (CA; EC 4.2.1.1.1) isoforms I, II, IX and XII. Among all compounds tested the 6-iodo 3g and the 7-fluoro 3i derivatives were the most potent inhibitors against the tumor associated CA IX and XII isoform (K(1)s 1.5 and 2.7 nM respectively for the hCA IX and K1s 0.57 and 1.9 nM respectively for the hCA XII).

The kinetic data reported here strongly support compounds of this type for their future development as radiotracers in tumor pathologies which are strictly dependent on the enzymatic activity of the hCA IX and XII isoforms. (C) 2017 Elsevier Ltd. All rights reserved.

Keywords

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Author Information

Reprint Address: Supuran, CT (reprint author)

+ Univ Firenze, Dipartimento Neurofarba, Sez Sci Farmaceut, Polo Sci, Via U Schiff 6, I-50019 Florence, Italy.

Reprint Address: Vullo, D (reprint author)

+ Univ Firenze, Dipartimento Chim, Lab Chim Bioinorgan, Rm 188,Via Lastruccia 3, Florence, Italy.

Addresses:

+ [1] Univ Firenze, Dipartimento Neurofarba, Sez Sci Farmaceut, Polo Sci, Via U Schiff 6, I-50019 Florence, Italy

+ [2] Int Islamic Univ, Kulliyyah Sci, Chem Dept, Kuantan, Malaysia

+ [3] Prince Sattam Bin Abdulaziz Univ, Coll Pharm, Pharmaceut Chem Dept, Al Kharj, Saudi Arabia

+ [4] Univ Firenze, Dipartimento Chim, Lab Chim Bioinorgan, Rm 188,Via Lastruccia 3, Florence, Italy