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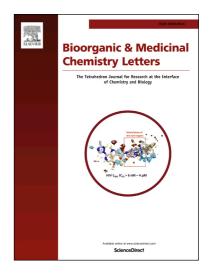
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ACCEPTED MANUSCRIPT

Sulfonamide inhibition profile of the γ -carbonic anhydrase identified in the genome of the pathogenic bacterium *Burkholderia pseudomallei* the etiological agent responsible of melioidosis

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Abstract. A new γ carbonic anhydrase (CA, EC 4.1.1.1) was cloned and characterized kinetically in the genome of the bacterial pathogen *Burkholderia pseudomallei*, the etiological agent of melioidosis, an endemic disease of tropical and sub-tropical regions of the world. The catalytic activity of this new enzyme, BpsCA γ is significant with a k_{cat} of 5.3×10^5 s⁻¹ and k_{cat}/K_m of 2.5×10^7 M⁻¹ x s⁻¹ for the physiologic CO₂ hydration reaction. The inhibition constant value for this enzyme for 39 sulfonamide inhibitors was obtained. Acetazolamide, benzolamide and metanilamide were the most effective (K_{IS} of 149-653 nM) inhibitors of BpsCA γ activity, whereas other sulfonamides/sulfamates such as ethoxzolamide, topiramate, sulpiride, indisulam, sulthiame and saccharin were active in the micromolar range (K_{IS} of 1.27 -9.56 μ M). As *Burkholderia pseudomallei* is resistant to many classical antibiotics, identifying compounds that interfere with crucial enzymes in the *B. pseudomallei* life cycle may lead to antibiotics with novel mechanisms of action.

Keywords: carbonic anhydrase, γclass, inhibitor, sulfonamide, sulfamate, acetazolamide, drug resistance, *Burkholderia pseudomallei*.

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