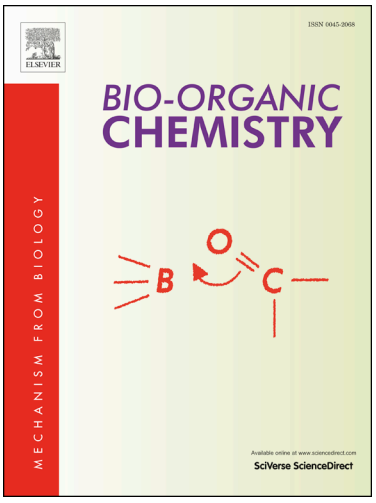

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1,2,4-Trisubstituted imidazolinones with dual carbonic anhydrase and p38 mitogen-activated protein kinase inhibitory activity

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Abstract: Various 1,2,4 trisubstituted imidazolin-5-one derivatives were synthesized and evaluated for their inhibitory activity against p38 mitogen-activated protein kinase (p38MAPK) and carbonic anhydrase (CA) enzymes aiming to explore potential dual inhibitors. Results revealed that compounds **3c, 3g, 3h, 4a, 6c** and **6d** were the most effective derivatives against p38αMAPK (IC_{50}= 0.14, 0.14, 0.056, 0.14, 0.13 and 0.14 μM, respectively) compared to sorafenib (IC_{50}= 1.58 μM) as standard drug. On the other hand, compound **4a** revealed the best inhibitory activity against all the tested carbonic anhydrase isoforms CA I, II, IV and IX with K_i values of 95.0, 0.83, 6.90 and 12.4 nM, respectively compared to acetazolamide with K_i values 250, 12.1, 74 and 12.8 nM, respectively. Therefore, compound **4a** can be considered as a potent dual p38αMAPK/CA inhibitor.

Keywords: Imidazoline-5-ones; sulphonamide derivatives; p38αMAPK inhibitors; carbonic anhydrase inhibitors.