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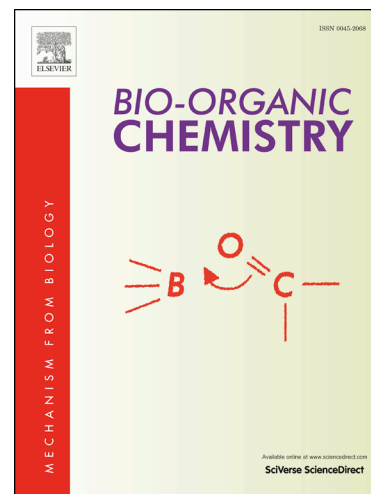
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## 1,2,4-Trisubstituted imidazolinones with dual carbonic anhydrase and p38 mitogen-activated protein kinase inhibitory activity

Hanan H. Georgey<sup>a</sup>, Fatma M. Manhi<sup>b</sup>, Walaa R. Mahmoud<sup>a,\*</sup>, Nehad A. Mohamed<sup>b</sup>, Emanuela Berrino<sup>c</sup>, Claudiu T. Supuran<sup>c</sup>

<sup>a</sup> *Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Cairo University, El-Kasr El-Eini Street, P.O. Box 11562 Cairo, Egypt*

<sup>b</sup> *National Organization for Drug Control And Research (NODCAR), Giza, Egypt.*

<sup>c</sup> *Università degli Studi di Firenze, Department NEUROFARBA, Pharmaceutical and Nutraceutical Chemistry Section, University of Florence, via Ugo Schiff 6, I-50019, Sesto Fiorentino, Firenze, Italy*

**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 p38 $\alpha$ MAPK ( $IC_{50}$ = 0.14, 0.14, 0.056, 0.14, 0.13 and 0.14  $\mu$ M, respectively) compared to sorafenib ( $IC_{50}$ = 1.58  $\mu$ M) 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 p38 $\alpha$ MAPK/CA inhibitor.

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**Keywords:** Imidazolin-5-ones; sulphonamide derivatives; p38 $\alpha$ MAPK inhibitors; carbonic anhydrase inhibitors.

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