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Synthesis, molecular docking, and biological activities of new cyanopyridine derivatives containing phenylurea

Hayreddin Gezegen, Meliha B. Gürdere, Ayşegül Dinçer, Oğuz Özbek, Ümit M. Koçyiğit, Parham Taslimi, Burak Tüzün, Yakup Budak, Mustafa Ceylan

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Abstract

A new class of cyanopyridine derivatives (**10a**–**e** and **11a**–**e**) containing the phenylurea unit was synthesized and tested against some metabolic enzymes including acetylcholinesterase (AChE), butyrylcholinesterase (BChE), and α-glycosidase (α-Gly). The new cyanopyridine derivatives showed K_i values in the range of 40.73 ± 6.54 to 87.05 ± 16.98 μM against AChE, 29.17 ± 4.88 to 124.03 ± 22.43 μM against BChE, and 3.66 ± 0.93 to 26.33 ± 5.05 μM against α-Gly. These inhibition effects were compared with standard enzyme inhibitors like tacrine (for AChE and BChE) and acarbose (for α-Gly). Also, these cyanopyridine derivatives with the best inhibition score were docked into the active site of the indicated metabolic enzymes. Finally, molecular docking calculations were made to compare the biological activities of the compounds against AChE (−8.81 kcal/mol for molecule **11d**), BChE (−3.52 kcal/mol for molecule **11d**), and α-Gly (−2.98 kcal/mol for molecule **11a**). After molecular docking calculations, the ADME/T analysis was performed to examine the future drug use properties of the new cyanopyridine derivatives containing phenylurea.

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