

# Nanomolar potency of imidazo[2,1-b]thiazole analogs as indoleamine 2,3-dioxygenase inhibitors

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## Abstract

Novel series of imidazo[2,1-b]thiazole analogs were designed, synthesized, and biologically evaluated as indoleamine 2,3-dioxygenase (IDO1) inhibitors. Imidazo[2,1-b]thiazoles 6, 7, and 8 showed inhibitory profiles against IDO1 at IC<sub>50</sub> values of 68.48, 82.39, and 48.48 nM, respectively, compared with IDO5L at IC<sub>50</sub> 67.40 nM. Benzo[d]imidazo[2,1-b]thiazoles 17, 20, and 22 showed promising IDO1 inhibition at IC<sub>50</sub> values of 53.58, 53.16, and 57.95 nM, respectively. Compound 7 showed a growth inhibitory profile at GI of 39.33% against the MCF7 breast cancer cell line, while 8 proved lethal to ACHN renal cancer cells. Cells treated with compounds 17 and 22 showed a typical apoptosis pattern of DNA fragments that reflected the G<sub>0</sub>/G<sub>1</sub>, S, and G<sub>2</sub>/M phases of the cell cycle, together with a pre-G<sub>1</sub> phase corresponding to apoptotic cells, which indicates that cell growth arrest occurred at the S phase. Molecular modeling simulations validated the potential of benzo[d]imidazo[2,1-b]thiazole analogs to chelate iron(III) within the IDO1 binding pocket and, hence, to have a better binding affinity via hydrophobic-hydrophobic interactions.

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