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Título	Synthesis, Selective Cytotoxic Activity against Human Breast Cancer MCF7 Cell Line and Molecular Docking of Some Chalcone-Dihydropyrimidone Hybrids
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Resumo	Designed Chalcone-Dihydropyrimidinone hybrid compounds were synthesized expeditiously. The hybridization was performed through the Copper-catalyzed Alkyne-Azide Cycloaddition (CuAAC) from the propargyloxy chalcones and azido-dihydropyrimidinones. The hybrid products were prepared in five steps with a 30–48% overall yield. Most of the compounds showed selective cytotoxicity and lower IC50 values (<10 µM) against MCF-7 (breast adenocarcinoma) cancer. Cytotoxicity was also observed against OVCAR-3 (ovary, adenocarcinoma), NCI/ADR-RES (ovary, multidrug-resistant adenocarcinoma), and U-251 (brain, glioblastoma) cell lines. The potency of the most active hybrids 9d, 9g, and 9h was greater than the individual parental compounds, suggesting the effectiveness of molecular hybridization on the cytotoxicity. Compounds 9d, 9g, and especially 9h showed high selectivity for breast cancer cells (MCF-7) regarding human keratinocytes (HaCaT). Molecular docking calculations for the 9d, 9g, and 9h hybrids in the active site of estrogen supported the hypothesis that the compounds act as ER-α antagonists, disrupting the cell proliferation process of MCF-7, corroborating the potency and selectivity observed for this tumoral cell line.
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