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# Design and synthesis of bis-triazole curcumin analogs as antiproliferative agents: Mechanistic insights from cell cycle analysis in MCF-7 cells

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**ABSTRACT** In the present work, a new series of modified curcumin analogs of 1,2,3-triazoles (bis-triazole curcumin) (**8-19**) were synthesized in good yields using a molecular hybridization strategy by click functionalization of a curcumin-pyrazole adduct. The synthesized compounds were characterized by spectral data, and curcumin hybrids **8-19** were evaluated *in vitro* by 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide assay for antiproliferative activity against four different human breast carcinoma cell lines. All the tested compounds have shown moderate-to-excellent antiproliferative activity, and among them, compounds **15** and **19** have shown a significant inhibition against all the cell lines when compared with curcumin and doxorubicin. Cell cycle analysis of compounds **15** and **19** on MCF-7 cell lines indicated greater accumulation of the cell population in the S phase for compound **15** by 59.87% and G0-G1phase for compound 19 by 62.98%. Cell cycle analysis suggests that the aforementioned compounds actively involve arrest of the S phase and the G0/G1 phase. Furthermore, docking studies were also conducted for all the compounds with the prominent endothelial growth factor receptor 2 target. Docking studies have shown higher glide scores, −6.400 and −6.578 kcal/mol, respectively, for **15** and **19**. ProTox 3.0 toxicity prediction showed $LD_{50}$ values in the range of 400–790 mg/kg, and all the compounds have a toxicologically safe profile. The results indicate that the curcumin-triazole hybrid adducts are promising lead to develop as antiproliferative agents.

**KEY WORDS** 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide assay, Antiproliferative, Click functionalization, Curcumin-triazoles, Human breast carcinomal cell lines, Molecular hybridization

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