

Synthesis, design, and examination of the cytotoxic effects and nuclear condensation properties of novel andrographolide-vanillin-1,2,3-triazoles

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Andrographolide is a bioactive labdane diterpenoid found in the leaves and stems of the *Andrographis paniculata* plant, which is native to South Asian countries such as India and Sri Lanka. Hybrid molecules produced by combining structural elements or pharmacophores from two or more parent compounds retain key features from the parent compound while potentially exhibiting novel or enhanced bioactivities. This paper presents the synthesis of andrographolide-vanillin-1,2,3-triazole hybrid analogues through a copper-catalysed azide-alkyne cycloaddition reaction, commonly known as the "click reaction," which enables the linkage of the three components. A series of 5 novel andrographolide-vanillin-1,2,3-triazole hybrid molecules have been synthesized and evaluated for their cytotoxic efficacy toward HELA cell lines. The results show that compound **7c** potentially induces cytotoxicity at three different concentrations compared with the other compounds in the series. Compared to the other analogues, **7c** induced significant cytomorphological abnormalities, including nuclear condensation in HeLa cells, as observed under both phase-contrast and fluorescence microscopes using Hoechst staining method.

Keywords: *Andrographis paniculata*, Andrographolide, Vanillin, 1,2,3-Triazole, 1,3-Dipolar cycloaddition