

Evodiamine stabilizes topoisomerase I-DNA cleavable complex to inhibit topoisomerase I activity

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摘要.

Abstract

Evodiamine (EVO), an alkaloidal compound isolated from *Evodia rutaecarpa* (Juss.), has been reported to affect many physiological functions. Topoisomerase inhibitors have been developed in a variety of clinical applications. In the present study, we report the topoisomerase I (TopI) inhibitory activity of EVO, which may have properties that lead to improved therapeutic benefits. EVO is able to inhibit supercoiled plasmid DNA relaxation catalyzed by TopI. Upon treatment 0~10 μ M EVO TopI was depleted in MCF-7 breast cancer cells in a concentration-dependent and time-dependent manner in 0~120 min. A K-SDS precipitation assay was performed to measure the extent of Top I-trapped chromosomal DNA. The ability of EVO to cause the formation of a TopI-DNA complex increased in a concentration-dependent manner, in that the DNA trapped increased by 24.2% in cells treated with 30 μ M. The results suggest that EVO inhibits TopI by stabilizing the enzyme and DNA covalent complex