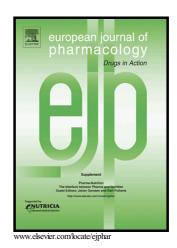
Author's Accepted Manuscript

A novel harmine derivative, *N*-(4-(hydroxycarbamoyl)benzyl)-1-(4- methoxyphenyl)-9H-pyrido[3,4-b]indole-3-carboxamide (HBC), as histone deacetylase inhibitor: in vitro antiproliferation, apoptosis induction, cell cycle arrest, and antimetastatic effects

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Abstract

This study aims to design and synthesize a novel harmine derivative N-(4-(hydroxycarbamoyl) benzyl)-1-(4-methoxyphenyl)-9H-pyrido [3,4-b]indole-3-carboxamide (HBC) as histone deacetylase (HDAC) inhibitor, and evaluate its antitumor activities and anti-metastasis mechanism. HBC not only exerted significant ant-proliferation activity against five human cancer cell lines, especially for HepG2 cell with an IC₅₀ value of 2.21 μ M, which is nearly three-fold lower than SAHA (IC₅₀ = 6.26 μ M), but also showed selective HDAC1/6 inhibitory effects in vitro. However, HBC had little effect on normal hepatic cells LO2. Furthermore, HBC simultaneously increased the acetylation of histone H3, H4, and α -tubulin, induced hypochromism by electrostatical

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