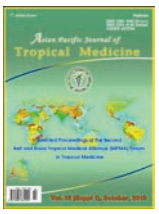

Asian Pacific Journal of Tropical Medicine

journal homepage: www.apjtm.org

doi: 10.4103/1995-7645.268165

Impact factor: 1.77

Penicilazaphilone C, a new azaphilone, induces apoptosis by blocking the Notch signalling pathway in gastric cancer

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Objective: To explore the molecular mechanisms of the anticancer activities of penicilazaphilone C against gastric cancer.

Methods: *In vitro* effects of penicilazaphilone C on cell growth, proliferation, and apoptosis were evaluated by MTT, BrdU, MTS, colony formation assays, Hoechst 33258 staining, and flow cytometry. Related proteins were examined by Western blotting assays. The expression of Notch receptor was analyzed using real-time PCR. In vivo antitumor activities of penicilazaphilone C were observed in nude mice.

Results: Compared to the controls, penicilazaphilone C suppressed cell proliferation and promoted apoptosis in MGC-803 and SGC-7901 cells. The Notch/PTEN/AKT axis was involved in the activating penicilazaphilone C-induced apoptosis. Penicilazaphilone C decreased levels of Notch, NICD, phospho-PTEN and phospho-AKT compared to controls. The penicilazaphilone C-induced inhibition of Notch-related protein expression levels and the resulting apoptosis could be reversed by overexpression of Notch1 or/and Notch2. Moreover, penicilazaphilone C inhibited tumor growth in mice bearing tumours derived from MGC-803 and SGC-7901 cells, respectively.

Conclusions: Penicilazaphilone C can induce the apoptosis by suppressing the activation of the proteolytic cleavage of the Notch receptor and subsequently blocking the PTEN/AKT signaling axis in gastric cancer cells. Thus, penicilazaphilone C is a potential alternative agent for the treatment of gastric cancer.

Keywords: Penicilazaphilone C; Notch signalling pathway; Gastric cancer; Apoptosis; Molecular mechanism

Article history:
Received 8 September 2019
Reevised 13 September 2019
Accepted 25 September 2019
Available online 7 October 2019

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Foundation project: This work was supported by the National Natural Science Foundation of China (Grant No. 81560484), and the Key Research and Development Project of Hainan Province (Grant No. ZDYF2019177).

How to cite this article: Zhao HG, Wang M, Lin YY, Zhou SL. Penicilazaphilone C, a new azaphilone, induces apoptosis by blocking the Notch signalling pathway in gastric cancer. Asian Pac J Trop Med 2019; 12(Suppl 1): 4.