

Anti-proliferative and anti-invasive properties of a purified fraction from *Streptomyces* sp. H7372.

Abstract

Secondary metabolites from actinomycetes especially the genus *Streptomyces* may be one of the most important sources for novel anticancer agents. A purified fraction from a novel actinomycete strain, *Streptomyces* sp. H7372, was elucidated in breast cancer cells. We have isolated three purified fractions from a novel strain, *Streptomyces* sp. H7372. One of the fractions, designated as 31-2, exhibited the strongest growth-inhibitory effect and thereby was selected for further studies. 31-2 exerted a growth-inhibitory effect on a panel of 15 human cancer and 2 non-malignant cell lines. In MCF-7 and MDA-MB-231 breast cancer cells, 31-2 induced a cytostatic (anti-proliferative) effect without causing cytotoxicity (cell death). Our data suggest that the cytostasis resulted from cell cycle arrest at the G1 phase in MCF-7 cells and at the S phase in MDA-MB-231 cells. Western blot analysis demonstrated a modulation of phosphorylation of the Rb and CDC2 proteins and of CDK4, cyclin D1 and cyclin D3 in the 31-2-treated breast cancer cell lines. The protein levels of CDK2, CDK6, and PCNA were not affected by 31-2 treatment. 31-2 also exhibited an anti-invasive effect in MDA-MB-231 cells. However, this effect is not attributed to the modulation of proteolytic activity in MDA-MB-231 cells as the enzymatic degradation of type IV collagen was not affected by 31-2. The 31-2 is a potent cytostatic and anti-invasive agent and modulates the cell cycle pathway. Together, these results will have important implications in searching for novel approaches to treat cancer.

Keyword: Breast cancer; Cell cycle; Cytostasis; Invasion; Proteolytic activity; *Streptomyces*