PHARMA Pharmacologia

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News & Comments

Siomycin A., Potential Agent in the Treatment of Gastric Cancer GC.

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One of the most prevalent malignancies worldwide is gastric cancer, which accounts for around 10% of all cancer-related deaths worldwide. Irinotecan, fluoropyrimidines (capecitabine and S-1), and other important chemotherapy drugs are used to treat GC. As a member of the forkhead box (Fox) family of transcription factors, FOXM1 has been linked to several aggressive human malignancies, including those of the cervix, liver, breast, prostate, and lung. Overexpression of FOXM1 in gastric cancer is associated with a poor prognosis and chemoresistance. Additionally, it has been noted that FOXM1 aids in the development, growth, and metastasis of human gastric cancer. Gram-positive bacteria are selectively inhibited by the thiazole antibiotic siomycin A, which contains sulphur. Siomycin A's impact on GC cells hasn't been studied, though. This study examined the effects of Siomycin A on the AKT/FOXM1 axis in gastric cancer cells.

The study was carried out at the Department of Traditional Chinese Medicine, Xinjiang Uygur Municipal People's Hospital, China. The American Type Culture Collection (ATCC) cell repository has provided the human gastric adenocarcinoma cell line (SGC-7901) and the healthy human gastric mucosa epithelial cell line (GES). SGC-7901 cells were expanded (1 105 cells/well) on 24-well plates and scraped with 200 L pipette tips. Afterwards, PBS washed the plates to remove any disconnected cells. Using the Cell Death Detection ELISA plus kit as directed by the manufacturer, apoptosis was found to have been induced in Siomycin A-treated cells (Sigma Aldrich, Merck KGaA). The expression of several proteins was determined using a western blot analysis. According to the figure legends, all data are shown as the Mean SEM of n independent measurements.

The effect of Siomycin A on cell migration was evaluated using a wound-healing experiment. 5 M Siomycin A significantly decreased the migration of GC cells in the wound healing assay as compared to the untreated control.

According to the findings, 5 M Siomycin A could only bridge the gap. Before being examined for apoptosis using the cell death detection ELISA PLUS, SGC-7901 cells were treated with Siomycin A (0, 2.5, and 5 M) for 24 hrs. DNA fragmentation, a crucial indicator of apoptosis, is the foundation of this investigation. DNA fragmentation was nearly 4 and 6.8 times higher in cells treated with 2.5 and 5 M Siomycin A than in the untreated control. The results of this investigation showed that Siomycin A significantly and dose-dependently inhibited GC cell proliferation. Siomycin A therapy significantly decreased cell migration in the gastric cancer cell line SGC-7901, according to in vitro cell migration

experiments. The study also investigated whether Siomycin A affects the FOXM1-linked AKT signalling pathway in gastric cancer cells. A sulphur-containing antibiotic called siomycin A, which has been shown to have anticancer activity against a variety of cancer cells by inhibiting FOXM1, preventing cell proliferation, and inducing apoptosis, is derived from an endophytic Actinomycin species found in the medicinal plant *Acanthopanax senticosus*. For the first time, the current study examines Siomycin A's impact on stomach cancer cells.

Recent investigations have demonstrated that siomycin A causes ROS-mediated cytotoxicity in ovarian cancer cells. Siomycin A is also known to cause pancreatic cancer to apoptosis. Siomycin A, like LY294002, may therefore inhibit the expression of FOXM1 in GC cells by a related mechanism.

The study focuses on how Siomycin A modifies the FOXM1-linked AKT signalling pathway in gastric cancer cells. In gastric cancer cell lines, siomycin A dramatically decreased AKT phosphorylation. Additionally, study observes that LY294002, a PI3K inhibitor, reduced the expression of both pAKT and FOXM1. Therefore, it's plausible that siomycin A, like LY294002, may inhibit FOXM1 expression in GC cells via a related route.

JOURNAL REFERENCE

Chen, J., X. Yu and B. Xu, 2022. Siomycin A induces cytotoxicity in gastric cancer cells by targeting AKT/FOXM1 axis. Int. J. Pharmacol., 18: 691-698.

KEYWORDS

AKT/FOXM1 axis, anticancer, gastric cancer, siomycin A, apoptosis, migration, akt phosphorylation