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In-vitro antitumor activity of new quaternary phosphonium salts, derivatives of 3-hydroxypyridine

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Abstract

© 2018 Wolters Kluwer Health, Inc. All rights reserved. This work presents the results of in-vitro biological activity studies of three novel anticancer agents, phosphonium salts based on the 3-hydroxypyridine scaffold, including one derivative of 4-deoxypyridoxine. Proliferation and viability of cells treated with these compounds was assessed by the colony formation and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assays. Effects of the compounds on apoptosis and cell cycle were studied by flow cytometry using annexin V-FITC/propidium iodide and propidium iodide staining, respectively. The influence of the compounds on mitochondrial membrane potential and intracellular reactive oxygen species was evaluated using tetramethyl rhodamine ethyl and DCFHA staining. Western blot analysis was used to study the changes in the expression of Bcl-xL, Bax, and caspase-3 apoptotic proteins. The treatment of ovarian adenocarcinoma cells OVCAR-4 with the tested compounds inhibited the growth and induced cell cycle arrest in the G1 phase. 3-Hydroxypyridine derivatives induced apoptosis by hyperexpression of Bax and caspase-3, whereas 4-deoxypyridoxine derivative induced cell death partly by reactive oxygen species generation and caspase-3 hyperexpression. These results indicate that the quaternary phosphonium salts studied represent potential therapeutic agents for the treatment of ovarian cancer.

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Keywords

3-hydroxypyridine, 4-deoxypyridoxine, apoptosis, cell cycle, cytotoxicity, OVCAR-4

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