Introduction

ON 01910.Na (Estybon™) is a potent anticancer antimitotic agent currently in clinical trials for the treatment of solid tumors. It is a non-ATP-competitive small molecule inhibitor of Plk1, a crucial mitotic kinase that regulates the entry of eukaryotic cells into mitosis. Plk1 is essential for spindle organization and assembly, and its inhibition leads to mitotic arrest and apoptosis in tumor cells [1]. Studies have shown that ON 01910.Na is a potent and selective inhibitor of cyclin-dependent kinases (CDKs) and has shown promising results in preclinical trials [2].

Materials and Methods

Cell viability assay

Cell viability was determined using the sulforhodamine B (SRB) assay. Cells were seeded at different densities in 96-well plates and treated with various concentrations of ON 01910.Na, nocodazole, taxol, vinblastine, colchicine, and okadaic acid. After 24 hours, the cells were fixed and stained with SRB solution. The dye was then solubilized and the absorbance at 492 nm was measured.

Results and Discussion

1) Exposure of tumor cells to anticancer mitotic inhibitor, ON 01910.Na, resulted in cell cycle arrest at mitosis, that is correlated with RGSH expression.

2) All tubulin agents tested, both tubulin polymerization enhancers and depolymerizing agents were able to produce RGSH.

3) Cytotoxic drug concentrations of antimitic drugs were correlated with those of RGSH expression.


5) Roscovitine and caffeine inhibited RGSH and mitotic Cdc25C.

6) Okadaic acid, known PP1/PP2A inhibitor, caused mitotic arrest, expression of RGSH and apoptosis similar to ON 01910.Na.

These findings suggest that ON 01910.Na is a RGSH phosphatase inhibitor.

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References
