A new platinum-based prodrug candidate: Its anticancer effects in B50 neuroblastoma rat cells

Beatrice Rangone, Beatrice Ferrari, Valentina Astesana, Irene Masiello, Paola Veneroni, Ilaria Zanellato, Domenico Osella, Maria Grazia Bottone

PII:	S0024-3205(18)30496-X
DOI:	doi:10.1016/j.lfs.2018.08.048
Reference:	LFS 15895
To appear in:	*Life Sciences*
Received date:	12 June 2018
Revised date:	27 July 2018
Accepted date:	20 August 2018

Please cite this article as: Beatrice Rangone, Beatrice Ferrari, Valentina Astesana, Irene Masiello, Paola Veneroni, Ilaria Zanellato, Domenico Osella, Maria Grazia Bottone , A new platinum-based prodrug candidate: Its anticancer effects in B50 neuroblastoma rat cells. Lfs (2018), doi:10.1016/j.lfs.2018.08.048

A new platinum-based prodrug candidate: its anticancer effects in B50 neuroblastoma rat cells.

Beatrice Rangone[1§], Beatrice Ferrari[2§], Valentina Astesana[2], Irene Masiello[2], Paola Veneroni[2], Ilaria Zanellato[1], Domenico Osella[1], Maria Grazia Bottone[2]*

[1]Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale "A. Avogadro", viale Teresa Michel 11, 15121 Alessandria, Italy.

[2]Dipartimento di Biologia e Biotecnologie "L. Spallanzani", Università di Pavia, via Ferrata 9, 27100, Pavia, Italy.

(§ Both authors contributed equally to this work)

Corresponding author

*****Maria Grazia Bottone

Dipartimento di Biologia e Biotecnologie "L. Spallanzani", Università di Pavia,

via Ferrata 9, 27100, Pavia, Italy.

Email: bottone@unipv.it

ABSTRACT

Aims: Neuroblastoma is a rare cancer that affects children, mostly under the age of 5. This type of cancer starts in very early forms of immature nerve cells or developing cells found in embryo or fetus. To date cisplatin represents one of the most potent antitumor agent known, however, the onset of systemic side effects and the induction of drug resistance limit its use in the clinic for long-term treatment. In the present study we have analysed the effects of a new compound of platinum(IV) conjugates, named Pt(IV)Ac-POA, which is able to generate a synergistic antineoplastic action when released along with cisplatin upon intracellular Pt(IV) →Pt(II) reduction.

Main methods: To assess the growth inhibition of the compounds under investigation, a cell viability test, *i.e.* the resazurin reduction assay was used on the B50 neuroblastoma rat cells. Further analysis on the cell cycle and metabolic alterations were carried out through flow cytometry. Morphological changes and activation of different cell death pathways after treatment, were observed at transmission electron microscope and by immunocytochemistry at fluorescence microscopy. Protein expression was examined by western blot analysis.

Key findings: This compound bearing bioactive axial ligand, such as the active histone deacetylase inhibitor (HDACi) (2-propynyl)octanoic acid (POA), induced cell death through different pathways at a concentration ten times lower than cisplatin.