Title:	The molecular response of vanadium complexes of nicotinoyl hydrazone in cervical cancers—A possible interference with HPV oncogenic markers
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Keywords:	Nicotinoyl Hydrazone Vanadium Complexes Cervical Cancers HPV Oncogenic
Issue Date:	2014
Publisher:	Elsevier Inc.
Citation:	Life Sciences, 116(2), pp.90-97.
Abstract:	Aims: Hydrazones belonging to the class of NNO donor Schiff bases are reported to have extensive anti-viral activity and anti-neoplastic activity against certain cancers such as colon cancer, hepatocellular carcinoma and testicular cancer. Here we aim to study the possible effects of two novel nicotinoyl hydrazones on Human papillomavirus (HPV) infected cervical cancers. Main methods: The effect of vanadium complexes on the proliferation of SiHa and HeLa cells was analyzed using MTT assay. The apoptotic potentials of the complexeswere assessed by their ability to induce DNA condensation as well as loss of mitochondrial membrane potential. Caspase activity assay and DNA content analysis were performed to understand the mechanism of apoptotic induction. RT-PCR analysis of cell cycle genes, GADD45, p53, p21 and HPV specific oncogenes, E6 and E7 were used to elucidate the molecular mechanism of the complexes. Key findings: OVK 49 exhibits an increased apoptosis inducing potential when compared to OVK 89 inHPV16 positive SiHa cells compared to HPV18 positive HeLa. A down regulation for E6 and E7mRNA transcripts along with the induction of p53 protein in SiHa cellswere observedwhen treatedwith OVK 49 indicating that OVK 49 might have promising anti-cancer activity against HPV16 positive cervical cancers. Significance: This is the first study demonstrating that vanadium complexes could induce a p53 dependent apoptotic mechanism in high risk HPV16-positive cervical cancers.
Description:	Only IISERM authors are available in the record.
URI:	https://www.sciencedirect.com/science/article/abs/pii/S0024320514007607 (https://www.sciencedirect.com/science/article/abs/pii/S0024320514007607) http://hdl.handle.net/123456789/2773 (http://hdl.handle.net/123456789/2773)
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