

## Antiproliferative and Apoptotic Effects of Vanadyl Sulphate on *H-Ras* Transformed 5rp7 Cells

Hatice Mehtap Kutlu, Djanan Vejselova

Anadolu University, Faculty of Science, Department of Biology, 26470, Eskisehir, Turkey

Metal based drugs have successfully been used in the detection and treatment of a variety of diseases [1]. Despite the advantages in early diagnostic and treatment of cancer, there is essential to develop new alternative of drugs. A number of *in vitro* studies have revealed that vanadium shows its antitumor effects on various cell lines [2]. Moreover, it is shown that vanadium compounds may show cytotoxic effects through DNA cleavage and fragmentation, *in vitro* [3]. According to these studies, here in we aimed to investigate the cytotoxic and antiproliferative effect of vanadyl sulphate *in vitro*, also to detect the effect of this agent on *H-Ras* transformed 5RP7 cells ultrastructure.

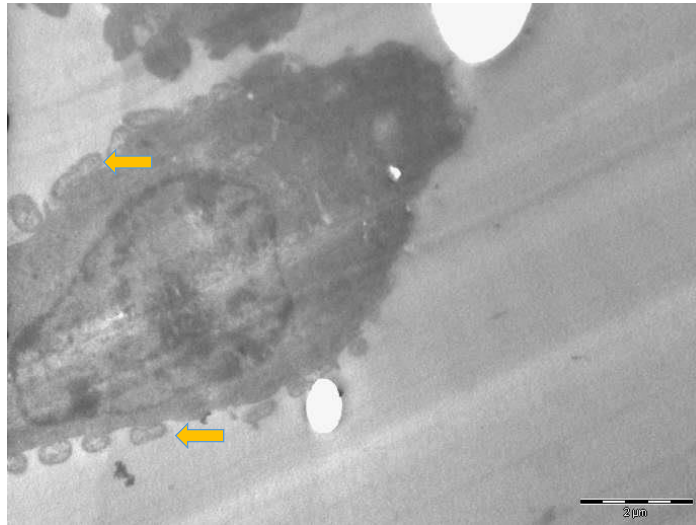
For detecting the cytotoxic effects, the stock solution (in distilled water) of vanadyl sulphate, was further diluted with culture medium to 10, 20, 30, 40, 50, 60, 70, 80, 90 and 100 $\mu$ M concentrations and applied on *H-Ras* 5RP7 cells ( $1 \times 10^4$  cells per well) for 24 hours. The plates were read on ELISA reader (ELX808) at wavelength of 540 nm ( $n=3$ ). From the Elisa reader results, the 50% inhibition concentration ( $IC_{50}$ ) of the cells was determined to be 35 $\mu$ M.


For ultrastructural changes, *H-Ras* 5RP7 cells incubated with 35 $\mu$ M for 24 hours were fixed with 2,5% glutaraldehyde (in 0,1M phosphate buffer, pH 7.4) and left in buffer overnight at +4 °C. After being embedded in agar and post fixed in %2 osmium tetroxide, the cells were dehydrated in graded ethanol (70%, 90%, 96% and 100%). Dehydrated cells were embedded in EPON 812 epoxy (Germany) and sectioned on ultramicrotome (LEICA UC6, Germany). Structural and ultrastructural changes of these cells were observed on transmission electron microscope (TEM) and photographed.

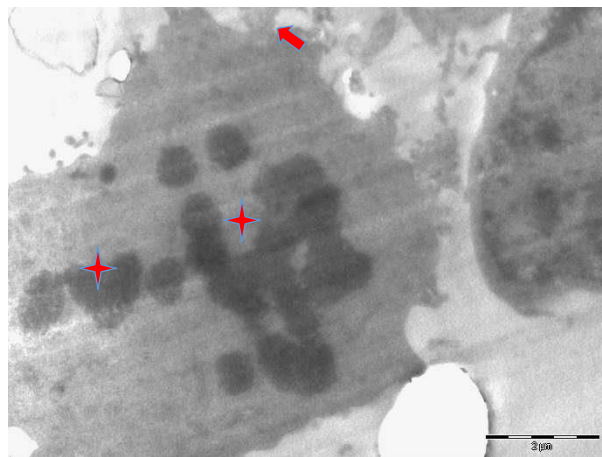
Our results demonstrated that vanadyl sulphate showed high sitotoxicity on *H-Ras* transformed 5RP7 cells in low concentrations. Also, in our results it is shown the structure and ultrastructural changes like membrane blebbing and nuclear fragmentation as apoptotic sparks on *H-Ras* transformed 5RP7 cells caused by vanadyl sulphate via transmission electron microscopy (TEM). According to these sparks, vanadyl sulphate has induced apoptosis in *H-Ras* transformed 5RP7 cells. Consequently, we can say that vanadyl sulphate with its effects on *H-Ras* transformed 5RP7 cells may expose well inspiration for designing of pharmaceutical products helpful in cancer treatment.



### References:

- [1] B Thati, European Journal of Pharmacology **602** (2009), 203–214.
- [2] J Kieler, A Gromek, NI Nissen, Acta Chir Scand **343** (1965), 154–164.
- [3] HJ Thompson, DN Chasteen, L Neeker, Carcinogenesis **5** (1984), 849–851.



**Figure 1.** Transmission electron micrograph of 5rp7 cell treated with  $IC_{50}$  value of vanadyl sulphate for 24 hours (10kx).  : Membrane blebbings.



**Figure 2.** Transmission electron micrograph of 5rp7 cell treated with  $IC_{50}$  value of vanadyl sulphate for 24 hours (10kx).  : Nuclear fragmentations;  Membrane blebbing