

## TOXICOLOGICAL EVALUATION OF MEPACRINE AND INTERFERON $\alpha$ -2A ON U87-MG AND VERO CELL CULTURE

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Mepacrine is an anti-protozoal agent no longer used as anti-malarial drug because of its toxicity. In previous studies we observed that mepacrine can act as anti-proliferative agent on MCF-7 cells (1), moreover we observed that the molecule is characterised by an aliphatic chain similar to that of polyamines whose activation is closely associated with cell proliferation. Aim of the present study was to test the activity of mepacrine on human glioblastomas cells (U87-MG) using interferon  $\alpha$ -2a as reference drug and to compare the effects of both on a control cell line. Methods: Vero cells (chosen as control line) and human glioblastomas cells (U87-MG) were cultured in EMEM (+37°C in 5% CO<sub>2</sub> in air) and treated with increasing concentrations of mepacrine (from 3.3  $\mu$ M to 100  $\mu$ M) and interferon  $\alpha$ -2a (from 0.000728  $\mu$ M to 0.9  $\mu$ M). Trypan blue exclusion test, MTT test and western blotting test were performed and the results analysed statistically by the *student t test*. Results from MTT test indicate that the anti-proliferative effect of mepacrine on U87-MG is evident from 24 hours, while Vero cells are inhibited from 48 hours. Moreover, DL<sub>50</sub> values were significantly different: 49.65  $\mu$ M on Vero cells e 34  $\mu$ M on U87-MG cells. The comparison with interferon  $\alpha$ -2a clearly shows a higher activity of the antitumour drug as the DL<sub>50</sub> is reached at very low concentrations: 0.55  $\mu$ M on Vero cells and 0.57  $\mu$ M on U87-MG. Finally, preliminary results from the *western blotting* test performed on U87-MG cells treated with mepacrine 34  $\mu$ M indicate that, even if *p 53* expression is unmodified, *bcl-2* expression is reduced from 24 hours thus confirming what we observed in the MTT test. The comparison between DL<sub>50</sub> values of mepacrine and interferon  $\alpha$ -2a outlines the presence of a selective cytotoxicity towards U87-MG which is evident only in the cultures treated with mepacrine: DL<sub>50</sub> values of interferon  $\alpha$ -2a on Vero and U87-MG cells are very similar (0.55  $\mu$ M and 0.57  $\mu$ M). As regard the mechanism of action, we suppose that the presence of the aliphatic chain both in mepacrine and in natural polyamines could be at the basis of a probable antagonising effect towards the proliferative action of polyamines on neuronal cell replication. In conclusion, even if it is known that mepacrine toxic effects are not negligible we suppose that the results of our experiments could offer a contribute to the research on the neurodegenerative and tumoural diseases.

1) Rossi T., Coppi A., Zandomenighi G., Lodi S., Ruberto A. and Baggio G. (2004):  
*Anticancer Res.* 24 (5D): 3614.