IJAE
Vol. 117, n. 2 (Supplement): 73, 2012
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Antitumor activity of fenretinide encapsulated in novel based PLA microspheres

Stefano Focaroli[1], Viviana Salvatore[1], Silvia Bolzani[1], Pietro Gobbi[3], Alessandra Ruggeri[1] and Isabella Orienti[2]

[1] Dipartimento di Scienze Anatomiche Umane e Fisiopatologia dell'Apparato Locomotore, University of Bologna, Bologna, Italy
[2] Department of Pharmaceutical Sciences, University of Bologna, Bologna, Italy
[3] Department of STeVA, University "Carlo Bo", Urbino, Italy

Several studies reported fenretinide (4-HPR) can be used as antitumoral drug in many types of cancer cell lines such as neuroblastoma, mammary carcinoma and melanoma. In vitro 4-HPR inhibits growth of neuroblastoma in a dose dependent manner with an high antitumor activity at 5–10 μM (Ponzoni et al., 1995).The main disadvantage of 4HPR in clinical application is its lipophilic behavior which hinders the possibility to maintain therapeutic concentration for long period of time.

To bypass this drawback, new drug delivery systems consisting in polylactide (PLA) or polylactide-co-glycolid (PLGA) microspheres were developd. A novel solvent extraction method based on the co-precipitation of PLA or PLGA with gelatin has been utilized. Phosphatidylcholine (PC) or dextrin (DX) were added to improve the hydrophilic character of the microsphere surface.

After a preliminary study of physical characteristics in terms of encapsulation efficiency, mean size and release profile of drug, PLA/gelatin/dextrin MS were chosen to test the antitumor activity in SH-SY5Y neuroblastoma cell line.

After 3 and 24 hours of treatment a cell viability of 50 % and 0% was observed respectively. Empty MS did not affect the cell viability at the same time points. High resolution SEM showed an high bioadhesion of PLA/gelatin/dextrin microspheres to cell membrane. Cell uptake experiments demonstrated an high intracellular concentrations of fenretinide in the presence of the PLA/gelatin/dextrin microspheres rather than in the presence of pure fenretinide.

In conclusion, 4-HPR loaded in PLA/gelatin/dextrin microspheres represent a powerful tool for drug delivery systems for hydrophobic antitumor drugs whose therapeutic potential is hindered by their low availability.

References

Ponzoni M et al. (1995) Differential effects of N-(4-hydroxyphenyl) retinamide and retinoic acid on neuroblastoma cells: apoptosis versus differentiation Cancer Res., 55: 853–861.

Keywords: Microparticles, PLA, PLGA, dextrin, fenretinide, antitumor activity.