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Name of Presenter: Paraskevi Zagana

University/Company Name: FORTH/ICE-HT, Patras

Address: Stadiou Street, Platani, Patra 265 04, Greece

Contact Email: voulazagana@yahoo.gr

Contact Phone Number: +306980370599

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IN VITRO STUDY OF DOXORUBICIN ENCAPSULATION INTO ARSONOLIPOSOMES

Paraskevi Zagana^{2*}, Spyridon Mourtas², Anastasia Basta², Sophia G. Antimisiaris^{1,2}

¹ Department of Pharmacy, University of Patras, Greece

²Institute of Chemical Engineering Sciences (FORTH/ICE-HT), Patras, Greece

* Email: voulazagana@yahoo.gr

Arsonoliposomes, are liposomes that incorporate arsonolipids in their membranes and have been studied previously, in terms of their stability and antitumor activity [1, 2]. They demonstrate significant toxicity towards cancer cells while being less toxic towards normal cells. Doxorubicin (DOX), is a commonly used anti-cancer drug which is currently used in the clinic as in the form of PEG-liposomes.

In this study, we sought to investigate the possibility to encapsulate DOX into arsonoliposomes and arsonoliposomes that are modified with a curcumin derivative (TREG), in order to study at a latter step, if the DOX-arsonoliposome combined system demonstrates additive or even synergist anticancer activity. PEGylated arsonoliposomes and TREG-arsonoliposomes composed of DSPC/Chol/PEG-2000-DSPE/Arsonolipid/TREG (in some cases) were prepared and the loading of DOX was attempted by applying the active loading method protocol. A drug/lipid ratio (D/L) of 1/7 (w/w) was always used, while the effect of using different temperatures (40° C and 60° C) and different time periods of incubation (15, 30, 60 and 90 min), on the DOX encapsulation in arsonoliposomes and TREG-arsonoliposomes, was tested. In all cases, liposomes were purified after the loading process and the % DOX entrapment efficiency was calculated based on initial/final D/L ratio.

Results show that, the active-loading protocol succeeds to encapsulate high percents of DOX into arsonoliposomes (up to 99%) and TREG-arsonoliposomes (up to 89%); Maximum loading was demonstrated when the incubation was carried out at 40° C, for arsonoliposomes and 60° C for TREG-arsonoliposomes. Considering the duration of incubation, in both cases DOX encapsulation was highest after 90 min. DOX-loaded arsonoliposomes and TREG-arsonoliposomes are currently tested for their anticancer activity towards different types of cancer cells, in vitro, and the first results are interesting.

References:

- [1] Zagana P, et al. (2009) Arsonoliposome interaction with cells in culture. Effect of pegylation and lipid composition. *J Mol Nutr Food Res* 53:592–599
- [2] Gortzi O, et al. (2002) Arsonoliposomes, a Novel class of arsenic-containing liposomes: effect of palmitoyl-arsonolipid-containing liposomes on the viability of cancer and normal cells in culture. *Pharm Res* 19:79–86

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