

**BIOLOGICAL EFFECTS OF LIPOSOMAL FORMULATION OF
DIMIQ, POTENTIAL ANTITUMOR INDOLO[2,3-*B*]QUINOLINE
AGENT ON HEPATOMA MORRIS 5123 CELLS**

KATARZYNA SUCHOSZEK-ŁUKANIUK^{1*}, ANNA JAROMIN², WANDA
PECZYŃSKA-CZOCH³, ŁUKASZ KACZMAREK⁴, MARIA MALICKA-
BŁASZKIEWICZ¹ and ARKADIUSZ KOZUBEK²

¹Department of Cell Patology, Institute of Biochemistry and Molecular Biology,
University of Wrocław, Przybyszewskiego 63/77, 51-148 Wrocław, Poland,

²Department of Lipids and Liposomes, Institute of Biochemistry and Molecular
Biology, University of Wrocław, Przybyszewskiego 63/77, 51-148 Wrocław,
Poland, ³Institute of Organic Chemistry, Biochemistry and Biotechnology,

Wrocław University of Technology, Wybrzeże Wyspiańskiego 27, 50-370
Wrocław, Poland, ⁴Pharmaceutical Research Institute, Rydygiera 8,

01-793 Warszawa, Poland

Currently considerable interest has arisen for the synthesis of indoloquinoline alkaloids derivatives, due to their potential biomedical and pharmaceutical value. The cytotoxic and antitumor activity of DIMIQ (5,11-Dimethyl-5*H*-indolo [2,3-*b*]quinoline), synthetic analog of neocryptolepine, alkaloid isolated from *Cryptolepis sanguinolenta* makes this compound a potential antitumor agent. More extensive clinical use of this agent is delayed due to lack of appropriate delivery system as this compound has very low solubility in aqueous media.

The cytotoxic effect of free and liposome-entrapped DIMIQ was evaluated against hepatoma Morris 5123 cells cultured *in vitro*. The cells, derived from experimentally induced and rapidly growing hepatoma Morris 5123 tumour, were exposed to the different concentrations of the drug. The treatment of the cells for 24 h with both free DIMIQ and its liposomal formulation resulted in significant changes in the cells morphology and was accompanied by the reduction of cell viability to compare with control, non-treated cells. This cytotoxic effect was correlated with the drug concentration. DNA analysis revealed characteristic for apoptosis large-scale fragmentation of DNA (300-50 kb fragments). This fragmentation was observed only for the highest tested concentration of DIMIQ (10 µg/ml in culture medium) and was not followed by further internucleosomal DNA fragmentation.

A significant difference between the cytotoxic effect of free DIMIQ and its liposomal formulation was observed only for the lowest tested concentration of the drug (0,1 µg/ml). At this concentration DIMIQ encapsulated in liposomes caused much higher reduction in the cell viability than its free form. These may indicate that DIMIQ incorporation within liposomes enhances the drug cytotoxic effect to compare with free DIMIQ administration, thus suggesting the more effective drug uptake when encapsulated in liposomes.

* E-mail: annak@ibmb.uni.wroc.pl