

# *Review of Clinical Pharmacology and Pharmacokinetics*

ΕΠΙΘΕΟΡΕΣΕ ΚΛΙΝΙΚΕΣ ΦΑΡΜΑΚΟΛΟΓΙΑΣ ΚΑΙ ΦΑΡΜΑΚΟΚΙΝΗΤΙΚΕΣ  
ΕΠΙΘΕΩΡΗΣΗ ΚΛΙΝΙΚΗΣ ΦΑΡΜΑΚΟΛΟΓΙΑΣ ΚΑΙ ΦΑΡΜΑΚΟΚΙΝΗΤΙΚΗΣ  
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## Letter from Guest Editor

The progress and contributions of 20<sup>th</sup> century pharmacology has been immense with over 20 pharmacologists to have received Nobel Prizes. This field of medical studies covers many areas; it is built upon and at the same time incorporates many disciplines such as biochemistry, biology physiology, pathology, anatomy, molecular biology, while the development of new analytical and experimental techniques and instruments has given a new boost in pharmacological research. Yet, although a remarkable progress has been made in developing new drugs and in understanding how they act, the challenges are endless. Integrating a depth of knowledge in many related scientific disciplines, pharmacologists offer a unique perspective to solving drug and chemical related problems which impinge on human health, with ultimate goal the treatment and prevention of major diseases.

The 5<sup>th</sup> Panhellenic Congress of Pharmacology focuses on four *hot* subjects: Regenerative Pharmacology, Herbal Medicines, Pharmacology of Abuse and Dependence, and Education in Pharmacology.

- *Regenerative Pharmacology* is one of the newest areas in Pharmacology, represents a groundbreaking field of research and has the potential to radically alter the treatment of diseases and disorders.

- *Herbal Medicines* have acquired an important percentage among the drug used; according to WHO 80% of people worldwide rely on herbal medicines for some aspect of their primary health care. This continuously increasing use of plant medicines imposes the need for establishing new regulations.

- *Pharmacology of Abuse and Dependence*, still not a well defined area, presents a lot of challenge for researchers and clinicians.

- *Education in Pharmacology* remains a hot subject in the Medical education, following the knowledge *explosion* of the last decades accompanied by a decreasing reliance on didactic teaching. The crucial question is: how and what should we teach?

We hope that the round table discussions along with the invited lectures, included in this abstract book, will raise new and intriguing ques-

tions that will further stimulate research, and will contribute to new therapeutic approaches and attitudes.

I would like to thank the Editorial Board of *Review of Clinical Pharmacology and Pharmacokinetics* in particular Journal Editors Prof. S.T. Plessas and Dr C.T. Plessas for invitation and for providing the suitable and high-standard forum through which new research findings will become available to the scientific community.

*The Guest Editor*

*Charis Liapi*

Assist. Professor in Pharmacology  
Medical School, University of Athens  
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## Cell Toxicity and Fluorescence Spectroscopy Studies of Carboxyl, Amine and Hydroxyl Terminated Dendrimers

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**Key words:** Cell toxicity, dendrimer, lipid bilayer, fluorescence spectroscopy

Nanotechnology is the most promising multidisciplinary field concerning the targeted delivery of bioactive molecules. Among the nanomolecules synthesized during the last decades, dendrimers seem to be ideal drug carriers as they exhibit zero polydispersity index and full structure control, characteristics that lead to reproducible pharmacokinetic behaviour. An ideal dendrimeric carrier of bioactive molecules should be non-toxic, non-immunogenic and biodegradable.

This study presents the effects of Pamam G3.5, Pamam G4 and PG1 dendrimers on cell toxicity and model membrane fluidity. Chinese hamster fibroblasts (cell line B14) were used as cellular model. The proliferation of the cells was measured using MTT assay. The morphological changes of cells were examined by fluorescent microscopy. The fibroblasts were exposed to various concentrations of dendrimers (0-90 µM) and various incubation times for 2h, 24h and 72h. Obtained results show that tested dendrimers (carboxyl terminated - PAMAM 3.5 and amine terminated - PAMAM 4) significantly reduced cell viability and caused cell morphological changes of cells. In contrast, PG1 dendrimer did not demonstrate a cytotoxic activity *in vitro*. Also red blood cells haemolysis assay was carried out in

order to determine the toxic effect of dendrimers on human red blood cells.

Incorporation of the dendrimers into membranes is supposed to change their physical properties with consequences to signal transduction and membrane protein activities. The physical parameters membrane fluidity are considered also in presented investigations. The measuring was carried out using large unilamellar vesicles (LUV) formed from three different lipid compositions: dimyristoylphosphatidylcholine (DMPC), dipalmitoylphosphatidylcholine (DPPC), dioleoylphosphatidylcholine (DOPC) phospholipids with final concentration 300 µM in presence of increasing amounts of dendrimers, using 1 µM 1,6-diphenyl-1,3,5-hexatriene (DPH) or trimethylammonium-diphenyl-hexatriene (TMA DPH) as fluorescent labels. The results showed that incorporation of the PAMAM 3.5, PAMAM 4 and PG1 dendrimers in the bilayer of LUV change partially the membrane anisotropy. This leads to the hypothesis that dendrimer incorporation into membranes is governed by their ability to change membrane fluidity. The results demonstrate that investigated dendrimers can play an important role in biological function of cells and cell membranes.



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