

# *Review of Clinical Pharmacology and Pharmacokinetics*

ΕΠΙΘΕΟΡΗΣΗ 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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## The Role of Oxidative and Nitrosative Stress Mechanisms in Symptomatic Carotid Disease

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**Key words:** Atheromatosis, plaque instability, oxidative stress, nitrosative stress, oxidized LDL

### INTRODUCTION

Oxidative stress contributes to the atherosclerotic process but its role in carotid plaque instability is unclear. We evaluated the oxidative mechanisms in atheromatic disease, their role in plaque instability and symptomatic carotid disease.

### METHODS

Thirty six patients undergoing endarterectomy were evaluated. Oxidized LDL (ox-LDL), malondialdehyde (MDA), nitrotyrosine (NT) and protein carbonyl (PCs) levels were determined in the atheromatic plaques in all cases. Differences between stable and unstable plaques, symptomatic and asymptomatic patients, >90% and <90% stenosis were evaluated. Cellular phenotype, nitrotyrosine (NT), and metalloproteinase (MMP9) expression were determined using immunohistochemistry. MMP9 expression was further verified using Western blotting. Twenty normal cadaveric carotids were the control group in our study.

### RESULTS

ox-LDL levels were significantly higher in unstable versus stable carotid plaques ( $p < 0.01$ ) as well as in symptomatic compared to asymptomatic patients ( $p < 0.01$ ). NT levels were significantly higher in unstable compared to stable plaques ( $p = 0.0186$ ). There were no significant differences in MDA and PCs levels between any groups. A statistically significant increase in NT and MMP9 expression was found in unstable versus stable plaques ( $p < 0.01$  and  $p < 0.01$ , respectively) and symptomatic versus asymptomatic patients ( $p = 0.0365$  and  $p = 0.0156$ , respectively), a result further verified with Western blotting. Furthermore, ox-LDL levels correlated significantly with NT ( $p = 0.0314$ ) and MMP9 ( $p = 0.0043$ ) levels.

### CONCLUSIONS

ox-LDL is an important oxidative factor which contributes to the instability of the atheromatic plaque through nitrosative stress and MMP9.



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