Review of Clinical Pharmacology and Pharmacokinetics

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ΕΠΙΘΕΩΡΗΣΗ ΚΛΙΝΙΚΗΣ ΦΑΡΜΑΚΟΛΟΓΙΑΣ ΚΑΙ ΦΑΡΜΑΚΟΚΙΝΗΤΙΚΗΣ
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GENERAL INFORMATIONS

REVIEW OF CLINICAL PHARMACOLOGY AND PHARMACOKINETICS

publishes Applied Pharmacology and Current Therapeutics Reviews, Review Articles on Drugs and Drug Therapy, Original Papers and Practical Therapeutics Articles.

The *scientific standard* of the papers, which are accepted for publication, is controlled by the Editorial Board or by other Experts in the various fields of Pharmacology and Pharmacokinetics.

Manuscripts: These should mention, on the first page, the *Title*, *Author(s)* and the *Name of the Institution* at which the work was done. The complete *address* of the author, including Postal area code number, should be given under the rubric *Send reprint requests to*. Papers should follow the general form: *Introduction, Materials and Methods, Results, Discussion* and *References*. Drugs must be referred to by their generic or chemical name, but may be identified by trade name in parenthesis or o footnote. All papers should be submitted in duplicate.

Summary: A summary in English (maximum length 200 words) must accompany all manuscripts.

Key words: A list of key words should be submitted.

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Papers should be submitted to the Editors-in-Chief: Prof. S.T. Plessas or Dr C.T. Plessas.

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INVITED SPEAKERS

ORAL AND POSTERS PRESENTATIONS

Letter from Guest Editor

The progress and contributions of 20th 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 5th 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
Chair of Hellenic Society of Pharmacology

REVIEW OF CLINICAL PHARMACOLOGY AND
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Medical Foods and Dietary Supplements: Minimal Requirements for Safe Clinical Use

T.C. Theoharides

Professor of Pharmacology and Internal Medicine, Immnunopharmacology and Drug Discovery Laboratory, Department of Pharmacology and Experimental Therapeutics, Tufts University School of Medicine, Tufts Medical Center, Boston, MA USA; Massachusetts Drug Formulary Commission (1986-2008) (www.mastcellmaster.com)

The increased decline in pharmacology teaching, the uncontrollable increase in drug prices, the increased fear of obscure diseases, such as chronic fatigue syndrome, and the lack of rational and sufficient regulations have propelled the use and misuse of supplements to a multibillion, multinational industry with little if any oversight. It is estimated that 7/10 people use some dietary supplement, there are >40,000 products available and >100 new products are introduced every year. The potential direct and indirect health dangers stem from inflated and unproven claims, impure ingredients, questionable sources and quality of preparation, unwanted interactions with drugs and foods, as well as often use instead of rational, evidence-based treatments. A case in point is Ma Huang (ephedrine alkaloids) that has been linked to numerous deaths and strokes, but it took over 10 years and an act of Congress to have it banned in the USA. No supplement should be permitted as a drug if published evidence indicates that it has no effect on a disease process. A relevant example is glucosamine (1500 mg/day), which has repeatedly been shown to be ineffective in osteoarthritis and can interfere with insulin therapy in diabetics, yet numerous products are sold in Greece both as prescription and dietary supplements. In addition, chondroitin sulfate, which is often added to glucosamine, commonly derives from cow cartilage that is banned because of “mad cow” disease, but the source is not disclosed; moreover, it has a molecular weight of >1 million Daltons and <5% is absorbed in powder form, making it essentially useless. Finally, no cartilage “replenishment” is likely to work unless joint inflammation is blocked. The EU has created a ‘positive list’ of approved supplements, but the amounts are not defined. All non-prescription dietary supplements should be required to include a warning box, such as the one mandated by the US Federal Trade Commission, that any statements/claims have not been approved by the USA Food and Drug Administration FDA), and to provide a least evidence of: (a) Good Manufacturing Practices certificate of the site of production, (b) exact amounts, (c) purity, (d) source of active ingredients, and (e) any allergenic ingredients. Even though the US FDA does not have authority to regulate dietary supplements, it does issue a *Certificate of Free Export* if these criteria are met, clearly establishing a way to differentiate those products of superior quality and safety. For *medical foods*, evidence should be provided that the claimed active ingredients replenish/supplement those affected by a disease process, as shown by published studies, and some indication of the extent of oral absorption. Over 60% of consumers are not aware that neither safety nor efficacy or these products is approved. Ethical, medical and economic reasons mandate that appropriate regulatory actions are well overdue.

SELECT REFERENCES

Ashar B.H., Miller R.G., Pichard C.P., Levine R., Wright S.M.: Patients' understanding of the regulation of dietary supplements. *J. Community Health 33*: 22-30 (2008)

Bijlsma J.W., Lafeber F.P.: Glucosamine sulfate in osteoarthritis: the jury is still out. *Ann. Intern. Med. 148*: 315-316 (2008)

Clegg D.O., Reda D.J., Haris C.L., et al.: Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N. Engl. J. Med. 354*: 795-808 (2006)
Eberhardie C.: Nutritional supplements and the EU: is anyone happy? *Proc. Nutr. Soc. 66*: 508-511 (2007)
Felson D.T.: Glucosamine and chondroitin sulfate in knee osteoarthritis: where now? *Nat. Clin. Pract. Rheumatol. 2*: 356-357 (2006)
Gulati O.P., Berry Ottaway P.: Legislation relating to nutraceuticals in the European Union with a particular focus on botanical-sourced products. *Toxicology 221*: 75-87 (2006)
Hampton T.: Efficacy still uncertain for widely used supplements for arthritis. *JAMA 297*: 351-352 (2007)
Hass D.J., Lewis J.D.: Quality of manufacturer provided information on safety and efficacy claims for dietary supplements for colonic health. *Pharmacoepidemiol. Drug Saf. 15*: 578-586 (2006)
Jordan M.A., Haywood T.: Evaluation of internet websites marketing herbal weight-loss supplements to consumers. *J. Altern. Complement. Med. 13*: 1035-1043 (2007)
Morrow J.D.: Why the United States still needs improved dietary supplement regulation and oversight. *Clin. Pharmacol. Ther. 83*: 391-393 (2008)
Pham T., Cornea A., Blick K.E., Jenkins A., Scofield R.H.: Oral glucosamine in doses used to treat osteoarthritis worsens insulin resistance. *Am. J. Med. Sci. 333*: 333-339, (2007)
Rozendaal R.M., Koes B.W., van Osch G.J., et al.: Effect of glucosamine sulfate on hip osteoarthritis: a randomized trial. *Ann. Intern. Med. 148*: 268-277 (2008)
Sadovsky R., Collins N., Tighe A.P., Brunton S.A., Safeer R.: Patient use of dietary supplements: a clinician's perspective. *Curr. Med. Res. Opin. 24*: 1209-1216 (2008)
Theoharides T.C.: Sudden death of a healthy college student related to ephedrine toxicity from a ma huang-containing drink. *J. Clin. Psychopharmacol. 17*: 43743-43749 (1997)
Theoharides T.C., Bielory L.: Mast cells and mast cell mediators as targets of dietary supplements. *Ann. Allergy Asthma Immunol. 93(2 Suppl 1)*: S24-34 (2004)

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