

Review of Clinical Pharmacology and Pharmacokinetics

ΕΠΙΘΕΟΡΗΣΗ ΚΛΙΝΙΚΗΣ ΦΑΡΜΑΚΟΛΟΓΙΑΣ ΚΑΙ ΦΑΡΜΑΚΟΚΙΝΗΤΙΚΗΣ
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CONTENTS

INVITED SPEAKERS

M. GÖTHERT.....	83
<i>Changes in pharmacological and functional properties of human 5-HT receptors by genetic, splice and subunit variation</i>	
P. HONKAKOSKI....	85
<i>The role of nuclear receptor in regulation of CYPs</i>	
C. SAMPAIO.....	86
<i>Neuroprotection: The difficult journey from the bench to the bedside</i>	
P. ATHANASIOU.....	87
<i>Biological factors: New perspectives in the treatment of autoimmune diseases</i>	
CH. FLORDELLIS, P. PAPATHANASSOPOULOS.....	88
<i>Multi-drug targeting as a new basis in Pharmacology</i>	
E. KASTRITIS.....	89
<i>Modern therapy of multiple myeloma</i>	
M. KOUTSILIERIS.....	90
<i>Pathophysiology of osteoplastic metastasis in prostate cancer: Therapeutic implications</i>	
Z. PAPADOPOULOU-DAIFOTI.....	91
<i>Sex differences in drug response</i>	
D. DUKA.....	92
<i>Neurobiological mechanisms underlying drug addiction: Is there a common pathway?</i>	
A. GRAVANIS.....	93
<i>Regenerative Pharmacology</i>	
I. CHINOU.....	94
<i>Introduction to herbals</i>	
P. GALANOPOULOU-COUVARI.....	95
<i>Herbal and dietary supplement – drug interactions: Evidence for clinical significance</i>	
W. KNÖSS.....	97
<i>Herbal medicinal products in Europe</i>	
B. MATHIOUDAKIS.....	98
<i>The legal situation regarding the use of vitamins, minerals and certain other ingredients in foods</i>	
T.C. THEOHARIDES.....	99
<i>Medical foods and dietary supplements: Minimal requirements for safe clinical use</i>	
DRAGO F.....	101
<i>Docendo Discimus: Teaching Pharmacology in the Modern Europe</i>	
T. GRIESBACHER.....	102

Medical curricula between sharpening Universities' individual profiles and the need for speed: Effects on Pharmacology teaching in Austria

S. MAXWELL.....103
How can we best prepare medical students to be safe and effective prescribers?

J.S. PAPADOPOULOS.....104
Knowledge or attitude?

T.C. THEOHARIDES.....105
Pharmacology: From basic principles to translational medicine to clinical practice

ORAL AND POSTERS PRESENTATIONS

I. ANDREADOU, S. PARASCHOS, E.K. ILIODROMITIS, A. ZOGA, P. MAGIATIS, S. MITAKOU, L. KAKLAMANIS, A.L. SKALTSOUNIS, D.TH. KREMASTINOS.....107
Antiatheromatic and hypolipidemic activity of Chios mastic gum in anesthetized rabbits

O. ASIMAKI, N. SAKELLARIDIS, D. MANGOURA.....109
CB1R-dependent activation of Fyn tyrosine kinase and protein kinase C delta, PKC δ , in lipid rafts

E. BEGAS, E. KOUVARAS, V. TSIOKOU, E.K. ASPRODINI.....113
In vivo evaluation of CYP1A2 and CYP2A6 activities in a Greek population during menopause

A. BIBIS, G. DIMOGERONTAS, K. KOUZELIS, A. ZARROS, C. LIAPI.....115
Lazaroids: A new category of neuroprotective agents

A. BOULTADAKIS, G. GEORGIADOU, P.A. TARANTILIS, N. PITSIKAS.....118
Effects of the active constituents of Crocus Sativus L., crocins, in an animal model of anxiety

I. CHARALAMPOPOULOS, V. MINAS, N. AVLONITIS, T. CALOGEROPOULOU, A. GRAVANIS.....119
Synthetic spiro-neurosteroid analogs exerting structure-specific neuroprotective effects

E. CHATZAKI, C. PASXOS, M. LAMBROPOULOU, S. ANAGNOSTOULIS, CH. CHARSOU, E. CHOURIDOU, E. MICHAILIDOU, F. PAPACHRISTOU, TH.C. CONSTANTINIDIS, C. SIMOPOULOS.....122
Corticotropin releasing factor (CRF) and liver apoptosis

- O. CHOULIARA, A. POLISSIDIS, M. DOSI, A. GALANOPOULOS, E.TZAVARA, M. MARSELOS, Z. PAPADOPOULOU-DAIFOTI, C. SPYRAKI, K. ANTONIOU.....124
Behavioral effects and dopaminergic indices following THC administration in two rat phenotypes
- TH.C. CONSTANTINIDIS, E. VAGKA, P. DALLIDOU, P. BASTA, V. DRAKOPOULOS, E. CHATZAKI.....126
Occupational exposure of health care workers to chemotherapeutic agents: A Study in Greek Hospitals
- E.P. DASKALOPOULOS, G. RENTESI, M.A LANG, M. MARSELOS, M. KONSTANDI.....129
Hepatic drug metabolizing efficacy modifications after exposure to stress
- E. DIMITRIADI., M. NIKOLAIDOU, P. PAPPAS, M. MARSELOS.....131
Sex differences in Pharmacokinetics of Doxorubicin
- CH. DOKOS, K. KALOUSIS, A. KOUYOUMTZIS, M. MIRONIDOU-TZOUVELEKI.....133
Chemotherapy of osteosarcoma: Beyond conventional approaches to future concepts
- D. ECONOMOU, E. PAPAKONSTANTINOU, I. KLAGAS, ATH. SAKADAMIS, A. SIOGA.....138
Hyaluronic acid induces wound closure by primary human skin fibroblasts in a wound healing model
- H. FRANGOY, E. NIKOLOUSSIS, N. MASSOURIDOU, T. VAVILIS, E.-N. EMMANOUIL.....141
Caspase-3 activity in pregnant rat spleen and lymph nodes after treatment with Cycloheximide and the development of malignant breast tumor in experimental animals: Case report
- A. GALANOPOULOS, A. POLISSIDIS, O. CHOULIARA, Z. PAPADOPOULOU-DAIFOTI, K. ANTONIOU.....145
Glutamatergic alterations following cannabinoid administration
- C. GIAGINIS, A. ZIRA, S. THEOCHARIS, A. TSANTILI-KAKOULIDOU.....146
Simple physicochemical properties as effective filters for risk estimation of drug transport across the human placental barrier
- M. GIANNAKOULI, A.J. ALETRAS, E. GIANNOPOULOU.....149
Antagonistic effect of TGF- β 1 on the IL-1 β -induced expression of MMP-1 in human fibroblasts of different tissue origin
- E.-M. GEORGANTA, G. MAZARAKOU, A. AGALOU, Z. GEORGOUSI.....152
The C-termini of the μ - and δ - opioid receptors differentially bind to signal transducers and Activators of transcription, STAT5A and STAT5B
- CH. HADJIMICHAEL, S. SAVVA, A. ANDREOU, S. THEOCHAROUS.....156
Physicians and the use of antibiotics in Cyprus
- C. HADJICOSTA, M. MIRONIDOU-TZOUVELEKI.....159
Eph receptors and ephrin ligands: Back to the origin in the therapy of cancer
- A. HATZISOTIRIOU, D. KAPOUKRANIDOU, M. ALBANI.....163
Assessment of motoneuron death during development following central and peripheral deaf-ferentation
- Z. IAKOVIDOU-KRITSI, K. AKRITOPOULOU, M.T. EKONOMOPOULOU, T. LIALIARIS, D. MOURELATOS AND E. MIOGLOU-KALOUP-TSI.....166
Genotoxic and cytostatic effect of atypical antipsychotic drugs in normal human lymphocytes cultures
- I. ILIAS, M. ALEXIOU, K. MICHALAKIS, G. MITIOS, E. VENAki, S. NIKOPOULOU.....169
Study of the effect of statin antilipidemic therapy on the thyroid
- M. IORDANIDOU, A. TAVRIDOU, M.V. VASSELIADIS, K.I. ARVANITIDIS, J. PETRIDIS, D. CHRISTAKIDIS, V.G MANOLOPOULOS.....170
The role of polymorphisms in 5-HT_{2c} receptor gene in type 2 diabetes mellitus and obesity in the caucasian population
- K. KALOKASIDIS, D. MOLYVA, V. MIRTSOU, H. DEDI, B. KOKKAS, A. GOULAS.....174
The effect of rupatadine on histamine-induced oedema formation and TNF- α gene expression in the rat paw
- C. KANI, K. PAPANIKOLAOU, A. PEHLIVANIDIS, Z. PAPADOPOULOU-DAIFOTI.....176
Cholinesterase inhibitors and memantine in vascular dementia: A systematic review of randomized controlled trials
- D. KAPOUCRANIDOU, R. KOTAKIDOU, M. PONTIKA, D. HADJIPAVLOU-LITINA.....178
Effects from chronic iron administration on functional organs: Correlation with free Radicals
- CH. KARACHALIOS.....181
Salmonella enterica Serovar Typhi Ty21a expressing HPV Type 16 L1 as a potential live vaccine against cervical cancer and typhoid fever

- I. KARAMOUZIS, F. KESIDON, E. HASAPOPOULOU, C. MANOLOPOULOS, B. PAPAGEORGIOU, M. GIANNOULIS, E. SAMPANOPOULOU, D. MICHAILIDOU, TH. DARDAVESSIS, M. KARAMOUZIS, I. PIDONIA.....182
False positive tumour markers CA 15-3, CEA, CA 125 and CA 19-9 in patients with homozygous β -thalassaemia, sickle cell / β -thalassaemia and thalassaemia intermedia
- G. KARKOULIAS, K. KYPREOS, P. PAPATHANASOPOULOS, CH. FLORELLIS.....185
Sustained activation of CREB is required for neuronal differentiation of α_2 -AR transfected PC12 cells
- D.S. KATSIABAS, S.K. MAVRIDIS, I.S. PAPPAS.....189
Expression of cytochrome P450s and transcription factors Pxr and Car in canine tissues
- K. KATSIKARIS, I. SKOPELITIS, A. PAPAIONANNOU, A. GOTSI, N. KARAGIANNIDIS.....193
A pharmacoeconomic comparison study of an lc/ms method used for the bioequivalence study of Donepezil compared with a similar HPLC method for the same substance
- K. KOSMA, A. SIANNI, K. LIATSOS, C. LEOTSAKOU, A. KALOGEROPOULOU, V. ROUMPOS.....195
Effects of long-term antipsychotic treatment of oxidative defense system parameters
- A. KOTSIU, E. CHATZIGIANNI, A. PITSICALI, C. TESSEROMATIS.....198
Cholesteryl ester transfer protein (CETP) changes under the influence of saturated fat diet and anabolic treatment in rats
- M. KOUTSIUMPA, M. HATZIAPOSTOULOU, C. MIKELIS, E. PAPADIMITRIOU.....201
The stimulatory effects of aprotinin on human endothelial and prostate cancer cells are mediated by pleiotrophin
- M. KOUTSOVITI-PAPADOPOULOU, TH.A. PSARRA, G.C. BATZIAS.....203
Lower esophageal sphincter relaxing agents: An in vitro comparative study in the rabbit
- M. KOUTSOVITI-PAPADOPOULOU, L. XU, I. DEPOORTERE, L. THIELEMANS, TH. THIJS, TH.L. PEETERS.....207
In vitro responses of the guinea pig gastrointestinal tract to homologous motilin
- E. KOUVARAS, T. KILINDRIS, A. VASILAKI, E.K. ASPRODINI.....212
Acute in vivo exposure to fentanyl reduces GABA immunoreactivity in the CA1 area of the rat hippocampus
- L.J. LEONTIADIS, M.-P. PAPAKONSTANTINOY, M. SARRIS, Z. GEORGIOUSSI.....214
RGS4 and RGS2 differentially modulate opioid receptor signaling
- CH.I. LIAKOU, A. KAMAT, D. NG TANG, H. CHEN, J. SUN, CH. LOGOTHETIS, P. SHARMA.....217
Anti-CTLA-4 therapy in bladder cancer patients alters immune responses by increasing IFN γ production and decreasing the CD4⁺FOXP3⁺ regulatory T cells in the tumor microenvironment
- CH. LIAPI, A. ZARROS, S. THEOCHARIS, H. AL-HUMADI, F. ANIFANTAKI, E. GKROUZMAN, Z. MELLIOS, N. SKANDALI, S. TSAKIRIS.....221
Lanthanum effects on the adult rat brain antioxidant status and adenosinetriphosphatase activities: Modulation by L-cysteine
- A. LYMPEROPOULOS, W.J. KOCH.....224
Adrenal beta-arrestin 1 promotes physiological aldosterone production
- CH. MAGLARAS, M. PARAVA, P. PAPADOPOULOS, D.TSIPTSIOS, P. BEREDIMAS.....227
Pharmaceutical approach in mild cognitive impairment. Is it advisable? Recent data and prospects
- I. MAIMARI, CH. DOKOS, M. MIRONIDOU-TZOUVELEKI.....230
Brain wave patterns and steroids administration
- F.M. MALAMAS, C.G. THOMAS, T. STEFOS, A. TSATSOULIS, A.M. EVANGELOU.....232
The antagonizing effects of N-acetyl-cysteine on prolactin induced proliferation of human breast cancer cells
- G. MANTA, S. TARAVIRAS, E. KOUVELAS, A. MITSACOS.....235
Developmental heterogeneity in splicing of the postnatal rat retinal N-methyl-D-aspartate glutamate receptor 1
- A. MATRALIS, A. KOUROUNAKIS.....238
Hypolipidaemic and antioxidant properties of novel squalene synthase inhibitors
- M.C. MAVROGIORGOU, P. STAVRINOY, P. PAPPAS, G. MILIARAS, K. POLYZOIDIS, M. MARSELOS.....241
Expression of drug-metabolizing proteins in human brain tumors: Preliminary results
- M. MAVRIKAKI, G.G. NOMIKOS, G. PANAGIS.....242

- Evaluation of the effects of different mood stabilizers in a rat model of euphoria*
 TH. MAVRAKANAS, E. TSIRELLA, M. MIRONIDOU-TZOUVELEKI.....243
Glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in the treatment of type 2 diabetes
 M. MIRONIDOU-TZOUVELEKI, CH. DOKOS, M. ANDRONOGLU, P. PAPADIMOULI, K. KALOUSIS.....246
Administration of antiplatelet agents in cardiovascular disorders: Results from a clinical study
 M. MIRONIDOU-TZOUVELEKI, CH. DOKOS, K. KALOUSIS.....250
Serum butyrylcholinesterase activity as a marker of aging process in drug metabolism: Study in Greek aging population
 M. MIRONIDOU-TZOUVELEKI, CH. DOKOS.....254
Statins and bone formation: Proposed methods of implementing statins innovation in osteoporosis
 M. MIRONIDOU-TZOUVELEKI, A. ANOGEIANAKI, CH. DOKOS, D. KOUTSONIKOLAS, J. LIAGOURIS, G. ANOGIANAKIS.....256
The effect of orlistat on blood glucose and body weight in an onset diabetic rat model
 K. NAZOS, M.-T. BASSI, N. BRESOLIN, K. PANTOS.....259
The first identified mutation associated to alternating hemiplegia of childhood (AHC) in a Greek Family: Clinical and genetical approach
 M. NIKOLAIDOU, P. PAPPAS, K. ANTONIOU, M. MARSELOS.....263
Effects of a selective cyclooxygenase inhibitor on behavioural and neurochemical parameters
 Z. PANAGI, P. BOUNTOURIS, E. PAPADIMITRIOU, M. SKOUROLIAKOU, F. KALFARENTZOS.....264
Preliminary evaluation of preoperative and short-term (1 year) postoperative serum fat-soluble vitamin levels in super-obese patients undergoing A rouxen-Y gastric bypass with biliopancreatic diversion (RYGBP/BPD) malabsortive operation
 M. PANTELIDOU, K. DIMAS, A. GEORGOPOULOS, S. HATZIANTONIOU, C. DEMETZOS...265
Preparation, characterization and in vitro evaluation of liposome-incorporated curcumin on colorectal cancer cell lines
 G.K. PAPADIMAS, K.N. TZIROGIANNIS, M.D. DEMONAKOU, S.D. SKALTSAS, A.D. GRYPIOTI, K.T. KOURENTZI, K.N. ALEXANDROPOULOU, K. SOURLIS, M.G. MYKONIATIS, G.I. PANOUTSOPOULOS.....267
Hepatic regeneration after 60-70% and 30-34% partial hepatectomy in the rat
 P.K. PANAGOPOULOS, S. TSARTSALIS, CH. DOKOS, M. MIRONIDOU-TZOUVELEKI.....269
New kids on the block: Statins in the fight against Alzheimer's Disease
 P. PAPAIOANNIDOU, A. KAMBAROUDIS, V. VLAHOVIC-PALCEVSKI, A. SABO, L. PEJAKOV, B. BEOVIC, R. VELICKOVIC-RADOVANOVIC, E. KARAMANLIS, A. RASKOVIC, C. PAPANIKOLAOU, M. JAKOVLJEVIC, H. CARAGEORGIOU, I. DIAMANTIS, G.M. BENONI, L. CUZZOLIN, J. PETROVIC, S. JANKOVIC, G. HATZITHEOHARIS, G. VELO, N. HARLAFTIS, TH. GERASIMIDIS.....273
Quality of perioperative chemoprophylaxis in General Surgery: Preliminary results of ASPPOC in South Europe
 P. PAPAIOANNIDOU, K. NANASSIS, A. SABO, V. VLAHOVIC-PALCEVSKI, L. PEJAKOV, O. HORVAT, M. JAKOVLJEVIC, P. SELVIARIDIS, G.-M. BENONI, L. CUZZOLIN, Z. TOMIC, S. JANKOVIC, G. VELO.....276
Quality of perioperative chemoprophylaxis in Neurosurgery: Preliminary results of ASPPOC in South Europe
 P. PAPAIOANNIDOU, P. AKRITOPOULOS, G.-M. BENONI, L. CUZZOLIN, G. VELO.....279
Quality of perioperative chemoprophylaxis in Orthopedics Surgery: Preliminary results of ASPPOC in Greece and Italy
 P. PAPAIOANNIDOU, D. VAVILIS, G.-M. BENONI, L. CUZZOLIN, G. VELO, B. TARLATZIS, J. BONTIS.....282
Quality of perioperative chemoprophylaxis in Obstetrics and Gynecology: Preliminary results of ASPPOC in Greece and Italy
 P. PAPAIOANNIDOU.....285
Theoretical and practical issues of cognitive development in problem based learning
 M. PARAVA, CH. MAGLARAS, D. TSIPTSIOS, M. DOULGERAKIS, P. BEREDIMAS.....288
Succinylcholine in rapid sequence induction (RSI): How safe is its use when there is evidence of intracranial changes?
 S.M. PIPERAKIS, K. KONTOGIANNI, G. KARANASTASI, C. SIFFEL, A. CEBULSKA-WASILEWSKA, R. MARKOS, Z. IAKOVIDOU-KRITSI, M.M. PIPERAKIS.....291
Effects of pesticides on exposed populations from four European Countries

- N. PITSIKAS, S. ZISOPOULOU, I. PAPPAS, N. SAKELLARIDIS.....294
The selective 5-HT₆ receptor antagonist Ro 04-6790 attenuates psychotomimetic effects of the NMDA receptor antagonist MK-801
- P.M. PITYCHOUTIS, K. NAKAMURA, P.A. TSONIS, Z. PAPADOPOULOU-DAIFOTI.....295
Neurochemical alterations following acute immune stimulation: A male versus female study
- S. PLAKAS, I. SPANOS, G. DIMOGERONTAS, E. ROKAS, M. PAPADOPOULOS, A. ROVLIAS, E. KONSTANDINIDIS.....296
Gliadel wafers in the treatment of malignant glioma: Our experience
- E. POLAKIS, M. LAMBROPOULOU, C. CHAR-SOU, C. CHEIMONIDOU, K. CHALKIADAKI, E. CHATZAKI.....297
The expression of the corticotropin releasing factor (CRF) system of neuropeptides and receptors in mouse microglia cells
- A. POLISSIDIS, O. CHOULIARA, A. GALANOPoulos, E. TZAVARA, M. MARSELOS, Z. PAPADOPOULOU-DAIFOTI, K. ANTONIOU.....300
Dopaminergic modifications following win 55,212-2 administration in the conditioned place preference paradigm
- CH. POURZITAKI, TH. TZELLOS, CH. SARDELI, G. PAPAZISIS, E. AMANITI, D. KOUVELAS..302
Evidence-based evaluation of emergency care treatment algorithms: 15 dominant myths
- C. POURZITAKI, G. KANELLOS, I. KLAGAS, A. KRITIS.....304
Combined treatment of aspartyl protease inhibitor and NMDA antagonist in Pc12 cells after glutamate excitotoxicity
- C. POURZITAKI, H. LOGOTHETI, C. SARDELI, G. PAPAZISIS, P. ARAMPATZIS, D. KOUVELAS.....308
Pregabalin combined with epidural analgesia in chronic cancer pain patients
- TH.A. PSARRA, TH. THIJS, A. DIEZ-FRAILE, I. DEPOORTERE, G.C. BATZIAS, TH.L. PEETERS, M. KOUTSOVITI-PAPADOPOULOU.....310
Pharmacologic characteristics of the rabbit lower esophageal sphincter
- G. RAGIA, A. TAVRIDOU, K. ARVANITIDIS, E. NIKOLAIDIS, G. BOUGIOUKAS, V.G. MANOLOPOULOS.....315
Frequencies of eNOS gene polymorphisms - 786T>C and 894G>T in the Greek Population
- G. RENTESI, K. ANTONIOU, M. MARSELOS, M. SYRROU, M. KONSTANDI.....318
Long-term consequences of early maternal deprivation in behavioral and neurobiological responses of adult rat
- A. RUCINSKA, K. GARDIKIS, M. IONOV, M. JOKIEL, T. FELEKIS, B.R. STEELE, C.G. SCRETTAS, C. DEMETZOS, M. MICHA-SCRETTAS, M. BRYSEWSKA, T. GABRYELAK.....319
Cell toxicity and fluorescence spectroscopy studies of carboxyl, amine and hydroxyl terminated dendrimers
- CH. SARDELI, TH. TZELLOS, E. AMANITI, G. PAPAZISIS, K. KARAKOULAS, CH. POURZITAKI, D. KOUVELAS.....320
Deciding on the best treatment strategy for recurrent febrile seizures: An evidence-based Medicine approach
- P. SEMERTZIDIS, S. DOUMA, K. PETIDIS, A. TRIANTAFYLLOU, E. GALIAGOUSI, P. PAPAETHIMIOU, N. PAPADOPOULOS, N. KARTALI, A. PYRPASOPOULOU, M. DOUMAS, C. ZAMBOULIS.....322
Efficacy of amlodipine in older hypertensive patients (>55 years) not controlled with inhibitors of the renin-angiotensin system or beta blockers
- A. SIANNI, A. GANOTOPOULOU, K. KOSMA, K. LIATSOS, N. KARAGIANNI, E. LASKOS, D. VASILOPOULOS.....323
Effects of statins on key biochemical indexes of patients with acute ischemic cerebrovascular stroke
- F. SIGALA, A. PAPALAMBROS, K. FILIS, S. MARKANTONIS, M. DEMOPOULOU, P. SIGALAS, A. KOTSINAS, A. NIFOROU, B. GORGOLIS, I. ANDREADOU.....326
The role of oxidative and nitrosative stress mechanisms in symptomatic carotid disease
- V. SOURLAS, V. ATHANASIOU, A. VASILAKI.....327
Effect of somatostatinergic analogues on the ischemia-induced release of [³H]-D-aspartate and [³H]-GABA from rat retina and hippocampus
- H. SOUKI, G. VRIONI, M. KATRAMADOU, D.G. HELA, H. CARAGEORGIOU.....329
Serum pseudocholinesterase levels after chronic exposure to fenthion and correlation with morbidity (cancer, liver diseases, respiratory and neurological diseases)
- C. SPANOU, N. ALIGIANNIS, A. L. SKALT-SOUNIS, D. KOURETAS.....336
Effect of leguminosae family plant extracts and polyphenolic fractions on topoisomerase I-induced nicking of DNA

- TH. STROUBINI, A. PERELAS, CH. LIAPI, D. PERREA, I. DONTAS, M. TRAPALI, P. GALANOPOULOU.....339
Effects of sibutramine treatment on food intake, serum lipoproteins and TNF- α levels in rats fed standard laboratory or three isocaloric diets
- A. TRIANTAFYLLOU, S. DOUMA, K. PETIDIS, P. SEMERTZIDIS, E. GALIAGOUSI, P. PAEFTHIMIOU, N. PAPADOPOULOS, N. KARTALI, A. PYRPASOPOULOU, M. DOUMAS, C. ZAMBOULIS.....343
The implementation of British Hypertension Society Guidelines results in improved blood pressure control in young hypertensives
- B. TSAKMAKI, G. PAPADOPOULOS.....344
The introduction of the use of stimulants for attention deficit and hyperactivity in children (and adolescents)
- ATH. TSIOKANOS, ATH. JAMURTAS, P. SCHAMASCH, P. PAPALEXIS, CHR. TSITSIMPIKOU.....347
Statistical data collected during urine collection for doping control at the Athens 2004 Olympic Games and recommendations to improve the urine collection process
- E. TSIRELLA, M. MIRONIDOU-TZOUVELEKI.....350
Nitrous oxide for conscious sedation in Pediatric Dentistry
- E. TSIRELLA, M. MIRONIDOU-TZOUVELEKI.....353
Side effects of agents used in local anaesthesia
- TH. TZELLOS, G. PAPAZISIS, E. AMANITI, CH. SARDELI, CH.POURZITAKI, D. TAHMATZIDIS, D. KOUVELAS.....355
Pregabalin as a new treatment strategy for neuropathic pain in spinal cord injury: An evidence based evaluation
- TH. TZELLOS, I. KLAGAS, E. PAPAKON-STANTINO, K. VAHTSEVANOS, S. TRIARIDIS, ATH. KYRGIDIS, ATH. PRINTZA, E. ZVINTZOU, G. KARAKIULAKIS.....358
Differential expression of matrix metalloproteinases 2 and 9 in basal cell carcinoma, photo-exposed and photo-protected skin
- A.S. VESKOUKIS, M.G. NIKOLAIDIS, A. KYPAROS, D. KOKKINOS, E. VARAMENTI, D. KOURETAS.....360
The Effect of allopurinol on protein carbonyls and swimming performance in rats
- E. YIANNAKOPOULOU.....363
Cephalosporin induced haemolytic anaemia in surgical patients: Systematic review
- C. GIAGINIS, A. ZIRA, S. THEOCHARIS, A.TSANTILI-KAKOULIDOU.....368
Property distribution in the chemical space of PPAR- γ agonists: Evaluation of drug-like characteristics
- A.I. LIAKOU, K. ARABATZI, C.I. LIAKOU, M.J. THEODORAKIS.....366
Impact of obesity on cytokine secretion patterns following an oral glucose tolerance test in individuals with normal glucose tolerance

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

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Neuroprotection: The difficult Journey from the Bench to the Bedside

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Neurodegenerative diseases are a varied assortment of central nervous system disorders characterised by the gradual and progressive loss of neural tissue or nerve cells. Two of such diseases that have a major public health impact are Alzheimer Disease (AD) (5% of the population older than 65 years) and Parkinson Disease (PD) (1% of the population older than 65 years).

Currently, symptomatic treatment of AD is only modestly efficacious (anticholinesterase inhibitors, memantine). On the other hand the symptomatic treatment of the motor symptoms of PD is highly efficacious (levodopa, dopamine agonists, MAO-B inhibitors, COMT inhibitors, deep brain stimulation). Yet, despite these circumstantial differences both diseases are far from being controlled. All the expectations and dreams about controlling AD or PD are mostly based in the concept of halting or slowing the progression of disease, mostly by interfering with the processes that lead to neuronal death.

Target Discovery is very much disease specific. The amyloid and tau hypothesis underlying the physiopathology of AD have been a fertile field to generate compounds to be tested in clinical trials. AD Epidemiological research also contributed to the identification of clinically testable compounds (AINES, COX-2 inhibitors, statins, estrogens). In the field of PD the most recent advances in target search have been accrued in the field of genetics. However, so far most of the compounds tested in clinical trials have been supported by non-genetic

concepts: mitochondrial dysfunction, oxidative stress (selegiline, CoQ10, creatinine).

Until now not a single compound succeeded to be proven as being a disease modifier (neuro-protector) in clinical trials. There are many reasons to justify this daunting scenario, which we intend to discuss in some details. Those reasons can be classified in 2 main types: (1) the compound is not sufficiently active to have clinical expression. (2) The clinical trial design and implementation are not adequate to detect the clinical expression of the effect. For the time being our evaluation of the data available suggests that the first reason is the most common.

The lack of high potential compounds is probably the biggest shortcoming in the field. However many of the bottlenecks are technological or methodological and must be mastered if a disease modifying intervention is to be found. At the lab level issues like the lack of positive predictability of in vitro and in vivo models must be solved. Methods to establish plausible dose ranges must be developed. This, in part, depends on the validation of biomarkers.

At the clinical level the validation of progression biomarkers is critical (diagnostic and progression biomarkers should be distinguished). To much emphasis and work have been put, so far, in innovative trial designs (futility, two period designs).

We will summarize the controversy surrounding these topics, providing our personal insights on the matter.

VOLUME 22, 2008 ☼ No 2
CONTENTS

- AGALOU A. 152
 AKRITOPOULOS P. 279
 AKRITOPOULOU K. 166
 ALBANI M. 163
 ALETRAS A.J. 149
 ALEXANDROPOULOU K.N. 267
 ALEXIOU M. 169
 AL-HUMADI H. 221
 ALIGIANNIS N. 336
 AMANITI E. 302,320,355
 ANAGNOSTOULIS S. 122
 ANDREADOU I. 107,326
 ANDREOU A. 156
 ANDRONOGLOU M. 246
 ANIFANTAKI F. 221
 ANOGEIANAKI A. 256
 ANOGIANAKIS G. 256
 ANTONIOU K. 124,145,263, 300,318
 ARABATZI K. 369
 ARAMPATZIS P. 308
 ARVANITIDIS K.I. 170,315
 ASIMAKI O. 109
 ASPRODINI E.K. 113,212
 ATHANASIOU P. 87
 ATHANASIOU V. 327
 AVLONITIS N. 119
 BASSI M.-T. 259
 BASTA P. 126
 BATZIAS G.C. 203,310
 BEGAS E. 113
 BENONI G.M. 273,276,279,282
 BEOVIC B. 273
 BEREDIMAS P. 227,288
 BIBIS A. 115
 BONTIS J. 282
 BOUGIOUKAS G. 315
 BOULTADAKIS A. 118
 BOUNTOURIS P. 264
 BRESOLIN N. 259
 BRYSEWSKA M. 319
 CALOGEROPOULOU T. 119
 CARAGEORGIU H. 273,329
 CEBULSKA-WASILEWSKA A. 291
 CHALKIADAKI K. 297
 CHARALAMPOPOULOS I. 119
 CHARSOU C. 122,297
 CHOURIDOU E. 122
 CHATZAKI E. 122,126,297
 CHATZIGIANNI E. 198
 CHEIMONIDOU C. 297
 CHEN H. 217
 CHINOU I. 94
 CHOULIARA O. 124,145,300
 CHRISTAKIDIS D. 170
 CONSTANTINIDIS TH.C. 122, 126
 CUZZOLIN L. 273,276,279,282
 DALLIDOU P. 126
 DARDAVESSIS TH. 182
 DASKALOPOULOS E.P. 129
 DEDI H. 174
 DEMETZOS C. 265,319
 DEMONAKOU M.D. 267
 DEMOPOULOU M. 326
 DEPOORTERE I. 207,310
 DIAMANTIS I. 273
 DIEZ-FRAILE A. 310
 DIMAS K. 265
 DIMITRIADI. E. 131
 DIMOGERONTAS G. 115,196
 DOKOS CH. 133,230,246,250, 254,256,269
 DONTAS I. 339
 DOSI M. 124
 DOULGERAKIS M. 288
 DOUMA S. 322,343
 DOUMAS M. 322,343
 DRAKOPOULOS V. 126
 DRAGO F. 101
 DUKA D. 92
 ECONOMOU D. 138
 EKONOMOPOULOU M.T. 166
 EMMANOUIL E.-N. 141
 EVANGELOU A.M. 232
 FELEKIS T. 319
 FILIS K. 326
 FLORDELLIS CH. 88, 185
 FRANGOU H. 141
 GABRYELAK T. 319
 GALANOPOULOS A. 124,145, 300
 GALANOPOULOU-COUVARI P. 95,339
 GALIAGOUSI E. 322,343
 GANOTOPOULOU A. 323
 GARDIKIS K. 319
 GEORGANTA E.-M. 152
 GEORGIADOU G. 118
 GEORGOPOULOS A. 265
 GEORGOUSI Z. 152,214
 GERASIMIDIS TH. 273
 GIAGINIS C. 146,368
 GIANNAKOULI M. 149
 GIANNOPOULOU E. 149
 GIANNOULIS M. 182
 GKROUZMAN E. 221
 GORGOU LIS B. 326
 GÖTHERT M. 83
 GOTSI A. 193
 GOULAS A. 174
 GRAVANIS A 93,119
 GRIESBACHER T. 102
 GRYPIOTI A.D. 267
 HADJICOSTA C. 159
 HADJIMICHAEL CH. 156
 HADJIPAVLOU-LITINA D. 178
 HARLAFTIS N. 273
 HASAPOPOULOU E. 182
 HATZIANTONIOU S. 265
 HATZIAPOSTOULOU M. 201
 HATZISOTIRIOU A. 163
 HATZITHEOHARIS G. 273
 HELA D.G. 329
 HONKAKOSKI P. 85
 HORVAT O. 276
 IAKOVIDOU-KRITSI Z. 166, 291
 ILIAS I. 169
 ILIODROMITIS E.K. 107,
 IONOV M. 319
 IORDANIDOU M. 170
 JAKOVLJEVIC M. 273,276
 JAMURTAS ATH. 347
 JANKOVIC S. 273,276
 JOKIEL M. 319
 KAKLAMANIS L. 107
 KALFARENTZOS F. 264
 KALOGEROPOULOU A. 195
 KALOKASIDIS K. 174
 KALOUSIS K. 133,246,250
 KAMAT A. 217
 KAMBAROUDIS A. 273
 KANELLOS G. 304
 KANI C. 176
 KAPOUCRANIDOU D. 163,178
 KARACHALIOS CH. 181
 KARAGIANNI N. 323
 KARAGIANNIDIS N. 193
 KARAKIULAKIS G. 358
 KARAKOULAS K. 320

- KARAMANLIS E. 273
 KARAMOUZIS I. 182
 KARAMOUZIS M. 182
 KARANASTASI G. 291
 KARKOULIAS G. 185
 KARTALI N. 322,343
 KASTRITIS E. 89
 KATRAMADOU M. 329
 KATSIABAS D.S. 189
 KATSIKARIS K. 193
 KESIDON F. 182
 KILINDRIS T. 212
 KLAGAS I. 138,304,348
 KNÖSS W. 97
 KOCH W.J. 224
 KOKKAS B. 174
 KOKKINOS D. 360
 KONSTANDI M. 129,318
 KONSTANDINIDIS E. 296
 KONTOGIANNI K. 291
 KOSMA K. 195,323
 KOTAKIDOU R. 178
 KOTSINAS A. 326
 KOTSIU A. 198
 KOURENTZI K.T. 267
 KOURETAS D. 336,360
 KOUROUNAKIS A. 238
 KOUTSILIERIS M. 90
 KOUTSIOUMPA M. 201
 KOUTSONIKOLAS D. 256
 KOUTSOVITI-
 PAPADOPOULOU M. 203,207,
 410
 KOUVARAS E. 113,212
 KOUVELAS D. 235,302,308,
 320,355
 KOUYOUMTZIS A. 133
 KOUZELIS K. 115
 KREMASTINOS D.TH. 107
 KRITIS A. 304
 KYPAROS A. 360
 KYPREOS K. 185
 KYRGIDIS ATH. 358
 LAMBROPOULOU M. 122,297
 LANG M.A. 129
 LASKOS E. 323
 LEONTIADIS L.J. 214
 LEOTSAKOU C. 195
 LIAGOURIS J. 256
 LIAKOU A.I. 369
 LIAKOU CH.I. 217,369
 LIALIARIS T. 166
 LIAPI C. 81,115,221,339
 LIATSOS K. 195,323
 LOGOTHETI H. 308
 LOGOTHETIS CH. 217
 LYMPEROPOULOS A. 224
 MAGIATIS P. 107
 MAGLARAS CH. 227,288
 MAIMARI I. 230
 MALAMAS F.M. 232
 MANGOURA N. 109
 MANOLOPOULOS C. 182
 MANOLOPOULOS V.G. 170,
 315
 MANTA G. 235
 MARKANTONIS S. 326
 MARKOS R. 291
 MARSELOS M. 124,129,131,
 241,263,300,318
 MASSOURIDOU N. 141
 MATHIOUDAKIS B. 98
 MATRALIS A. 238
 MAVRAKANAS TH. 243
 MAVRIDIS S.K. 189
 MAVRIKAKI M. 242
 MAVROGIORGOU M.C. 241
 MAXWELL S. 103
 MAZARAKOU G. 152
 MELLIOS Z. 221
 MICHALIDOU D. 182
 MICHALIDOU E. 122
 MICHALAKIS K. 169
 MICHA-SCRETTAS M. 319
 MIKELIS C. 201
 MILIARAS G. 241
 MINAS V. 119
 MIOGLOU-KALOUPTSI E. 166
 MIRONIDOU-TZOUVELEKI M.
 133,159,230,243,246,250,254,
 256,269,350,352
 MIRTSOU V. 174
 MITAKOU S. 107
 MITIOS G. 169
 MITSACOS A. 235
 MOLYVA D. 174
 MOURELATOS D. 166
 MYKONIATIS M.G. 267
 NAKAMURA K. 295
 NANASSIS K. 276
 NAZOS K. 259
 NG TANG D. 217
 NIFOROU A. 326
 NIKOLAIDIS E. 315
 NIKOLAIDIS M.G. 360
 NIKOLAIDOU M. 131,263
 NIKOLOUSSIS E. 141
 NIKOPOULOU S. 169
 NOMIKOS G.G. 242
 PANAGI Z. 264
 PANAGIS G. 242
 PANAGOPOULOS P.K. 269
 PANOUTSOPOULOS G.I. 267
 PANTELIDOU M. 265
 PANTOS K. 259
 PAPACHRISTOU F. 122
 PAPADIMAS G.K. 267
 PAPADIMITRIOU E. 201,264
 PAPADIMOULI P. 246
 PAPADOPOULOS G. 344
 PAPADOPOULOS J.S. 104
 PAPADOPOULOS M. 296
 PAPADOPOULOS N. 322,343
 PAPADOPOULOS P. 227
 PAPADOPOULOU-DAIFOTI Z.
 91,124,145,176,295,300
 PAPAETHIMIOU P. 322,343
 PAPAGEORGIOU B. 182
 PAPAIOANNIDOU P. 273,276,
 279,282,285
 PAPAIONANNOU A. 193
 PAPAKONSTANTINOU E. 138,
 358
 PAPAKONSTANTINOU M.-P.
 214
 PAPALAMBROS A. 326
 PAPALEXIS P. 347
 PAPANIKOLAOU C. 273
 PAPANIKOLAOU K. 176
 PAPATHANASOPOULOS P.
 88,185
 PAPAZISIS G. 302,308,320,
 355
 PAPPAS I. 294,189
 PAPPAS P. 131,241,263
 PARASCHOS S. 107
 PARAVA M. 227,288
 PASCHOS C. 122
 PEETERS TH.L. 207,310
 PEHLIVANIDIS A. 176
 PEJAKOV L. 273,276
 PERELAS A. 339
 PERREA D. 339
 PETIDIS K. 322,343
 PETRIDIS J. 170
 PETROVIC J. 273
 PIDONIA I. 182
 PIPERAKIS M.M. 291
 PIPERAKIS S.M. 291
 PITSICALI A. 198
 PITSIKAS N. 118,294
 PITYCHOUTIS P.M. 295
 PLAKAS S. 296
 POLAKIS E. 297
 POLISSIDIS A. 124,145,241

- POLYZOIDIS K. 241
 PONTIKA M. 178
 POURZITAKI C. 302,304,308,
 320,355
 PRINTZA ATH. 358
 PSARRA TH.A. 203,310
 PYRPASOPOULOU A. 322,
 343
 RAGIA G. 315
 RASKOVIC A. 273
 RENTESI G. 129,318
 ROKAS E. 296
 ROUMPOS V. 195
 ROVLIAS A. 296
 RUCINSKA A. 319
 SABO A. 273,276
 SAKADAMIS ATH. 138
 SAKELLARIDIS N. 109,294
 SAMPAIO C. 86
 SAMPANOPOULOU E. 182
 SARDELI C. 302,308,320,355
 SARRIS M. 214
 SAVVA S. 156
 SKALTSAS S.D. 267
 SCHAMASCH P. 347
 SCRETTAS C.G. 319
 SELVIARIDIS P. 276
 SEMERTZIDIS P. 322,343
 SHARMA P. 217
 SIANNI A. 195,323
 SIFFEL C. 291
 SIGALA F. 326
 SIGALAS P. 326
 SIMOPOULOS C. 122
 SIOGA A. 138
 SKALTSOUNIS A.L. 107,336
 SKANDALI N. 221
 SKOPELITIS I. 193
 SKOUROLIAKOU M. 264
 SOUKI H. 329
 SOURLAS V. 327
 SOURLIS K. 267
 SPANOS I. 296
 SPANOU C. 336
 SPYRAKI C. 124
 STAVRINOY P. 241
 STEELE B.R. 319
 STEFOS T. 232
 STROUBINI TH. 339
 SUN J. 217
 SYRROU M. 318
 TAHMATZIDIS D. 355
 TARANTILIS P.A. 118
 TARAVIRAS S. 235
 TARLATZIS B. 282
 TAVRIDOU A. 170
 TAVRIDOU A. 315
 TESSEROMATIS C. 198
 THEOCHARIS S. 146,221,368
 THEOCHAROUS S. 156
 THEODORAKIS M.J. 369
 THEOHARIDES T.C. 99,105
 THIELEMANS L. 207
 THIJS TH. 207,310
 THOMAS C.G. 232
 TOMIC Z. 276
 TRAPALI M. 339
 TRIANTAFYLLOU A. 322,343
 TRIARIDIS S. 358
 TSAKIRIS S. 221
 TSAKMAKI B. 344
 TSANTILI-KAKOULIDOU A.
 146,368
 TSARTSALIS S. 269
 TSATSOULIS A. 232
 TSIOKANOS ATH. 347
 TSIOKOU V. 113
 TSIPTSIOS D. 227,288
 TSIRELLA E. 243,250,353
 TSITSIMPIKOU CHR. 347
 TSONIS P.A. 295
 TZAVARA E. 124,300
 TZELLOS TH. 302,320,355,358
 TZIROGIANNIS K.N. 267
 VAGKA E. 126
 VAHTSEVANOS K. 358
 VARAMENTI E. 360
 VASILAKI A. 212,327
 VASILOPOULOS D. 323
 VASSEILIADIS M.V. 170
 VAVILIS D. 282
 VAVILIS T. 141
 VELICKOVIC-RADOVANOVIC
 R. 273
 VELO G. 273,276,279,282
 VENAKI E. 169
 VESKOUKIS A.S. 360
 VLAHOVIC-PALCEVSKI V.
 273,276
 VRIONI G. 329,
 XU L. 207
 ZAMBOULIS C. 322,343
 ZARROS A. 115,221
 ZIRA A. 146,368
 ZISOPOULOU S. 294
 ZOGA A. 107
 ZVINTZOU E. 358
 YIANNAKOPOULOU E. 363

