24th World Congress on
Pharmacology
&
7th World Heart Congress
August 19-20, 2019 Vienna, Austria

Scientific Tracks & Abstracts

Day 1

Day-1

SESSIONS

Clinical Pharmacology and Receptor Theory | Cardio Vascular Pharmacology | Pharmacokinetic and Pharmacodynamic | Drug Screening and Discovery | Topical Medicine and Infectious Diseases | Advances in Pharmacological Research | Biochemical Pharmacology

Chair: **Maria I Yablonskay,** Russian National Research Medical University, Russian Federation

SESSION INTRODUCTION

Title: **Biomarkers in brain-derived exosomes assist the diagnosis of neurodegenerative diseases**
Gal Bitan, University of California, USA

Title: **The project of experimental testing of the hypothesis regarding the effect of sodium phenylbutyrate for reducing dopamine depletion in the brain in Lesch-Nyhan syndrome using new personalized genetic HPRT1-deficient mouse as a pharmacological model**
Maria I. Yablonskay, Russian National Research Medical University, Russian Federation

Title: **Forming statin response in patients with coronary heart disease in presence of acute respiratory viral infections by means of genetic markers**
Galina S. Mal, Kursk State Medical University, Russian Federation

Title: **MicroRNA 103 inhibitor as a potential promising therapeutic target for myocardial infarction**
Ayman Selim, October University for Modern Sciences and Arts (MSA), Egypt

Title: **Circulating betatrophin in relation to metabolic, inflammatory Parameters, and oxidative stress in patients with type 2 diabetes mellitus**
Bland Bayar Khaleel, Preventive Health Directorate, Iraq

Title: **Finding a medical solution to calcium oxalate urolithiasis: Which agents have the best dissolution potential? An integrative review**
Samuel P.B.Drawbridge, BVetMed MRCVS, UK

Title: **Orthosteric- versus allosteric-dependent activation of the GABAA receptor requires numerically distinct subunit level rearrangements**
Jahanshah Amin, University of South Florida, USA

Title: **Clinical benefit of training asthmatic libyan patients on how to use metered dose inhalers by using 2Tone trainer**
Walid Y Tarsin, University of Tripoli, Libya

Biomarkers in brain-derived exosomes assist the diagnosis of neurodegenerative diseases

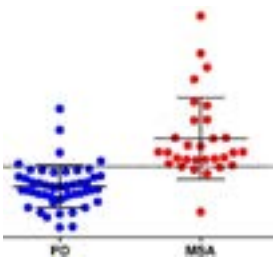
Gal Bitan[1], Suman Dutta[1], Irish del Rosario[2], Kimberly Paul[2], Jose-Alberto Palma[3], Susan L. Perlman[1], Wayne W. Poon[4], Horacio Kaufmann[3], Brent L. Fogel [1], Jeff M. Bronstein[1] and **Beate Ritz[2]**
[1,2,4]University of California, USA
[3]New York University School of Medicine, USA

Statement of the Problem: Biomarkers for neurodegenerative diseases are urgently needed. Definite diagnosis for most diseases is possible only postmortem and the rates of misdiagnosis are high. Monitoring progression and treatment effects using clinical criteria is inefficient due to high variability. Current biomarker strategies, such as brain imaging and cerebrospinal fluid analysis have major drawbacks. An attractive alternative is analysis of biomarkers in brain-derived exosomes isolated from the blood.

Methodology & Theoretical Orientation: We examined α-synuclein in neuronal and oligodendroglial exosomes as a diagnostic biomarker for distinguishing between Parkinson's disease (PD) and multiple system atrophy (MSA). α-Synuclein deposition is found as Lewy bodies in PD and glial cytoplasmic inclusions, primarily in oligodendrocytes, in MSA. We compared cohorts of healthy control individuals, patients with PD, and patients with MSA.

Findings: α- Synuclein concentration in both exosome populations were significantly higher in the two diseases than in the controls and in MSA relative to PD. The total α-synuclein levels separated MSA from control with high sensitivity and specificity, whereas the PD group separated only moderately from the other groups. However, the ratio between the α- synuclein levels in the oligodendroglial relative to the neuronal exosomes separated the two disease groups with high sensitivity and specificity. The ratio also correlated significantly with progression of motor symptoms in the PD group.

Conclusion & Significance: Measurement of α-synuclein in brain-derived exosomes offers a minimally invasive means for analyzing biomarkers for PD and MSA, suggesting that in the relatively near future these two diseases could for the first time be diagnosed with high sensitivity and specificity, and their progression could be monitored, using a simple blood test.



Biography

Gal Bitan, PhD, received his PhD in organic chemistry from the Hebrew University of Jerusalem, Israel. Following postdoctoral training at Harvard Medical School and affiliated hospitals, he joined the faculty at UCLA where he is currently a Professor of Neurology. Dr. Bitan's research program focuses on neurodegenerative diseases caused by abnormal protein self-assembly, such as Alzheimer's and Parkinson's diseases. He has made seminal contributions to the study of amyloid-protein oligomers and has been developing novel drug candidates and biomarker measurements for these diseases.

24th World Congress on Pharmacology
&
7th World Heart Congress

August 19-20, 2019 Vienna, Austria

The project of experimental testing of the hypothesis regarding the effect of sodium phenylbutyrate for reducing dopamine depletion in the brain in Lesch-Nyhan syndrome using new personalized genetic HPRT1-deficient mouse as a pharmacological model

Maria I. Yablonskay[1], Vladislav A. Kalmykov[2], Yuliya Yu. Silaeva[2], Victoria Yu. Voinova[1] and **Alexey V. Deykin[2]**
[1]Russian National Research Medical University, Russian Federation
[2]Institute of Gene Biology of the Russian Academy of Sciences, Russian Federation

Lesch-Nyhan syndrome is an X-linked inborn error of purine metabolism which is caused by mutations in the HPRT1 gene encoding the purine recycling enzyme hypoxanthine-guanine phosphoribosyltransferase (HPTR), the prevalence is approximately 1:380000. The disease manifests during the first year of life and is characterized by uric acid overproduction and urate nephropathy combined with severe neurologic dysfunction including cognitive impairment, dystonia, choreoathetosis, spasticity and self-injurious behavior. Overproduction of uric acid is controlled well with allopurinol. But until now, there is no sufficiently effective pharmacologic therapy for neurologic dysfunction in Lesch-Nyhan syndrome. We hypothesized that HPRT deficiency leads to hyperactivation of guanine deaminase (GDA), which has the same localization and expression levels in the brain as HPRT. GDA irreversibly converts guanine to xanthine with the release of ammonia. Local excess of ammonia in brain structures triggers a cascade of pathological processes resulting in impaired transport and release of dopamine in the nigrostriatal pathway, hyperactivation of the NMDA receptors and combined hyperactivation of adenosine and dopamine receptors, neuronal insensitivity to exogenous dopamine. We offer to test the effect of ammonia binding remedy Sodium Phenylbutyrate for reducing dopamine depletion in the brain. To test this hypothesis, we created a new personalized genetic HPRT1-deficient mouse model. We used the CRISPR-Cas9 genomic editing system to introduce the deletion of 8Val in the first exon of the HPRT1 gene in the mouse model. This hemizygous mutation is the cause of Lesch-Nyhan syndrome in one of the patients observed in our clinic. Despite the fact that Hprt-deficient mice do not demonstrate a clinical complex characteristic of patients with Lesch-Nyhan syndrome, they have depletion of dopamine in the same brain structures. These models should be used in studies of brain metabolism and preclinical studies of the effectiveness of new treatments for this disease.

Recent Publications :

1. Fu R., Jinnah H.A. (2011) Genotype-phenotype correlations in Lesch-Nyhan disease: moving beyond the gene. Journal of Biological Chemistry 287(5): 2997–3008.
2. Torres R.J., Puig J.G. (2007) Hypoxanthine-guanine phosophoribosyltransferase (HPRT) deficiency: Lesch-Nyhan syndrome. Orphanet Journal of Rare Disseases 2: 48.
3. Fairbanks L.D., Jacomelli G., Micheli V., Slade T., Simmonds H.A. (2002) Severe pyridine nucleotide depletion in fibroblasts from Lesch-Nyhan patients. Biochemical Journal 366(Pt 1): 265–272.
4. Deutsch S.I., Long K.D.B., Rosse R.B., Mastropaolo J., Eller J. (2005) Hypothesized deficiency of guanine-based purines may contribute to abnormalities of neurodevelopment, neuromodulation and neurotransmission in Lesch-Nyhan syndrome. Clinical Neuropharmacology 28: 28–37.
5. Meek S., Thomson A.J., Sutherland L., Sharp M.G., Thomson J., Bishop V., et al. (2016) Reduced levels of dopamine and altered metabolism in brains of HPRT knock- out rats: a new rodent model of Lesch-Nyhan Disease. Scientific Reports 6: 25592.

6. Bayat A., Christensen M., Wibrand F., Duno M., Lund A. (2015) Mild Lesch–Nyhan Disease in a Boy with a Null Mutation in HPRT1: An Exception to the Known Genotype–Phenotype Correlation. JIMD Reports 18: 135- 137.
7. Kosenko E., Montoliu C., Giordano G., Kaminsky Yu., Venediktova N., Buryanov Ya., Felipo V. (2004) Acute ammonia intoxication induces an NMDA receptor-mediated increase in poly(ADP-ribose) polymerase level and NAD+ metabolism in nuclei of rat brain cells. Journal of Neurochemistry 89: 1101-1110.
8. Göttle M., Prudente C.N. Fu R., Sutcliffe D., Pang H., Cooper D., Veledar E., et al. (2014) Loss of dopamine phenotype among midbrain neurons in Lesch-Nyhan disease. Annals of Neurology 76(1): 95-107.
9. Rice M.E. (2011) H2O2: a dynamic neuromodulator. The Neuroscientist 17(4): 389-406.

Biography

Maria I. Yablonskaya has passion in clinical genetics and especially in diagnostics and management of inherited metabolic diseases.

Notes:

Forming statin response in patients with coronary heart disease in presence of acute respiratory viral infections by means of genetic markers

Galina S. Mal
Kursk State Medical University, Russia

Statement of the Problem: Development of CHD associated with atherosclerosis. One of the main pathogenetic causes of atherosclerosis development is inflammation, being an important atherogenesis component. Any acute infection may be the etiological factor which activates chronic inflammation in the atherosclerotic plaque, involving the cytokine system. A number of studies demonstrate the relation between an increase of cytokine level and the signs of atherosclerosis destabilization and CHD. The purpose of this study is to describe the drug response variability in CHD patients with an acute viral infection.

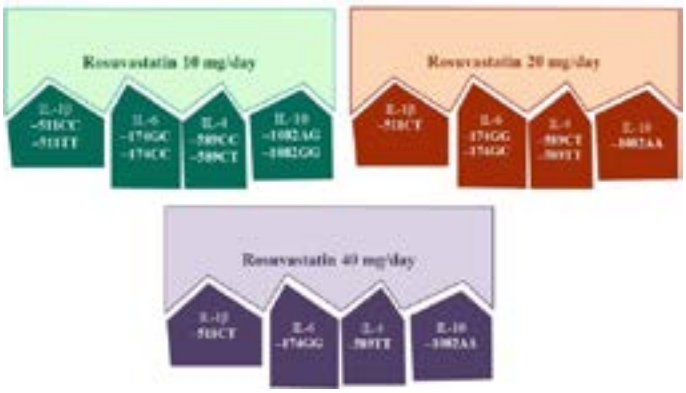
Methodology & Theoretical Orientation: The study involved 170 CHD patients, 120 of whom also had infections (ARVI). The LDL-C and cholesterol levels were determined in the blood serum using an enzymatic method. Genotyping of polymorphisms IL-1β –511C>T, IL-6 –174G>C, IL-4 –589C>T, IL-10 –1082G>A was performed using a PCR method on the CFX96 Bio-Rad Laboratories amplifier (USA).

Findings: Carriership of –511TT genotype were diagnosed with the lowest LDL-C level and a high HDL-C level ($p<0.05$), which confirmed the hypolipidemic statin effect. Carriers of –511CC genotype had the increased LDL-C levels. Carriership homozygous –1082GG genotype demonstrated the association with the level of Cholesterol ($P=0.003$). When the anti-inflammatory cytokine (IL-4, IL-10) level increased, C level decreased ($P<0.05$). The analysis of correlation between pro- /anti-inflammatory cytokine gene genotypes revealed the activity of genotypes –511TT (IL-1β gene), –174CC (IL-6 gene), –589TT (IL-4 gene), and –1082GG (IL-10 gene) in maintaining chronic inflammation stability ($P=0.012$).

Conclusion & Significance: The obtained correlations contributed to the preparation of personalized HLP pharmacotherapy algorithm in CHD patients in presence of ARVI. The presence of heterozygous –511CT genotype for –511C>T polymorphism of the IL-1β gene, homozygous –174GG genotype for –174G>C polymorphism of the IL-6 gene, and homozygous –1082AA genotype for polymorphism –1082G>A of the IL-10 gene did not lead to reaching the target LDL-C level.

Recent Publications:

1. Babu BM, Reddy BP, Priya VH et al. (2012) Cytokine gene polymorphisms in the susceptibility to acute coronary syndrome. Genetic Testing and Molecular Biomarkers 16(5): 359-365
2. Chen L, Liu L, Hong K et al. (2012) Three genetic polymorphisms of homocysteine-metabolizing enzymes and risk of coronary heart disease: a meta-analysis based on 23 case-control studies. DNA and Cell Biology 31(2): 238-249
3. Guan X, Yang W, Sun X et al. (2012) Association of influenza virus infection and inflammatory cytokines with acute myocardial infarction.
4. Inflammation Research 61(6): 591-598
5. Loppnow H, Zhang L, Buerke M et al. (2011) Statins potently reduce the cytokine-mediated IL-6 release in



SMC/MNC cocultures. Journal of Cellular and Molecular Medicine 15(4): 994-1004

6. Yu GI, Cho HC, Cho YK et al. (2012) Association of promoter region single nucleotide polymorphisms at positions -819C/T and -592C/A of interleukin 10 gene with ischemic heart disease. Inflammation Research 61(8)

Biography

Mal Galina Sergeevna throughout the 30 years dealing with the actual problems of cardiology, pharmacology and clinical pharmacology. In 1993 she defended her thesis and was awarded the degree of candidate of medical sciences. In 2005, defended her doctoral thesis and awarded the degree of doctor. Since 2005 she has been working as a professor of pharmacology. She is the author of 500 scientific papers. Develops issues of pharmacological correction of atherosclerosis of coronary heart disease, arterial hypertension. Studies pharmacogenetic approaches to the modification of the drug response in cardiac patients. Her approach to optimizing treatment is based on the pharmacokinetic, pharmacodynamic and pharmacogenetic aspects of the treatment of cardiac patients. That allows to implement personalized medicine in real life. She and her students present their work internationally.

Notes:

MicroRNA 103 inhibitor as a potential promising therapeutic target for myocardial infarction

Ayman Selim, Mai A. Zaafan, Amr M. Abdelhamid, Amr Mohamed Alaa, Bana Ammar, Shahd Yehia, Al Hasnaa Abdel Tawwab, Asmaa Esmail, Heba Abdelhakim and **Yara Hamdy**
October University for Modern Sciences and Arts (MSA), Egypt

Myocardial infarction (MI) is myocardial cell death due to severe and prolonged ischemia produced from atherosclerosis-related coronary artery disease. MI triggers a cascade of events and reparative phases end with myocardial cell necrosis. MicroRNA (miR) is non-coding single stranded RNA that regulates protein expression. miR-103 is used to regulate expression of Fas-associated death domain (FADD) which decreases necroptosis of ischemic myocardium. The study aims to investigate the modulatory effect of up-regulating mRNAs translation processes of myocardial infarction induced with Isoprenaline HCL 100 mg/kg (ISO) by injecting miR-103 inhibitor. Eighteen mice (15-25 gm) were allocated into three groups; Group A (control) received normal saline, Group B received ISO and Group C received ISO and miR-103 inhibitor. Mice were sacrificed by cervical dislocation under urethane anesthesia. Blood and hearts samples were collected for biochemical analysis of miR103, FADD, receptor interacting protein kinase (RIPK), nuclear factor-kB (NF-kB), tumor necrosis factor-α (TNF-α), interleukine-6 (IL-6),Troponin-I and creatine kinase-MB (CK-MB). In addition, hearts were used for histopathological examination. Results showed that administration of miR-103 antagomir leads to increase in FADD protein levels in group C compared to A and B. While miR-103, RIPK, NF-kB, TNF-α and IL-6 showed high levels of expression in group B that is attenuated in group C. Troponin-I and CK-MB also supported the previous results. Histopathological test showed normal histological structure in groups A and C while focal degeneration in myocardium in B. Accordingly, these results indicate a promising suppression of MI manifestations upon inhibition of miR-103.

Notes:

Circulating betatrophin in relation to metabolic, inflammatory Parameters, and oxidative stress in patients with type 2 Diabetes mellitus

Bland Bayar Khaleel[h], Alan Bapeer Hassan[a], Sherwan Ferman Salih[b], Israa Issa Hassan[a], Farsat Saeed Saadi[d], Deldar Morad Abdulah[e*], Idris Haji Ahmed[f] and **Sherzad Majeed Taher[g]**

[a,b,e,g]University of Duhok, Iraq
[d]Duhok General Directorate of Health, Iraq
[f]Azadi Teaching Hospital, Iraq
[h]Preventive Health Directorate, Iraq

Aims: Recently, it was suggested that betatrophin has a role in controlling pancreatic b cell proliferation and lipid metabolism, however, its role in human subjects has not been established yet. The predicting role of betatrophin and MDA along with other biochemical indicators in type 2 diabetes mellitus (T2DM) in a sample of the Iraqi population was examined in the present investigation.

Methods: A total of 31 patients diagnosed with T2DM and 30 adult subjects without diabetes were matched in age and gender in a case-control study. Logistic and linear regression models were performed

to examine the role of MDA and betatrophin in T2DM and triglyceride, respectively.

Results: The study confirmed a higher concentration of LDL (124.45 vs. 102.70 mg/dL; P ¼.001) and TG (191.13 vs. 103.83 mg/dL; P < .0001), insulin (18.40 vs. 10.97 mU/mL; P < .0001), and Hs. CRP (5.39 vs. 2.80 mg/L; P ¼.033) in diabetic patients compared to the controls. No significant difference in betatrophin and MDA was found between diabetic patients and non-diabetic healthy subjects. The study

Showed triglyceride as the only predictor of T2DM (P ¼.028). Similarly, total cholesterol (P < .0001), HDL (P ¼.001), LDL (P < .0003), and MDA (P ¼.010) were shown as predictors of triglyceride in diabetic patients.

Conclusion: The present study that triglyceride is a direct and MDA is an indirect predictor for T2DM.

Recent Publications:

1. Hu H, Sun W, Yu S, Hong X, Qian W, Tang B, et al. Increased circulating levels of betatrophin in newly diagnosed type 2 diabetic patients. Diabetes Care 2014:DC_140602.
2. Vetere A, Choudhary A, Burns SM, Wagner BK. Targeting the pancreatic b-cell to treat diabetes. Nat Rev Drug Discov 2014;13(4):nrd4231.
3. Yi P, Park J-S, Melton DA. RETRACTED: betatrophin: a hormone that controls pancreatic b cell proliferation. Elsevier; 2013.
4. [5] Zhang R, Lipasin. A novel nutritionally-regulated liver-enriched factor that regulates serum triglyceride levels. Biochem Biophys Res Commun 2012; 424(4):786e92.
5. Yi P, Park J-S, Melton DA. Perspectives on the activities of ANGPTL8/betatrophin. Cell 2014;159(3):467e8.
6. [23] Fenzl A, Itariu BK, Kosi L, Fritzer-Szekeres M, Kautzky-Willer A, Stulnig TM, et al. Circulating betatrophin correlates with atherogenic lipid profiles but not with glucose and insulin levels in insulin-resistant individuals. Diabetologia 2014;57(6):1204e8.

7. Gusarova V, Alexa CA, Na E, Stevis PE, Xin Y, Bonner-Weir S, et al. ANGPTL8/ betatrophin does not control pancreatic beta cell expansion. Cell 2014;159(3): 691e6.

Biography

Bland Bayar has is expertise in management and Prevention of Diabetes mellitus. He is a head of non communicable disease in Duhok city north of Iraq (Kurdistan) he is a clinician and part time lecturer at shexan polytechnic college and has many activities in prevention of non communicable and specially diabetes mellitus. This research was done to evaluate the role betatrophin and it is relation to type 2 diabetes mellitus patients.

Notes:

24th World Congress on Pharmacology
&
7th World Heart Congress

August 19-20, 2019 Vienna, Austria

Finding a medical solution to calcium oxalate urolithiasis: Which agents have the best dissolution potential? An integrative review

Samuel P.B.Drawbridge
BVetMed MRCVS, UK

Calcium urolithiasis is a disease of major concern given its high prevalence, welfare and economic implications, and complications associated with current treatment and prevention strategies. A large number of publications were evaluated in this review to determine chemicals most evidential of calcium oxalate dissolution potential, the most prevalent stone component. The relevant literature was sourced through a keyword search of several online databases, and studies included if they showed evidence of an agent exhibiting dissolution activity upon calcium oxalate powder, crystals or stones. A critical analysis of these chemicals was undertaken, to determine those most efficacious, whilst also considering safety of medical use. This evaluation revealed citrates to be the most promising candidates for future research, given *in vivo* and *in vitro* data. Other factors influencing dissolution were also considered, including the ability of the immune system to dissolve calcium oxalate crystals.

Recent Publications:

1. Raheem, O.A., Khandwala, Y.S., Sur, L.R., Ghani, K.R., Denstedt, J.D, 2017. Burden of urolithiasis: trends in prevalence, treatment and costs. Eur. Urol. Focus, 3, 18-26.
2. Chutipongtanate, S., Chaiyarit, S., Thongboonkerd, V., 2012. Citrate, not phosphate, can dissolve calcium oxalate monohydrate crystals and detach these crystals from renal tubular cells. Eur. J. Pharmacol. 689, 219-25
3. Phillips, R., Hanchanale, V.S., Myatt, A., Somani, B., Nabi, G., Biyani, C.S., 2015. Citrate salts for preventing and treating calcium containing kidney stones in adults. Cochrane database of systematic reviews, Issue 10.
4. Cicerello, E., Merlo, F., Gambaro, G., Maccatrozzo, L., Fandella, A, Baggio, B., Anselmo, G., 1994. Effect of alkaline citrate therapy on clearance of residual renal stone fragments after extracorporeal shock wave lithotripsy in sterile calcium and infection nephrolithiasis patients. J. Urol. 151, 5-9.
5. Soygur, T, Akbay, A, Kupeli, S., Effect of potassium citrate therapy on stone recurrence and residual fragments after shockwave lithotripsy in lower caliceal calcium oxalate urolithiasis: a randomised controlled trial. J. Endourol. 16, 149-152.
6. Saso, L, Valentini, G., Leone, M.G., Grippa, E., Silvestrini, B., 1998. Development of an in vitro assay for the screening of substances capable of dissolving calcium oxalate crystals, Urol Int. 61 (1998) 210-214.

Biography

A practitioning veterinarian Samuel Drawbridge is very passionate about medicine, but also has a deep interest in chemistry. Pharmacology allows a combining of these two disciplines. His current research involves exploring medical solutions to calcium oxalate based urolithiasis. He hopes to develop a solution that could be used to dissolve calcium oxalate uroliths by direct irrigation of the urinary tract, as well as discovering those agents best suited for prevention of this disease. This research allowing him to improve the health and welfare of humans and animals, beyond that of working as a general practitioner.

Orthosteric- versus allosteric-dependent activation of the GABAA receptor requires numerically distinct subunit level rearrangements

Jahanshah Amin and **Meena S. Subbarayan**
University of South Florida, USA

Anesthetic molecules act on synaptic transmission via the allosteric modulation of ligand-gated chloride channels, such as hetero-oligomeric α1β2γ2 GABAA receptors. To elucidate the overall activation paradigm via allosteric versus orthosteric sites, we used highly homologous, but homooligomeric, ρ1 receptors that are contrastingly insensitive to anesthetics and respond partially to several full GABA α1β2γ2 receptor agonists. Here, we co-expressed varying ratios of RNAs encoding the wild-type and the mutated ρ1 subunits, which are anesthetic-sensitive and respond with full efficacy to partial GABA agonists, to generate distinct ensembles of receptors containing five, four, three, two, one, or zero mutated subunits. Using these experiments, we then demonstrate that, in the pentamer, three anesthetic-sensitive ρ1 subunits are needed to impart full efficacy to the partial GABA agonists. By contrast, five anesthetic-sensitive subunits are required for direct activation by anesthetics alone, and only one anesthetic-sensitive subunit is sufficient to confer the anesthetic-dependent potentiation to the GABA current. In conclusion, our data indicate that GABA and anesthetics holistically activate the GABAA ρ1 receptor through distinct subunit level rearrangements and suggest that in contrast to the global impact of GABA via orthosteric sites, the force of anesthetics through allosteric sites may not propagate to the neighboring subunits and, thus, may have only a local and limited effect on the ρ1 GABAA receptor model system.

Recent Publications:

1. Walters RJ, Hadley SH, Morris KDW, and Amin J: Benzodiazepines act upon $GABA_A$ receptors via two distinct and separable mechanisms. (2000) Nature Neuroscience; 3(12): 1274-1281.
2. W, Hadley SH, Lüddens H, Amin J: Ketamine, But Not Phencyclidine, Selectively Modulates Cerebellar $GABA_A$ Receptors Containing α_6 and δ Subunits. (2008) Journal of Neuroscience 28(20): 5383-5393.
3. Morris KW and Amin J: Insight into the mechanism of action of neuroactive steroids. (2004) Mol Pharmacol; 66:56-69.
4. Hadley SH & Amin J: Rat $\alpha_6\beta_2\delta$ GABAA receptors exhibit two distinct and separable agonist affinities. (2007) Journal of Physiology 581.3:1001-1018.
5. Amin J, Subbarayan MS. Orthosteric-versus allosteric-dependent activation of the GABAA receptor requires numerically distinct subunit level rearrangements (2017). Scientific Reports 7 (1), 7770, 1-16.

Biography

J Amin laboratory has a primary interest in GABAA and NMDA receptor-channels. We have studied the structure/function relationship of subtypes of GABAA receptors to enhance our understanding of the molecular mechanism of action of sedative/hypnotic drugs. By co-expression of wild-type with anesthetic-sensitive subunits of GABAA receptors, we have determined the minimal number of subunits required for orthosteric- versus allosteric-dependent activation of GABAA receptor channels. The laboratory is also focused on drug discovery with particular interest in ketamine. In the last several years, we have synthesized a number of ketamine analogues and characterized their molecular actions on the NMDA and GABAA receptors. One oxime analogues of ketamine has shown great promise in terms of molecular signature on NMDA and GABAA receptors and in an animal model test for antidepressants.

Clinical benefit of training asthmatic Libyan patients on how to use metered dose inhalers by using 2Tone trainer

Walid Y Tarsin
University of Tripoli, Libya

Bronchial asthma is a serious chronic inflammatory disease of the respiratory system. Aerosol inhalation as a route of drug delivery has become well-known in therapy of asthma. This study was aimed to evaluate if the use of 2Tone helps patients maintain the correct inhalation technique after training and can improve the clinical benefit. 125 Libyan adult asthmatic patients were engaged from Tripoli Medical Centre, 2017. At the first clinical visit; 38, 44 and 43 patients were included as C, VT and 2T groups, respectively. Their IFR through an MDI was measured using an In-Check Dial. Patients in 2T group were trained on how to use the 2Tone Trainer according to its PIL and practiced inhaling through this training aid to familiarize themselves with the different sounds according to the IFR. At the second clinic visit for all the patients was held six weeks later, each patient was assessed in the same manner as on the first visit. Results indicate a significant positive correlation between percent predicted FEV1 and PEFR with all AQLQ domains. Patients in the 2T group showed reduced IFR of about double that in VT group whereas in the C group, there was no significant difference in IFR. However, comparison of IFR between VT vs. 2T groups at visit one showed no statistical significant difference. On the other hand, at visit two, comparison between all the groups showed a highly significant difference. Thus, this study shows that 100% and 29% of the patients in the C and VT groups were inhaling at a high IFR while the 2T group shows only one patient (3%) was inhaling at the high flow rate while the rest of the patients managed to obtain the optimum IFR needed for the MDIs. Thus, the findings strongly recommend the importance of the use of the 2T device to train the patients to slow their IFR.

Recent Publications:

1. Altman P, Wehbe L, Dederichs J, Guerin T, Ament B, Moronta MC, et al. Comparison of peak inspiratory flow rate via the Breezhaler®, Ellipta® and HandiHaler® dry powder inhalers in patients with moderate to very severe COPD: a randomized cross-over trial. BMC Pulmonary Medicine 18 (2018): 100.
2. Chapman KR, Boulet LP, Rea RM, Franssen E. Suboptimal asthma control: prevalence, detection and consequences in general practice. European Respiratory Journal 31 (2008): 320-325.
3. Giraud V, Allaert FA, Roche N. Inhaler technique and asthma: feasability and acceptability of training by pharmacists. Respiratory Medicine 105 (2011): 1815-1822.
4. Tarsin W, Hshad NA, Elshamli I, Sherif FM. A clinical benefit of training asthmatic patients on how to use metered dose inhalers by using the 2tone trainer in Libya. Journal of Pharmacy and Pharmacology Research 3 (2019): 028-040 DOI: 10.26502/fjppr.0018
5. Virchow JC, Crompton GK, Dal Negro R, Pedersen S, Magnan A, Seidenberg J, et al. Importance of inhaler devices in the management of airway disease. Respiratory Medicine 102 (2008): 10-19.

Biography

Tarsin has his expertise in evaluation of drug delivery reproducibility from different inhalation products using Pharmacokinetic methods and *In-vitro* characterisation of inhaled products focussing on DPI and MDI. He had several Clinical trials using the inhalation profile recorder to determine the total emitted dose and the fine particle mass of different inhalers *in vitro* by means of inhalation simulator (The Electronic Lung). He focused on clinical trials to identify which inhaled product to prescribe to an asthmatic patient and those with Chronic Obstructive Pulmonary Disease (COPD) using the In-Check Dial. He has built this model after years of experience in research, evaluation, teaching and administration in hospital and education institutions in the UK and Libya.

SESSIONS

Arrhythmias | Heart Failure | Cardiac Nursing and Health Care | Hypertension

Chair: **Naranjan S Dhalla,** University of Manitoba, Canada

SESSION INTRODUCTION

Title: **Effectiveness of combine therapy using allapinin and cardiac glycosides for suppression of supraventricular paroxysmal tachyarrhythmias in patients with ischemic heart disease**
Kapustnyk Yurii, Ukrainian Medical Stomatological Academy, Ukraine

Title: **Prognostic Value of speckle tracking echocardiography in peripartum cardiomyopathy patients: A long term single center study**
Doaa A Fouad, Assiut University, Egypt

Title: **Coagulation proteins C&S and cases of cardiac thrombi**
Elizabeth B. Simon, New York Institute of Technology, USA

Title: **Increased blood viscosity implies clustering of multiple metabolic abnormalities in essential hypertension**
Fumihiro Tomoda, Fukui Health Science University, Japan

Effectiveness of combine therapy using Allapinin and cardiac glycosides for suppression of supraventricular paroxysmal tachyarrhythmias in patients with ischemic heart disease

Kapustnyk Yurii
Ukrainian Medical Stomatological Academy, Ukraine

Paroxysmal atrial fibrillation and paroxysmal supraventricular tachycardia can be treated using several preparations. Author of this abstract has developed the new method of treatment for paroxysmal supraventricular tachyarrhythmia's including such disorder of cardiac rhythm in patients with severe heart failure. In accordance with this method combination of preparations with antiarrhythmic action (allapinin + cardiac glycosides) is used.

Allapinin is the alkaloid of bromhydrate lappaconitine. This alkaloid was extracted from the perennial plant. It can be extracted from the wild plant of the aconite, which belongs to the group of buttercup plants. It is produced in tablets at 50 mg and in solution for intravenous or intramuscular administration: 1% solution in ampoules at 2 ml. Allapinin occupies the special place among antiarrhythmic agents of the 1st class according to Vaughan-Williams classification. It differs from agents of IA and IB subclass. Being different from quinidine, procainamide, gilurytmal and others agents of the 1st class of antiarrhythmic drugs allapinin in effective antiarrhythmic doses has small influence on the width of ventricular QRS complex, P-Q interval and Q-T interval. Allapinin in doses, which provide denominated antiarrhythmic effect, unlike the other antiarrhythmic drugs, does not lead to reduction of the system arterial pressure and to negative inotropic action in myocardium fibers.

In accordance with the new method of treatment of paroxysmal supraventricular tachyarrhythmias a cardiac glycoside – digoxin (lanoxin) in dose 0,25 mg or strophantin in dose 0,25 mg is administered intravenously. Then in 20-30 minutes after administration of cardiac glycoside allapinin is used intravenously in dose 30-40 mg

In case of suppression of paroxysmal tachyarrhythmia prophylactic treatment must be administered using the above preparations. Allapinin is administered orally in daily dose 75 mg (25 mg 3 times daily). In combination with allapinin digoxin is used orally in dose 0,25 mg (1 tab) 1-2 times daily. In case of positive result of therapy the daily dose of allapinin can be reduced to 50 mg (1 tablet 2 times a day) and digoxin - to the minimum effective one, which is 0,25 mg (1 tablet) once a day.

The criterion of such positive result of therapy is occurrence of the periods without paroxysms of tachyarrhythmia, which are greater than 1,5-2 periods. Such periods occurred earlier between paroxysms of tachyarrhythmia. Thus, this therapy provides prophylactic effect in respect to occurrence of tachyarrhythmia attack.

The significant advantage of this method is the possibility of using it for the patients with severe heart failure. Unlike the majority of other antiarrhythmic drugs of synthetic origin allapinin does not have any negative inotropic action in effective antiarrhythmic doses. For the patients with cardiac failure this cardiac glycoside leads to improving of metabolism in myocardial cells. Such improvement of myocardium metabolism contributes to the elimination of paroxysmal tachyarrhythmias.

The most expressive effect of combined therapy is observed in case of intravenous administration of allapinin in single dose 30-40 mg and cardiac glycoside in 20-30 minutes after using allapinin. Such combination of these agents is conditioned by their pharmacodynamics. The beginning of antiarrhythmic effect occurred only in 10-15 minutes after its intravenous administration. The maximal effect of allapinin is achieved in 20-40 minutes after using this antiarrhythmic drug. This property of allapinin is conditioned by the time of intravenous administration of cardiac

glycoside. Such therapy was realized with 37 patients having ischemic heart disease and supraventricular paroxysmal tachyarrhythmias. They were included in the main group of patients.

To control the effectiveness of the combined therapy the monotherapy only using intravenous administration of allapinin in single dose 40-50 mg was realized with 38 patients having ischemic heart disease and supraventricular paroxysmal tachyarrhythmias.

The therapy results in the main and in the control group of patients are submitted in the table.

Table

№	Form of paroxysmal tachyarrhythmia	Number of patients in main group	Positive result of therapy	Number of patients in control group	Positive result of therapy
1.	Paroxysmal supraventricular tachyarrhythmia	16	12	15	8
2.	Paroxysmal form of atrial fibrillation	14	11	15	7
3.	Paroxysmal form of atrial flutter	7	5	8	3

The use of cardiac glycoside increases the antiarrhythmic effect of allapinin. This combined treatment is more efficient in comparison with the monotherapy with the help of only one preparation (allapinin). Such combined use of these two medicines contributes to shortening of the time, which is needed for suppression of tachyarrhythmia paroxysm. After the renew of the normal sinus rhythm the supporting treatment (oral administration of allapinin and cardiac glycosides) must be administered in the earliest possible period.

Notes:

Prognostic value of speckle tracking echocardiography in peripartum cardiomyopathy patients: A long term single center study

Doaa A Fouad, Hatem Abdel-Rahman Helmy, Safwat Abdelrady Salman, Hanan Galal Abdel-Azeem and **Ahmed Mohammed Moheb El-Din**
Assiut University, Egypt

Patients who died had significantly impaired GLS and GCS vs. those improved (-9.07±0.65 vs.-16.09±2.57%, -8.17±3.1 vs. -14.02±2.62 %, P<0.01)). More reduction was noted in apical GCS (-6.97±4.67 vs. -17.43±6.75%). Patients with persistent LV dysfunction and those who died were presented later than improved (18±11.79 vs.7.5±4.93 days postpartum)

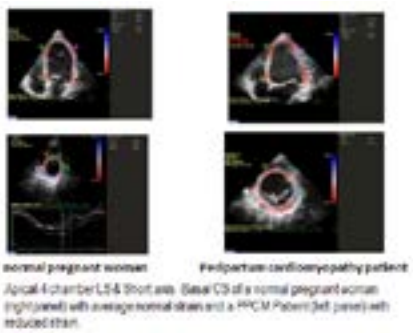
Conclusion & Significance: Longitudinal and circumferential strains are depressed in PPCM patients. 2D-STE can be used as an objective marker of LV dysfunction in PPCM patients at long term.

Recommendation: A larger multicenter study is recommended. Meanwhile, STE is advised whenever PPCM is suspected.

Statement of the Problem: Although peripartum cardiomyopathy (PPCM) is a rare disease, its frequency is higher in some regions including Egypt. It can result in morbidity and mortality of 5- 32%. Identifying prognostic indicators of women with PPCM is of paramount importance. Speckle tracking echocardiography (STE) was found helpful to assess early changes of left ventricular function and mechanics; however its prognostic value is still under investigation.

Methodology & Theoretical Orientation: This is a case-control prospective study that included 25 PPCM patients admitted to the cardiology and woman health hospitals of Assiut University, Egypt from September 2016-December 2018 and 20 control pregnant women. Clinical assessment, 2-D echocardiography and STE were done to study population upon inclusion, and at scheduled quarterly visits.

Findings: Patients age was 29.9±7.68 years, 75% presented in the postpartum period. At presentation, LVEF was impaired in patients vs. controls (33.2±8.84 % vs. 62.65±5.61 %, P<0.001), STE showed reduction of GLS (-10.08±6.76 vs.-19.49±2.82), GCS (-11.65±3.34 % vs.-23.63±2.93%) (P<0.001). Patients were followed-up for a median of 13.5 months where 9 improved (LVEF≥50%), 7 partially improved (LVEF=40-49%), 4 had persistent LV dysfunction (LVEF<40%), 4 died. Along the study; GLS & GCS increased significantly (-13.03±4.53% to -20.18±1.75), (-13.28±3.37% to -22.53±4.82%) in improved patients



Recent Publications:

1. Shimaa Khidr, Mark Doyle, Geetha Rayarao, Mohamed Abdel Ghany, Hosam Hasan-Ali, Doaa A Fouad, William Belden and Robert W Biederman (2019) Pulmonary vein remodeling following pulmonary vein isolation in patients with atrial fibrillation-do pulmonary veins represent only an epiphenomenon? A cardiac MRI study. Cardiovascular Diagnosis and Therapy, 9(1):8-17.
2. Doaa A Fouada, Sherif H Zakib, Hosam H Elarabya, Ahmed Abdelgaleela and Marwan S Mahmoud (2019) Validation of right ventricular pacing response during supraventricular tachycardia in mechanistic diagnosis (transition zone). J Curr Med Res Pract 2:25-31.
3. Naglaa K Idriss, Aliaa AY Mosa, Abdel- Rahim MA Maeki, Doaa A Fouad, Hosney Ali Hassen, Mahmoud Abdelsabour and Sherif Sayed (2018) Role of endothelial biomarkers in patients with coronary artery disease. J Tissue Sci Eng. 9:56.
4. Ayman K M Hassana, Doaa Ahmed Fouada and Abeer Refaiy (2017) Demographic features and prevalence of myocarditis in patients undergoing transarterial endomyocardial biopsy for unexplained cardiomyopathy. The Egyptian Heart Journal (2017) 69():29-35.
5. Mostafa S K Tawfeek, Doaa M Raafat, Khaled Saad, Naglaa K Idriss, Sherif Sayed and Doaa A Fouad (2016) Plasma levels of neutrophil gelatinase-associated lipocalin in children with heart failure . Therapeutic advances in cardiovascular disease, 10(1):30-36.

Biography

Doaa A Fouad is a Professor of Cardiovascular Medicine at Assiut University, Egypt. She was the Head of Cardiovascular Medicine Department from 2013-2016. During this period, she gave a lot of effort to complete the modern facilities and introduce up-to-date equipments in the New Heart University Hospital. She has a long expertise in interventional cardiology in the fields of Device therapy, electrophysiology, and PCI of coronary artery disease. In addition, she has an expertise in different echocardiographic modalities. She has more than 50 publications in these fields with a special interest in diagnosis and management of myocardial disease and heart failure. She is a Member of the Egyptian Society of Cardiology, Egyptian Cardiac Rhythm Association (ECRA), and the European Society of Cardiology (ESC).

Notes:

Coagulation proteins C&S and cases of cardiac thrombi

Elizabeth B Simon
New York Institute of Technology, USA

Statement of the Problem: Protein S or Protein C deficiency leads to uncommon thrombophilia that precipitates clotting in unusual sites. Thrombotic episodes of under 40-50 years of age are rare without a thrombophilia. Clotting- related clinical presentations are common among Asian populations compared to others. Several case reports illustrate young patients with arterial thrombosis associated to inherited PS deficiency. Physiological changes in pregnancy also predisposes to thrombosis in the presence of underlying anticoagulant deficiencies. Clinicians need to have an understanding about this phenomenon to provide optimal care.

Methodology & Theoretical Orientation: A systematic analysis of cases with PS or PC deficiency manifested as cardiac thrombi using multiple databases presented 40 recent articles. Based on the complexity of the clinical manifestations, diagnostic measures and interventions 5-7 cases were chosen for further exploration.

Findings: Abnormal clotting in unusual sites triggered morbidity and mortality in younger (under 50 years of age) clientele. The focus of such thrombosis management is to restore hemostasis by reestablishing perfusion. Occasionally, surgical interventions may be necessary to accomplish this goal. Diagnosis of the underlying problem and prevention of further episodes is based on immunoassays and family history. The clients may need anticoagulation for at least three to six months.

Conclusion & Significance: P S and PC deficiency- related cardiac thrombi are not a commonly seen anomaly. Yet clinicians should be alert to identify abnormal clotting problems in acutely ill patients. Astute history taking, thorough physical exam skills and understanding of the concept will help in early diagnosis and management.

Recent Publications:

1. Bhandary S P, Papadimos T J, Essandoh M K and Apostolakis J (2015) Massive intracardiac thrombosis during coronary artery bypass grafting surgery. Int J Crit Illn Inj Sci. 5(1):56-58.
2. Kenichiro Uchida, Mitsuharu Hosono, Toshihiko Shibata, Daisuke Kaku, Tomonori Yamamoto, Takafumi Terada, … Mizobata, Y. (2016). Surgical treatment for thoracoabdominal intra-aortic thrombus with multiple infarctions: a case report. Journal of Medical Case Reports, 10:1-5.
3. Kurniawan M Z and Pratanu I (2015) Sub-acute stent thrombosis and in-stent restenosis associated with antiplatelets clopidogrel resistance and protein S deficiency. Folia Medica Indonesiana, 51(4):214-220.
4. Pahuja M, Ainapurapu B and Abidov A (2017) Large left ventricular thrombus in a patient with systemic and venous thromboembolism secondary to protein C and S deficiency. Case Rep Cardiol. 2017:7576801.
5. Sabzi F and Faraji R (2014) Cardiac left ventricular thrombus in protein C deficiency. Nigerian Medical Journal 55(4):354-355.

Biography

Elizabeth B Simon is an experienced Academician as well as a Clinician. She is committed to facilitate clinical learning through case studies. During her 24 years of academic tenure, she has published and presented in national and international forums and journals. She was a Fulbright Scholar during 2015-2016 in India teaching Critical care Nursing.

Increased blood viscosity implies clustering of multiple metabolic abnormalities in essential hypertension

Fumihiro Tomoda
Fukui Health Science University, Japan

In skeletal muscle, increased blood viscosity can reduce nutritional blood supply and thereby influencing insulin sensitivity, uric acid production and oxygen utility. Although blood viscosity elevates in hypertension, the associations of blood viscosity with limbs circulation and metabolism reminded to be elucidated in hypertension. In 116 untreated essential hypertensives without apparent cardiovascular damages, blood viscosity, forearm vascular resistance and biochemical indices were measured by falling-ball microviscometer, venous-occlusion plethysmography and laboratory tests, respectively. The relationships between blood viscosity and the other measured parameters were evaluated. Forearm vascular resistance correlated positively with blood viscosity (r=0.240). Concomitantly with the increase in blood viscosity, both plasma insulin and HOMA ratio elevated without changes in blood glucose (r=0.238, 0.205). Additionally, serum uric acid, plasma lactate and C-reactive protein also elevated together with the increase in blood viscosity (r=0.404, 0.286, 0.199). In essential hypertensives, increase blood viscosity was associated with the worsening of insulin sensitivity, uric metabolism, aerobic metabolism and inflammation as well as the reduction in limbs blood flow. The increased blood viscosity could imply the clustering of multiple metabolic abnormalities in essential hypertension.

Recent Publications:

1. Ohara M and Tomoda F (2015) T Pubertal administration of antiserum against nerve growth factor regresses renal vascular remodeling in spontaneously hypertensive rats. Clin Exp Pharmacol Physiol. 42(6):687-694.
2. Takiwaki M and Tomoda F (2014) Increased levels of small dense low-density lipoprotein cholesterol associated with hemorheological abnormalities in untreated, early-stage essential hypertensives. Hypertens Res. 37(11):1008-1013.
3. Yamazaki H and Tomoda F (2014) Renal vascular structural properties and their alterations by removal of uraemic toxins in a rat model of chronic kidney disease. Clin Exp Pharmacol Physiol. 41(3):238-245.

Biography

Fumihiro Tomoda is a Professor at Fukui Health University. He belongs to Japanese Society of Internal Medicine, Japanese Society of Nephrology, Japanese Society of Hypertension, Japanese Society for Dialysis Therapy and Japanese Circulatory Society. Currently, he is in the position of Editor-In-Chief for the Journal of "Insights in Blood Pressure". He is a Specialist in Clinical Nephrology and Cardiology and he has Medicine Doctor's degree and was awarded at Toyama Medical and Pharmaceutical University. His researches focus on sympatho-adrenal system and its clinical implication in hypertension, renal vascular structural remodeling and its possible influences on renal hemodynamics in hypertensive or CKD animal models and hemorheologic characteristics and its clinical implication in cardiovascular disease.

Notes:

24th World Congress on
Pharmacology
&
7th World Heart Congress
August 19-20, 2019 Vienna, Austria

Scientific Tracks & Abstracts
Day 2

Day-2

SESSIONS

Clinical Pharmacology and Receptor Theory | Cardio Vascular Pharmacology | Pharmacokinetic and Pharmacodynamic | Drug Screening and Discovery | Topical Medicine and Infectious Diseases | Advances in Pharmacological Research | Biochemical Pharmacology

Chair: Maria I Yablonskay, Russian National Research Medical University, Russian Federation

SESSION INTRODUCTION

Title: Drug addiction and treatment compliance
Shirley Taniguchi, University of São Paulo, Brazil

Title: The effects of inhaled rapamycin solid lipid particle size on transport across lung epithelial cells
Emelie Land, The University of Sydney, Australia

Title: A prospective cross-sectional study to evaluate the economic burden of patients diagnosed with depression in a tertiary care hospital
Femina Dawer, Grant Govt. Medical College and Sir J.J Hospital, India

Title: Pharmacokinetic and pharmacodynamic considerations for drugs binding to alpha-1-acid glycoprotein
Sherri A Smith, Relay Therapeutics, USA

Title: Screening of kinase inhibitor library revealing lead compounds for treatment of Cystic echinococcosis
Jun Li, The First Affiliated Hospital of Xinjiang Medical University, China

Title: Neurological actions of honeybee products
Hesham El-Seedia, Uppsala University, Sweden

Drug addiction and treatment compliance

Shirley Taniguchi
USP - São Paulo/Brazil

Statement of the Problem: Neuroleptic-induced extrapyramidal symptoms may hinder adherence to drug rehabilitation treatment.

Methodology and Theoretical Orientations: This study included 32 patients (mean age of 33.61±1.90) admitted to a public mental health service in São Paulo (Brazil) due to psychotic symptoms associated with illicit drug use.

Findings: A total of 80.65% of patients were addicted to alcohol alone or alcohol plus cocaine or crack, while 19.35% were addicted to cocaine or crack cocaine. Psychosis (73.08%), aggressive behavior (7.69%), and withdrawal syndrome (11.10%), while no effects were registered in the remaining 7.69%. Among cocaine abusers, we observed hallucinations and delirium (50%), cardiovascular effects (27.76%), and psychomotor agitation (11.12%), while no effects were observed in the remaining 11.10%. Among crack users, we observed hallucinations and delirium (50%), and cardiovascular effects (37.50%), while no effects were observed among the remaining 12.50% of patients. Hallucinations, delirium, psychomotor agitation and psychosis were treated with typical or atypical neuroleptics (96.88%) or anticonvulsants (3.12%). A total of 80.64% of patients receiving neuroleptics had extrapyramidal symptoms (acute dystonia akathisia, pharmacological parkinsonism), which were treated with a centrally acting anticholinergic drug-biperiden (60%) or anticonvulsants/antihistaminics (40%).

Conclusions and significance: Professionals should reconsider the use of typical neuroleptics to treat drug-induced hallucinations, delirium and psychosis. Their side effects make it difficult for patients to adhere to treatment Thus, any neuroleptic-induced side effects should always be carefully monitored.

Recent Publications:

MELATTO, I. ; Pequeno, M.D.L. ; SANTOS, A. ; GILBERTO, H. ; MALHEIROS, D. ; ROPERO PELÁEZ, F.J. ; TANIGUCHI RODRIGUES, G. ; MAGALHÃES, J. ; Taniguchi, S. . Hypothyroidism in psychiatric patients. EUROPEAN PSYCHIATRY , v. 41, p. S839-S840, 2017.

BATISTELLA, J. ; HIDA, G. ; MALHEIROS, D. ; RODRIGUES, G. TANIGUCHI ; PELÁEZ, F.J. ROPERO ; MAGALHÃES, J. ; Taniguchi, S. . Pathologies related to depression in elderly patients. EUROPEAN PSYCHIATRY , v. 41, p. S543, 2017.

TAMARINDO, A. ; VOGEL, C. ; HIDA, G. ; MALHEIROS, D. ; Ropero, J.; Taniguchi, S. . The sedation could consist in a therapeutic strategy in advanced cancer conditions. European Psychiatry (Paris) , v. 33, p.

S500, 2016.

ROPERO PELÁEZ, FRANCISCO JAVIER ; TANIGUCHI, SHIRLEY . The Gate Theory of Pain Revisited: Modeling Different Pain Conditions with a Parsimonious Neurocomputational Model. Neural Plasticity , v. 2016, p. 1-14, 2016.

Citações: 1

Taniguchi, S.; MARTINS, R. MASTELARO ; VOGEL, C. ; Ropero, J. ; MASON, R. . Initial Palliative Care Drugs' Side Effect. European Psychiatry (Paris) , v. 30, p. 1507-1507, 2015.

Taniguchi, S.; MASTELARO MARTINS, R. ; VOGEL, C. ; Ropero, J. ; SALMAN, S. ; ALBUQUERQUE, R. . Neuroleptic Administration to Oncologic Patients Under Palliative Care. European Psychiatry (Paris) , v. 30, p. 1506, 2015.

BATISTELA, J. ; SALMAN, S. ; ROPERO PELÁEZ, J. ; LEON, B. ; MASON, R.; Taniguchi, S. . EPA-1812 - Alzheimer's disease treatment related nausea side effect. European Psychiatry (Paris) , v. 29, p. 1, 2014.

Citações: 17| 18

BATISTELA, J. ; ROPERO PELÁEZ, J. ; VITORELI, R. ; NEGRÃO, A. ; SALMAN, S. ; SOARES, A. ; Taniguchi, S. . EPA-1806 - Motor symptoms related to alzheimer's disease treatment. European Psychiatry (Paris) , v. 29, p. 1, 2014.

Citações: 17| 18

BATISTELA, J. ; ROPERO PEL EZ, F. ; TAMARINDO, A. ; SILVA, S. ; FRIZZO, E. ; SALMAN, S. ; Taniguchi, S. . EPA-1446 - Antiparkinsonian drug related hallucination. European Psychiatry (Paris) , v. 29, p. 1, 2014.

Citações: 17| 18

FELTRIN, M. ; CENTRONI, A. ; Ropero Pelaez, J. ; DIAS, S. ; THAMINNY, M.; MASON, R. ; NEGRAO, A. ; Taniguchi, S. . PO-0932 Nausea Related To Sevoflurane Anaesthesia. Archives of Disease in Childhood , v. 99, p. A555-A556, 2014.

FELTRIN, M. ; CENTRONI, A. ; Ropero Pelaez, J. ; MONTEIRO, F. ; ARENAS, S. ; SILVA, I. ; RIBEIRO, M. ; Taniguchi, S. . PO-0933 Pharmacological Treatment Of Emergence Agitation Related To Sevoflurane Anaesthesia. Archives of Disease in Childhood , v. 99, p. A556-A556, 2014.

Biography

Shirley earned her M.S. in Pharmacology at the University of São Paulo in 1993. From 1994-1996, she worked as a researcher for the Japanese Ministry of Education in the Department of Pharmacology at the University of Kitasato in Tokyo. She has been an instructor in Pharmacology since 1997 and a researcher at the Medical School at the University of São Paulo (Faculdade de Medicina /Universidade de São Paulo). Shirley has been teaching undergraduate Pharmacology classes within Healthcare courses under the theme 'Education to Prevent the Misuse of Drugs'.

Her assistance is requested whenever there is difficulty associated with the pharmacological treatment in any given sector within different hospitals. Through research projects registered with the Ministry of Health, Shirley accesses and analyzes medical records to propose pharmacological care to complement patients' treatments and minimize risks.

Shirley has assisted in research with drugs in the Intensive Care Unit, Urgent Care, sedation in oncology, and in Psychiatry, Geriatrics and Pediatrics departments.

Notes:

The effects of inhaled Rapamycin solid lipid particle size on transport across lung epithelial cells

Emelie Land, Lyn M. Moir, Daniela Traini, Paul M. Young and **Hui Xin Ong**
The University of Sydney, Australia

Background: Lymphangioleiomyomatosis (LAM) is a rare lung disease characterized by the uncontrolled growth of smooth like muscle cells (LAM cells) in the lungs that can spread to other body parts via the lymphatic system Current treatment for LAM is oral Rapamycin, which is limited by its low bioavailability (~15%) and side effects [1, 2]. It's been shown that particles of approximately <1000nm with a negative surface charge are able to enter the lymphatic system [3].

Aim: The current study aimed to determine the optimum size of Rapamycin solid lipid nanoparticles (SLN) that will facilitate drug entry into the lymphatic system through the inhaled route in order to increase lung bioavailability, reduce systemic side effects and potentially have increased efficacy.

Methods: Three different sized (1-3) of Rapamycin-SLN: 200, 500 and 800nm, were produced by dissolving Rapamycin and glyceryl behenate in methanol and dichloromethane. The organic solvents were evaporated prior to mixing with hot Tween80 (1.5 %w/v) solution. The solution was either homogenized (1700rpm) or passed through a membrane with specified pore sizes mini-extruder before being freeze-dried overnight. Size and charge were determined using a Zetasizer. Transepithelial drug transport of the formulations was evaluated *in-vitro* using a Calu-3 air-liquid interface bronchial epithelial cell model.

Results: All Rapamycin-SLNs formulations had negative surface charge (table 1) and average particle sizes: 237 ± 1.8nm, 583 ± 1.3nm and 790 ± 2.3nm, respectively. The formulations showed varying encapsulation efficiencies ranging from 65.8 to 97.32%. The transport studies showed that 83 ± 4.2% and 68 ± 2.5 % of SLN200 and SLN500 formulations were transported, respectively, across the epithelium after 4hrs compared to 22 ± 2.15% of the SLN800 formulation.

Conclusion & Discussion: The current study showed that Rapamycin-SLN with negative surface charge and size of approximately 200nm is able to cross the lung epithelium faster than larger particles. Future studies will be expanded to evaluate the entry of these SLN particles

Recent Publications:

1. Smolarek, T.A., et al., Evidence that lymphangiomyomatosis is caused by TSC2 mutations: chromosome 16p13 loss of heterozygosity in angiomyolipomas and lymph nodes from women with lymphangiomyomatosis. Am J Hum Genet, 1998. 62(4): p. 810-5.
2. Kumasaka, T., et al., Lymphangiogenesis-mediated shedding of LAM cell clusters as a mechanism for dissemination in lymphangioleiomyomatosis. Am J Surg Pathol, 2005. 29(10): p. 1356-66.
3. Videira, M.A., et al., Lymphatic uptake of pulmonary delivered radiolabelled solid lipid nanoparticles. J Drug Target, 2002. 10(8): p. 607-13.

Biography

Emelie Landh completed her Bachelor in Medical Sciences, majoring in Pharmacology at the University of Sydney in 2013. She went on to complete a Graduate Diploma in Pharmacology with the Respiratory Technology Group at the Woolcock Institute of Medical research at the University of Sydney in 2014. She is currently at the end of the second year of her PhD under the supervision of Dr. Hui Xin Ong with the Respiratory Technology Group. Her PhD project involves developing an inhaled combination treatment using Solid-Lipid Nanoparticles for treating Lymphangioleiomyomatosis (LAM).

A prospective cross-sectional study to evaluate the economic burden of patients diagnosed with depression in a tertiary care hospital

Femina Dawer and **Dinesh Dhodi**
Grant Govt. Medical College and Sir J.J Hospital, India

Statement of the Problem: Depression is a common psychiatric disorder having important medical, social and psychological consequences. It is a disorder associated with enormous burden in terms of reduced quality of life as well as direct and indirect costs. It is a well -known fact that the majority of the economic burden of depression results from non- depression expenditures. Hence, the study was undertaken to evaluate economic burden of depression. The purpose of this study is to evaluate the cost off depression in terms of direct and indirect costs.

Methodology & Theoretical Orientation: 150 patients diagnosed with depression attending psychiatry OPD at Sir J.J. Group of Hospitals, Mumbai, fulfilling the inclusion criteria were explained about the study. Written informed consent were taken. Direct and Indirect costs were recorded in Structured Case Record Forms by interviewing the patients. Cost driving factors were identified.

Findings: Total annual direct cost was 6,378.16 INR while annual Indirect Cost was INR 16,860. Annual cost of Depression was 1NR 23,238.16/331.97 USD per patient. Total cost was 16.30% of per capita GDP 2018 among Depression patients in India. The annual economic burden of depression in India is 1.2% of GNP of India.

Conclusion & Significance: The indirect cost was almost thrice the direct costs. Hospitalisation cost and loss of working days due to depression was contributed the most to the direct costs and indirect costs respectively. Economic burden of Depression is found out to be 16.30% of per capita GDP in year 2018-2019.

Recommendation: Multi-centric studies to evaluate pharmaco-economic burden across the country and analyse the burden of the disease. Thus, shifting the approach to prevention rather treatment reducing the economic burden of the illness.

Recent Publications:

1. Bromet E, Andrade LH, Hwang I, Sampson NA, Alonso J, de Girolamo G, et al. Cross-national epidemiology of DSM-IV major depressive episode. BMC Med 2011; 9:90.
2. Wittchen HU, Jacobi F. Size and burden of mental disorders in Europe—a critical review and appraisal of 27 studies. Eur Neuropsychopharmacol. 2005;15: 357-376
3. Karampampa K, Borgström F, Jönsson B. Economic burden of depression of society. Medicographia. 2011;33(2):163-8.
4. Luppa M, Heinrich S, Angermeyer MC, Konig HH, Riedel-Heller SG. Cost-ofillness studies of depression: a systematic review. J Affect Disord. 2007;98: 29-43
5. Sarkar S, Mathan K, Sakey S, Shaik S, Subramanian K, Kattimani S. Cost-of-treatment of clinically stable severe mental lilnesses in India. Indian Journal of Social Psychiatry. 2017 Jul 1;33(3):262.
6. Sobocki P, Ekman M, Agren H, Runeson B, Jonsson B. The mission is remission: health economic consequences of achieving full remission with antidepressant treatment for depression. Int J Clin Pract. 2006; 60:791-798.

Biography

Femina Dawer a postgraduate resident in department of Pharmacology, Grant Govt Medical College and Sir J.J Group of Hospitals, Mumbai, India is dedicated towards clinical research both in experimental and clinical aspects. Considering different modalities while doing a research helps in giving a wisdom to explore impact of various factors in treating a patient. With the intent of helping the population this study was conducted to explore the financial aspect and calculate the burden of the disease comparing it with international available data. Thus, helping the patients by spreading a word.

Notes:

24th World Congress on Pharmacology
&
7th World Heart Congress

August 19-20, 2019 Vienna, Austria

Pharmacokinetic and Pharmacodynamic considerations for drugs binding to alpha-1-acid glycoprotein

Sherri A Smith
Relay Therapeutics, USA

According to the free drug hypothesis only the unbound drug is available to act at physiological sites of action. Albumin, the most abundant plasma protein (~50 mg/mL), and alpha-1-acid glycoprotein (AAG, ~1 mg/mL) are both involved with drug binding and distribution. While albumin levels are similar across species, marked species, age, and disease state differences in AAG expression, homology and drug binding affinity have been reported. Drug binding to plasma proteins can help aid and improve the translation of pharmacokinetic/pharmacodynamic (PK/PD), safety margin predictions, and relationships from preclinical species to human as well as adults to neonates (Smith and Waters, 2019). The impact of AAG binding on PK has been reported for multiple drug/candidate molecules including pinometostat (Smith et al., 2016), vismodegib (Gianetti et al., 2011), imatinib (Widmer et al., 2006), and UCN-01(Fuse et al., 1998). Obtaining accurate fraction unbound (fu) values, especially for highly bound drugs, is critical to PK and safety predictions (Di et al., 2017). The role of plasticizers used in blood collection bags has recently been reported to contribute to inaccurate overestimation of fu for drugs that preferentially bind to AAG (Butler et al., 2015, Ingram et al., 2019). Experimental considerations as well as recommendations for understanding the potential impact of AAG on PK through drug discovery and early development will be reviewed.

Recent Publications:

1. Smith S and Waters N (2019) Pharmacokinetic and pharmacodynamic considerations for drugs binding to alpha-1-acid glycoprotein. Pharm Res 36(2):30, doi.org/10.1007/s11095-018-2551-x.
2. Smith S, Gagnon S, Waters N. (2016) Mechanistic investigations into the species differences in pinometostat clearance: impact of binding to alpha-1-acid glycoprotein and permeability-limited hepatic uptake. Xenobiotica, 47(3)185-93, doi: 10.3109/00498254.2016.1173265.
3. Gianetti A, Wong H, Dijkgraaf G, Dueber E, Ortwine D, Bravo B et al. (2011) Identification, characterization, and implications of species-dependent plasma protein binding of the oral hedgehog pathway inhibitor vismodegib (GDC-0449). J Med Chem, 54(8):2592-601, doi: 10.1021/jm1008924.
4. Widmer N, Descosterd L, Csajka C, Leyvraz S, Duchosal M, Rosselet A, et al. (2006) Population pharmacokinetics of imatinib and the role of alpha-acid glycoprotein. Br J Clin Pharmacol, 62(1):97-112, doi: 10.1111/j.1365-2125.2006.02719.x.
5. Fuse F, Tanni H, Kurata N, Kobayashi H, Shimada Y, Tamura T, et al. (1998) Unpredicted clinical pharmacology of UCN-01 caused by specific binding to human alpha 1-acid glycoprotein. Cancer Res, 58(15):3248-53.
6. Di L, Breen C, Chambers R, Eckley S, Frick R, Ghosh A. et al. (2017) Industry perspective on contemporary protein-binding methodologies: considerations for regulatory drug-drug interaction and related guidelines on highly bound drugs. J Pharm Sci, 106(12):3442-52, doi: 10.1016/j.xphs.2017.09.005.
7. Butler P, Frost K, Barnes K, Smith S, Rioux N, Waters N (2015) Impact of blood collection method on human plasma protein binding for compounds binding preferentially to α-1-acid glycoprotein. Drug Metab Rev, doi: 10.1080/03602532.2016.1191843.
8. Ingram N, Dishinger C, Wood J, Hutzler JM, Smith S, Huskin N (2019) Effect of the Plasticizer DEHP in Blood Collection Bags on Human Plasma Fraction Unbound Determination for Alpha-1-Acid Glycoprotein (AAG) Binding Drugs. AAPS J 16;21(1):5, doi: 10.1208/s12248-018-0276-8.

Biography

Sherri Smith is experienced in drug metabolism and Pharmacokinetics (DMPK) of small molecules from discovery through clinical development in the pharmaceutical industry. Recent publication efforts have focused on explaining discrepancies in plasma protein binding values due to interference of plasticizers commonly used in blood collection bags, to highlight species, ontogeny, and disease state differences in expression of α-1-acid glycoprotein (AAG) and to provide examples where human PK of drugs have been impacted by preferential binding to AAG. The overall aim is to bring attention to the relevance of accurate measurement of fraction unbound for the prediction human PK and pharmacodynamics.

Notes:

Screening of kinase inhibitor library revealing lead compounds for treatment of cystic echinococcosis

Jun Li, Tian Wang, WenJing QI, Li He and WenBao Zhang*
The First Affiliated Hospital of Xinjiang Medical University, China

Aims: The metacestode stage of two *Echinococcus species*, E. granulosus sensu lato and E. multilocularis cause cystic echinococcosis (CE) and alveolar echinococcosis (AE), respectively. These diseases remarkably impact on the health of population. Although surgical removal of cyst is the cure treatment, about 90% of patients with echinococcal infection are treated by albendazole. However, as the drug is not parasiticidal, the patients with AE or CE have to take the drug for a long time, even for the whole life. The treatment of these diseases urgently need an effective drug.

Material and Methods: In the study, by using *in vitro* cultivation of E. granulosus protoscoleces and micro-cysts, we primarily screened 378 kinase inhibitors at 5 μM, which revealed 51 compounds showing killing efficacy. Further using 1 μM, 7 compounds were keeping killing efficacy *in vitro*. Dose-response assays revealed that 2 of the compounds, S2243 and S2895, had LC50 value below 2.5 μM. We then incubated cysts of E. granulosus collected from infected mice with S2895 and S2243 at 20 μg/L, which resulted in 60% of the cysts dead in 24 h. For *in vivo* efficacy trial, BALB/c mice were transferred with 50 micro-cysts and after 3 month postinfection, each of the mice was orally given these two drugs a dose of 15 mg/kg of body weight for one month. An increase in cyst mortality rate was observed compared to that of those collected from control mice.

Conclusions: Our study identifies that the two kinase inhibitors showed parasiticidal in both *in vitro* and *in vivo*, indicating these two inhibitor may be the lead-compounds for drug development against echinococcosis.

Recent Publications:

1. Jianling Bao,Jun Li(2018) Donald McManus. Echinococcus granulosus infection results in an increase in Eisenbergiella and Parabacteroides genera in the gut of mice, Frontiers in Microbiology.29 November 2018.
2. Hui Wang, Jun Li (2018) Echinococcus granulosus sensu stricto: silencing of thioredoxin 4 peroxidase impairs the differentiation of protoscoleces into 5 metacestodes. Parasite 25, 57.
3. Zhuang-Zhi Zhang,Wen-Bao Zhang(2018)Dog vaccination with EgM proteins against Echinococcus granulosus.[J]. Infectious Diseases of Poverty,7(1):61.
4. Mei Yang, Wenbao Zhang(2017)Cloning and characterization of an Echinococcus granulosus ecdysteroid hormone nuclear receptor HR3-like gene.[J]. Parasite-journal De La Societe Francaise De Parasitologie, 24:36
5. Weisi Wang, Jun Li(2017)In vitro and in vivo efficacies of novel carbazole aminoalcohols in the treatment of cystic echinococcosis. J Antimicrob Chemother. Jul 24. doi: 10.1093/jac/dkx250.
6. Wu C, Li J(2017)Genetic variation of mitochondrial genes among Echinococcus multilocularis isolates collected in western China. Parasit Vectors. May 30;10(1):265. doi: 10.1186/s13071-017-2172-y.
7. Wang H, Li J (2016) In vitro culture of Echinococcus multilocularis producing protoscoleces and mouse infection with the cultured vesicles. Parasites & Vectors.Jul 25;9(1):411

Biography

Jun Li is a professor of Xinjiang Medical University and a senior research fellow of State Key Laboratory of Pathogenesis, Prevention and Treatment of High Incidence Diseases in Central Asia, Xinjiang Medical University, Urumqi, China. He received her B. Sc from Xinjiang Medical University. In 2004, she obtained her PhD at the University of Queensland working on developing diagnosis tool for detecting cystic echinococcosis. She then spent 3 years working on PanBio for developing diagnosis kit for infectious diseases. From 2008-2013, she worked on molecular biology of Echinococcus as a senior research officer in Molecular Parasitology Laboratory, Infectious Diseases Division, QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia. She has published more than 30 papers/articles in the international journals in her research career.

24th World Congress on Pharmacology
&
7th World Heart Congress

August 19-20, 2019 Vienna, Austria

Neurological actions of honeybee products

Hesham El-Seedi[a,b,c*], Shaden Khalifa[d,e], Jianbo Xiao[f], Aida Abd El Wahed[a,b,g], Lei Chenh Mohamed Farag[i,j] and **Ghulam Abbas[c,k*]**

[a]Uppsala University, Sweden
[b]Menoufia University, Egypt
[c]University of Karachi, Pakistan
[d]Stockholm University, Sweden
[e]Karolinska Institute, Sweden
[f]University of Macau, China
[g]Agricultural Research Centre, Egypt
[h]Fujian Agriculture and Forestry University, China
[i]Cairo University, Egypt
[j]The American University in Cairo, Egypt
[k]Ziauddin University, Pakistan

Statement of the Problem: According to the World Health Organization, two billion people will be aged 60 years or older by 2050. Aging is a major risk factor for a number of neurodegenerative disorders. These age-related disorders currently represent one of the most important and challenging health problems have impact on the economic and social. Therefore, much attention has been directed towards the design and development of neuroprotective agents derived from natural sources.

The honeybees (Apis mellifera L.) have several products, including honey, propolis, royal jelly, bee venom, and bee pollen. Bee products meet the criteria of being natural products that have long-recognized medicinal properties. Historically, bee products nutritional and medicinal values have been considered for thousands of years by Ancient Egyptian, Persians, Romans and Chinese in supplementary nutrition and alternative diets. Bee products are often sold as nutritional supplements and/or health products, and with potential anticancer, antimicrobial activities, antioxidant, anti-nociceptive, and anti-inflammatory. Bee products polyphenols have neuroprotective actions via quench biological reactive oxygen species that cause neurotoxicity and aging as well as the pathological deposition of misfolded proteins, such as amyloid beta.

In the current talk will concerned on the neuroprotective of bee products and its ingredients against neurogernatives diseases including Alzheimer's disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis and depression.

Recent Publications:

1. Biotech N, Corporation M, Road J, Gung C, Hospital M, Science M, Health, N (2007). Propolin G, a prenylflavanone, isolated from Taiwanese propolis, induces caspase-dependent apoptosis in brain cancer cells. Journal of Agricultural and Food Chemistry, 55: 7366–7376.
2. Giampieri F, Quiles JL, Orantes-Bermejo FJ, Gasparrini M, Forbes-Hernandez TY, Sánchez-González C, Battino M (2018). Are by-products from beeswax recycling process a new promising source of bioactive compounds with biomedical properties? Food and Chemical Toxicology 112:126–133.
3. Kumar A, Sehgal N, Kumar P, Padi SSV, Naidu P. (2008). Protective effect of quercetin against ICV colchicine-induced cognitive dysfunctions and oxidative damage in rats. Phytotherapy Research 22: 1563–1569.
4. Squillaro T, Schettino C, Sampaolo S, Galderisi U, Di Iorio G, Giordano A, Melone MAB (2018). Adult-onset brain tumors and neurodegeneration: Are polyphenols protective? Journal of Cellular Physiology, 233:3955–3967.

5. Tomás A, Falcão SI, Russo-almeida P, Vilas-boas M (2017). Potentialities of beebread as a food supplement and source of nutraceuticals: Botanical origin , nutritional composition and antioxidant activity. Journal of Apicultural Research 8839.
6. Unno K, Takabayashi F, Yoshida H, Choba D, Fukutomi R, Kikunaga N, Hoshino M (2007). Daily consumption of green tea catechin delays memory regression in aged mice. Biogerontology 8: 89–95.

Biography

Hesham R. El-Seedi working in the area of isolation, structure elucidation and synthesis of biologically active natural products from medicinal plants, marine and bee products. Recently, we started also a project on nanoparticles synthesis. Prof. Hesham is a former fellow of the Japanese Society of Promotion of Science (JSPS), Faculty of Science and Technology, Keio University, Japan, under direction of Prof. Shosuke Yamamura and Prof. S. Nishiyama. Throughout his carrier, he worked in pioneer internationally recognized laboratories including Geneva University, Switzerland, in collaboration with Prof. Kurt Hostettmann, Kunglia Tekniska Högskola (KTH), Stockholm, Sweden (since 2007), Faculty of Pharmacy, Uppsala Biomedical Center, Uppsala University, Sweden and Menoufia University, Egypt. He was appointed as Adjunct Faculty Professor at the International Center for Chemical and Biological Sciences (ICCBS), Karachi, Pakistan, 2017 and was rewarded two Swedish Research Links grants for the 2017-2019.He has published peer-reviewed international research articles and scientific papers, reviews, chapters in Peer-Reviewed International Journals

Notes: