Poster Presentations

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Lin28a expression protects against streptozotocin-induced β-cell destruction and prevents diabetes in mice

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Lin28a is a highly conserved RNA-binding protein that represses the miRNA let-7. Lin28a is highly expressed in embryonic stem cells (ESCs) and is involved in ESC differentiation. Lin28a also functions as a reprogramming factor for induced pluripotent stem (iPS) cells. A previous study showed that Lin28a modulates glucose metabolism, insulin sensitivity, and promotes cancer cell proliferation. Lin28a overexpression enhances cell proliferation and facilitates glucose transport in the mouse pancreatic β-cell line Min6. To investigate the effect of Lin28a expression on β-cells, cells were treated with the appropriate streptozotocin (STZ) concentrations. Pancreatic β-cells overexpressing Lin28a showed higher survival than mock cells. Furthermore, Lin28a was found to promote proliferation and inhibit apoptosis in STZ-treated cells. In addition, Lin28a-overexpressing cells show enhanced glucose transport. Lin28a inhibits let-7 expression and activates the PI3K/Akt signaling pathway. In addition, this study aimed to identify the relationship between Lin28a and type 1 diabetes *in vivo* using Lin28a-overexpressing transgenic (Tg) mice. Lin28a Tg mice showed enhanced glucose transport and increased insulin secretion. We performed STZ experiments to mimic diabetes *in vivo*. Lin28a-overexpressing mice were found to have lower blood glucose levels and higher survival following STZ treatment of pancreatic β-cells. The islet of Langerhans in Lin28a-overexpressing mice secretes more insulin than in WT mice when subjected to STZ treatment. In conclusion, Lin28a expression protects against STZ-induced pancreatic β-cell destruction and promotes cell proliferation in pancreatic β-cells. The results indicate that Lin28a improves the function of the islet of Langerhans in mice.

Speaker Biography

Jain Jeong is currently studying for PhD at Kyungpook National University in Korea. His current laboratory research work is focusing on elucidating gene function and their relation to diseases using various transgenic mice models.

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Hydroalcoholic extract obtained from *Eugenia punicifolia* leaves and its effect in improving injury induced by gastric ischemia- reperfusion in male and female rats

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Introduction: *Eugenia punicifolia* (Kunth) DC. (Myrtaceae), popularly known as "murta", is a shrub largely distributed in the Amazon region and Savanna biome. The leaves of this medicinal plant are popularly used as a natural therapeutic agent to treat inflammation, wounds and infections.

Aim: The aim of this study was to evaluate the gastric healing effect against ulcer induced by ischemia and reperfusion (I/R).

Material & Methods: The gastric ulcers were induced by I/R in male and female (intact and ovariectomized) Wistar rats, according to the method described by Ueda *et al*. Hydroalcoholic extract from *Eugenia punicifolia* leaves (HEEP - 125 mg/kg – lower effective dose of previous assays, dose-response curve), lansoprazole (30 mg/kg) or vehicle (saline – 0.9%; 10 mL/kg) were administered during 6 days to determine the healing effects of the subacute treatment. After treatments, the rats were killed and the stomach removed for analysis of lesions areas (mm^2) and biochemical parameters such as: superoxide dismutase (SOD - antioxidant), myeloperoxidase (MPO - inflammation marker), malondialdehyde (MDA - lipid peroxidation marker), catalase (CAT - antioxidant) and reduced glutathione (GSH - antioxidant). The results are expressed as mean ± standard error of the mean and statistical significance was determined by ANOVA followed by Dunnett's test ($p<0.05$). Animal Research Ethical Committee n. 675.

Results & Discussion: The results show that the treatment with lansoprazole and HEEP during 6 consecutive days significantly healed the gastric ulcers decreasing the lesion area (males [63.43% and 73.68%]; intact females [68.80% and 52.83%]; ovariectomized females [50.39% and 43.13%]; respectively) when compared with their control group treated with vehicle. There are no significant changes between healing area of ovariectomized females and males rats treated with HEEP for 6 days ($p>0.05$). But when compared intact females with males, our results showed that the latter presents decrease in the lesion area after the treatment with the HEEP ($p<0.01$). Our results indicate that HEEP administered for 6 days presents curative effects against the I/R induced lesions increasing GSH levels ($p<0.0001$) in intact females. The biochemical parameters evaluated in this study are not related to the healing of the gastric mucosa of males and ovariectomized females.

Conclusion: Treatment with HEEP administered during 6 consecutive days in male and female rats (intact and ovariectomized) after gastric injury induced by I/R, could heal the mucosa with a significant increase in GSH levels, acting as antioxidant.

Speaker Biography

Périco L L possess a Bachelor's degree in Pharmacy from the Faculdades Adamantinenses Integradas (2010), a Master's degree in Biological Sciences (Pharmacology) from the Institute of Biosciences of Botucatu at the São Paulo State University (UNESP) (2014). She is currently a Doctoral student in Pharmacology and Biotechnology at Institute of Biosciences of Botucatu (UNESP), where she works on the following topics: Pharmacology of Natural Products, with an emphasis on medicinal plants with antiulcerogenic, anti-inflammatory, antinociceptive and antidiarrheal activity. She participates in the thematic project: "Standardized herbal medicines for the treatment of chronic diseases". During the Master's degree, she worked with animal models for gastroprotection. She currently works with animal models for the evaluation of hormonal effects on gastric ulcer healing. Her current project is titled: The role of the hydroalcoholic extract from the leaves of *Eugenia punicifolia* in experimental peptic ulcer disease: characterization of anti-inflammatory, healing and antiapoptotic mechanisms of action.

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In vitro assessment of the toxic effects of an AKWATON based-disinfectant on human tissues

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The purpose of this study is to prove the potential safe use of AKWATON as a new antimicrobial product. Many service products are often removed from the market due to their toxic effects on the human body or to their aggressiveness towards the environment. Antimicrobial products such as disinfectants may contain harmful ingredients that can cause disease. Some disinfecting products are corrosive or irritating; others produce strong odors, which in the long run can cause real health problems. AKWATON is a new disinfectant, member of the family of guanidine polymers. Its bactericidal, fungicidal and sporicidal properties have been demonstrated and widely documented. In this study, the toxic effects of AKWATON and of three well known commercial antimicrobial products currently on market, were evaluated and compared on various human tissues including eyes, lung, skin and liver cells. The testing were performed using the TB (Trypan blue) and MTT (3-(4, 5-Dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide) methods. Cell-cultures and the different tests done, showed that the AKWATON based-disinfectant was much less toxic, killing many fewer cells than the commercial disinfectants. It spared more than 64% of skin cells; 65% of lung (IMR-90) cells; 66% of eye cells (ARPE-19) and 64% of liver (Hep-G2) cells while some well-known disinfectants currently marketed killed 100% of cells. This study demonstrated that AKWATON can be used as an odorless, colorless, non-corrosive and harmless disinfectant for hospital, agriculture industry, farming, food service and household facilities or as antiseptic.

Speaker Biography

Mathias Oulé holds a Bachelor's degree in Mathematics, a Master's degree in Biochemistry from the University of Abidjan (Côte d'Ivoire), a Master's degree in Microbiology and a Doctorate in Microbiology from Laval University (Québec). Since 2000, he is Professor of Microbiology at Saint-Boniface University (Winnipeg, MB); Head of the Department of Biological Sciences from 2006 to 2010. For several years, he has been researching on AKWATON, a microbicidal polymer with high solubility in water, odorless, colorless, non-corrosive and harmless, to fight nosocomial infections and superbugs. In 2012, the Society for General Microbiology (SGM) issued press release on his studies on AKWATON's sporicidal activity, published in the *Journal of Medical Microbiology* (JMM).

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Safety and biosimilarity of ior®LeukoCIM compared to Neupogen® based on toxicity, pharmacodynamic and pharmacokinetic studies in the Sprague-Dawley rat

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This study examined the safety, pharmacodynamic and pharmacokinetic biosimilarity of the human recombinant filgrastim products iorRLeukoCIM and NeupogenR following a 28-day repeated subcutaneous dose administration in male and female Sprague-Dawley rats with a 14- day recovery period. Safety profiling was based on clinical observations, clinical pathology and pathology findings for control rats dosed with vehicle and rats dosed either with 15, 75 and 150 µg/kg of iorRLeukocim or 150 µg/kg of NeupogenR. Adverse clinical findings for both iorRLeukoCIM and NeupogenR were similar and consisted of mild to moderate forelimb alopecia; skin lesions (scab formation on the shaved dorsal region) and mild to severe swelling of the hock-joint (tarsal joint) and hind limb, alone or accompanied with lameness in high dose group animals which was more prominent in males. All adverse findings were fully reversible. As expected, iorLeukoCIMR and NeupogenR both increased white blood cell and neutrophil levels in rats and to a similar extent for high dose iorRLeukoCIM and NeupogenR. The pharmacokinetics of filgrastim following dosing with iorRLeukoCIM was well behaved and comparable for high dose iorRLeukoCIM and NeupogenR. The results of this study imply that iorRLeukoCIM and NeupogenR had safety profiles, pharmacodynamic responses and toxicokinetic profiles that were biosimilar.

Speaker Biography

Nuris Ledon has a PhD in Pharmaceutical Sciences since 2000. She is also an Auxiliary Professor and Senior Researcher at Molecular Immunology Center, La Havana, Cuba with 25 years of experience. She counts with two Master´s degrees, one in Pharmacology and other in Business Administration. She has published more than 50 articles on subjects like Pharmacology and Toxicology of different drugs. She has participated in numerous congress and summits and has tutored several theses.

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Inhibition of ERKs/RSK2/IκBα signaling axis by magnolin suppresses cancer cell invasion and migration

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Previously, our study demonstrated that IκBα phosphorylation at Ser32 by RSK2, a kinase regulated their activity by ERK1 and 2, induced NF-κB transactivation activity through IκBα destabilization, and magnolin inhibited ERK1 and 2 activities by targeting of the ERK active pocket. However, the role of magnolin in cell migration has not been clearly elucidated. Here, we found that magnolin inhibited NF-κB transactivation activity by suppression of ERK1/2/RSK2 signaling pathway. We demonstrated that magnolin abrogated increase of EGF-induced COX-2 protein level and wound healing in a dose dependent manner. In human lung cancer cells such as A549 and H1975 which harbor constitutive active Ras and EGFR mutants, respectively, we found that magnolin suppressed wound healing and cell invasion in Boyden chamber assay in a dose dependent manner. Importantly, gene expressions and activities of MMP-2 and -9 were inhibited by magnolin treatment. Notably, E-cadherin levels, an epithelial marker, was elevated by magnolin treatment and N-cadherin, Snail, Vimentin levels, mesenchymal markers, were suppressed by magnolin treatment in a dose dependent manner. In addition, the knockdown or knockout of RSK2 in A549 lung cancer cells or MEFs revealed that magnolin targeting ERKs/RSK2 signaling suppressed epithelial-mesenchymal transition. These results demonstrated that magnolin is beneficial for the anti-invasion and -migration in cancer metastasis.

Speaker Biography

Sun-Mi Yoo is an Ph. D. course sudent at the College of Pharrmacy, The Catholic University of Korea. Ms Yoo graduated B. S. degree at the Yonsei University (Life science) and entered graduate school of M. S./Ph. D. joint program on major of Pharmecutical Biochemistry in 2014 supervised by professor Yong-Yeon Cho. Ms. Yoo has studied on the protein-protein interaction and signaling network involved in cell transformation, cancer metastasis anc chemoresistance. Ms. Yoo found that ERKs/RSK2 signaling pathway plays a key role in cancer cell metastasis and molecular targeting of ERKs using magnolin, a natural compound abendently found in magnolia flos, strongly suppressed cancer cell migration and invasion. Moreover, During the M. S./Ph. D. course, she has identified a novel signaling pathway involved in chemoresistance through p90RSKs.

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Tet1 overexpression leads to anxiety-like behavior and enhanced fear memories via the activation of calcium-dependent cascade through Egr1 expression in mice

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Ten-eleven translocation methylcytosine dioxygenase 1 (Tet1) initiates DNA demethylation by converting 5-methylcytosine (5-mC) to 5-hydroxymethylcytosine (5-hmC) at CpG-rich regions of genes, which plays a key role in adult neurogenesis and memory. In addition, the overexpression of Tet1 with 5-hmC alteration in patients with psychosis has also been reported, for instance in schizophrenia and bipolar disorders. The mechanism underlying Tet1 overexpression in the brain, however, is still elusive. In the present study, we found that Tet1-transgenic (Tet1-TG) mice displayed abnormal behaviors involving elevated anxiety and enhanced fear memories. We confirmed that Tet1 overexpression affected adult neurogenesis with oligodendrocyte differentiation in the hippocampal dentate gyrus of Tet1-TG mice. In addition, Tet1 overexpression induced the elevated expression of immediate early genes (IEGs), such as Egr1, c-fos, Arc, and Bdnf followed by the activation of intracellular calcium signals (i.e., CamKII, ERK, and CREB) in prefrontal and hippocampal neurons. The expression of gamma-aminobutyric acid (GABA) receptor subunits (Gabra2 and Gabra4) fluctuated in the prefrontal cortex (PFC) and hippocampus. We evaluated the effects of Tet1 overexpression on intracellular calcium-dependent cascades by activating the Egr1 promoter *in vitro*. Tet1 enhanced Egr1 expression, which may have led to alterations in Gabra2 and Gabra4 expression in neurons. Taken together, we suggest that the Tet1 overexpression in our Tet1-TG mice can be applied as an effective model to study various stress-related diseases that show hyperactivation of intracellular calcium-dependent cascades in the brain.

Speaker Biography

Wookbong Kwon is currently studying for PhD at Kyungpook National University in Korea. His current laboratory is focusing on elucidating gene function and their relation to diseases using various transgenic mice models.

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Characterization of methionine oxidized human recombinant erythropoietin by nano LC-ESI-MSMS; Isoform distribution and biological activity

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Methionine (Met) oxidation is a significant form of protein damage caused by endogenous or environmental oxidizing agents. In this study we examined the effect of increasing levels of Methionine-54 oxidation on the isoform distribution and biological activity of the human recombinant erythropoietin. Mass spectrometry was applied to determine and compare the Met oxidation level of three batches of human recombinant erythropoietin. Isofrom distribution of the analyzed products was assessed by capillary zone electrophoresis (CZE) method. The calculated area percent of isoforms 2-4 which belongs to more acidic glycoforms, were decreased with increasing the level of methionine oxidation in all samples. Also, the results showed that the percent of isoforms 5-8 (more basic) were increased in all samples along with the elevating Met oxidation level. The *in vivo* biological activity of proteins was decreased by increasing the level of oxidation. In conclusion, Met oxidation level in human recombinant erythropoietin showed significant association with the net charge and isoform distribution of the glycoprotein and could be applied for monitoring and validation of production processes and quality control assessments.

Speaker Biography

M Reza Khorramizadeh, is a full Professor at Tehran University of Medical Sciences (TUMS), directs Biosensor Research Center and newly instituted Zebra Fish Core Lab at Endocrinology and Metabolic Molecular-Cellular Sciences Institute. Concurrently, he is a 2nd affiliation to the Dept. of Medical Biotechnology, School of Advanced Technology in Medicine, TUMS.

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Pistacia atlantica subspecies kurdica mastic gum resin, a potent and novel natural plant metabolite for cancer treatment

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The present study is focused on investigating the anticancer effect of *Pistacia atlantica* subspecies kurdica mastic gum resin (MGR) on the proliferation of various cancerous and noncancerous human cell lines exploiting MTT assay, microscopic evaluations, flow cytometry, caspase activity and qPCR. The MTT results showed that the mastic gum resin (0.01-100 µM) is selectively induced death of cancer cells in a dose and time-dependent manner. Significant suppression of proliferation of human cancerous cells was seen with IC_{50} value of 15.34±0.21, 11.52±0.18, 8.11±0.23 µg/mL and 5.2±0.8 µg/mL at 72 hours of treatment respectively for bile duct cancer (cholangiocarcinoma) (KMBC), pancreatic carcinoma (PANC-1), gastric adenocarcinoma (CRL-1739), breast adenocarcinoma (MCF-7) and colonic adenocarcinoma (COLO205). On the other hand, normal human colon fibroblasts (CCD-18Co) have not showed adverse effect after treatment with various doses of a natural resin. The study also showed that a natural resin at a concentration of 5.2±0.8 µg/mL for 72 h early signs of apoptosis as evidenced by confocal microscopy imaging. Flow cytometry studies showed that the natural resin significantly ($P<0.05$) arrests COLO205 cells at G2/M phase of cell cycle. On the other hand, we revealed that, the antiproliferative effect of natural resin on COLO205 cells is through the apoptotic intrinsic pathway via activation of caspases -3 and -9. In conclusion, the results revealed that natural resin can be further developed as chemotherapeutic compound for the treatment of cancers especially colon cancer.

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Molecular modeling- a tool for postulating the mechanism of drug interaction: glimepiride alters the pharmacokinetics of sildenafil citrate in diabetic nephropathy animals

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The present study evaluates the possible drug interaction between glimepiride (GLIM) and sildenafil citrate (SIL) in streptozotocin (STZ) induced in diabetic nephropathic (DN) animals and also postulates the possible mechanism of interaction by molecular modeling studies. Diabetic nephropathy was induced by single dose of STZ (60 mg/kg, ip) and confirms it by assessing the blood and urine biochemical parameters on 28th day of its induction. Selected DN animals were used for the drug interaction between GLIM (0.5 mg/kg, p.o.) and SIL (2.5 mg/kg, p.o.) after 29th and 70th day of protocol. Drug interaction was assessed by evaluating the plasma drug concentration using HPLC-UV and also determined the change in the biochemical parameter in blood and urine. Mechanism of the interaction was postulated by molecular modeling study using Maestro module of Schrodinger software. DN was confirmed as there was significant alteration in the blood and urine biochemical parameter in STZ treated groups. The concentration of SIL increased significantly ($p<0.001$) in rat plasma when co-administered with GLIM after 70th day of protocol. Molecular modelling study revealed few important interactions with rat serum albumin and CYP2C9. GLIM has strong hydrophobic interaction with binding site residues of rat serum albumin compared to SIL. Whereas CYP2C9 and GLIM has strong hydrogen bond with polar contacts and hydrophobic interactions than SIL. Present study concludes that bioavailability of SIL increases when co-administered chronically with GLIM in the management of DN animals and mechanism has been supported by molecular modeling studies.

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Comparative toxicological evaluation of the combined therapy of finasteride and alfuzosin to lauric acid and myristic acid in male rats

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Benign prostate hyperplasia (BPH) is a urological disorder caused by the noncancerous enlargement of the prostate as men age. As the prostate enlarges, it can constrict the urethra, inducing various symptoms including a weak urinary stream, incomplete bladder emptying, nocturia, dysuria and bladder outlet obstruction. Conventionally used drugs like 5 α -reductase inhibitors and α adrenoceptors antagonists are used to treat benign prostatic hyperplasia, but they possess various side effects like impotence, decreased libido, ejaculation disorder, gynaecomastia, dizziness, upper respiratory tract infection, headache, fatigue and chest pain, also it was found in our previous study combination of fatty acid like lauric and myristic acid can be used for treatments of benign prostatic hyperplasia with minimum side effects so present study undertaken to compare side effects of conventionally used drugs and fatty acid, and hence so present study investigated to compare toxicological potential of combined therapy with doses of finasteride and alfuzosin to lauric and myristic acid orally administered for 28 days to male Sprague Dawley rats. Male animals were randomized into three groups of six animals each one: a control group treated only with the vehicle and two groups treated with combination of, Finasteride (50 mg/kg)+Alfuzosin (50 mg/kg) {FA}, and Lauric acid (180 mg/kg) + myristic acid (70 mg/kg) {LA}, respectively. The variables analyzed were done like mortality, clinical signs, body weight, food consumption, hematology and blood parameters, relative organ weight and histopathological findings. Treatment with FA and LA combined therapy significantly reduced the relative organ weight of sex organs in animals treated. In conclusion, the combined therapy orally administered to male rats did not induce toxicological effects except the atrophy of the accessory sex organs related to FA administration, weight gain in fatty acid treatment groups so results show both combinations are relatively safe for the treatments of benign prostatic hyperplasia.

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Yi Shen Pin Gan Fang-a Chinese herb formula is effective in treating the ultra-high risk for psychosis population

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Objective: To investigate the effect of Yi Shen Pin Gan Fang-a Chinese Herb Formula in treating the Ultra High Risk for Psychosis population compared with aripiprazole.

Method: 54 Ultra High Risk for Psychosis population, matched for age, gender, handedness and education, were randomly assigned to receive either Yi Shen Pin Gan Fang and aripiprazole placebo or aripiprazole (5–10 mg/day) and Yi Shen Pin Gan Fang placebo for a 12-week period. At baseline, 4th week, 8th week, 12th week, clinical effect was evaluated with the Structured Interview for Prodromal Syndromes (SIPS), Positive and Negative Syndrome Scale (PANSS) and the Global Assessment of Functioning Scale (GAF), side effect was measured by Udvalg for Kliniske Undersogelser (UKU). Neurocognitive function was assessed at baseline and 12th week.

Result: For GAF, PANSS and SIPS, there was no difference between two groups (F=0.04, 0.05, 0.15, P>0.05), there was significant improvement since 4th week till 12th week in each group compared with baseline (F=27.16 59.91, 55.92, 0.05, 0.15, P<0.001). Compared with baseline, for the Trail Making test, there is no difference between and intra groups (P>0.05); In Chinese Medicine Treatment group, Verbal Learning test, Visual Memory test, CPT and Stroop-(colour/word) test were significant improved (P<0.05); For Aripiprazole Treatment group, only Verbal Learning test, Stroop-word test were significant improved (P<0.05). No obvious side effects were found in Yi Shen Pin Gan Fang treatment group.

Conclusion: Yi Shen Pin Gan Fang was effective in treating Ultra High Risk for Psychosis population.

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Comparative performance of Sprague-Dawley rat hearts using DMSO and DMF as cryoprotectants

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Purpose: Heart transplantation is one of the most effective treatment options for congestive heart failure. Current organ storage methods can preserve the human heart for only about four to six hours. The organ donor pool could be dramatically increased if the preservation time could be lengthened and hearts stored for weeks or even months prior to transplantation. This study describes the performance characteristics of explanted Sprague-Dawley rat hearts before and after cryopreservation using 10% dimethylsulphoxide (DMSO) and 30% dimethylformamide (DMF) in Tyrode solution.

Methods: A modified Morgan perfusion model was used for this study. Male Sprague- Dawley (ethical approval AREC/2009/09/002) hearts were harvested and arrested in a cold (<10°C) Tyrode solution (pH 7.4) for 5 minutes. The hearts were mounted on the aorta and vena cava to allow reperfusion in a doubled walled water jacket at 37 °C for baseline performance studies. The hearts (n=3) were cooled to 4, -20, -80 and -196°C (liquid nitrogen), and stored for 6 hours. This study was extended to 48 hours and 7 days at -196 °C (n=6). Cardiac output (aortic and coronary) and an electrocardiogram were obtained during baseline studies, followed by cryopreservation and after thawing at times T0, 10, 20, 40, 60, 120 min, 6, 8, 12 and 24 hours. Reperfused hearts were monitored for as long as possible. Ethical approval (AREC/2009/09/002) for the use of laboratory animals was obtained from the Tshwane University of Technology, Ethics Committee and the Animal Ethics committee before experimental work commenced.

Discussion: The average heart rate of the Sprague-Dawley rats reduced from 396 beats/minutes to 184 beats/minutes after anaesthesia. The average survival time of the hearts under the experimental conditions were seven hours 32 minutes with an average aortic output at 8 hours of 0.62 ml and 0.52 ml at 12 hours for DMF and 0.61 ml for 8 hours and 0.35 ml for DMSO at average survival time of 9 hours 44 minutes. A 100 % recovery after cryopreservation with DMSO and DMF was achieved after storage for 6 hours, 48 hours and 7 days in liquid nitrogen. DMSO and DMF were equally effective cryoprotectants in this study.

Conclusion: It was possible to preserve the hearts outside the body longer than eight hours as previously studied to 168 hour (7days) at –196°C with 100% recovery using both DMSO and DMF as cryoprotectant.

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Nature's own remedies: *Allium cepa* - does it offer new options for the treatment of epilepsy?

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A number of processes are thought to contribute to the development of epilepsy including increased excitatory synaptic transmission, neuronal cell death and development of aberrant innervations pattern in part arising from axonal growth. Recent findings indicate that adhesion molecules and their receptors play an important role in these processes and contribute significantly in epileptogenesis. Among the adhesion molecules, cell surface glycoproteins CD44 and CD90 are reported to be up-regulated after neuronal injury or epilepsy. Focus of this study was to evaluate the effect of classical anticonvulsants i.e., diazepam and phenytoin and an essential oil of *Allium cepa* AC-31B on the expression of these markers in the PTZ-induced model of epilepsy. Here we tested the hypothesis that anticonvulsant therapy that can reduce the level of CD44/CD90 expression *in vivo* model of epileptogenesis can be used to control the underlying process of epileptogenesis. Targeting CD44/CD90 might be a novel therapeutic target in neurological disorders. Mice weighing 20-25 gm were subjected to PTZ-induced kindling and their seizure-related behaviors were monitored. Once stage 4 seizures were prominent, animals were sacrificed and the brain samples were collected for the determination of CD44/CD90 expression. The results revealed that AC-31B not only halts the development of epileptogenesis in PTZ-kindled mice but also significantly reduced the expression of CD44/CD90. Based on these observations, we suggest that AC-31B can be effectively used to control the underlying pathology of epileptogenesis. This finding uncovers a potential effect of AC-31B in epileptogenesis and may provide a new therapeutic target that can be harnessed for the prevention of epilepsy development or progression.

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Speciation of inorganic and organic selenium in human serum samples based on isopropyl 2-[(isopropoxycarbothiolyl) disulfanyl] ethane/ionic liquid by ultrasound-assisted dispersive liquid-liquid microextraction

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A simple *in-vitro* speciation of inorganic selenium (SeIV and SeVI) and organic selenium (Se-Cys, Se-T, Se-Alb Se-M) in human biological samples based on isopropyl 2-[(isopropoxycarbothiolyl) disulfanyl] ethane thioate (IICDET) as a complexing agent were studied by ultrasound-assisted dispersive liquid-liquid bio-microextraction (USA-DLLMBE). In first stage, 100 µL (≈0.1 g) of hydrophobic ionic liquid of C8MIM [PF6] were only added to organic selenium (Se-Cys, Se-M, and Se-ALB) in 10 mL of standard solution and human serum, urine and plasma samples that were thermally extracted into IL phase at human biological pH in 10 min and after dilution with 100 µL of acetone, directly determined by electro thermal atomic absorption spectrometry (ET-AAS). In second stage, after separation IL from sample, inorganic selenium (Se IV) in remained samples was com plexed by IICDET and extracted to IL at pH=4 (R-S2Se-R). After reduction Se (VI) to Se (IV) by HCl with temperature 130 ^{0}C, inorganic Se speciation was obtained based on total Se determination. After optimized conditions, the enrichment factor (EF), Linear range and limit of detection (LOD) for inorganic selenium were obtained 25.2, 0.02- 1.35 µg L-1 and 5 ng L-1 in human biological samples respectively. The validation of methodology was achieved by certified reference material (CRM) and ICP-MS.

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Nanomaterial drug products: Manufacturing and analytical perspectives

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The increasing use of nanotechnology, including nanoparticles, in the preparation of drug products requires both manufacturing and analytical considerations in order to establish the quality metrics suitable for performance and risk assessment. A range of different nanoparticle systems exists including (but not limited to) nano-drugs, nano-additives and nano-carriers. These systems generally require more complex production and characterization strategies than conventional pharmaceutical dosage forms. The advantage of using nanoparticle systems in pharmaceutical science is that the effective and desired function of the material can be designed through modern manufacturing processes. The systematic nomenclature allows for greater understanding of the drug product under evaluation based on available data from other nanoparticle reports. Analytical considerations of nano-drugs, nano-additives and nano-carriers and the way in which they are measured are directly connected to quality control. Ultimately the objective is to consider the entire nano-drugs, nano-additives and nano-carriers product life cycle with respect to its manufacture, use, and eventual fate. The tools and approaches to address the needs of these products exist; it should be the task of the pharmaceutical scientists and those in related disciplines to increase their understanding of nanomedicine and its novel products.

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