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Gyu-Un Bae, Clin Exp Pharmacol 2017, 7:4 (Suppl)
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An isoflavone compound Daidzein elicits myoblast differentiation and myotube growth

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The reduced regenerative capacity of muscle stem cells contributes to aging or disease-related skeletal muscle atrophy. Daidzein, a natural isoflavone from Leguminosae, improves insulin sensitivity in skeletal muscle and prevents TNF-α induced muscular atrophy. However, the molecular mechanisms by which daidzein exerts these beneficial effects are currently unknown. In this study, we determined the effect and molecular mechanisms by which daidzein might improve skeletal muscle function. Similarly to the results with TNF-α, daidzein treatment prevented myotube atrophy triggered by Dexamethasone (DEX) via Akt activation. Furthermore, daidzein promoted myoblast differentiation in a dose-dependent manner through activation of promyogenic kinases, Akt and p38MAPK. Daidzein treatment strengthened MyoD activation by enhancing its heterodimer formation with E protein. Additionally, daidzein induced myotube growth, through activation of Akt/mTOR/S6K pathway. Moreover, daidzein increased MyoD-dependent myogenic conversion of fibroblast and myogenic differentiation. Taken together, daidzein has a potential as a therapeutic or nutraceutical remedy to improve muscle function and to treat aging or disease-related muscle loss and weakness.

Biography

Gyu-Un Bae has completed his PhD from Sungkyunkwan University and Postdoctoral studies from Harvard University, School of Medicine. He has published more than 54 papers in reputed journals and has been serving as an Editorial Board Member of Archives of Pharmacal Research.

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Fatma Sultan Kilic et al., Clin Exp Pharmacol 2017, 7:4 (Suppl)
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The role of nicotinic receptors in the effects of galangin in the Morris water maze

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Eskisehir Osmangazi University, Turkey

Introduction & Aim: Enhancing cholinergic transmission is suggested to improve cognitive functions. We aimed to investigate the effects of galangin, a flavonoid compound that is reported to inhibit acetylcholinesterase enzyme, on mecamylamine-induced spatial memory impairments in rats.

Methods: Morris water maze test was used to investigate the spatial memory. Galangin 50 (100 mg/kg) was administered acutely 30 minutes before the impairment of spatial memory by a nicotinic receptor antagonist (mecamylamine injection). Donepezil (1 mg/kg) used as a reference drug. Distance to platform and time spent in escape platform quadrant were recorded and analyzed with Ethovision XT version 9.0 (Noldus, Wageningen, Netherlands). Results were statistically analyzed with one-way ANOVA.

Results: Mecamylamine significantly increased the distance to platform and decreased the time spent in the escape platform quadrant compared to control group. Galangin 100, but not 50 mg/kg significantly decreased the distance to platform and increased the time spent in the escape platform quadrant compared to mecamylamine group comparable to donepezil 1 mg/kg.

Conclusion: Galangin 100 g/kg may improve memory comparable to donepezil and nicotinic receptors may be involved in this effect.

Biography

Fatma Sultan Kilic has completed her PhD from Anadolu University, Turkey. She has been working as an Academic Member and also contunuing her PhD at Faculty of Education. She has published more than 45 papers in reputed journals.

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Effects of selective PDE-2 inhibitor BAY60-7550, PDE-5 inhibitor Sildenafil and PDE-9 inhibitor PF-04447943 on learning and memory in the passive avoidance test in naive mice

Guner Ulak, Emine Bektaş, Füruzan Yıldız Akar, Oguz Mutlu and **Faruk Erden**
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Phosphodiesterases (PDE) are enzymes that hydrolyze cAMP and/or cGMP throughout the body, including the brain. Preventing the breakdown of cAMP by PDE inhibitors promotes memory. PDE inhibitors present a novel therapeutic approach with which to arrest cognitive decline or possibly reverse the decline with cognition enhancement. The aim of this study was to investigate effects of BAY 60-7550 (a PDE2 inhibitor), Sildenafil (a PDE5 inhibitor) and PF-04447943 (a PDE9 inhibitor) on emotional memory in naive mice using Passive Avoidance (PA) test. Mice were trained in a one trial step-through PA apparatus for evaluating emotional memory; whereas, decrease in retention latency indicate an impairment of memory. BAY60-7550 (1 and 3 mg/kg), Sildenafil (3 and 10 mg/kg) or PF-04447943 (1 and 3 mg/kg), (n=12-15 per group) was administered intra-peritoneally 30, 60 and 60 minutes, respectively before the acquisition session of PA test. One way Anova post hoc Tukey's test was used for the statistical analysis of the data. The results of this study revealed that there was significant difference between the first day latency of the animals. Drug treatment, significantly prolonged the retention latency of PA test in the second day compared to control group (3 mg/kg BAY 60-7550 vs. control $p<0.05$, 10 mg/kg Sildenafil vs. control $p<0.05$, 3 mg/kg PF-04447943 vs. control $p<0.01$). Our results confirm that BAY 60-7550, Sildenafil and PF-04447943, enhance emotional memory of mice in the PA test. Further studies and different cognition models are needed to support our results and enlighten whether these effects are test dependent or not.

Biography

Guner Ulak has completed her PhD from Dicle University, School of Medicine and Postdoctoral studies from Kocaeli University, School of Medicine, Turkey. She is the Director of Pharmacology Department, Kocaeli University, Turkey. She has published more than 70 papers in English, 45 in Turkish and has given many poster presentations.

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Furuzan Yildiz Akar et al., Clin Exp Pharmacol 2017, 7:4 (Suppl)
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Effects of selective PDE-2 inhibitor BAY60-7550 and PDE-9 inhibitor PF-04447943 on olfactor memory in Social Transmission of Food Preference (STFP) test in naive mice

Furuzan Yildiz Akar, Emine Bektaş, Oguz Mutlu, Güner Ulak and **Faruk Erden**
Kocaeli University, Turkey

Phosphodiesterases (PDEs) are enzymes that hydrolyze cyclic AMP (cAMP) and/or cyclic GMP (cGMP) throughout the body, including the brain. Accumulating evidence indicates that the inhibition of phosphodiesterase (PDE) activity may be a particularly interesting mechanism for memory enhancement. PDE inhibitors present a novel therapeutic approach with which to arrest cognitive decline or to possibly reverse this decline with cognitive enhancement. The aim of this study was to investigate effects of BAY 60-7550, a PDE2 inhibitor and PF-04447943, a PDE9 inhibitor on olfactory memory in naive mice using social transmission of food preference (STFP) test. Hippocampus-dependent non-spatial olfactory memory was studied using the STFP. In the STFP test, the ratio of the weight of the cued food eaten and the total weight of food eaten was used as a measure of food preference. Higher percentage of cued food/total food eaten reflects better performance in olfactory memory. BAY60-7550 (1 and 3 mg/kg) and PF-04447943 (1 and 3 mg/kg) (n=12 per group) were administered intraperitoneally 30 and 60 minutes, respectively before the retention session of STFP test. One way Anova post hoc Tukey's test was used for the statistical analysis of the data. BAY 60-7550 and PF-04447943 significantly increased % cued food/total food eaten compared to the control group. BAY 60-7550 and PF-04447943 also decreased total food consumption compared to the control group but it was not significant. Our results confirm that BAY 60-7550 and PF-04447943 enhance olfactory memory of naive mice in the STFP test.

Biography

Füruzan Yildiz Akar has completed her PhD and Postdoctoral studies from Kocaeli University, School of Medicine, Turkey. Presently she is working as an Associate Professor at the Kocaeli University, School of Medicine. She has published more than 50 papers in english and has many poster presentations.

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Li Zhou et al., Clin Exp Pharmacol 2017, 7:4 (Suppl)
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The reproductive toxicity of ZishenYutai pill on rats and offspring in perinatal period

Li Zhou, Juan Jiang, Yang Yang, Da-wei Yan, Li Xu, Li-ming Chong and **Zu-Yue Sun**
Shanghai Institute of Planned Parenthood Research Hospital, China

Objective: ZishenYutai Pill (ZYP) is one of the most commonly used Chinese medicines in prevention of early pregnancy loss due to threatened and recurrent miscarriage. Although it is widely used, its toxicity during perinatal period has not been well understood. Its main components include Radix Codonopsis, Radix Dipsaci, Polygoni multiflori, *Atractylodes macrocephala, Morinda officinalis, Eucommia ulmoides*, Semen cuscutae and Radix rehmanniae praeparata. In recent years, the research on ZYP has been increased year by year. Previous studies have shown that ZYP combined with phloroglucinol is significantly effective in the treatment of threatened abortion.

Methods: Pregnant rats (F_0) were exposed to 6 g/kg, 12 g/kg and 24 g/kg body weight/d of ZYP by intragastric administration from gestation day 15 (GD_{15}) to through parturition and lactation up to weaning i.e., post-natal day 21 (PND_{21}). Water and propylthiouracil (PTU, 15 mg/kg) were used as the negative control and positive control respectively. The mating was done between the treatment (ZYP or PTU) group and negative control group when the F1 pups were born on 63 days.

Results: The reproductive capacity of F_0 and F_1 generation decreased significantly after PTU exposure ($P<0.05$), however the body weight and reproductive ability of F_0, the physical development and feed consumption of F_1 as well as the reproductive ability and survival rate of F_2 rats were not significantly changed in the ZYP group compared with the negative control group ($P>0.05$).

Conclusion: There was no statistically significant evidence of perinatal toxicity under ZYP exposure.

Biography

Li Zhou has completed her PhD from Beijing Institute of Pharmacology and Toxicology and Postdoctoral studies from Chinese Academy of Medical Sciences. She is the Deputy Director of National Evaluation Centre for the Toxicology of Fertility Regulating Drug. She has published more than 40 papers in China and abroad reputed journals.

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Han Yan et al., Clin Exp Pharmacol 2017, 7:4 (Suppl)
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Testicular toxicity characters and mechanisms of hydroxyurea on rats

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Objective: Apoptosis plays a dominant role in both spontaneous spermatogenesis and germ cell death. This study was aimed to investigate the functions of related genes in testicular germ cell death induced by Hydroxyurea (HU).

Method: Wild-type (WT) and FasL Transgenic (TG) DBA/C57BL mice were intraperitoneal injected with 400 mg/kg HU. 12 hours later, testes were collected. Histomorphology of testis was observed by stained with Periodic Acid Schiff (PAS). Apoptosis was assessed by TUNEL assay. mRNA and protein levels of related genes were evaluated by quantitative RT-PCR and Western blot respectively.

Results: The 2×2 factorial design comparative experiments between WT and TG mice showed that the TG mice exhibited a higher basal apoptotic index. The basal mRNA levels of Fas and FasL and protein levels of Fas, FasL, Caspase-3, Caspase-8 and Caspase-9 in TG mice were also higher than that in WT mice. 12 hours after injection of HU, the testicular tubules exhibited no significantly morphological changes but remarkably increased apoptosis index in both WT and TG mice, with the latter having the higher amplitude. Although HU up-regulated the mRNA of apoptosis related genes such as Fas and FasL in both TG and WT mice, the increased amplitude were more obvious in TG mice. By Western blot analysis, apoptosis related proteins Fas, FasL Caspase-3, Caspase- 8 and Caspase-9 were significantly increased in both WT and TG mice, with TG mice exhibiting a greater up-regulation.

Conclusion: Germ cell apoptosis induced by HU treatment may be related to the FasL mediated signal transduction pathway.

Biography

Han Yan has completed the masters in Quality Assurance from National Evaluation Centre for the Toxicology of Fertility Regulating Drug. She has published more than 20 papers in China and abroad reputed journals.

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Zu-Yue Sun et al., Clin Exp Pharmacol 2017, 7:4 (Suppl)
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The research progress and biomarker research of chronic prostatitis

Zu-Yue Sun, Li Zhou and **Yu-ling Jia**
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Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) is an important public health problem. CP/CPPS is a poorly understood entity characterized by pelvic or perineal pain, irritative voiding symptoms and sexual dysfunction, and from a clinical point of view, is truly lacking a cause that would allow a more rational-driven therapy. As a common genitourinary disease of adult male, diagnosis, treatments and prognostic monitoring of prostatitis have always been the focus of clinical attention, as a result of its setbacks, such as complex pathogenesis and clinical symptoms, lacking specificity in medication and its high rate of recurrence and so on. Currently, there isn't a golden standard in diagnosis of prostatitis, while the detection of biomarkers can be helpful for the diagnosis, treatment and prognostic monitoring of prostatitis. Following significant improvements of the methods of detection in biological fluids, a number of prostate inflammation biomarkers were identified and quantified, in peripheral blood, urine and seminal plasma. In fact, White Blood Cells (WBC) count in Expressed Prostatic Secretions (EPS) has long been considered as the marker of prostatitis. However, it does not appear to be the optimal marker of inflammation and the current categorization of chronic prostatitis/chronic pelvic pain syndrome IIIB and asymptomatic inflammatory prostatitis as inflammatory or non-inflammatory based on WBC count appears to offer little clinically useful information and whilst WBC can be found in the prostatic fluid or seminal plasma of asymptomatic men as well as in that of men with pelvic pain. Also, the measures of the NIH-CP Symptom Index in symptomatic men show no correlation with WBC in EPS or seminal plasma. As the prostatitis biomarkers, cytokines/chemokine may have high sensitivity and good specificity. Cytokines are regulatory proteins released by various cellular subtypes that promote intercellular communication and immune responses. Chemokines are a subset of cytokines that recruit and activate immune cells to sites of inflammation. Interleukin 8 (IL-8) is a pro-inflammatory cytokine and plays an important role in different inflammatory diseases. Significant correlations between IL-8 levels and symptom score results were found. IL-8 values strongly correlated with CP/CPPS. Moreover, the patients with higher levels of IL-8 reported the worst symptoms. The study has shown that IL-8 was significantly elevated compared to controls in patients with CP/CPPS IIIA, CP/CPPS IIIB and benign prostatic hyperplasia (BPH). IL-8 is a reliable biomarker in seminal plasma for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and for BPH and also the IL-8 levels were correlated with symptom scores and serum PSA values, increasing its value as a biomarker for prostate inflammation. Monocyte Chemoattractant Protein-1 (MCP-1) and macrophage inflammatory protein-1α (MIP-1α) recruit monocytes and macrophages via their release from fibroblasts and macrophages in joints of patients with rheumatoid arthritis and perpetuate the inflammatory process. For MCP-1 and MIP-1α, chronic pelvic pain syndrome subtypes had statistically higher levels than the control group and patients with benign prostatic hyperplasia. MCP-1 and MIP-1α within the prostatic fluid in both chronic pelvic pain syndrome subtypes provide candidate future biomarkers for chronic pelvic pain syndrome. In addition, macrophage inflammatory protein-1α increase in expressed prostatic secretions provides a new marker for clinical pain in chronic pelvic pain syndrome patients. Given these findings prostatic dysfunction likely has a role in the pathophysiology of this syndrome.

Biography

Zu-Yue Sun is the Research Director of National Evaluation Centre for the Toxicology of Fertility Regulating Drug. He has published more than 312 theses in China and abroad reputed journals.

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Yan-qiang Liu, Clin Exp Pharmacol 2017, 7:4 (Suppl)
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Genistein inhibition of OGD-induced neuronal death *in vitro* experiment

Yan-qiang Liu
Nankai University, China

In the present study, we established an *in vitro* model of hypoxic-ischemia via exposing PC12 cells and primary neurons of newborn rats to oxygen-glucose deprivation (OGD) and observing the effects of genistein, a soybean isoflavone on hypoxic-ischemic neuronal viability, apoptosis, voltage-activated potassium (K_v) and sodium (Na_v) currents and glutamate receptor subunits expression. The results indicated that OGD exposure reduced the cell viability, increased apoptosis, decreased the GluR2 expression and decreased the voltage-activated potassium currents in PC12 cells and genistein partially reversed the effects induced by OGD. In primary neurons, OGD exposure reduced the viability and increased the apoptosis of brain neurons. Meanwhile, OGD exposure caused changes in the current-voltage curves and current amplitude values of voltage-activated potassium and sodium currents. OGD exposure also decreased GluR2 expression and increased NR2 expression. However, genistein at least partially reversed the effects caused by OGD in primary neurons. The results suggest that hypoxic-ischemia caused neuronal apoptosis/death is related to an increase in K^+ efflux, a decrease in Na^+ influx, a down-regulation of GluR2 and an up-regulation of NR2. Genistein may exert some neuroprotective effects via the modulation of K_v and Na_v currents and the glutamate signal pathway mediated by GluR2 and NR2.

Biography

Yan-qiang Liu has completed his PhD in Nanjing Agricultural University and Postdoctoral study in Chinese Military Medicine Academy, also visiting and co-operative studies in Pisa University. He is also the Professor of College of Life Sciences Nankai University, China. He has published more than 80 papers in reputed journals and has been serving as an Editorial Board Member of Acta Nutrimenta Sinica and the referee of many academic journals.

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Suliman Alghurair, Clin Exp Pharmacol 2017, 7:4 (Suppl)
DOI: 10.4172/2161-1459-C1-020

Assessment of pharmacists' knowledge regarding counseling patients about chronopharmacology of antihypertensive drugs (calcium channel blockers, α & β blockers)

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The General Directorate of Medical Services of Armed Forces, KSA

Statement of Problem: Some pharmacists are not aware of chronopharmacology and the importance of counseling patients about appropriate time to take their anti-hypertensive drugs.

Purpose of Study: To measure pharmacists knowledge about chronopharmacology of anti-hypertensive medications (Calcium Channel Blockers, α & β Blocker) and to assess pharmacist's practice when providing patient counseling for hypertensive patient's. A convenient sample of community pharmacists in Riyadh, Saudi Arabia were given questionnaire that contains closed and open ended questions. Data then analyzed by using descriptive statistics using Microsoft Office Excel 2010 to provide an overview of the quantitative data collected.

Methodology: This is a descriptive cross-sectional survey that was conducted by recruitment of convenient sample of pharmacists from community pharmacies in Riyadh, Saudi Arabia. Questionnaires that contain closed and open-ended questions were given to the sample. Data then analyzed by using descriptive statistics using Microsoft Office Excel 2010 to provide an overview of the quantitative data collected.

Findings: Forty six (46) community pharmacists participated in the survey. Almost half of the sample (54%) agreed that blood pressure has two peaks (9:00 AM and 7:00 PM). Likewise, half of the pharmacists participated in the survey think that some medications can be taken at time patients preferred either in the morning or evening. In addition, most of the pharmacists (93%) rated their counseling to patients as a good counseling.

Conclusion: This study indicates that pharmacist's awareness of chronopharmacology and interaction with antihypertensive drugs and patients counseling about chronopharmacology and adherence to time when taking antihypertensive agents need further improvement.

Biography

Suliman Alghurair has his experience in studying patient's adherence to medications and measurement of factors that influence patient's adherence to medications. He is also interested in studying patient-pharmacist relationship and patient satisfaction.

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Kevser Erol et al., Clin Exp Pharmacol 2017, 7:4 (Suppl)
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Effects of anandamide and agmatine on cisplatin-induced neurotoxicity *in vitro*

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Objective: Cisplatin is a widely used antineoplastic drug in the treatment of malignancies. Cannabinoids have shown analgesic features in neuropathic pain models. Agmatine has also been shown to relieve neuropathic pain in different animal models. The aim of this study was to investigate the *in vitro* effects of anandamide, a cannabinoid receptor agonist and agmatine on cisplatin-induced neurotoxicity on primary dorsal root ganglia.

Materials & Methods: Primary cultures of DRG were also prepared from 1-day old rats. The toxic effects of cisplatin were evaluated by incubating the cells with cisplatin (50-500 µm). Concentration of 200 µm of cisplatin which showed submaximal neurotoxicity was used alone and with 10-500 µm concentration of agmatine or with anandamide (10-1000 µm) for determining its possible neuroprotective activity. MTT assay was used to detect the toxicity of DRG cells. Results were evaluated by using ELISA test system at a wavelength of 450 nm.

Results: Cisplatin had concentration-dependent neurotoxic effects on DRG *in vitro* and high concentration of anandamide attenuated cisplatin neurotoxicity. But agmatine could not alter the neurotoxic effect of cisplatin.

Conclusions: We suggest that exogenous cannabinoid may represent a promising new protective strategy against cisplatin neurotoxicity.

Biography

Kevser Erol has completed her PhD from Dicle University and Postdoctoral studies from Anadolu University, School of Medicine. She is the Director of Department of Pharmacology and has published more than 125 papers in reputed journals.

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Rashida Bashir et al., Clin Exp Pharmacol 2017, 7:4 (Suppl)
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Exploring ethnopharmacological potential of Australian native old man saltbush and wattle seed with untargeted metabolic profiling and structural elucidation with mass spectrometry

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Currently, there are 119 drugs of known structure that are still extracted from higher plants and used globally in allopathic medicine. Ethnomedical and traditional medicinal use of Australian aboriginal plants can provide information that is useful to pre-screen them for experimental pharmacological studies. Australian aboriginal people use old man saltbush topically as a medicine for cuts and stings and wattle seeds as a mild sedative for rheumatism or indigestion. This study intended to attract the attention of ethnopharmacologists to focus on the unexplored potential of both edible plants. Recent advances in bioanalytical technologies have emerged as a critical tool in the process of drug discovery and development. Non-targeted metabolomics with Reaction Flow Chromatography-Post Column detection-Ferric reducing Antioxidant potential assay (RF-PCD-FRAP) and LC-ESI-MS analysis implies that Australian native saltbush and wattle seed are rich sources of antioxidants. Underivatized and derivatized reactions were simultaneously monitored to attain information of complex samples. Analytes were identified by MS and MS^2 with the ESI mass spectra under the same conditions in both positive and negative ionization modes. Isorhamnetin, Rhamnetin, Asarone, Nookatone, Brevifolin and Apocynin Quinic acid, Citric acid, Gallic acid, Quinovic acid, β-D-glucoside, D-Pantothenic acid and 4”-0-beta glucose 4-p-Coumaroylquinic acid were the main bioactives found within samples, which may be responsible for their well-known therapeutic roles of these plants. Both samples have exhibited superior antioxidant capacity and comprise predominantly of flavonols, anthocyanin, phenolic acids and contains bioactives with known therapeutic potential in cardiovascular, neurodegenerative and other chronic diseases that play a major role in the prevention/delay of diseases.

Biography

Rashida Bashir has previously completed Masters of Biotechnology and Bachelor of Pharmaceutical Sciences. She has recently submitted her PhD thesis in the area of Natural Products and Bioanalytical Chemistry under the supervision of Dr. Peter Mahon and Professor Enzo Palombo.

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Rational drug use among physicians and nurses who work in a university hospital

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Introduction & Aim: At the meeting which is assembled at Nairobi, World Health Organization (WHO) described rational drug use as easy access to adequate drug in the meaning of period and dosage and for lowest cost. According to 2006 WHO data, worldwide reserved fund for drug expenditure is 859 billion US Dollar. As a result of irrational drug use, bacterial resistance occurs against antibiotics and affects treatments. This research was conducted to study knowledge and attitude of college, hospital, physicians and nurses towards rational drug use.

Materials & Methods: This is a descriptive study and it was conducted between 1-15 April 2016 in college and hospital, physicians and nurses (n=316) who work at college and hospital form the sample of this study. However, due to unwillingness of participation 212 (67.08%) individual were included in the study. Data were collected by survey form, which was made from literature review. Ethical approval was taken before the application of the study.

Results: 32.8% of physicians had 11 to 15 years of professional experience, 87.5% of the participants reported that they are specialist physician, 44.3% of the nurses had 11 to 15 years of professional experience, 79.1% of the nurses reported that they participated in-service training, 68.70% of physicians stated that they participated in rational drug use training, 35.9% of physicians participating in the study reported that they made an adverse report. When prescribing, they stated that they used the *Vade mecum* (71.9%) as information source. Only a minority of participants (7.8%) reported that they had a poor knowledge about bioequivalence, pharmacological properties (4.7%) and warnings. About 18.8% of physicians reported that they were discussing with their patient if they did not prescribe the medicine desired by the patient. They said that 20.3% of the physicians never interacted with other medicines or foods, 12.5% never gave information about drugs, 53.4% of the participants stated that medication was omitted or not applied, 49.3% said that the medication was applied at the wrong time and 18.9% said the medication was applied to the wrong patient. It was found that 10.8% of the participants were warnings and precautions and 8.1% of them had very poor knowledge of drug interactions. When informational conditions were being evaluated, warnings-precautions and drug interaction were reported by nurses as very bad (respectively 10.8% and 8.1%).

Conclusions: Drug use problems continue despite important advancements in Turkey. The physicians' knowledge and attitude were comparable but need further improvement. The nurses do not have sufficient information about rational drug use and they reported that they do make drug administration errors. They need periodic reinforcement about rational drug use. Drug policies should be shaped accordingly.

Biography

Kevser Erol has completed her PhD from Dicle University and Postdoctoral studies from Anadolu University, School of Medicine. She is the Director of Department of Pharmacology and has published more than 125 papers in reputed journals.

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Se-Young Choung et al., Clin Exp Pharmacol 2017, 7:4 (Suppl)
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Anti-diabetic effects of water extract of *Dendropanax morbifera* leaves in db/db mice

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Kyung Hee University, South Korea

In the present study, we investigate the effect of the water extract of *Dendropanax morbifera* leaves (DLE) on anti-diabetic activity in the diabetic db/db mice. 6-week-old male db/m+ and 5 groups of db/db mice were treated with metformin or DLE for 6 weeks, db/m+ group (normal), db/db group (control), metformin group (positive control, 200 mg/kg) and the DLE groups (50, 100, 200 mg/kg). The oral administration of DLE or metformin significantly lowered serum glucose, insulin, HbA1c, c-peptide and serum lipid levels (TG, TC) in db/db mice. Additionally, the safety of 6 weeks administration of DLE was confirmed when considering that the level of AST, ALT and BUN in serum were within the normal range. Histological analysis with H&E staining indicated that DLE treated group showed the higher number of hepatic nucleus compared to the db/db group. To understand the molecular mechanism of DLE, the expression level of genes associated with diabetes was measured in liver and muscle tissue. The expression of glucose metabolism and transport genes (glucokinase, glucose transporter type-2 and 4) and glycogen synthase of db/db mice was increased by DLE. On the other hand, DLE treatment resulted in decreased expression level of gluconeogenesis related genes such as glucose-6-phosphatase, phosphoenolpyruvate and carboxykinase. These results suggest that DLE may have the possibility to ameliorate type-2 diabetes. Therefore, DLE could be extensively used as a functional food for mitigating type-2 diabetes.

Biography

Se-Young Choung has completed his PhD from Tokyo University, Graduate School of Pharmacy. He is the Professor of Kyung Hee University College of Pharmacy and the President of Korean Accreditation Council for Pharmacy Education. He has published more than 30 papers in reputed journals and has been serving as an Editorial Board Member of repute.

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Efficacy and safety of Daclatasvir plus Asunaprevir therapy for Taiwanese patients with genotype 1b hepatitis C virus infection

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Kaohsiung Medical University, Taiwan

All oral Direct Acting Antivirals (DAAs) achieve high Sustained Virological Response (SVR) rates in patients with chronic hepatitis C Virus (HCV) infection. In Asian countries, the dual therapy with Daclatasvir and Asunaprevir was reported well tolerated and achieved high SVR rates in patients with chronic HCV genotype 1b infection. Recently, the dual therapy has been reimbursed by the National Health Insurance in Taiwan. The studies aimed to survey the efficacy and safety of dual therapy with Daclatasvir and Asunaprevir in Taiwanese patients with HCV genotype 1b infection. Total 19 patients (8 males and 11 females, mean age: 65 years) without the NS5A resistance-associated substitution have been treated with dual therapy for 24 weeks and followed up for 12 weeks. All 19 patients achieve negative HCV RNA at end of therapy and at 12 weeks after cessation of therapy (SVR12). The mean (range) baseline AST, ALT and total bilirubin (T-bil) levels were: 80.6 (30-224) IU/L, 89.0 (34-230) IU/L and 0.71 (0.29-1.24) mg/dL, respectively. In all patients, there was neither significant increase of these liver function markers up to 2 times' upper limit of normal nor acute exacerbation or decompensation at 12 weeks after therapy. The highest AST, ALT and T-bil levels were 39 IU/L, 47 IU/L and 1.21 mg/dL, respectively. We concluded that dual therapy achieved very high SVR rates and was well tolerated in Taiwanese patients with HCV genotype 1b infection. Further results of large number of treated patients are expected.

Biography

Chia-Yen Dai has completed his MD, Master and PhD degrees from Kaohsiung Medical University, Kaohsiung, Taiwan. He is the Director of Health Management Center and Occupational and Environmental Medicine, Kaohsiung Medical University Hospital and a Full Professor of Hepatology, Internal Medicine, College of Medicine, Kaohsiung Medical University. He has published more than 220 papers in reputed journals with more than 50 papers.

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Quasi emulsion spherical crystallization technique based environmentally responsive Tulsion® (pH dependent) microspheres for colon specific delivery

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Statement of the Problem: pH-dependent sustained-release Tulsion® microspheres bearing clarithromycin were developed for colon specific release so that a broad spectrum of diseases can be treated well.

Methodology & Theoretical Orientation: Clarithromycin bearing Tulsion® microspheres were prepared using quasi-emulsion solvent diffusion method (spherical crystallization technique) with thermocoat L 30 D-55. Both, clarithromycin and thermocoat L 30 D-55 were evaluated for *in vitro* toxicity assay against human red blood cells. Ratiometric optimization of different solvents using phase diagrams was performed on amount of good solvent, bridging liquid, dispersing liquid and poor solvent.

Findings: Both, clarithromycin and thermocoat L 30 D-55 were found to be non-hemolytic during *in vitro* toxicity assay against human red blood cells. The developed microspheres were evaluated for the recovery (67.27±3.3%), average particle size (52.0±0.46 µm) and encapsulation efficiency (61.0±3.1%). Scanning electron microscopy and transmission electron microscopy revealed that the microspheres were smooth in surface and spherical in shape, respectively. The drug release study was conducted at different pH of GIT and it gave a pH dependent release for clarithromycin.

Conclusion & Significance: The manuscript reported the debut work on thermocoat L 30 D-55 based novel drug delivery system, the polymer is safe to be used, quasi emulsion spherical crystallization technique is a good technique to prepare microspheres, the prepared microspheres provides sustain release profile as well as targeting to colon.

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Detection of mineral nutrients and toxic elements in Yemeni sesame oil by inductively coupled plasma-optical emission spectrometry (ICP-OES)

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Abundance and mineralogical residence of 12 elements have been determined by inductively coupled plasma-optical emission spectrometry (ICP-OES) in 120 samples of Yemeni sesame oil collected from different provinces. Over two years of analysis, the results show no significant differences in terms of the physicochemical parameters. Calcium content was found between 3.021 and 9.656 mg/kg, this cation making up 50% of the total mineral content. The two other most abundant minerals were potassium (0.824-4.251 mg/kg) and magnesium (0.811- 4.742 mg/kg). Heavy metal (Cd, Pb, Cu, Sn and Zn) content was very low. The use of chemometrics in this work allowed establishing discriminant models for optimization to determine the trace elements content in oil samples.

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Surface electromyography analysis of blepharoptosis correction by transconjunctival incisions

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Upper eyelid movement depends on the antagonisticactions of orbicularis oculi muscle and levatoraponeurosis. Blepharoptosis is an abnormal droopingof upper eyelid margin with the eye in primaryposition of gaze. Transconjunctival incisions forupper eyelid ptosis correction have been a welldevelopedtechnique. Conventional prognosishowever depends on clinical observations and lacksof quantitatively analysis for the eyelid musclecontrolling. This study examines the possibility ofusing the assessments of temporal correlation insurface electromyography (SEMG) as a quantitativedescrip- tion for the change of muscle controllingafter operation. Eyelid SEMG was measured frompatients with blepharoptosis preoperatively andpostoperatively, as well as, for comparative study,from young and aged normal subjects. The data wereanalyzed using the detrended fluctuation analysismethod. The average DFA a index values for all ofthe eyes from the young and aged normal groups andthe patient group from before and after the operationsare plotted in Fig. 7. The results show that thetemporal correlation of the SEMG signals can becharacterized by two indices asso- ciated with thecorrelation properties in short and long time scalesdemarcated at 3 ms, corresponding to the time scaleof neural response. Aging causes degradation of thecorrelation properties at both time scales, and patientgroup likely possess more serious correlationdegradation in long-time regime which wasimproved moderately by the ptosis corrections. Wepropose that the temporal correlation in SEMGsignals may be regarded as an indicator forevaluating the performance of eyelid musclecontrolling in postoperative recovery.

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Coenzyme Q10-evoked stimulation of nitric oxide-related dilation of the rat aorta

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This study examined whether coenzyme Q10 can improve NO dependent vasodilatation in the rat aorta after pre-incubation or intravenous administration. In initial experiments, intact isolated aortic rings were incubated with CoQ10 or L-arginine. In further experiments, CoQ10 was administered intravenously in anesthetized rats, and then in 2 hours, aorta was isolated. In both cases, after preliminary preparation the isolated aortic rings were tested for Ach induced NO dependent relaxation. ACh elicited a concentration dependent relaxation of phenylephrine pre-contracted aortic rings. Relaxant responses to ACh were markedly potentiated after pre-incubation with CoQ10 or L-arginine. The maximum relaxant responses (%) were significantly increased from 64.1±5.3 (control) to 89.8±3.0 and 83.6±3.0 (CoQ10 and L-arg, respectively). The pD2 (-lgEC50) value in control study was 5.81±0.28, after pre-treatment with CoQ10 or L-arg were 7.59±0.16 and 7.26±0.32, respectively. There was no difference between CoQ10 and L-arginine groups. After intravenous administration, the relaxant responses to ACh were significantly increased in CoQ10-treated group (94.2±2.0) compared with controls (68.1±4.4). pD2 values were also different between control and treatment groups (5.79±0.29 vs. 8.14±0.65, respectively). Thus, CoQ10 improved NO mediated vasodilation in rat aorta as well as substrate for eNOS-L-arginine. Our data show that exogenous intravenously administered CoQ10 is able to improve rapidly NO dependent vasodilation in rat aorta, likely due to accumulation of CoQ10 in the vessel wall. Improvement of endothelial function can contribute, at least in part, to beneficial effects of CoQ10 in cardiovascular diseases associated with endothelial dysfunction.

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Alcohol exposure suppresses neural crest cells generation and differentiation during early chick embryo

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It is now known that excess alcohol consumption during pregnancy can cause fetal alcohol syndrome (FAS) in which several characteristic craniofacial abnormalities are often visible. However, the molecular mechanisms of how excess ethanol exposure affecting cranial neural crest cells (CNCCs), the progenitor cells of the cranial skeleton, is still not clear. In the study, we investigated the effects of ethanol exposure on CNCCs migration both in early chick embryo and *in vitro* explant culture. First of all, we demonstrated that ethanol treatment caused Alizarin red-stained craniofacial developmental defects including parietal defect. Second, immunofluorescent staining with neural crest special markers indicated that CNCCs generation was inhibited by ethanol exposure and, double immunofluorescent stainings (Ap-2α/PHIS3, HNK1/BrdU and AP-2α/c-caspase3) revealed that ethanol exposure inhibited CNCCs proliferation and increased apoptosis. In addition, it inhibited NCCs production by repressing the expression level of key transcription factors which regulate neural crest development by altering expression of Epithelial-Mesenchymal Transition (EMT)-related adhesion molecules in the developing neural crests. In sum, we have provided experimental evidence that excess ethanol exposure during embryogenesis disrupts CNCCs survival, EMT and migration, which in turn causes defective cranial bone development.

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Bax inhibitor-1 inhibits Acetaminophen-induced hepatotoxicity by reducing ER stress through regulating the RIDD activity of IRE1α

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Acetaminophen (APAP) overdose is the most frequent cause of acute liver failure in young adults and is primarily caused by CYP2E1 driven conversion of APAP into NAPQI, a hepatotoxic metabolite. This will lead to the ER stress, activation of UPR and the proapoptotic events, due to the reduced glutathione level and perturbation in the redox balance. Bax inhibitor-1 (BI-1) is an evolutionarily conserved ER-membrane resident protein that suppresses cell death by regulating ER stress response. In this study we examined the role of BI-1 in APAP induced ER stress and in regulation of IRE1alpha, an endoribonuclease UPR molecule known to degrade the mRNA through the process called RIDD. Our result showed that APAP induced ER stress was reduced in BI-1 over expressing cells. BI-1 knockout mice showed massive hepatic toxicity and large number of cytoplasmic vacuoles as revealed by H&E staining. Further it increased ALT and AST levels, protein oxidation and lipid peroxidation. We observed reduction of CYP2E1, a RIDD substrate, expression in BI-1 overexpressing cells. To examine the possible relation of BI-1 in CYP2E1 lower expression in the ER stress, we hypothesized that BI-1 may regulate the IRE1 response. As, it is known that XBP1s requires oligomer state of activated IRE1a and this XBP1s is reduced in BI-1 expressing cells but at the same time phosphorylation of IRE1 was also observed. So, it indicates that in BI-1 overexpressing cells IRE1alpha is activated but held in dimer state for extended time compare to PC cells. In consequence, the dimer state of activated IRE1a has the RIDD activity and helps in initial adaptive stress response by reducing the further load of protein synthesis during ER stress. As a consequence CYP2E1 mRNA degraded and resultantly lesser conversion of APAP to toxic metabolite. So, our results suggest a role for BI-1 in in the regulation of RIDD activity in early adaptive responses against APAP induced ER stress.

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3,4-methylenedioxymethamphetamine-induced neurotoxicity improves following exercise in the hippocampus of adult rats

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3,4-methylenedioxymethamphetamine (MDMA) or ecstasy impairs the learning and memory. As the exercise can improve the memory, herein we investigated the effects of treadmill exercise on memory and long term potentiation in relation to apoptosis, neurotrophic factors and stress oxidative in the hippocampus of MDMA-treated rats. Male Wistar rats received multiple injections of MDMA and exercised for one month on a treadmill. Long Term Potentiation (LTP) and memory function were assessed using electrophysiology and Morris water maze. Lipid peroxidation and expression of caspase 3 and Brain Derived Neurotrophic Factor (BDNF) were examined by thiobarbituric acid assay test and western blot, respectively. Treadmill exercise could improve MDMA-induced LTP disruption and memory impairment. Caspase 3 expression decreased in the exercise group compared to MDMA group. BDNF expression decreased in MDMA group and treadmill exercise could increase that. Exercise caused the reduction in lipid peroxidation in the hippocampus. Exercise seems could be a useful strategy for treating memory impairment through up-regulation of BDNF and decrease in apoptosis in the hippocampus.

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Anti-aging drugs: where do we stand and where are we going?

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Taking into account the extraordinary complexity of mechanistic pathways underlying aging process, the recognition of these pathways and development of anti-aging interventions seems a challenging task. Significant progress, however, has been achieved in this research field during the past years. Efforts to increase healthspan through pharmacological agents and supplements targeting aging-related pathological changes are now in the spotlight of geroscience. The attempts to increase healthspan are currently focused on slowing the basic biological processes of aging such as cellular senescence, mitochondrial dysfunction, age-related decline of stress resistance, dysregulated cellular energy sensing/growth pathways, impaired proteostasis, deteriorated stem cell function/bioavailability, as well as inflammation/oxidative stress. A number of pharmacological agents targeting basic aging pathways to extend lifespan and healthspan (i.e., antioxidants, calorie restriction mimetics, autophagy inductors, etc.) are currently under investigation. Experimental studies have showed that extension of life span is usually accompanied by delayed or reduced morbidity including cardiovascular disease, neurodegeneration and tumors. Another way for anti-aging drug discovery is evaluating the pharmacological agents already approved by the FDA and other regulatory agencies for the treatment of particular conditions associated with aging, such as beta-blockers, metformin, statins, as well as anti-inflammatory medications. Supplementation with substances having anti-aging properties can, however, resulted in some cases in unfavorable effects as well. For example, in meta-analyses of observational studies and randomized controlled trials conducted in well-nourished and healthy populations, long-term antioxidant supplementation has been shown to be occasionally associated with undesirable consequences for the health and all-cause mortality. In a modern pharmacy, anti-aging is likely one of the most promising markets because the target group can potentially include each person. Current marketing research indicates that most people are willing to pay for long-term pharmacological therapy to prevent or delay the aging-related decline in physical and mental functions. Optimistic predictions of the feasibility of health- and life-extending interventions, however, should certainly be critically discussed in the light of their ethical, economic and social implications. Only after in-depth examination and following comprehensive debates, the implementation of such approaches in clinical practice will be possible.

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