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BIOCHEMICAL AND BIOLOGICAL EFFECTS OF IRISIN IN A MODEL OF DIABETES MELLITUS

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Diabetes mellitus (DM) is a highly prevalent health problem affecting more than 425 million people worldwide. It is associated with several detrimental complications such as neuropathy, nephropathy, retinopathy and cardiovascular diseases. Irisin is a novel hormone that plays a role in metabolism by stimulating the browning of white adipose tissue (WAT) into beige adipose tissue which acquires properties that are like those of brown adipose tissue (BAT). Several studies have attempted to characterize the roles of irisin in DM and obesity; however, contradictory results have been reported and physiological roles of irisin have been questioned by several researchers. In our study, we investigated the role of irisin in controlling glucose levels and insulin secretion in STZ-induced DM model and the mechanism by which irisin exerts its beneficial effects both *in vivo* and *in vitro*, using a variety of biochemical, morphological and cell biology techniques. We showed that irisin did not cause any significant reduction in weight or fasting blood glucose; however, it caused a significant glucose reduction 30 minutes after glucose challenge. Our data also showed that irisin co-localizes with insulin in pancreatic β-cells in both normal and diabetic animals while it co-localizes with glucagon only in diabetic animals. Moreover, irisin was also detected in skeletal muscle, visceral and subcutaneous adipose tissues. Irisin also reduced triglycerides and increased the level of high density lipoprotein (HDL) and total protein. We also provided evidence that irisin treatment can modulate the tissue level of different peptide hormones such as insulin, glucagon, incretins and leptin. In addition, irisin possesses a potent antioxidant activity and reversed oxidative stress induced by DM. Our *in vitro* investigations showed that irisin can stimulate the release of insulin from pancreatic β-cells. Irisin could be a potential therapeutic agent in the management of DM.

BIOGRAPHY

Mahgoub M is a Pharmacist who has been practicing since graduation in 2009 until date. He has worked in different settings like community pharmacy, hospital pharmacy and ambulatory healthcare centre in United Arab Emirates. In addition, his passion towards pharmacological research has encouraged him in obtaining his master's degree in 2012 and PhD. His focus is in diabetes mellitus pharmacology and particularly in discovering new agents that can assist in controlling hyperglycaemia and reversing complications associated with diabetes.

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DANCE AND ROBOT THERAPY FOR COGNITIVE ABILITY

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Introduction: Our preliminary trial revealed the correlation between cognitive ability and active ability, blood vessel age, and stress. From this result, a method to eliminate stress and favorably influence blood vessels and activity capacity was examined. We developed a method where elderly participants danced to familiar music while executing brain training tasks. Furthermore, we considered how this brain training dance could be done alongside a robot for a healing effect.

Methods: For comparison before and after the intervention, a cognitive ability test was used. A ten-word memory test measured immediate reproduction and delayed reproduction. A code conversion test and word recall test were also used. Then, impressions and the demand for robot therapy were investigated.

Results: The brain training dance continued once a month for three months, and cognitive tests were conducted before and after. Data of 102 people were analyzed. The score of the cognitive test items (immediate memory, delay of memory, recurrence of transcoding) was analyzed by a paired t-test and showed significant improvement after therapy ($p<0.05$). Responses were received from 62 people for the free description of the robot therapy. 24 of the largest people wanted robots as partners, 15 people healed through heart-to-heart interaction, eight people healed through dancing and singing, four people trained their brains, and four people wanted body care.

Discussion & Conclusion: The brain training dance to familiar music improved cognitive abilities. This activity can relieve stress. Following this study, we want to evolve the brain training dance that the robot can do and increase the volume of fun activities available to the elderly.

BIOGRAPHY

Kazue Sawami is a Professor at Nara Medical University and completed her PhD at Health Science. Her research is about the cognitive abilities of elderly people.

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ROLE OF NANO-CURCUMIN IN DIABETIC CARDIOMYOPATHY

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Diabetes is a long-lasting disorder in the metabolism of proteins, fats, and carbohydrates. It is described as an increase in blood glucose. Diabetes results leads from either insulin deficiency or malfunction. According to statistics, 2.8% of the world's population suffers from this disease and it is expected to increase to more than 5.4% by 2025. These leads to the diabetes complication and one of the major complications are diabetic cardiomyopathy [DCM]. The main reason of the uncontrolled change of DCM is microangiopathy, which consequences in cardiac structural and functional modifications, such as apoptosis of the myocardium, myocardial interstitial fibrosis, and perfusion abnormality of the heart muscles. It was described that capillary basement membrane thickening and microaneurysms were witnessed in patients with DCM. Once the myocardial interstitial fibrosis in diabetes patients has developed, it cannot be inverted, and a poor forecast of the diseases is commonly expected. Therefore, it is important to recognize appropriate therapeutic goals notably at the initial stage of DCM. Numerous biological methods have been shown to interpretation for the pathogenesis and progression of DCM, including diabetes oxidative stress, cardiomyocyte apoptosis, endoplasmic reticulum stress, myocardial insulin resistance, endothelial dysfunction, mitochondrial dysfunction, and autophagy. Amongst which, oxidative stress is supposed to be important mechanism through which diabetes mellitus induces DCM. Reactive oxygen species are chemically responsive chemical species containing oxygen, including peroxides, superoxide, hydroxyl radical, and singlet oxygen. Mitochondrion is the main factory in which diabetes mellitus creates excessive mitochondrial superoxide. The diabetes mellitus induced overproduction of mitochondrial superoxide indications to increased development of advanced glycosylation end products, expression of the receptor for AGEs, and activation of protein kinase C, the polyol pathway, and the hexosamine pathway. In case of the additional ROS not being balanced or removed via the action of endogenous antioxidative enzymes or exogenous antioxidant molecules, an increased oxidative stress occurs, which can consequence in damage to proteins, lipids, and DNAs in cardiomyocyte. These harmful effects finally lead to the transformation of the diabetic heart, followed by its dysfunction the antioxidative effect of natural products on the attenuation of DCM has been extensively investigated in recent years, showing promising outcomes. Curcumin is a natural compound isolated from curcuma longa and has been widely used in indigenous medicine. Attention has been paid to the antioxidative effect of curcumin on DCM. Curcumin was establishing to reduce myocardial capillary sclerosis; attenuate cardiac tissue damage, myocardial cell hypertrophy, and apoptosis; reduce extracellular protein accumulation; and preserve left ventricular function in the hearts of STZ-induced diabetic rats. Mechanistically, curcumin was originated to increase HO-1, catalase, superoxide dismutase, and GSH. Although curcumin was found to have antioxidative effects on DCM, the exact goal through which curcumin applied the functions remained uncertain. Gene sensation and silencing approaches could aid the examination of the exact mechanism of antioxidative role induced by curcumin. Hence from above discussion it can be concluded that the curcumin can be the choice of treatment for DCM.

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MULTIMECHANISTIC ANTIFIBROTIC EFFECT OF IRON CHELATORS: IMPLICATIONS OF INFLAMMATORY AND FIBROGENIC MEDIATORS

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Background & Aim: Iron overload is one of mechanisms by which HCV causes oxidative stress that may contribute to liver fibrosis and carcinogenesis. The therapeutic benefit of adding iron chelators to treatment regimen of HCV patients are warranted because: firstly, clinical data reported that excess iron deposits are found in the liver samples from about 20% of HCV-positive patients. Secondly, hepatic iron load enhances the levels of eukaryotic initiation factor 3, which is essential for HCV translation. Through an international joint project entitled investigating the coagulation profiles and the role of iron in patients with hepatitis C virus (HCV): impact of iron chelators in attenuating thrombosis and liver fibrosis, we investigated the potential antifibrotic effects of different iron chelators, and the underlying mechanisms through studying different oxidative stress, inflammatory and fibrotic markers.

Methods: Liver fibrosis was induced using concanavalin A (Con A; 15 mg/kg/w for six weeks, iv) and rats were treated with iron chelators (deseferoxamine, defriprone or defrasirox) three times per week for six weeks. Histopathology and iron homeostasis pathway were elucidated. Then different oxidative stress, inflammatory and fibrosis markers were assessed such as hydroxyproline, TGF-beta, alpha-SMA, CD4, NF-kB, TNF-alpha, iNOS, COX-2, IL6 and INF-γ.

Results: Collectively, it was found that iron chelators possess potent antifibrotic effects due to their antioxidant and anti-inflammatory properties as well as maintenance of iron homeostasis.

Conclusion: The present project may open a new scenario for the clinical usefulness of iron chelators in treatment of liver fibrosis associated conditions in the future.

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ANTIBACTERIAL ACTIVITY AND PHYTOCHEMICAL ANALYSIS OF WILD *ORIGANUM SYRIACUM* ESSENTIAL OIL COMMONLY USED IN THE WEST BANK

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Origanum syriacum (O syriacum) is a very popular edible and medicinal plant in the East Mediterranean countries. The current study employed microwave-ultrasonic assisted hydro distillation (MAUHD) to produce EO from four wild *O syriacum* samples. Gas chromatography coupled with mass spectrometer detector (GC/MS) was used for phytochemical analysis. Assessment of their antibacterial and antioxidant potentials *in vitro* was carried out. Sesquiterpenes (24-39%) α-humulene and caryophellene in addition to oxygenated monoterpenes (26-41%) thymol and carvacrol represent the bulk of phytochemicals detected by GC-MS analysis. Thymol-rich EOs were found to be most effective against *Staphylococcus aureus* and methicillin-resistant *Staphylococcus aureus* (MRSA) (MIC 0.4 mg/mL). Carvacrol and α-humulene rich chemo type EO from Bethlehem, exhibited the highest inhibitory effect of *Pseudomonas aeruginosa* (MIC of 1.6 mg/mL). Interestingly, γ-terpinene-rich EO from Jerusalem and Bethlehem showed promising antibacterial properties against *Enterococcus faecium* and MRSA (MIC 100 and 200µg/mL respectively). In conclusion, the current study supports the use of MAUHD as a time-saving, cost-effective, environment-friendly method for production of high quality *O syriacum* EO for potential use in the treatment, prevention and adjuvant therapy against bacterial infections without compromising the quantity.

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MITIGATION OF DRUG-INDUCED HEPATOTOXICITY BY NOVEL PHENOLIC ACID-ISONIAZID MUTUAL PRODRUGS: DESIGN, SYNTHESIS, KINETICS AND BIO EVALUATION

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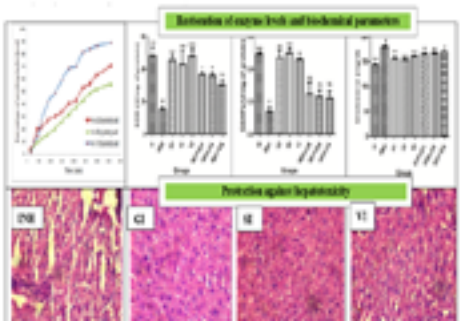
Aims & Objective: To overcome hepatotoxicity caused by long term use of anti-tubercular agent isoniazid (INH), a novel hepato-protective prodrug strategy was developed by combining INH with phenolic acids as antioxidant carriers for probable synergistic effect.

Methodology: INH was conjugated with antioxidant phenolic acids through a bioreversible amide linkage using Schotten Baumann technique. Synthesized prodrugs were characterized by spectral analysis and *in vitro* release kinetics was studied by HPLC. Hepatoprotective potential was evaluated in male Wistar rats by performing the liver function tests, oxidative stress markers and histopathology studies.

Results: Prodrugs resisted hydrolysis in acidic (pH 1.2), basic (pH 7.4) buffers and rat stomach homogenates whereas hydrolyzed significantly (56.03-88.62%) in intestinal homogenates over a period of 6h. All the prodrugs were effective in abating oxidative stress and re-establishing the normal hepatic physiology. Especially the effect of prodrugs of INH with gallic acid and syringic acid in restoring the levels of enzymes superoxide dismutase and glutathione peroxidase and abrogating liver damage was noteworthy.



Conclusion: The findings of this investigation demonstrated that the reported mutual prodrugs can add safety and efficacy to future clinical protocols of tuberculosis treatment.

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INVESTIGATION OF ANTI-LEUKEMIC AND ANTI-CLASTOGENIC POTENTIALS OF SOME MEDICINAL PLANTS KNOWN FOR THE TREATMENT OF LEUKEMIA IN OGBOMOSO, NIGERIA

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Leukemia is a cancer of the blood and bone marrow that is characterized by uncontrolled proliferation of immature blood cells that originate from mutated hematopoietic stem cells. Globally, leukemia accounts for about 200 and 22000 deaths annually. The side effects of chemotherapy in leukemia treatment have necessitated the search for natural products especially medicinal plants as alternative therapy. Therefore, this study investigated some medicinal plants that are popularly used for the treatment of leukemia in Ogbomoso for possible anti-leukemic and anti-clastogenic activities. Leukemia was induced with 400 mg/kg body weight of benzene intraperitoneally. 100 g of the pulverized plant leaves were extracted in four liters distilled water and the extract was fractionated using the solvent-solvent extraction method. The anti-leukemic potentials were evaluated by microscopic examination of peripheral blood and bone marrow smear for the presence of blast. Chromosomal damage was evaluated in the mice bone barrow smear using the micronucleus assay. The antioxidant activity was assayed by measuring the level of reduced glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) in the liver homogenate of mice. The hematological parameters were analyzed using standard method. Liver samples of treated mice were processed for histological analysis using heamoxylin and Eosin stains. The aqueous extract of the selected plants exhibited significant ($p<0.05$) anti-clastogenic activity while *N lotus* and *M lucida* showed significant ($p<0.05$) anti-leukemic potential. Aqueous extracts of *M lucida* and *X aethiopica* caused significant ($p<0.05$) increase in the number of RBC, hemoglobin concentration and packed cell volume. Treatment of mice with *N lotus* and P stratiotes caused improvement in liver cyto-architecture relative to the control. Treatment with the fractions of *N lotus* significantly ($p<0.05$) reduced the number of micro nucleated polychromatic erythrocyte in the bone marrow. Ethyl acetate fraction of *N lotus* treated group showed significant ($p<0.05$) anti-leukemic activity. Fractions of *N lotus* increased the number of red blood cell, hemoglobin concentration and packed cell volume. Administration of fractions of *N lotus* to mice caused significant ($p<0.05$) increase in CAT activity, SOD activity and GSH concentration. The histological indices showed improvement in general cyto-architecture in the mice treated with ethyl acetate and butanol fraction groups of N lotus. In conclusion, this study affirms the anti-leukemic and anti-clastogenic activities of some traditionally acclaimed anti-leukemic plants in Ogbomoso. Therefore, further studies should be done to isolate and characterize the active components of extracts and deduce the possible mode of action.

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EFFECTS OF ALUMINIUM OXIDE NANOPARTICLES ON SOME BLOOD PARAMETERS IN FEMALE WISTAR RATS

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Nanoparticles (<100 nm) containing metals are being used various fields of technology and released to the environment, causing contamination of food supplies. Thus, the present work was undertaken to investigate the effects aluminium oxide nanoparticles (Al2O3) sized 40 nm after its administration to female Wistar rats. Following 14 days oral administration of Al2O3 nanoparticle (0, 0.5, 5, 50 mg/kg b.w./day), the levels of 19 serum biomarkers (glucose, cholesterol, creatinine, urea, triglycerides, bilirubin, protein, ALP, ALT, AST, cortisol, T3, T4, estradiol, prolactin, IgG, IgM, total oxidant, total antioxidant) belonging to different metabolic systems and the activities of osmoregulation enzymes (Na, K-ATPase, Mg-ATPase, CaATPase) in the erythrocyte were measured. Except the lowest Al2O3 dose, Na, K-ATPase activity (up to 76%) decreased significantly ($P<0.05$) following Al2O3 administrations, while Al2O3 did not alter the activities of Mg-ATPase and Ca-ATPase in the erythrocytes. Al2O3 administration caused an increase (167%) in the levels of total oxidants in the serum, while total antioxidant levels were not altered by Al2O3. The levels of the liver enzymes, ALT and AST did not change significantly, while ALP levels increased (58%) following Al2O3 administration. The levels of the immune system parameters (IgM, IgG) did not change significantly. The levels of estradiol and T3 decreased (up to 83%) significantly, while the levels of prolactin, cortisol and T4 did not change significantly. An increase (240%) in bilirubin level and a decrease (73%) in triglyceride level were also noted in the serum of Al2O3 administrated rats. The present study demonstrated that oral administration of Al2O3 to female rats altered many parameters in the serum and ATPase activities in the erythrocyte and suggests carrying out further research to enlighten better the environmental fate of nanoparticles.

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RELATIONSHIP BETWEEN ON-SITE ORAL FLUID TESTING AND THC PLASMA CONCENTRATIONS IN MARIJUANA SMOKERS

Simon N and Alvarez J C
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The study aim was to define the pharmacokinetic of delta-9-tetrahydrocannabinol (THC) and 11- OH-THC following two inhaled doses of cannabis and to evaluate the relationship between THC plasma concentrations and on-site oral fluid screening device Drugwipe 5S® in chronic and occasional marijuana smokers, 30 healthy male volunteers: 15 regular (1-2 joints/day) and 15 occasional (1-2 joints/week) consumers aged 18-34 were included. Blood concentrations of THC were measured after controlled inhalation of 10 mg or 30 mg. Blood samples were collected 5, 15, 30 minutes, 1, 2, 4, 6, 8, 10, 12 and 24 hours after the end of the joint, and an oral fluid test was carried out at the same times up to six hours with a final test at 24 h before leaving the study. First, a population PK analysis was performed using a non-linear mixed effects modelling. Then, the relationship between a positive oral fluid testing and several covariates was evaluated using a logistic regression analysis. For THC, the best base model used three-compartments with zero-order input and first-order output. The group had a significant effect on relative bioavailability (F1). Chronic cannabis users had a 2.41 times greater value of F1 than the occasional users. Dose achieved to non-linearity with a decrease by 0.68 of F1 for 30 mg compared to 10 mg. For 11-OH-THC, the model was a two-compartments with first-order input. The logistic model describing the probability of a positive oral fluid testing included the THC plasma concentrations (estimate 246, IC95: 169-547) and the group (estimate -1.81, IC95: -3.09- -0.78) with an intercept of -1.20 (-2.36- -0.47). This study described a non-linear relative bioavailability of THC with higher doses leading to a lower exposure. Further, with a same THC concentration, users who smoke cannabis occasionally have a higher probability to be screened positive compared to daily users.

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EVALUATING THE NECESSITY OF A POISON CONTROL CENTER IN CAMEROON: THE KNOWLEDGE AND PERCEPTION OF HEALTH CARE PROFESSIONALS IN THE LAQUINTINIE HOSPITAL AND THE BONASSAMA DISTRICT HOSPITAL IN DOUALA

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Introduction: A cross sectional study was carrying out on the necessity of creating a poison control center in Cameroon, by evaluating the knowledge and perception of health care professionals in the Laquintinie hospital and the Bonassama District hospital in Douala, based on two years (2014 to 2015) record files reviewed of poison victims.

Material & Method: The materials used in this experiment are: A4 white sheets, respiratory mask, disposable gloves, a data analysing tool (Microsoft Excel 2010) and questionnaire. A questionnaire was used in data collection to access the knowledge of health care professionals on poisoning and poison control centre regarding proper poison management (group I). And to further evaluate group I, two years poison victims' files (records) were reviewed at the level of the emergency and paediatric units. The data obtained were analyzed using Microsoft Excel 2010 and the results were displaced on frequency tables, and in percentages and figures.

Results: The perception and knowledge of the 66 health care professionals accessed in the study; revealed that none of the participants had a formal training on poison management and none of the hospitals involved, had established poison management guidelines. 23,182 patients' files were reviewed; of which 245 files were recorded as poison victims: 62% (152) as voluntary, 38% (93) as involuntary, 4% (10) death case recorded inclusive; with a prevalence of 1% been observed for poisoning from the sorted hospitals.

Conclusion: The relative low knowledge of health care professionals on poisoning and the absence of poison management guidelines in hospitals still make poison management in Cameroon a complex issue. Cameroon is therefore highly in need for policies on poison management.