Metabolism

Chairpersons: DD Ramdath, M Coombs

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Leonotis nepetifolia leaf extracts as a hepatoprotective agent against the harmful effects of acetaminophen-induced toxicity in mice

A Williams, YN Clement, S Nayak, AVC Rao, E Uchee-Nwache
Units of Pharmacology, Biochemistry, Pathology and Microbiology and Anatomy, Faculty of Medical Sciences, The University of the West Indies, St Augustine, Trinidad and Tobago
E-mail: *williams.arlene@gmail.com*

Objective: To investigate the hepatic activity of *Leonotis nepetifolia* leaf extracts in an acetaminophen-induced toxic model.
Design and Methods: Oven dried leaves were extracted in methanol or 0.9% warmed saline solution. Swiss albino mice (n = 4–6) were pre-treated with methanol or aqueous extract at a dose of 250 to 1000 mg/kg orally for three days followed by a toxic dose of acetaminophen, 550 mg/kg orally. Post-treated animals were given one toxic non-lethal dose of acetaminophen, 550 mg/kg one hour before a dose of extract. Negative (-) control normal saline, and the positive (+) control, a toxic non-lethal acetaminophen dose, 550mg/kg, were used for evaluation. Animals were observed over 24 hours after final dose; serum enzymes, histology and antioxidant enzymes glutathione reductase (GR) and peroxidase (GPx) levels were assessed.
Results: Pre- and post-treatments of *L nepetifolia* at all doses showed a complete reversal of the effect on acetaminophen toxicity with serum levels of alanine transaminase (ALT) and aspartate aminotransferase (AST) closer to normal at a 95% confidence level ($p < 0.05$). Histopathology of the liver tissue showed that *L nepetifolia* attenuated the hepatocellular necrosis caused by the toxic dose of acetaminophen. Glutathione perioxidase increased with a reduction of GR levels for both extract-treated compared to the acetaminophen-treated animals.
Conclusion: Both the pre- and post- treatments of *Leonotis nepetifolia* extracts prevented acute liver damage induced by acetaminophen toxicity. We propose that hepatic protection of *L nepetifolia* leaf extract may be due to components of the plant exhibiting a direct effect to reduce toxicity of acetaminophen metabolism.

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Effect of high glucose on the expression of genes and proteins involved in insulin signalling in cardiomyocytes

S Singh, DD Ramdath
Department of Pre-Clinical Sciences, Faculty of Medical Sciences, The University of the West Indies, St Augustine, Trinidad and Tobago; Guelph Food Research Centre, Guelph, Canada
E-mail: *shamjeet.singh@sta.uwi.edu*

Objectives: To study the effect of hyperglycaemia on gene and protein expression along the insulin signalling pathway in cardiomyocytes and to ascertain whether these changes can be modulated by anthocyanin.
Design and Methods: Adult rat cardiomyocytes were isolated and incubated with 100, 200, or 400 mg/dL glucose. RNA was subsequently used to quantify gene expression along the insulin signalling pathway using real time polymerase chain reaction (PCR) and PCR arrays. In separate experiments, cardiomyocytes were incubated with 100, 300, or 300 mg/dL glucose plus 30 mM bilberry anthocyanins. Sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) and Western blotting was subsequently used to measure protein expression.
Results: Rat cardiomyocytes incubated with 200 mg/dL glucose significantly down-regulated 21 genes ($p < 0.05$), and up-regulated 11 ($p < 0.05$) when compared to controls (100 mg/dL); while 400 mg/dL changed the expression of 17 genes. In separate experiments, 300 mg/dL glucose significantly decreased protein kinase B (Akt) expression ($p < 0.05$) and increased the p*-Akt/Akt ratio ($p < 0.05$).
Conclusions: Changes in protein and gene expression in response to hyperglycaemia may contribute to physiological dysfunctions observed in heart failure.

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Cardiovascular structure and function in adult survivors of severe acute malnutrition

IA Tennant, AT Barnett, DS Thompson, J Kips, MS Boyne, EE Chung, AP Chung, C Osmond, MA Hanson, PD Gluckman, P Segers, JK Cruickshank, TE Forrester
The University of the West Indies, Kingston, Jamaica; Ghent University, Belgium; University of Southampton, UK; University of Auckland, New Zealand; St Thomas' Hospital, London, UK
E-mail: *ingrid@landscreek.net, kennedy.cruickshank@kcl.ac.uk*

Background: Severe acute malnutrition (SAM) presents in early childhood as either an oedematous or non-oedematous phenotype, with metabolic effects which may persist into adulthood. We hypothesised that cardiovascular structure and function would differ between survivors and persons never exposed to SAM (controls) and between phenotypes of SAM.
Design and Methods: We recruited adult survivors of SAM, 54 with previous non-oedematous, and 62 the oedematous phenotype, and 45 age/sex/body mass index (BMI)-matched community controls. Standardized anthropometry, blood pressure (BP), 2D-echocardiography, carotid and femoral artery ultrasound, brachial, radial and carotid tonometry were performed. Cardiac indices, left ventricular mass (LVM) index and outflow tract (LVOT) diameter, carotid and femoral intima-media thickness (IMT), carotid-femoral pulse wave velocity (PWV) and augmentation index were derived. Visceral fat mass (VFM) was assessed by CT scan. All variables were expressed as standard deviation (SD) scores.
Results: Mean age for all was 28.8 ± 7.8 years (55% men). Adjusting for age, sex, height and weight, SAM survivors combined had mean (SE) reductions for LVOT diameter of 0.67 (0.16, $p < 0.001$), cardiac output (CO) 0.53 (0.16, $p = 0.001$), stroke volume (SV) 0.44 (0.16, $p = 0.009$), femoral IMT 0.71 (0.19, $p < 0.001$) and PWV 0.32 (0.15, p=0.03) compared to controls. Visceral fat mass and BP did not differ between groups, nor did cardiovascular parameters between phenotypes.
Conclusions: Adult survivors of SAM had lower arterial stiffness, CO, SV and LVOT diameter compared to controls, probably due to effects on cardiac development. However, there was no apparent adverse impact on vascular structure and function, perhaps because the participants were young with a lean body habitus.

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Programming of lean body mass and resting metabolic rate in healthy Jamaican children

C Taylor-Bryan, A Badaloo, M Boyne, C Osmond, TE Forrester
Tropical Medicine Research Institute, The University of the West Indies, Kingston, Jamaica
E-mail: *carolyn.taylorbryan@uwimona.edu.jm*

Objective: To examine the effect of birth anthropometry on lean body mass (LBM) and resting energy expenditure (REE) in healthy children in a longitudinal cohort.
Design and Methods: One hundred and twenty-nine children from a longitudinal cohort with recorded birth anthropometry were recruited at an average age of 11 years and re-evaluated seven years later. After an overnight fast, weight, height and bioelectrical impedance were measured. Lean body mass was calculated and REE was measured by indirect calorimetry.
Results: Birth weight was positively associated with LBM at age 11 years ($p = 0.02$) but not at 18 years ($p = 0.09$). Length at birth was positively associated with LBM at both ages ($p = 0.025$ and 0.026, respectively). Birth weight was positively associated with REE at age 11 years and 18 years ($p = 0.039$ and 0.036, respectively). Birth length was positively associated with REE at 18 years ($p = 0.009$) but not at 11 years ($p = 0.120$).
Conclusions: Weight and length at birth are associated with LBM and REE in childhood and these effects persists into adulthood.

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Effects of methionine supplementation on cysteine and glutathione production in malnourished children

AV Badaloo, CO Green, JW Hsu, C Taylor-Bryan, M Reid, TE Forrester, F Jahoor
Tropical Metabolism Research Unit, The University of the West Indies, Kingston, Jamaica; Children's Nutrition Research Center, Baylor College of Medicine, Houston, Texas, USA
E-mail: *asha.badaloo@uwimona.edu.jm*

Objective: To determine if methionine supplementation would augment cysteine production and consequently glutathione (GSH) synthesis in children with oedematous severe acute malnutrition (SAM).
Design and Methods: Total cysteine flux and rates of cysteine and GSH synthesis were measured using stable isotope tracer methodology in eight males and eight females in the fed state at 2.7 ±0.5 days (stage 1), 7.7 ±0.8days (stage 2); and at 14.4 ±1.4 days (stage 3) after admission. The subjects randomly received equimolar

supplement (0.6 mmol/kg/d) of methionine (n = 8) or alanine as control (n = 8) immediately after stage 1study. Cysteine release from body protein was calculated as total flux minus the sum of cysteine intake and its *de novo* synthesis.

Results: Cysteine flux derived from protein was significantly faster at stage 2 compared to stage 1 in the methionine group but not in the alanine group ($p < 0.05$). Also, change in plasma cysteine concentration from stage 1 to 2 was significantly greater in the methionine group compared to the alanine group ($p < 0.05$). However, total cysteine flux and its *de novo* synthesis were not different between the groups. There was no group difference in GSH rate of synthesis and concentration.

Conclusions: Despite the effects of enhancing release of cysteine from body protein and plasma cysteine concentration, the methionine supplement had no significant effect on total cysteine flux or on synthesis rates of cysteine and GSH. Increased dietary intake may be necessary to meet the total demand for cysteine in oedematous SAM.