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ANTI-HYPERGLYCEMIC ACTIONS OF *NIGELLA SATIVA* MEDIATED BY INHIBITION OF CARBOHYDRATE DIGESTION AND ABSORPTION IN THE GUT

Afra Haque, Abir Huzaifa, Afrina Sanju, Nur-A-Safa, Kazi Ishtiaq Ahmad, Mahbub Hasan, Kamol Krishna Nandy and **JMA Hannan**
Independent University, Bangladesh

Previously *Nigella sativa* seeds have been documented as a traditional herbal treatment for diabetes. Anti-hyperglycemic activity of its seed extract, in the postprandial state, indicates that the extract may interfere with the glucose absorption in the gut. The present study aims to explore the mechanism of its anti-hyperglycemic activity related to the inhibition of carbohydrate digestion and absorption in the gut. The dried powdered seeds of *N sativa* were extracted with methanol. Rats were fasted for 20 h prior to the experiment. Sucrose (2.5g/Kg/5ml), average 443mg) with or without extract (0.5 g/kg) was administered orally. Following administration rats were sacrificed after 30 min,60 min, 120 min respectively. Sucrose malabsorption was evaluated in the rats by measuring the amount of sucrose remaining in six different parts of gastrointestinal tract. With ice- cold saline (10 ml) each segment was washed out, for acidifying H_2SO_4 (2 ml) was added and centrifuged at 3000 rpm for 10 min. To hydrolyze the sucrose the supernatant thus obtained was boiled for 2 hours and then neutralized with NaOH (approximately 2.5 ml). Glucose Oxidase (GOD-PAP) method was used to measure the amount of glucose liberated from residual sucrose in the gastrointestinal tract. From the amount of liberated glucose the sucrose content in the gastrointestinal tract was calculated. When extract of *N sativa* was administered simultaneously with the sucrose load, the residual sucrose content in the GI Tract was increased significantly ($p<0.01$) and ($p<0.05$ respectively) in the stomach at 30min and 1h, especially in the upper intestine at 1h, in the middle intestine at 1h, in the lower intestine at 30min and 2h ($p<0.01$), in small intestine, large intestine and cecum at 30min and 1hr. The anti-hyperglycemic activities of *N sativa* in *Long Evans rat* are related to retardation of intestinal carbohydrate digestion and absorption in the gut.

BIOGRAPHY

Afra Haque completed her bachelor of pharmacy from East West University (EWU), Dhaka, Bangladesh. During her bachelors program she has done her thesis project on Pharmacology on the topic "Anti-hyperglycemic activity of *Nigella sativa* plant seed on *Long Evans rat*" under the supervision of JMA Hannan. She has been awarded dean's list scholarship and full free scholarship during her bachelors program.

jma_hannan2002@yahoo.com

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MOMORDICA CHARANTIA INHIBITS CARBOHYDRATE DIGESTION AND ABSORPTION IN THE GI TRACT

Mahbub Hasan, Kazi Ishtiaq Ahmad, Limu Parvin, Kamol Krishna Nandy and **JMA Hannan**
Independent University, Bangladesh

Momordica charantia fruits has been widely used as a traditional drug throughout Asia. The goal of the present study is to explore the mechanism of its anti-hyperglycemic activity related to the inhibition of carbohydrate digestion and absorption in the gut. The dried-powder-fruits of *M charantia* were extracted with methanol. Sucrose malabsorption was assessed in 20 h-fasted rats by determining the portion of sucrose remaining in six different parts of gastrointestinal tract after sucrose administration (2.5 g/kg b.w). Inhibition of glucose absorption in the gut was evaluated by utilizing the in situ perfusion of small intestine. For investigation of disaccharides activity, the extract was orally administered orally to 20 h-fasted rats. The small intestines of the sacrificed rats were isolated and homogenized after 60 min. At 37 °C, 40 mmol sucrose mixed homogenate (l) was incubated for 60 min. Disaccharides activity was determined by glucose generated as a result of sucrose digestion as mol-mg glucose/protein/h. After administration of *M charantia* extract with the sucrose load was shown that the residual sucrose quantity was increased significantly ($p<0.01$) in the gastrointestinal tract, particularly in the upper intestine after 30 min, in the whole intestine and cecum after 60 min and 120 min. At 240 min sucrose was not traceable in the gut. During 30 min of perfusion the intestinal glucose absorption with glucose was almost constant. When *M charantia* extract was administrated with the glucose solution, the glucose absorption percentage was decreased during whole perfusion period ($p<0.05$). Disaccharidase (sucrose) activity was significantly ($p<0.01$) decreased in extract treated rats. In conclusion, the anti-hyperglycemic action of *M charantia* fruit-fed-red are mediated partly via: delayed intestinal carbohydrate digestion and absorption.

BIOGRAPHY

Mahbub Hasan has recently completed masters of pharmacy, on clinical pharmacy and molecular pharmacology from East West University and also completed bachelor of pharmacy from Stamford University, Bangladesh. His research work was done on active supervision of JMA Hannan. He has published review scientific articles in reputed journals on "Nanotechnology drug delivery system: Tools in advances pharmaceutical & healthcare and contemporary investigation on nasal spray drug delivery system". Also has an international Conference Paper on "Gastro retentive: A novel drug delivery system" on 4-5 February 2017 Dhaka, Bangladesh.

mahbubhasan.cr7@gmail.com

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HOW SWEET IT IS—AN INTIMATE HISTORY OF DIABETES AND INSULIN

Abraham solomon
Florida Gulf Coast University, USA

Understanding and appreciating the history in medicine is important, if we are to fully value where we are and where we are likely to go. The History of diabetes and its scourge on humanity dates back centuries. The diagnosis of diabetes has been relatively easy, and was essentially a death sentence for those affected by this disease. The understanding of the metabolism and physiology of diabetes has proved impossible until the 1920's. When an obscure Canadian Surgeon, Banting had a spark of an idea at 2 am one cold night in London Ontario, that led to a series of experiments that permitted the discovery of insulin. This discovery and the subsequent purification of insulin has not provided an absolute cure But has offered a solution to a chronic disease that affects many organs and has changed countless lives for the better. The eventual manufacture of Insulin on a grand scale was also significant. Like all good history it is based on the intimate struggles, passions, and drive of those individuals whose fruits we can see in the present, and possibly beyond. Banting and his associates went on to win the Nobel Prize shortly after their discovery and purification of insulin. Today the disease is still potentially deadly, but we have the means to save the lives of our diabetic patients.

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STATUS PASSAGES IN YOUNG ADULTHOOD AS A RISK FACTOR FOR THE NUTRITION BEHAVIOR

Alexandra Sept
Technical University of Munich, Germany

Status passages are planned or unplanned transitions like from work life to retirement or from living as a couple to living as a family. Especially young people experience many status passages like the transition from school to university or from living at parent's home to moving out and living in a own flat. This transitions cause changes in lifestyle and behavior. Additional to changes because of status passages, adolescents are faced with many challenges like finding their identity, building up a system of moral and develop an own future perspective. Transitions in young adulthood, like the replacement of the parents by moving out of the parental home or the change from school to university are associated with many changes and also changes in the personal nutrition. Because young adults have many new freedoms and opportunities to try out and the focus is not always on the nutrition, the main criteria the nutrition has to comply with are fast, easy to get, delicious and cheap. The consumption of fast food, convenience food and snacks, for example, is particularly attractive for adolescents, as it is a distinction from the adult culture of eating, which is characterized by rules such as eating on a table, using cutlery and having fixed mealtimes. The young adults have to achieve autonomy, develop themselves personally and form a nutrition behavior that fits in their way of life. In this work the focus is on the practice of nutritional behavior in adolescence and young adulthood. Within the framework of the interdisciplinary research cluster enable, that develops strategies for a healthier nutrition in different stages of life, two focus groups with young women and men between and guided narrative interviews describe the personally perceived changes in nutrition behavior and provide information on the criteria that determine these changes.

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ON OBSERVATION OF POSITION IN QUANTUM THEORY

Alexey A Kryukov
University of Wisconsin-Milwaukee, USA

Newtonian and Schrodinger dynamics can be formulated in a physically meaningful way within the same Hilbert space framework. This fa was recently used to discover an unexpected relation between classical and quantum motions that goes beyond the results provided by t Ehrenfest theorem. A formula relating the normal probability distribution and the born rule was also found. Here the dynamical mechanism responsible for the latter formula is proposed and applied to measurements of macroscopic and microscopic systems. A relationship between the classical Brownian motion and the diffusion of state on the space of states is discovered. The role of measuring devices quantum theory is investigated in the new framework. It is shown that the so-called collapse of the wave function is not measure me specific and does not require a "concentration" near the Eigen states of the measured observable. Instead, it is explained by the comm diffusion of state over the space of states under interaction with the apparatus and the environment. This in turn provides us with a bas reason for the definite position of macroscopic bodies in space.

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DIABETES AND COGNITIVE BRAIN FUNCTION: IS DIABETES AN ACCELERATED FORM OF AGEING?

Amer Kamal Al Ansari
Arabian Gulf University, Bahrain

The aim of the present study was to examine learning and hippocampal synaptic plasticity in ageing and diabetes. Many of the processes which have been implicated in the pathogenesis of brain ageing are also involved in the development of diabetic complications. We investigated Morris water maze performance and examined hippocampal synaptic plasticity ex vivo in young adult and aged diabetic and non-diabetic rats. Rats were examined after 2 months of diabetes, which produces half-maximum deficits in synaptic plasticity in young adult rats. Aged rats were examined at 2 years of age, when they have developed moderate changes in synaptic plasticity due to aging alone. Significant learning impairments were observed in young adult diabetic rats compared with controls. These impairments were even greater in aged diabetic animals. In hippocampal slices from young adult diabetic animals, long-term potentiation was impaired compared with controls. In contrast, induced long-term depression was enhanced in slices from diabetic rats compared with controls. It is concluded that both diabetes and ageing affect learning and hippocampal synaptic plasticity. The cumulative deficits in learning and synaptic plasticity in aged diabetic rats indicate that the effects of diabetes and ageing on the brain could interact. Relative fEPSP slopes after different conditioning stimuli in hippocampal slices from young adult (Left) and aged animals (right). Diabetic animals in both groups show enhanced LTD and depressed LTP expressions when compared to the controls. Young diabetic animals had comparable defects to the aged control group indicating that DM acts like an accelerated ageing process.

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DOES THE HAES APPROACH CHANGE WHAT WE KNOW ABOUT THE TREATMENT OF OBESITY?

Amy Helms
New Hope Counselling and Wellness Center, USA

If our current attempts at weight management and the treatment of obesity demonstrate less than stellar long-term results, should we rethink the way we approach treatment? There is no debate that the rising obesity rates are problematic on both individual and public health levels; however, the solution to this problem leaves much room for debate. The impact of obesity at the public health level has caused the greatest concern. Obesity rates have been a target for public health as chronic health conditions have increased at the same time. Despite the public scrutiny over our growing obesity rates, treatment has remained one dimensional- through the medical model. Media reports show individual responsibility for obesity as high as seventy-two to ninety eight percent, while the scientific literature report is being closer to forty percent. While having the goal to treat obese individuals, health professionals have demonstrated fat-bias toward patients and endorsed significant stereotypes for obese individuals. Weight bias does not appear to differ in professionals who focus their careers on the management of obesity, further demonstrating the stigma obese individuals face on a daily basis. Once the extent of this stigma is fully understood, better interventions can be developed. Traditional approach to obesity management has shown little long-term effectiveness with participants regaining on average 30% to 40% of their lost weight within 1 year, and longer-term follow-up (2–5 years) showing a gradual return to baseline weight levels or above. Such interventions have focused on pharmacological, surgical, and behavioral strategies. Possibly a worse effect is individual stigma left after one does not see promised results. The shift from weight-focused model to the HAES challenges all key assumptions about weight management and the obesity-associated diseases. Rather, HAES

1. encourages body acceptance,
2. Supports intuitive eating, and
3. supports active embodiment.

Further, this model suggests that any strategy should promote a healthy lifestyle that is sustainable. This may or may not include body weight. The HAES approach explores the individual's feelings, life experiences, and their own embodiment to discover the root of the problem. While a new approach, literature does support its effectiveness compared to other treatment, which provides a false hope to individuals due to the high rates of regain. HAES focuses on intuitive eating, body acceptance, and moving for activity- not caloric reduction. The HAES approach has been effective for women with metabolic syndrome, premenopausal women, and clinically obese women. The most promising results are reducing psychological distress and increasing cardiorespiratory fitness. When compared with traditional treatment, HAES has shown to be sustainable long-term while improving self-esteem and long-term follow-up. In addition to the long-term maintenance, HAES provides psychological benefits to women experiencing disordered eating or chronic dieting behaviors, something often missed under the traditional paradigm.

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LOW VITAMIN B12 INDUCES *DE NOVO* LIPOGENESIS IN HUMAN HEPATOCYTES

J Boachie[1], A Adaikalakoteswari[1], J Samavat[1], V Zammit[1], Z Irshad[1] and **P Saravanan[1]**
1Division of Metabolic and Vascular Health, Clinical Sciences Research Laboratories, Warwick Medical School, University of Warwick, University Hospital-Walsgrave Campus, United Kingdom

Background: There is increasing evidence that lipid metabolism in humans may be regulated by environmental factors including nutrients such as vitamin B12 (B12). B12 deficiency results in disturbance of 1-carbon metabolites [methylmalonyl coenzyme A (MMA), homocysteine and S-adenosyl homocysteine (SAH), S-adenosyl methionine (SAM) and methionine] that collectively favours lipogenesis leading to risk of cardiovascular diseases. In clinical studies, B12 deficiency is associated with higher BMI and dyslipidaemia (high triglycerides and low HDL). *In vitro* experiments in human adipocytes showed that low B12 results in hypomethylation of SREBF1, a master regulator of cholesterol biosynthesis. If similar effects happen in hepatocytes, this may explain the observation of dyslipidaemia in humans. In addition, the role of B12 in hepatic metabolism of lipids in humans is unexplored. Therefore, we investigated whether B12 deficiency affect hepatic *de novo* lipogenesis.

Methods: Human HepG2 cell line was cultured using custom made B12 deficient Eagle's Minimal Essential Medium (EMEM) and seeded in four different concentrations of B12 media such as 500nM (control), 1000pM, 100pM and 25pM (low) B12. Oil Red O (ORO) staining, gene expression assay using RT-qPCR, total intracellular triglyceride (TG) assay with commercial kit and *de novo* TG biosynthesis using radioactive flux assay were employed to examine the effect of B12 on lipogenesis.

Results: HepG2 cells in low B12 (25pM) had more lipid droplets that were intensely stained with ORO compared with less stained few oil droplets in control B12 (500nM) condition. Total intracellular TG levels were higher in low B12 hepatocytes. The gene expressions of nuclear transcription factors sterol regulatory element binding protein (SREBF1) and low density lipoprotein receptor (LDLR) were higher in low B12 conditions compared with control. Similarly, the gene expressions of the enzymes involved in *de novo* fatty acid synthesis [ATP citrate lyase (ACLY), Acetyl CoA carboxylase (ACC), fatty acid synthase (FASN) and elongation-of very-long-chain fatty acid (ELOVL6)], cholesterol biosynthesis [3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR), 3-hydroxy-3-methylglutaryl-CoA synthase 1 (HMCS1), Isopentenyl-Diphosphate delta Isomerase 1 (IDL1)] and TG biosynthesis [stearoyl CoA desaturase (SCD), glycerol-3-phosphate acyltransferase (GPAT), acylglycerol-3-phosphate acyltransferase (AGPAT), phosphatidic acid phosphatase-1 (Lipin1) and diacylglycerol acyl transferase 2 (DGAT2)] in low B12 conditions. Lastly, cellular uptake of radio-labelled fatty acid (14C-oleate) for *de novo* TG biosynthesis assessed by scintillation was about 80% higher in HepG2 cells cultured in low B12 condition.

Conclusion: Our data provide novel evidence that B12 deficiency dysregulates lipid metabolism in hepatocytes. Further studies are required to quantify the effect of this on circulating levels of lipid fractions as well as its epigenetic role on hepatocyte function.

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PRE-NATAL EPIGENETIC INFLUENCES ON ACUTE AND CHRONIC DISEASES LATER IN LIFE, SUCH AS CANCER: GLOBAL HEALTH CRISES RESULTING FROM A COLLISION OF BIOLOGICAL AND CULTURAL EVOLUTION

James E Trosko
Michigan State University, USA

Better understanding of the complex factors leading to human diseases will be necessary for both long term prevention and for managing short and long-term health problems. The underlying causes, leading to a global health crisis in both acute and chronic diseases, include finite global health care resources for sustained healthy human survival, the population explosion, increased environmental pollution, decreased clean air, water, food distribution, diminishing opportunities for human self-esteem, increased median life span, and the interconnection of infectious and chronic diseases. The transition of our pre-human nutritional requirements for survival to our current cultur-ally-shaped diet has created a biologically-mismatched human dietary experience. While individual genetic, gender, and developmental stage factors contribute to human diseases, various environmental and culturally-determined factors are now contributing to both acute and chronic diseases. The transition from the hunter-gatherer to an agri-cultural-dependent human being has brought about a global crisis in human health. Initially, early humans ate sea-sonally-dependent and calorically-restricted foods, during the day, in a "feast or famine" manner. Today, modern humans eat diets of caloric abundance, at all times of the day, with foods of all seasons and from all parts of the world, that have been processed and which have been contaminated by all kinds of factors. No longer can one view, as distinct, infectious agent-related human acute diseases from chronic diseases. Moreover, while dietary and environmental chemicals could, in principle, cause disease pathogenesis by mutagenic and cytotoxic mecha-nisms, the primary cause is via "epigenetic", or altered gene expression, modifications in the three types of cells (e.g., adult stem; progenitor and terminally-differentiated cells of each organ) during all stages of human development. Even more significantly, alteration in the quantity of adult stem cells during early development by epigenetic chemicals could either increase or decrease the risk to various stem cell-based diseases, such as cancer, later in life. A new concept, the Barker hypothesis, has emerged that indicates pre-natal maternal dietary exposures can now affect diseases later in life. Examples from the studies of the atomic bomb survivors should illustrate this insight.

Key words: barker hypothesis, adult stem cells, epigenetic, metabolic diseases, cell communication

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SERUM INSULIN RESPONSE AFTER ACUTE AND CHRONIC SUCRALOSE INGESTION IN HEALTHY PATIENTS WITH VARIABLE BODY MASS INDEX

Nallely Bueno-Hernández and **Galileo Escobedo**
General Hospital of Mexico, Mexico

In recent years, the consumption of non-caloric sweeteners (NCS) has considerably increased but several publications suggest that their use is associated with insulin resistance. Therefore the aim of this study was to determine the effect of chronic exposure to sucralose on the insulin metabolism and glucose in young, healthy adults with different body mass index stage.

Material and methods: A randomized, double-blind, placebo-controlled clinical trial was conducted in healthy volunteers with the homeostatic model assessment (HOMA index) less than 3.8, from 18 to 35 years aged and without metabolic alterations. Each patient was assigned to one of the 3 different intervention groups: 1) 48 mg/60 ml of sucralose, 2) 96 mg/60 ml of sucralose and 3) 60 ml of water, which should be a daily intake for 10 weeks. An oral glucose tolerance test was made to each patient (OGTT). The areas under the curve (AUC) of the OGTT were calculated and the data were analyzed with the statistical package SPSSv.17 with the Wilcoxon test considering a significant P value <0.05.

Results: We recruited 96 volunteers. The insulin AUC was significantly increased in the second OGTT on the 48 mg sucralose intervention group (AUC=9262 to 11398, P=0.02) and 96 mg of sucralose (AUC=6962 to 8393, p=0.03), but not the water group (AUC=9054 to 9396; P=NS). The basic metabolic characteristics such as urea, creatinine and monocytes were similar in the three groups. However, the final analysis in the group with the highest concentration of sucralose (96 mg/dL) showed significant changes at the serum concentrations of urea (22.3 mg/dL to 25.4 mg/dL), creatinine (0.78 mg/dL at 0.84 mg/dL) and monocytes (0.42 mg/dL to 0.36).

Conclusions: The chronic consumption of sucralose had a significant effect on the insulin and glucose metabolism in healthy young adults with different BMI.

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HIGH POWER/ENERGY OPTICS

Apollonov Victor Victorovich
Prokhorov GPI of Russian Academy of Sciences, Russia

The advent of the high power/energy laser has placed stringent requirements on the fabrication, performance and quality of optical elements employed within systems for most practical and special applications. Their high power/energy performance is generally governed by three distinct steps, firstly the absorption of incident optical radiation (governed primarily by various absorption mechanisms); secondly, followed by a temperature increase and response governed primarily by thermal properties and finally the element's thermo-optical and thermomechanical response, e.g., distortion, stress, birefringenous fracture, etc. All of which needs to be understood in the design of efficient, compact, reliable and versatile high-power/energy systems, under a variety of operating conditions such as pulsed, continuous wave, highly rep-rated or burst mode of varying duty cycles.

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FIBROBLAST GROWTH FACTOR 21 IN PREDICTION OF CORONARY ANGIOGRAPHY RESULT IN STABLE CORONARY ARTERY DISEASE PATIENTS

Matej Stančík
Comenius University, Slovakia

Background: FGF21 is adipokine affecting both glucose and lipid metabolism. Anti-apoptotic effect of FGF21 on the endothelium was previously proved.

Methods and Results: Transversal design performed on 203 subjects divided into subgroups based on the presence of hemodynamically significant coronary artery stenosis and stable coronary artery disease. Mean FGF21 concentration in stable coronary artery disease patients (323,16 ± 434,66 pg/ml) was significantly higher (t (201) = 2,082; p = 0,039; n = 203), than in healthy controls (266,46 ± 417,13 pg/ml). Multiple regression analysis proved, that the FGF21 measurement can´t be utilized as a surogate marker for the stable coronary artery disease. Contribution of the FGF21 measurement to the prediction of significant coronary stenosis was quantified using the hierarchical regression. Interaction analysis was used to detect between – variable interactions. The contribution of FGF21 added into the model based on known risk factors of significant coronary stenosis was small, yet statistically significant (2(4) = 25,606; p 0,001; n = 123; Nagelkerke R2 = 0,041; OR FGF21 = 2,366). Smoking was identified as the moderator of the direct effect between FGF21 and hemodynamically significant coronary artery stenosis. Adjusting for the moderator variable allowed us to build a regression model, in which the contribution of the FGF21 to the prediction of significant coronary stenosis was clinically relevant (2(3) = 30,778; n = 81; p 0,001; Nagelkerke R2 = 0,425; OR FGF21 = 7,013).

Conclusions: FGF21 can´t be utilized as a screening marker for the stable coronary artery disease in general population. FGF21 measurement has a potential to be utilized as a predictor of diagnostic coronary angiography result in non – smoking stable coronary artery disease patients. This work was supported by the SRDA (Slovak Research and Development Agency) grant: APVV – 14 – 0153, ARACS - Adipokine Regulation and Acute Coronary Syndrome in young adults.“ This work was supported by the VEGA (The Scientific Grant Agency of the Ministry of Education of the Slovak Republic) grant: VEGA 1/0160/16 „Diagnostic - prognostic relevance of adipocytokine network and glucose homeostasis assessment in cachexia.