Laboratory Studies

Chair: W McLaughlin and M Gossell-Williams

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Olanzapine-induced attenuation of the contracted isolated rat detrusor muscle strip

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Background: Antipsychotics have been documented to reduce bladder function in patients and antagonism of serotonin 5-HT_{2C} receptor has been implicated as the cause.
Objectives: The aim of this study was to determine the effect of olanzapine on the contracted isolated rat detrusor muscle strip.
Method: Detrusor muscle isolated from six male Sprague-Dawley rats (250–350 g) were divided into longitudinal strips and suspended in organ baths containing 10 mL of Krebs solution (mM: NaCl 119, KCl 4.7, $CaCl_2$ 1.25, $MgSO_4{\cdot}2H_2O$ 1.01, KH_2PO_4 1.2, $NaHCO_3$ 25 and glucose 11.1) with carbogen (95% O_2:5% CO_2) at 37 °C through double ringed electrodes connected to isometric force transducers attached to a Polyview data acquisition system. After equilibration at 0.5 g tension, the strips underwent electric field stimulation (EFS; 60 V, 0.5 ms duration, 10 s delay, 5 Hz frequency) while adding the selective 5-HT_{2C} receptor agonist, WAY-161503 (0.001 μM to 10 μM) cumulatively at half log concentrations. A concentration response curve was obtained using WAY-161503 in the absence and presence of olanzapine (0.003 nM to 3 nM) during EFS. Statistical analysis involved repeated measures of analysis of variance (ANOVA). Significant difference in treatments was assumed with $p \leq 0.05$.
Results: Electric field stimulation-induced contractions in the detrusor muscle was potentiated by WAY-161503 (range 0.10 ± 0.06 g to 0.25 ± 0.06 g; $p < 0.001$, F = 9.62) at the highest concentration of 10 μM. The potentiated contractions were reduced in the presence of olanzapine in a concentration dependent manner (range, -40.90 ± 25.71% to -81.07 ± 46.42%; $p \leq 0.001$, F = 8.031).
Conclusion: The results of the study suggest that olanzapine has the potential to reduce bladder contractility.

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Inositol hexakisphosphate (IP6) and inositol combination lowers fluid and food intake in Type 2 diabetes mellitus Sprague-Dawley rats

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Objective: Diabetes mellitus is a group of metabolic disorders characterized by hyperglycaemia. These metabolic disorders include alterations in carbohydrate, fat and protein metabolisms associated with absolute or relative deficiencies in insulin secretion and/or insulin action. There is currently no cure for the disease. This study was aimed at evaluating the effect of inositol hexakisphosphate (IP6) and an inositol nutraceutical product on blood glucose concentration, insulin resistance as well as fluid and food consumption in rats with Type 2 diabetes mellitus (T2DM).
Methods: Three groups of Sprague-Dawley rats were fed a high-fat diet followed by the administration of a low dose of streptozotocin to induce T2DM. The groups were assigned as follows: IP6 and inositol combination (IP6+INO), glibenclamide (Glib) and diabetic control (DC). Two groups of non-diabetic rats were fed normal diet and high-fat diet during the initial four weeks of the experiment. However, for the final four weeks, all rats were fed normal diet and given their respective treatment regimes. Non-fasting blood glucose, homeostatic model assessment (HOMA)-insulin resistance, food and fluid intake were assessed.
Results: Both glibenclamide and the combined IP6 and inositol supplement significantly reduced blood glucose concentration and insulin resistance. However, the IP6 and inositol combination was more effective in lowering fluid and food consumption in T2DM rats compared with glibenclamide treated rats ($p < 0.05$).

Conclusion: Treatment of T2DM rats with an IP6 and inositol combination improved glucose metabolism and ameliorated insulin resistance, polyphagia and polydipsia which are common symptoms of diabetes. Therefore, IP6 and inositol combination may be beneficial in the management of T2DM and the associated metabolic disorders.

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Effect of ATP-sensitive potassium channel inhibition on the vasorelaxant response to ketamine in diabetes mellitus

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Background: Diabetes mellitus (DM) is an independent and major risk factor for the development of endothelial dysfunction and impairment of potassium ion channel, thereby affecting vascular tone. This increases the risk of morbidity and mortality during surgery. The present study examined the responsiveness of blood vessels from diabetic rats to the anaesthetic agent ketamine in the presence of glibenclamide, a K_{ATP} potassium channel blocker.
Method: Diabetes mellitus was induced in Sprague-Dawley rats by intraperitoneal injection of streptozotocin (STZ) at 50 mg/kg body weight. After two weeks of DM, vascular response of the aortic rings from STZ-induced and age-matched Sprague-Dawley control rats to phenylephrine, acetylcholone, glibenclamide and ketamine was studied using standard organ bath procedures.
Results: The phenylephrine-induced contraction was significantly enhanced ($f = 30.157^b$, $p < 0.001$) and relaxation to acetylcholine was significantly reduced ($f = 23.887^b$, $p < 0.05$) in diabetic rats *versus* control. Ketamine-induced relaxation was significantly ($f = 32$, $p < 0.05$) enhanced in the presence of glibenclamide in diabetic aortic rings compared to control. Activation of potassium channel with nicorandil did not alter the relaxation response of diabetic rings to ketamine when compared to control groups.
Conclusion: The phenylephrine-induced contraction and endothelium-dependent relaxations are altered in the early stages of DM. Ketamine-induced relaxation is decreased in diabetic rats in the presence of glibenclamide. The results suggest that the relaxation response to ketamine is attenuated in DM, and K_{ATP} potassium channels are involved.

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Investigation of the anxiolytic and hypnotic potential of the leaves of the *Annona muricata* (soursop) in mice

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Objective: To investigate the anxiolytic and hypnotic potential of extracts of the leaves of the *Annona muricata* (soursop) in mice.
Methods: Anxiolytic activity of ethanolic and aqueous extracts of the *Annona muricata* was investigated using the hole-board test while hypnotic activity was investigated using the sleep-time test. The Hippocratic screen was used to investigate motor activity. Groups of six mice each were orally administered aqueous (2 and 6 g/kg) and ethanolic extracts (25 mg/kg) of the leaves of the plant, saline or diazepam (1.5 mg/kg). For the hole-board test, the effect of treatment on the propensity of mice to dip their heads through holes in the bottom of a chamber was noted over 10 minutes. Hypnotic activity was investigated by observing the effects of the respective treatments on the onset and duration of sleep induced by sodium pentobarbitone (30 mg/kg ip). In the Hippocratic screen, mice were observed for impairment in motor activity including ataxia, and loss of righting reflex within two hours of administration of the plant extracts.
Results: Extracts of the *Annona muricata* increased the duration and decreased the latency of head dips in the hole-board test and also reduced the overall motor activity ($p < 0.05$) of mice in the Hippocratic screen. Aqueous and ethanolic extracts (6 g/kg and 25 mg/kg, respectively) significantly increased the duration of barbiturate-induced sleep. These effects were similar to those of diazepam.
Conclusion: The study suggests anxiolytic and hypnotic activity of the leaves of the *Annona muricata*.

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The biochemical effects of biomagnetic therapy on Type II diabetic rats

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This study was done to determine the effects of biomagnetic therapy on non-fasting blood glucose levels in Type 2 diabetic (T2D) rats. For a gender unbiased research, both male and female streptozotocin-induced T2D Sprague-Dawley rats (16 each) weighing 195.5 ± 27.7 g were assessed, with and without biomagnetic therapy using 5000

gauss magnetic necklaces. Non-fasting blood glucose levels were measured in the blood collected from the tails, once weekly for sixteen weeks using a portable glucometer (Glucolab Blood Glucose Monitoring System). Results showed that there was a significant and consistent reduction of postprandial blood glucose levels over the experimental period for diabetic groups that were under the influence of biomagnetic therapy, with average blood glucose levels for the final month being 6.97 ± 3.27 mmol/L as compared to the non-treated diabetic rats (control) which averaged blood glucose levels of 31.13 ± 6.88 mmol/L. Results were compared to known goal blood glucose levels for diabetics. Biomagnetic therapy can facilitate the maintenance and management of Type 2 diabetes by lowering non-fasting blood glucose levels, because groups exposed to the biomagnetic therapy showed blood glucose levels trending to that of normo-glycaemic levels of 4.0–7.7 mmol/L.