

Effects of tualang honey on food intake and brain and body weight in adult male rats exposed to normobaric hypoxia

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Abstract

Hypoxia decreases food intake and body weight and increases brain weight. The effect of tualang honey on these parameters after hypoxia exposure is not clear. This study aimed to evaluate the effects of tualang honey on food intake and brain and body weight in adult male Sprague-Dawley rats exposed to hypoxia. The rats were divided into four groups (n = 12 per group): i) Non-hypoxic treated with sucrose, ii) Non-hypoxic treated with tualang honey, iii) Hypoxic treated with sucrose, and iv) Hypoxic treated with tualang honey. The rats were treated with either 1 mL of 7.9% sucrose or 0.2 g/kg tualang honey orally for 2 weeks. Then, the rats were subjected to ~11% continuous hypoxia for 7 days. Body weight and food consumption of the rats were recorded at the end of each week throughout the experimental period. The rats were anaesthetised with thiopental sodium and brain samples were collected and weighed using digital analytical balance. The hypoxic rats treated with sucrose and honey showed more significant decrease in food intake and body weight ($p < 0.05$) compared to non-hypoxic sucrose treated groups. In addition, there was significant increase in brain weight ($p < 0.05$) in hypoxia treated sucrose group compared to non-hypoxia treated sucrose group. Interestingly, there was significant decrease in brain weight ($p < 0.05$) in hypoxia treated honey group compared to hypoxia treated sucrose group. tualang honey has a therapeutic potential to regulate food intake and body weight and decrease in increased brain weight-induced hypoxia is possibly through its antioxidant properties.

The effect of tualang honey pre-treatment on hypoxia-induced cortical damage in adult male rats

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Abstract

Hypoxia induces neuronal damage and the effect of tualang honey to ameliorate hypoxia-induced neuronal damage has never been studied. This study aimed to evaluate the effects of tualang honey on the medial prefrontal cortex (mPFC) morphology and cholinergic system in rats exposed to normobaric hypoxia. Forty-eight male Sprague-Dawley rats were divided into four groups: (i) Sucrose-treated non-hypoxia, (ii) Sucrose-treated hypoxia, (iii) Tualang honey-treated non-hypoxia and (iv) Tualang honey-treated hypoxia. Oral sucrose (1 mL of 7.9%) and tualang honey (0.2 g/kg) were administered for 2 weeks prior to hypoxia. After 7 continuous days of exposure to hypoxia (~11%), the rats were sacrificed and the right and left hemispheres were separated. Histologic evaluation for right mPFC and ELISA estimation for acetylcholine (ACh) and acetylcholinesterase (AChE) for left hemispheres were conducted. Sucrose-treated hypoxic rats showed significant reduction in ACh and elevation in AChE concentrations in brain homogenates compared to sucrose-treated non-hypoxia groups. Interestingly, there were significant increase in ACh and decrease in AChE concentration among tualang honey-treated hypoxic rats compared to sucrose-treated hypoxic rats. In addition, there were decreased in neuronal counts in mPFC in sucrose-treated hypoxia group compared to sucrose-treated non-hypoxia groups. Tualang honey-treated hypoxia rats showed significant increase in neuronal count and preservation of morphology in mPFC compared to sucrose-treated hypoxia group. In conclusion, tualang honey can be used as an alternative treatment to protect against hypoxia-induced neuronal damage and the effect was possibly due to its cholinergic and antioxidant properties.

Minocycline and ifenprodil attenuated tactile allodynia by modulating the expression of DREAM and BDNF proteins in spinal cord of painful diabetic neuropathy rats

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Abstract

Painful diabetic neuropathy (PDN) is a serious complication resulted from prolonged hyperglycaemia in diabetes mellitus (DM) patients that severely affect their life routines. This study aimed to determine the effect of intrathecal administration of minocycline and ifenprodil on BDNF and DREAM proteins expression in spinal cord of streptozotocin-induced PDN rats. Forty-eight male Sprague-Dawley rats were randomly assigned into six groups consisting of non-diabetic (S+CB), PDN control and PDN rats treated with minocycline (M 80 or M 160) or ifenprodil (I 0.5 or I 1.0) at different doses. The rats were initially induced with DM by streptozotocin injection (60 mg/kg) and allowed for two weeks to develop into PDN condition. Von-Frey test was conducted on the rats to assess tactile allodynia on Day 0 (baseline), Day 14 (pre-treatment) and Day 22 (post-treatment). The rats were given intrathecal treatment of either minocycline or ifenprodil for seven days. The rats were then sacrificed and ipsilateral side of spinal cord tissue was collected for immunohistochemistry and western blot analyses. Minocycline and ifenprodil significantly attenuated tactile allodynia in dose-dependent manner ($p < 0.001$) compared to PDN control rats. Immunohistochemistry and western blot analyses revealed a significant attenuation of BDNF and DREAM proteins expression in dose-dependent manner ($p < 0.001$) after treated with minocycline and ifenprodil compared to PDN control rats. This study revealed the important modulation of BDNF and DREAM proteins expression in the spinal cord to attenuate tactile allodynia effect during the state of PDN through activation of microglial and NR2B receptor.

Repeated dose 12-weeks oral efficacy study on the hypotensive effects of *Syzygium polyanthum* aqueous extract in spontaneously hypertensive rats

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Abstract

Hypertension remains a major modifiable risk factor for cardiovascular disease (CVD). *Syzygium polyanthum*, a local herb found in Malaysia has been claimed traditionally as an antihypertensive treatment among Malays. Hence, this study aimed to investigate the hypotensive effects of repeated 12 weeks daily oral administration of an aqueous extract from *S. polyanthum* (AESP) leaves in spontaneous hypertensive rats (SHR). In this study, 18 SHR and six (6) male Wistar Kyoto (WKY) rats were used in four groups of rats. Group 1 (n = 6) and Group 2 (n = 6) received distilled water and were designated as negative control groups of WKY and SHR, respectively. In Group 3, SHR (n = 6) were subjected with 20 mg/kg losartan (positive control) and in Group 4, SHR (n = 6) received 1500 mg/kg AESP. The changes in systolic blood pressure (SBP) were measured biweekly to reflect the blood pressure changes using a non-invasive technique (tail-cuff method). AESP significantly reduced the SBP ($p < 0.001$) starting at week 4 and remained lowered until end of week 12. The SBP at the 12th week in the AESP-treated group was comparable to normal WKY and Losartan-treated groups. Thus, this study strongly suggests that *S. polyanthum* possesses the potential as an antihypertensive agent.

The antimalarial effect of concanamycin A on the V-type H⁺-ATPase of the *Plasmodium falciparum* digestive vacuole membrane

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Abstract

The ion pump known as a vacuolar-type H⁺-ATPase (V-type H⁺-ATPase) located on the digestive vacuole (DV) membrane of the malaria parasite, *P. falciparum* is thought to be responsible for the extrusion of H⁺ into the vacuole interior. The maintenance of the acidic DV is vital for the digestion of host cell hemoglobin and the subsequent process of heme detoxification. In this study, changes in the DV pH after treatment with concanamycin A, an inhibitor of V-type ATPase, were measured by flow cytometry. A standard pH calibration curve of FITC-dextran (a ratiometric pH indicator) was generated using saponin-permeabilized parasites in which the DV was preloaded with the pH indicator. These parasites were suspended in buffers of different pH in the presence of an ionophore, carbonyl cyanide 3-chlorophenylhydrazone (CCCP), to equilibrate intracellular compartments of parasites to external buffers of known pH. The ratio of the fluorescence intensities measured at two emission wavelengths (530 and 585 nm) of FITC dextran provides a quantitative measure of the DV pH. The average pH of the DV of untreated parasites (controls) was 5.52 ± 0.07 . However, treatment of the malaria parasites with concanamycin A (10 μ M) for 5 minutes resulted in the alkalization of the DV pH (7.28 ± 0.003). This result demonstrates the antimalarial effect of concanamycin A on the V-type H⁺-ATPase through the alkalization of the DV. Hence, this finding will be useful for validation of other antimalarial agents that might have the same mechanism of pH alteration of the DV.

The antimalarial activity of crude extracts of *Quercus infectoria* (manjakani) galls against the malaria parasite, *Plasmodium falciparum*

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Abstract

Quercus infectoria (manjakani) galls could potentially be employed as a relatively reasonable resource for a novel antimalarial drug candidate due to their simple extract preparation and abundance especially in tropical and subtropical regions. The galls of this plant have been reported to have various biological activities and medicinal properties, but its antimalarial activity has not been elucidated yet. This study aimed to determine the antimalarial activity of crude aqueous, ethanol, acetone and methanol extracts of *Q. infectoria* galls on asexual blood stages of a chloroquine-sensitive strain (3D7) of *P. falciparum* using a malarial SYBR Green 1 fluorescence-based (MSF) assay. The parasite development was evaluated microscopically using Giemsa-stained thin blood smears. Results show promising *in vitro* antimalarial activities of the acetone (IC₅₀ = 20.68 ± 2.16 µg/mL), aqueous (IC₅₀ = 21.32 µg/mL ± 8.81 µg/mL), ethanol (IC₅₀ = 22.46 ± 8.85 µg/mL) and methanol (IC₅₀ = 22.92 ± 9.65 µg/mL) extracts against the 3D7 parasites. The antimalarial effects of the extracts on the blood-stage parasites were associated with distinct morphological changes and parasite growth inhibition. The parasite development was inhibited and the parasites remained at the same ring stage after 24 and 48 hours of treatments, indicating that the bioactive components in these four extracts have an antimalarial action. Further studies to evaluate the possible cytotoxicity on normal cells and hemolytic effect on red blood cells of the extracts may provide greater reassurance regarding the safety of these products in humans.

A potential interaction between *Quercus infectoria* semi-purified fraction and pamidronate for management of osteoporosis

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Abstract

Current proclamation in traditional medicinal research has evidently documented successful finding in combination of herbal drug therapy, which could lead to potential increase in the therapeutic efficacy by increasing the bioavailability of drug. These provide promising strategies as well as alternative to overcome the compensatory mechanisms and off-target effects of synthetic drug. Bioactive natural polyphenols isolated from *Quercus infectoria* (QI) galls have been reported to play a role in bone formation by promoting new bone cell *in vitro*. This study aims to understand the potential effects of combination therapy between QI semi-purified fraction and osteoporotic drug (pamidronate) in comparison with individual therapy by performing bioavailability assay using MTT assay and screening of targeted specific osteoblast markers; Runt related transcription factor 2 (Runx2) and Osterix (Osx) by immunofluorescence staining in hFOB 1.19 osteoblast cell model. Our findings revealed that Runx2 and Osx were detected with higher fluorescence intensity along with rapid proliferation based on images acquired from immunofluorescence staining as compared to the individual treatment. Overall, this approach might provide the potential prospect of QI semi-purified fraction as an osteoporotic bone forming agent and is useful for identifying synergistic combinations of natural compounds for future osteoporotic therapeutic interventions.

***Syzygium polyanthum* improves renal damage secondary to hypertension**

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Abstract

Evidence has shown that there is a strong relationship between hypertension and kidney-disorder. Renal damage has become a major causative factor of hypertension. One of the local medicinal plants reported could be potentially served as an antihypertensive agent is *Syzygium polyanthum* (serai kayu). This study aimed to evaluate the effects of an aqueous extract of *S. polyanthum* (AESP) on the kidney morphology, damage secondary to prolonged hypertension. This study employed 21 male Spontaneously Hypertensive Rats (SHR), which were further divided into 3 groups (n = 7); untreated, Losartan-treated (20 mg/kg), and AESP-treated (1500 mg/kg) along with 7 male Wistar-Kyoto (WKY) rats as normal control orally treated for 92 days (subchronic). The effects of AESP on morphology improvement of the kidney was assessed using haematoxylin & eosin staining observation. Renal function test (RFT) was also evaluated in this study. There was a significant improvement of the structure of glomerulus in the group treated with AESP. There were more define Bowman's space, improved mesangial cell proliferation, reduced in thickness of the parietal layer of the renal corpuscle and elongated surrounding tubule. In contrast, there was no significant difference in RFT among the experimental groups despite there were significant morphological changes on the kidney due to hypertension, which proves their renal function remains intact. Thus, this study suggests that the oral administration of *S. polyanthum* has a renoprotective effect in improving renal morphology in hypertensive-renal damage of SHR rats.

Protective effects of tualang honey and its methanolic fraction against lipopolysaccharide-induced oxidative damage in the rats' hippocampus

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Abstract

Oxidative stress is a common pathogenic factor in neurodegenerative diseases. The present study was designed to investigate the protective effects of tualang honey (TH) and its methanolic fraction (MTH) against lipopolysaccharide (LPS)-induced oxidative stress in rats' hippocampus. Thirty five male Sprague Dawley rats were divided into five groups of seven individuals (n = 7): (i) control rats, (ii) untreated LPS rats (5 mg/kg) (iii) LPS rats treated with TH 200 mg/kg, (iv) LPS rats treated with MTH 150 mg/kg and (v) LPS rats treated with memantine 10 mg/kg. All treatments were administered intraperitoneally once daily for 14 days. The rats were sacrificed and the hippocampus was carefully dissected out, homogenized and stored at -80°C. Catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GPr), superoxide dismutase (SOD) and malondialdehyde (MDA) levels/activities were measured by using ELISA kits. Treatment with TH and MTH markedly reduced oxidative damage in rats' hippocampus as evidence by restoration in the activities of antioxidant enzymes (CAT, GPx and GPr) and decreased in MDA level comparable to LPS rats treated with memantine (a control drug). However, no significant differences were detected in SOD level in all groups. As a conclusion, TH and MTH exert their protective effects against LPS-induced oxidative damage in rats' hippocampus comparable to memantine.

Aortic oxidative stress reduction by Malaysian propolis in diabetic rats: An investigation of natural antioxidant therapeutics

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Abstract

Oxidative stress culminates diabetic vascular complications. Malaysian propolis extract (MP) possesses free radical scavenging, anti-atherogenic and vasorelaxing activities. However, *in vivo* antioxidative potential of MP on diabetic aorta has not yet been reported. This study aimed to determine oxidative stress status and antioxidative defenses in aorta of diabetic rats after MP supplementation. Adult male *Sprague Dawley* rats were randomized into five groups (n = 8/group): normoglycemia control (NG), diabetic control (DM), metformin-treated DM (DM+Met, 300 mg/kg/day), MP-treated DM (DM+MP, 300 mg/kg/day) and combined metformin and MP-treated DM (DM+Met+MP, dosage as former). Induction of DM was performed using streptozotocin (60 mg/kg/day, ip). Four-week treatment using oral gavage was initiated immediately following successful DM induction [fasting blood glucose (FBG) > 11.1 mM]. At the end of experiment, thoracic aortae were processed into 10% homogenates for calorimetric assays of malondialdehyde (MDA), protein carbonyl (PCO), superoxide dismutase (SOD) and catalase (CAT). CAT [18.3(13.4) vs. 5.2(6.33) U/mg protein] and SOD [3.5(2.2) vs. 1.1(1.3) U/mg protein/minute] were significantly raised in DM group compared to NG group. DM+MP group showed significant lower SOD [0.9(0.9) U/mg protein/minute] compared to DM group. No statistical difference was found in MDA and PCO. Reactive elevation of antioxidant enzymes precedes advanced lipid peroxidation and protein carbonylation in aorta of DM rats, suggest early compensated diabetic angiopathy pathogenesis. MP supplementation complements innate antioxidant defense systems to suppress oxidative stress. In this non-clinical proof of concept study, MP exhibits *in vivo* antioxidative potential as vasoprotection therapeutics for future exploration in clinical trial.

Expansion of human bone marrow CD34⁺ haematopoietic stem cells for adaptation of *Plasmodium knowlesi* to long-term *in vitro* culture

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Abstract

The simian malaria parasite, *Plasmodium knowlesi* is now recognised as a significant human pathogen causing malaria in Southeast Asia. The predilection of *P. knowlesi* for reticulocytes has hampered the establishment of its long-term *in vitro* culture system. Here, we demonstrated that human bone marrow CD34⁺ haematopoietic stem cells (HSCs) cultured in the presence of appropriate cytokines and growth factors, could be expanded to potentially generate a large number of reticulocytes for the long-term culture of *P. knowlesi in vitro*. Human bone marrow CD34⁺ cell line was expanded for nine days in serum-free expansion medium II (SFEM) supplemented with stem cell factor (SCF), thrombopoietin (TPO), FMS-like tyrosine kinase 3 (FLT3) and interleukin-6 (IL-6), and was subjected to four times of cell passage. The HSCs density and the population doubling level were determined for every passage. The data showed a raise in population doubling level along with the passage number, which indicates the expansion rates were increased up to five-fold. The expanded HSCs were cryopreserved at passage four, which allow the storage of HSCs to be used in the differentiation step to produce reticulocytes that are *P. knowlesi* target cells. In conclusion, we successfully expanded CD34⁺ HSCs from human bone marrow, which can offer a continuous source of reticulocytes required for the long-term *P. knowlesi* culture.

Knowledge, attitude and practice of food hygiene and safety among urban community in Bandar Utama Gua Musang, Gua Musang, Kelantan

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Abstract

Food hygiene and safety is an essential public health problem that affects all countries including Malaysia. It is important to have an understanding of the interaction on prevailing food hygiene and safety knowledge, attitude and practice among community in order to minimize the occurrence of foodborne illness. The main purpose of this study was to evaluate the level of knowledge, attitudes and practices regarding the aspect of food hygiene and safety among community at Bandar Utama Gua Musang, Gua Musang, Kelantan. A total of 123 participants was involved in the study. The data were collected from the participants through the instruments of questionnaire and analyzed using the SPSS version 24.0. Pearson's Chi Square Test was used to analyze the socio-demographic with level of knowledge, attitude and practices, determine association between knowledge level with attitude level, determine association between knowledge level and practice level, and determine association between attitude levels with practice level. In general, the participants' knowledge was low. Participants' level of attitude and practices were also low. There is no significant association between socio-demographic (age group, gender and education level) with level of knowledge, attitude and practices were observed. Furthermore, no significant association between knowledge and attitude ($p = 0.162$) and attitude with practices ($p = 0.435$). However, there was a significant association between knowledge and practice ($p = 0.003$).