Poster Exhibition

9. Therapeutics of Obesity and Metabolic Syndrome

PE 09-01 9. Therapeutics of Obesity and Metabolic Syndrome

Oxidative Stress and Obesity: Role of Peroxiredoxins

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Background: Accumulating evidence indicates that adipocyte oxidative stress plays an important role in the development of obesity and metabolic syndrome. Increased oxidative stress and mitochondrial dysfunction in obese adipocytes contribute to adipokine dysregulation, inflammation, and insulin resistance. Peroxiredoxins are a family of cellular thiol peroxidases scavenging peroxides. The precise role of peroxiredoxin on obesity is worth to discuss further. The objective of this study is to explore the mechanism by which peroxiredoxin in adipocytes on oxidative stress in obesity.

Method: We conducted a systematic review of the literature search in PubMed and Scopus databases using the terms from 2020 to June 2024. The following phrases were included in the process: (1) "obesity" AND "oxidative stress" AND peroxiredoxin"; (2) "metabolic syndrome" AND "oxidative stress" AND "peroxiredoxin"; (3) "obesity" AND "peroxiredoxin"; (4) "peroxiredoxin" AND "oxidative stress. We included articles that had the clear aim of investigating the role of peroxiredoxin on the risk of obesity or its metabolic complications. Additional articles not found in this search were identified by exploring references in key articles, as well as by individual searches of peroxiredoxin.

Results: The data demonstrated that peroxiredoxin 5 plays an essential role in regulating adipogenesis. Peroxiredoxin 5 overexpression significantly suppressed cytosolic and mitochondrial reactive oxygen species (ROS) generation. In addition, peroxiredoxin 5 regulated the AMP-activated protein kinase pathway and lipogenic gene (sterol regulatory element binding protein-1 and FAS) expression, and thereby inhibited lipid accumulation.

Conclusion: These data suggest that peroxiredoxin 5 may play an essential role in maintaining normal characteristics of adipocytes and that defect in peroxiredoxin 5 alters mitochondrial redox state and function, and adipokine expression in adipocytes, and thus leading to metabolic alteration. Collectively, peroxiredoxin 5 may be a valuable therapeutic target for the management of obesity and obesity-related metabolic diseases.

PE 09-02 9. Therapeutics of Obesity and Metabolic Syndrome

Protective potential of flaxseed lignan in high fat-diet/alloxan-induced diabetes in kidney and heart of female rats

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Background: Flax (Linum usitatissimum) seeds are among the richest sources of plant lignans. The lignans are a large group of low molecular weight polyphenols found in plants, particularly seeds, whole grains, and vegetables. Studies report fish oil based lipid emulsions contain high amounts of omega-3 polyunsaturated fatty acids. Hence, we assessed changes produced by the administration of flaxseed lignan secoisolariciresinol diglucoside (FLSD) on biomarkers related to lipid metabolism, cardiac functions and antioxidant systems in kidney of high fat-diet diabetic rats.

Methods: The study was carried out on 64 diabetic female albino rats; a high-fat diet (HFD) and a single dose of alloxan (25 mg/kg) were utilized for experimental model induction. Diabetic rats were received FLSD (50 ,100 and 200 mg/kg) intragastrically by gavage per day for 30 days.

Results: Administration of FLSD caused a remarkable recovery of kidney weight, heart function, and aldosterone level, particularly. The hypolipidemic activity of FLSD was confirmed by the normalization of total cholesterol, triglycerides, and low- and high-density lipoprotein cholesterol in diabetic rats. Inhibitory effects on albuminuria, creatinine, urea nitrogen, and n-acetyl-β-d-glucosaminidase verified FLSD's hepatic protective activity in diabetic rats. Furthermore, FLSD exerted beneficial modulation of creatinine kinase expression in heart, inflammatory factors and oxidative enzymes. Compared with untreated diabetic rats, FLSD decreased the expression of phosphor-AKT and phosphor-GSK-3β in the kidneys. Proapoptotic, cardiac biomarker and inflammatory markers were significantly improved and showing a great retain to their normal levels specifically in FLSD (200mg/kg)-treated groups.

Conclusion: FLSD has a great protective influence on kidney injury of HFD/alloxan-induced diabetic rats. These findings indicate that FLSD can be considered as a potential candidate for in vivo and clinical studies against various metabolic disease.

PE 09-03 9. Therapeutics of Obesity and Metabolic Syndrome

Study of MultI-eLectrode EndovaScular denervaTiOn in patieNts with type 2 diabetes mEllitus (MILESTONE): 6-month analysis from the first-in-human proof-of-concept study

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Background: Chronic elevation of sympathetic activity has been identified to induce insulin resistance and contributes to the development of type 2 diabetes mellitus (T2DM). This study aims to assess safety and glycemic indices at 6 months in the study of endovascular denervation (EDN) procedure, in patients with T2DM.

Method: Using a novel six-electrode catheter system, EDN was conducted on the celiac artery (CA), and aorta between CA and the superior mesenteric artery (SMA). The primary outcomes were evaluated by the safety, HbA1c, homeostasis-model assessment of insulin resistance (HOMA-IR), and fasting plasma glucose (FPG). The antidiabetic medication, lifestyle, physical condition, blood pressure (BP), and plasma biochemistry were also recorded.

Results: A total of 11 T2DM patients were included for analysis. The technical success was 100% and no severe treatment-related adverse events or major complications were observed. Both HbA1c and HOMA-IR significantly reduced at 6 months, from 9.9±1.6 to 8.0±2.4% (P = 0.005), and from 13.3 (IQR 5.9-46.1) to 6.0 (IQR 3.1-11.9) (P = 0.016), respectively. At 1, 3, and 6 months of follow-ups, FPG levels were 10.2±0.8, 10.1±1.2, and 9.6±1.7 mmol/L, respectively, compared to 15.4±1.6 mmol/L at baseline (P = 0.001, < 0.001, and < 0.001, respectively), and 2hPG levels were 11.8±3.0, 11.4±4.0, and 11.0±5.9 mmol/L, respectively, compared to 17.9±6.0 mmol/L at baseline (P = 0.001, 0.001, and 0.002, respectively). OGTT based 3-hour C-peptide release test showed improved beta-cell function (AUC 0.23 (IQR 0.18-0.32) vs. 0.28 (IQR 0.21-0.38) pmol/mL, P = 0.046). A reduction of daily insulin injection was also observed (24 (IQR 15.5-47) vs. 19 (IQR 9-27.5) IU, P = 0.018) without changes in lifestyle. Improvements of liver function were observed although physical conditions, BP, plasma norepinephrine, angiotensin II, and blood lipids were not changed during follow-ups.

Conclusion: The 6-month analysis from this trial shows that EDN using the novel six-electrode catheter system at the new sites of CA and aorta between CA and SMA elicits a clinically significant improvement in hyperglycemia in patients with T2DM, with good tolerability.

PE 09-04 9. Therapeutics of Obesity and Metabolic Syndrome

Anti-Obesity Effects of Fimasartan on High Fat Diet-Induced Obese Mouse Model

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Background: Obesity is a disease that has an abnormally large amount of fat accumulated in the body, and is caused by the collapse of energy balance due to excessive food intake and decreased activity.

Fimasartan is angiotensin II receptor inhibitor (ARB) for hypertension, and the results of studies on anti-obesity efficacy in obese mouse animal models and its mechanism are unknown. Therefore, this study was conducted to confirm the anti-obesity efficacy and mechanism of Fimasartan in diet induced obese (DIO) model.

Methods: C57BL/6 mice fed a high fat diet for 12 weeks to induce obesity and administered orally once a day for 4 weeks.

Grp78, sXBP1 mRNA expression was assessed by PCR in epididymal fat.

Hepatic fat accumulation was evaluated by H&E staining and Oil Red O staining.

Results: Repeated oral administration of Fimasartan to the DIO animal model for 4 weeks showed a dose-dependent weight loss(P<0.001). Plasma analysis showed a significant decrease in LDL-CHO levels in all treatment groups.

Hepatic triglyceride contents were significant decreased in all groups, especially in the Fimasartan 120 mg treatment group.

To identify the mechanism of action (MOA) of Fimasartan, PCR was performed to compare the gene expression of the ER stress marker Grp78 and sXBP1. There was a significant decrease in all treatment groups, especially in Fimasartan 24 mg treatment group. As a result of evaluating hepatic fat accumulation through H&E and Oil red O staining, the most effective fat reduction effect was shown in Fimasartan 120mg treatment group.

Conclusion: Our findings suggest that Fimasartan has an advantage in improving obesity when orally administered in the DIO mouse model, and this anti-obesity effect is thought to be due to a decrease in ER stress in adipocytes.

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The neuroprotective effect of exercise-induced hormone irisin in ischemic stroke

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Background: Stroke is a leading cause of death and disability worldwide. Obesity is an important risk factor for stroke, while exercise can reduce the incidence and the mortality associated with stroke. However, little is known about the mechanisms underlying the effect of obesity and exercise on the pathogenesis of stroke. Recent studies have highlighted the role of exercise-induced myokines in mediating the beneficial effect of exercise. Among the discovered myokines, irisin has been shown to exert neuroprotective role in brain disorders, such as Alzheimer's disease. In this study, the effect of exercise and exercise-induced myokine irisin was examined in ischemic stroke with obesity.

Method: Mice were fed a high-fat diet or a normal diet for 4 weeks and then exercised for 4 weeks, before subjected to transient middle cerebral artery occlusion (MCAO). FNDC5 knockout (KO) mice and plant-made human recombinant irisin was used to confirm the effect and mechanism of irisin in

Results: The results showed that exercise significantly reduced infarct size and increased survival rate compared to the HFD group. Inflammatory and apoptotic markers induced by HFD was also reversed in exercised group, while exercise increased tight junction factors. In addition, plasma irisin concentration and irisin expression in muscle and brain were all increased by exercise. In mice deficient in FNDC5, the precursor of irisin, MCAO-induced ischemic stroke was exacerbated, with aggravated inflammation and tight junction markers compared to control mice. Administration of recombinant irisin significantly reduced the size of cerebral infarction while increasing the expression of irisin receptor and M2 macrophage factors.

Conclusion: In conclusion, exercise and exercise-induced myokine irisin are suggested to exert neuroprotective effects on ischemic stroke.

PE 09-06 9. Therapeutics of Obesity and Metabolic Syndrome

Biological Importance Of Anthocyanin In Cardiovascular Disease (CVD): Therapeutic Role In Diabetic Cardiomyopathy With Their Molecular Mechanism

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Background: Medicinal plants and their derived plant extracts and active phytochemicals have numerous biological applications in the traditional medicine. Diabetes mellitus (DM) has been associated with cardiovascular disease (CVD). In the modern age, CVD is one of the main biological complications which affect many lives among people with diabetes. Further, diabetic CVD is associated with heart failure, coronary artery disease, ischemic heart disease, stroke, and diabetic cardiomyopathy (DCM). Anthocyanins are the pigments which gives bright colours to the fruits and vegetables. Anthocyanin has been widely studied for its medicinal properties and pharmacological effectiveness in medicine. Anthocyanins have numerous health beneficial potential in medicine, including anti-diabetic, anti-obesity effects and prevent CVD.

Methods: Biological potential of Anthocyanins class phytochemical have been investigated for their effectiveness against diabetic cardiomyopathy (DCM) and associated secondary complications in present work through scientific data analysis of numerous scientific research works. Biological potential of anthocyanin against isoproterenol-induced myocardial infarction has been investigated in the scientific research. Further, in another scientific research work, its effects on alleviated vascular inflammation in endothelial cells have been also described in the scientific fields. Other pharmacological activities of anthocyanin were also correlated in the present investigation in order to know its health beneficial aspects in medicine.

Results: Present work scientific data signified the biological importance and therapeutic effectiveness of anthocyanin in medicine. In cardiovascular scientific research, anthocyanin has been reported to exert cardioprotective effects against isoproterenol-induced myocardial infarction. However, in another scientific research work, anthocyanin reduced vascular inflammation in endothelial cells which signified its effectiveness against numerous cardiovascular disease complications. Further, some other scientific research work data revealed the biological importance of anthocyanin on dyslipidemia, promote vascular protection, ameliorate atherosclerosis, counteract obesity, and attenuate diabetic cardiomyopathy. Scientific research showed significant role of anthocyanin in modulating diabetic cardiovascular disease by modulating fibrosis, oxidative damage, inflammation, and apoptosis.

Conclusion: Present work signified biological importance of anthocyanin in cardiovascular disease, including diabetic cardiomyopathy.

PE 09-07 9. Therapeutics of Obesity and Metabolic Syndrome

Digital and Community-Based Peer Support Interventions for Cardiovascular and Metabolic Health in Malaysia

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Background: Cardiovascular diseases (CVD) and metabolic syndrome (MetS) are significant health challenges globally, particularly in underserved communities. We present the outcomes of two peer support interventions in low-income Malaysian communities. Study 1 discusses MYCardio-PEER, a digitally-enhanced peer support intervention targeting CVD risk reduction. Study 2 reports on PERSUADE, a community-specific nutrition and lifestyle behaviour program for Malaysian adults with MetS.

Method: MYCardio-PEER was developed using the Integrated Theory of Behaviour Change, incorporating literature review and stakeholder input to create culturally-relevant educational materials and activities. Trained peer leaders facilitated the 8-week program with educational videos and interactive content on heart-healthy behaviours. In contrast, PERSUADE involved 48 peers in a 3-month program focused on nutrition and lifestyle changes for adults with MetS. Statistical analyses assessed changes in nutrition intake, anthropometry, and metabolic parameters.

Results: MYCardio-PEER successfully created an engaging peer support intervention using digital resources, led by trained community members. Meanwhile, PERSUADE showed significant improvements in nutrition intake and physical activity, as well as slight improvements in anthropometric and metabolic parameters among adults with MetS.

Conclusion: Both interventions highlight the potential of peer support programs in addressing cardiovascular health and MetS in underserved communities. MYCardio-PEER and PERSUADE offer scalable approaches for promoting health behaviour change and improving health outcomes among vulnerable populations. Future research should focus on their long-term impact and scalability in diverse settings.

PE 09-08 9. Therapeutics of Obesity and Metabolic Syndrome

Puerarin modulates lipid metabolism in high-fat-diet-fed mice in association with gut microbiota via regulating SREBP-1/FAS/CD36 signaling pathways

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Background: Adipocyte differentiation, lipogenesis, lipolysis, and energy metabolism are just a few of the metabolic processes that can become dysregulated and exacerbate obesity. Anti-oxidation and anti-inflammatory qualities of puerarin have been shown to have protective effects against obesity, diabetes, and other cardiovascular illnesses, including atherosclerosis. The current study looked at the anti-obesity impact of YLGT in mice given a high-fat diet (HFD) and explored possible mechanisms through controlling the gut microbiota and SREBP-1/FAS/CD36 signaling pathways.

Methods: Adipocyte development in 3T3-L1 cells was examined as a result of PRN treatment in order to assess the anti-obesity potential of PRN in vitro. Mice were divided into three groups in order to assess its potential in vivo. Body weight, white fat mass (WAT), serum triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, glucose, insulin, and leptin, hepatic lipid accumulation, and gene levels related to lipid metabolism in the liver and WAT were all measured nine weeks after the start of the feeding regimen. We also assessed the study on facecal microbiota.

Results: When PRN was administered to 3T3-L1 cells in vitro, the result was a dose-dependent, effective inhibition of the cells' ability to differentiate into adipocytes. An in vivo study showed that SAE supplementation dramatically reduced the increases in body weight, liver weight, WAT mass, blood TG, TC, lipid, glucose, insulin, and leptin levels that were brought on by the HFD. It was discovered that PRN supplementation suppressed the expression of lipid metabolism-related proteins in the liver and WAT, such as SREBP-1, FAS, CD36, and PPARγ, in addition to downregulating the mRNA levels of transcription factors like Srebp and Pparg. These findings were consistent with the effects of PRN supplementation on liver weight and WAT mass. By suppressing transcription factors essential to adipogenesis and lipogenesis, PRN prevents fat formation in HFD-fed rats, indicating that it may be useful in avoiding obesity. An additional experiment using fecal microbiota transplantation shown that changes in gut microbiota, such as an increase in unclassified Muribaculaceae and a decrease in Colidextribacter, may be a significant factor in the inhibition of obesity by PRN.

Conclusion: In summary, there is great potential for using PRN in the treatment of obesity via modulating lipid metabolism and gut microbiota.

PE 09-09 9. Therapeutics of Obesity and Metabolic Syndrome

The Combination of Semaglutide and Selenium Supplementation Preserves Muscle Mass and Improves Thyroid Function in Obese Patient with Subclinical Hypothyroidism and Psoriasis: Case Report

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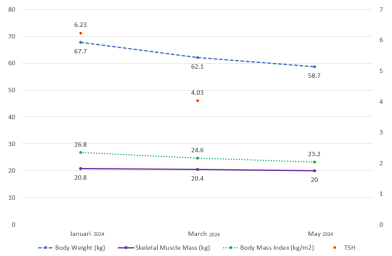
Background: Divergent outcomes have been observed in obesity management using semaglutide. Studies indicate that rapid weight loss following semaglutide injection, can result in loss of muscle and fat mass. Moreover, the relationship between semaglutide and various thyroid problems is still unclear, particularly regarding the development of semaglutide-induced subclinical hypothyroidism. Selenium is a trace mineral that has important biological functions and antioxidant properties, has been demonstrated to enhance thyroid function and maintain muscle mass.

Method: A 52-year-old woman with obesity and psoriasis experienced difficulties in managing her weight and psoriasis symptom. The patient was diagnosed with subclinical hypothyroidism and treated with weekly subcutaneous injection of 1 mg semaglutide, along with daily oral supplementation of 100 g selenium. The patient was instructed to adopt a healthy lifestyle, which involved adherence to the meal prescription and strength training program 2-3 times a week.

Results: After 5 months, decrement of 13% body weight and 4% skeletal muscle mass were observed. Semaglutide injection and selenium supplementation were well-tolerated, with no notable adverse effects. The serum TSH level returned to normal and psoriasis lesions showed significant improvement after 3 months. Studies have demonstrated that selenium can enhance mitochondrial biogenesis in skeletal muscle and improve thyroid function.

Conclusion: Selenium supplementation has the potential to reduce the adverse effects of semaglutide. The combination of semaglutide injection and selenium supplementation demonstrated a modest decrement of body weight, preservation of muscle mass, enhancement of thyroid function, and alleviation of psoriasis symptoms in obese patient with subclinical hypothyroidism and psoriasis.



PE 09-10 9. Therapeutics of Obesity and Metabolic Syndrome

Targeted Obesity Genes Single Nucleotide Polymorphisms, Diets, Lifestyles, and Obesity Indices: Nutrigenetics as a Predictive Model

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Background: There is a growing connection with nutrigenetics highlighting the influence of genetic factors on how individuals respond to dietary choices and impacting the prevalence of overweight and obesity. The study aims to explore different obesity genetic single nucleotide polymorphisms (SNPs), interact with diet-lifestyle factors, and influence the status of obesity.

Methods: A total of 290 Malaysian adults aged between 18-65 years old were recruited. A pre-tested, validated, structured, and self-administered questionnaire was utilized. Obesity was defined in terms of body mass index (BMI), waist circumference (WC), and body fat percentage (BF%). The Infinium Asian Screening Array-24 v1.0 BeadChip was used to genotype MC4R, INSIG2, FTO, and APOA genes. IBM® SPSS® Statistics v27 and Nutritionist Pro Version 4.0.0 were used for data analysis.

Results: A weak but positively significant correlation was found between dietary calories and BMI (r = 0.142, p=0.038). A positive significant correlation was revealed between energy (rpartial= 0.142, p=0.038), protein (rpartial= 0.154, p=0.025), alcohol (rpartial= 0.144, p=0.037), and WC. There were significant differences between FTO gene SNPs: rs11075989 (p=0.001), rs9936385 (p=0.001), rs8043757 (p=0.003), rs62033400 (p=0.002), rs7202116 (p=0.002), rs11075990 (p=0.002), and rs12149832 (p=0.002) and WC. The interaction between smoking and INSIG2 rs7566605 was significantly correlated with WC (rpartial= 0.186, p=0.012). In multivariate analysis, a significant positive association was shown between total daily energy expenditure and WC (adjusted-β=503, 95%CI= 0.007, 0.021, p<0.001). A significant positive association was found between dietary patterns high in carbohydrates, sugar, and fat and BMI, adjusted for gender and marital status (adjusted-β=0.349, 95%CI= 0.048, 0.650, p=0.024). The mean micronutrient index was significantly associated with BF% status (p=0.027). Increased dietary iron density index increased the odds of high BF% almost by 5-fold (AOR=4.70,95%CI=1.07, 20.55, p=0.040).

Conclusion: Findings of nutrient-gene interaction highlight the need to implement personalized nutrition and strategies to overcome obesity.

Keywords: Genetics, Metabolomics, Nutrient Density, Nutrition, Obesity, Public Health

PE 09-11 9. Therapeutics of Obesity and Metabolic Syndrome

Cardio Protective Effects of Red Sea Marine Sponge (Xestospongia Testudinaria) Extract In Heart Failure Rat

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Background: Heart failure persists as a widespread cardiovascular ailment distinguished by compromised cardiac function and concomitant vascular issues, such as endothelial dysfunction and oxidative stress. In the quest for innovative therapeutic approaches, this study endeavors to elucidate the potential efficacy of Xestospongia Testudinaria., a red sea marine sponge renowned for its rich content of bioactive compounds, in ameliorating cardiac dysfunction in rats subjected to experimentally induced heart failure.

Method: Male Wistar rats (200-250g, n=35) were randomly divided into 5 groups: Control, Xestospongia Testudinaria., Isoprenaline, Isoprenaline + Xestospongia Testudinaria. and Isoprenaline + Digoxin. Heart failure was induced for 14 days by using Isoprenaline (10mg/kg/s.c) daily followed by treatment for 14 days using X Xestospongia Testudinaria. (15mg/kg/o.g) and Digoxin (10/mg/kg/o.g). Control rats were given saline as a vehicle for ISO, Xestospongia spp. and Digoxin. Hemodynamic measurements, Electrocardiography (ECG), Cardiac Injury marker NT-proBNP, and histology analysis were assessed.

Results: Systolic blood pressure (SBP) in all ISO groups was significantly increased compared to the control group ($p<0.05$), and Xestospongia Testudinaria treatment managed to reduce the SBP. Besides that, Xestospongia Testudinaria treatment also significantly reversed the increase rat's heart rate (HR) in ISO-induced rats. The ECG patterns were also abnormal in ISO-induced rats, which were normalized in Xestospongia Testudinaria treated rats. Cardiac injury marker (NTpro-BNP) level was remarkably reduced by Xestospongia Testudinaria in the ISO group. Cardiac hypertrophy was evident by larger cardiomyocyte size and the fibrosis deposition was remarkable in ISO induced group. Interestingly, Xestospongia Testudinaria able to improve those conditions in ISO induced groups.

Conclusion: Xestospongia Testudinaria extract treatment was able to improve the hemodynamic functions, ECG readings, reduce NT-proBNP levels and reverse the cardiac structure; hence, highlighting its potential as an alternative treatment for heart failure conditions.

PE 09-12 9. Therapeutics of Obesity and Metabolic Syndrome

Coloring White Adipose Tissue as a Novel Therapeutic to Combat Obesity and its Metabolic Complications

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Background: Obesity is an urgent and worsening problem that is a major risk factor for morbidity and mortality. White adipose tissue (WAT) primarily functions in energy storage by accumulating fat, whereas brown adipose tissue (BAT) expends energy through thermogenesis. The transformation of WAT into BAT, referred to as "browning," has gained attention as a promising therapeutic approach for addressing obesity and its associated metabolic disorders. This review aims to summarize current methods and findings related to WAT browning and its potential benefits in obesity management.

Methods: We conducted a systematic search through Pubmed, Scopus, Cochrane Library, and EBSCO was conducted to find this topic, utilizing relevant MeSH terms. Keywords included "white adipose tissue browning," "brown adipose tissue," "obesity," and "metabolic disorders." The studies were selected based on relevance, and the quality of evidence and then critically appraised.

Results: Initially, 889 studies were identified, out of which 29 scientific papers met the inclusion criteria. Full-text articles were assessed, and six studies were selected for detailed analysis. According to the data analysis results, browning of WAT increases the body's energy expenditure, which can help in reducing overall body fat and combating obesity; improve insulin sensitivity and reduce the risk of metabolic disorders such as type 2 diabetes; contributes to better regulation of body temperature and energy balance. Recent research focuses on identifying molecular targets and pathways that can induce browning such as cold exposure that can promoting browning through the release of norepinephrine; pharmacological agents like β3-adrenergic agonists, thiazolidinediones show promise in promoting browning; and nutritional interventions including capsaicin and resveratrol that have been associated with increased browning activity.

Conclusion: The conversion of WAT to BAT offers a novel and effective strategy to combat obesity and its metabolic complications. Further research is necessary to develop safe and effective interventions for clinical use.

Keywords: white adipose tissue browning, brown adipose tissue, obesity, metabolic disorders

PE 09-13 9. Therapeutics of Obesity and Metabolic Syndrome

Potential Combination of Quercetin and Resveratrol as Obesity Therapy through Increased AMPKα1 Regulation, Increased Expression of Adiponectine Receptors, and Repairment of Intestinal Microbiota

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Background: Obesity has emerged as a global health concern, including in Indonesia, with its association with dyslipidemia, hypertension, glucose intolerance, heart disease, type II diabetes mellitus, cancer, osteoarthritis, and sleep apnea. The pathogenesis of obesity is intricately linked to disruptions in AMPKα1 phosphorylation. Additionally, alterations in the composition of intestinal microbiota contribute to the progression of obesity. While contemporary obesity therapies have been developed, they are not without limitations and are associated with various side effects. Therefore, this narrative review aims to explore alternative therapies that can either replace or enhance current therapeutic approaches.

Method: The literature search was conducted using PubMed, Cochrane Library, Science Direct, and Clinicaltrials.gov, utilizing keywords such as "new treatment," "obesity," "flavonoids", "quercetin", and "resveratrol". Our review indicates that the combination of quercetin and resveratrol holds promise in the context of obesity treatment.

Results: This combination can augment the AMPKα1 pathway, leading to the activation of SIRT1 and the inhibition of macrophage inflammation, thereby suppressing nuclear factor κB activation and reducing proinflammatory cytokine synthesis. Furthermore, increased expression of adiponectin receptors appears to enhance insulin sensitivity, decrease the expression of lipogenesis-related genes (PPARγ, ACC1, ACC2, and FAS), and improve glucose uptake. Additionally, quercetin and resveratrol may modulate intestinal microbiota, promoting the proliferation of beneficial bacteria with anti-inflammatory properties and potentially enhancing lipid metabolism while reducing harmful bacteria.

Conclusion: This review underscores the potential of the quercetin and resveratrol combination as a viable candidate for future alternative obesity treatment approaches, offering multiple avenues for therapeutic intervention.

PE 09-14 9. Therapeutics of Obesity and Metabolic Syndrome

Attenuation of COX-2 and PPARγ Expression by Puchea indica is Associated with Reduced Adiposity and its Related Complications

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Background: Obesity is a chronic, long-term health disease that progressively worsens over time. It is linked to a slew of complications that include ischemic heart disease, type 2 diabetes, an increased risk of stroke, cognitive dysfunctions, kidney problems, bone resorption, and so on. Therefore, it is necessary to search for pharmacological remedies for obesity. Medicinal plants are well utilized for the management of obesity and related complications. Here we made use of Pluchea indica, a species of flowering plant from the Asteraceae family. This study focused on demonstrating the effect of methanolic extract of P. indica leaf in obesity and related complications in high fat-induced obese mice.

Methods: Swiss albino mice were fed with high fat diet to induced obesity and the obese mice was treated with different doses of Pluchea indica leaves extract for eight weeks. Variation in the weight gain patter, food efficiency ratio, food intake behavior, adipocyte morphology, fat mass accumulation, serum cholesterol level, cardiac risk assessment, liver function, and creatinine levels were recorded. Moreover, IL-6, COX-2, MCP-1, and PPARγ expression at transcript level were also explored to know the changes in adipocyte specific genes associated with obesity and inflammation.

Results: The findings from our studies showed that the extract significantly reduced ($p < 0.05$) body weight gain and abdominal fat mass buildup, followed by a reduction in the levels of blood cholesterol. educed adipocyte sizes were also recorded in obese mice under treatment. Cardiac complication risk, hepatic function were altered positively. The extract was able to attenuate the mRNA expression of inflammatory adipokines like IL-6, COX-2, MCP-1, and PPARγ significantly, which is consistent with the biochemical outcomes.

Conclusion: All these biochemical and gene expression studies validated the potential of P. indica leaf to reduce adiposity and its associated factors.

PE 09-15 9. Therapeutics of Obesity and Metabolic Syndrome

Anti-Obesity Effects of Edible Bird Nest in High Fat-Cholesterol Diet-Induced Obese Rabbits via AMPK-Mediated Lipid Metabolism Pathway

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Background: Edible bird nest (EBN) is made from the saliva of swiftlets, and it is regarded as a highly nutritious and health restorative food. Growing evidence suggests that EBN is a potential functional food for managing metabolic disorders, which has initiated the present study to explore into novel therapeutic approach of EBN to improve obesity and its related disorders. Moreover, the role of EBN in preventing obesity has yet to be elucidated, and this study will be the first to report such activity. Therefore, the study aimed to determine the anti-obesity effect of EBN supplementation in high fat-cholesterol diet-induced obese rabbits via regulation of genes related to lipid metabolism mechanism via AMPK activation.

Method: Twenty-five young, male, New Zealand white rabbits aged 8-10 weeks-old with weights approximately 1.6 to 1.7 kg, were randomized into five groups (n=5): group I was the control, group II received high fat-cholesterol diet (HFCD), group III, IV and V received HFCD supplemented with Orlistat, EBN stew extract (SE) and EBN full stew (FS) for 12 weeks. In all groups, body weight, obesity index, visceral organ weights, serum lipid profile, leptin, adiponectin and free fatty acid levels were investigated. Histological evaluation was performed the assess the morphological changes in white adipose and liver tissues using Haematoxylin and Eosin staining. Additionally, the regulatory effect of EBN on lipid metabolism related genes were determined in adipose and liver tissues.

Results: Supplementation of SE and FS to HFCD-fed rabbits inhibited body weight gain and the mass of white adipose and liver tissues in the experimental rabbits. In addition, SE and FS supplementation attenuated lipid accumulation in adipose and liver tissues as displayed by Haematoxylin and Eosin staining. Serum lipid profile, adiponectin, leptin and free fatty acid concentrations were improved following SE and FS supplementation. The anti-obesity effect of EBN was achieved via regulation of genes involved in lipid metabolism mechanism, reflected with downregulation of ACACα, PLIN2 genes and upregulation of LIPE, LPL, PPARα and FFAR2 genes via AMPK activation.

Conclusion: The present study demonstrated for the first time, the functional properties of EBN as anti-obesity agent and proposed the underlying molecular mechanisms which mediated the effect via AMPK activation that regulate the expression of genes related to lipid metabolism.

PE 09-16 9. Therapeutics of Obesity and Metabolic Syndrome

Effect of Nelumbo nucifera Extracts and Regular Walking on Muscle Strength and Mass in Adults with Relatively Low Muscle Mass: A Randomized Controlled Trial

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Background: Previous in vitro and in vivo studies have confirmed the efficacy of Nelumbo nucifera leaves extracts (NM) in increasing muscle production and reducing muscle breakdown. In particular, NM improved muscle wasting through the regulation of muscle protein metabolism in DEX-induced muscle atrophy mice. However, the effect of oral NM supplementation on human muscle strength and mass is unclear. Therefore, we tested the effects and safety of consumption of NM combined with regular walking for 12 weeks on muscle strength and mass in older adults with relatively low muscle mass.

Methods: A randomized controlled trial was conducted on 80 adults between 19 and 71 years of age. Participants were randomized to receive either a placebo or 2,000 mg NM daily for 12 weeks. The indicator component of NM was Quercetin-3-O-glucuronide 24 to 37 mg/g. At baseline and 12 weeks after treatment, the following parameters of the participants were examined: knee strengths, handgrip strengths, body composition, blood tests, and 24-hour dietary recall. All participants were required to walk for 30–60 min/day for >3 days/week during the trial period. Physical activity was assessed using an exercise log during the study.

Results: Of the 80 participants, 73 completed the trial without reporting adverse effects. NM supplementation over 12 weeks did not increase knee or grip strength compared to the control group. Also, the two groups observed no differences in muscle mass or biomarkers. None of the participants experienced adverse events. The application of NM was well tolerated, and no notable adverse effect was reported in either group.

Primary outcome measure of the two groups

	Control group		Nelutri™ group		Adjusted difference of Control vs Nelutri™ 12 wk	P^1
	Baseline	12 wk	Baseline	12 wk		
Intention to treat (n=80)						
60 degree/s knee extension peak TQ (Right), Nm	90.76±31.16	96.03±28.55	82.28±30.35	86.91±28.97	-0.93 (-9.75, 7.90)	0.835
60 degrees/s knee extension peak TQ (Left), Nm	88.63±29.77	91.24±28.16	82.58±28.31	84.85±28.14	0.60 (-7.86, 9.06)	0.888
Per protocol (n=73)						
60 degree/s knee extension peak TQ (Right), Nm	91.29±30.30	96.99±27.21	84.20±30.58	89.35±28.66	-0.61 (-10.41, 9.19)	0.901
60 degrees/s knee extension peak TQ (Left), Nm	89.22±30.10	92.04±28.30	85.40±27.99	87.92±27.51	1.03 (-8.39, 10.46)	0.828

Values are mean ± SD or mean (95% CI).
[1]ANCOVA with adjustment for age, sex, and the changes from baseline in dietary total caloric intake and physical activity as covariates.

Conclusion: NM supplementation with regular walking did not improve remarkably muscle function compared to regular walking alone in adults with relatively low muscle mass.

PE 09-17 9. Therapeutics of Obesity and Metabolic Syndrome

Differences in Heart Rate, Blood Pressure and Cardiopulmonary Function according to Obesity during Cardiac Rehabilitation Program in Middle-Aged Men who have experienced Coronary Artery Disease

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Background: In Korea, Because of increasing patients with coronary heart disease, the need for a program that manages the heart was required in 1993, but related research is incomplete, and it is still on process. This research aimed to examine the functional difference before and after the cardiac rehabilitation program by dividing the two mid-age male groups who had experienced cardiovascular disease with obesity.

Method: The subjects, middle-aged 30 males who were diagnosed with acute myocardial infarction in 15 control group (NOG) and 15 obese group (OG). For 8 weeks, subjects was comparatively analyzed to effects of the cardiac rehabilitation program for heart rate, blood pressure and cardiopulmonary function according to obesity. Analysis was performed to two-way repeated measure ANOVA analyze the difference between before and after the cardiac rehabilitation program for each subject. And paired t-test was conducted to verify before and after changes.

Results: The results of this study are follows. Rest heart rate, the interaction effect between the group and time was found to be a statistically significant difference(p=.025). As a result of pre-post analysis within each group was significantly reduced in the NOG(p=.000). Maximum heart rate showed a significant difference according to the time of the main effect test(p=.020). Blood pressure at maximal systolic showed a significant difference according to the time of the main effect test(p=.009). Pre-post analysis within each group were significantly increased in the NOG(p=.037). Maximum oxygen intake showed a significant difference according to the time of the main effect test(p=.000). Pre-post analysis within each group were significantly increased in the NOG(p=.000), OG(p=.005). Rate-pressure product at stage 3 showed a significant difference according to the time of the main effect test(p=.045). Pre-post analysis within each group were significantly decreased in the NOG(p=.023). Rate-pressure product at maximal showed a significant difference according to the time of the main effect test(p=.006). Pre-post analysis within each group were significantly increased in the NOG(p=.049), OG(p=.047).

Conclusion: This study confirm that both groups are effective in cardiac rehabilitation programs and their effects are different. Therefore various cardiac rehabilitation programs have to follow-up studies are required in the future.

PE 09-18 9. Therapeutics of Obesity and Metabolic Syndrome

2 cases clinical experience of intragastric balloon for obese patients

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Background: Obesity, a chronic and recurrent disease, requires a multifaceted approach for effective management. Recent advancements in evidence-based care have expanded treatment modalities beyond conventional methods to include pharmacotherapy, endoscopic interventions, and metabolic surgery. In line with these developments, South Korea included the intragastric balloon procedure in its medical coverage in February 2024. This presentation aims to share our institution's experience with the intragastric balloon procedure.

Methods: Patients were selected based on established criteria for the intragastric balloon procedure. Preoperative evaluations included thorough medical history, and nutritional assessment. Detailed procedural steps of the intragastric balloon insertion were recorded.

Results: Case 1 : A 47-year-old male with initial weight of 118.6kg (BMI 38kg/m^2) have been managing only with hypertension medication. He received successful intragastric balloon placement on March 6th, 2024, following a 2kg weight loss through dietary counseling and antiobesity medication. No significant procedural complications noted. Follow-up on May 17th, 2024 revealed weight reduction to 99.1kg (BMI 31.49kg/m^2), achieving total weight loss of 19.5kg (16.44% TWL). Continued antiobesity medication during follow-up.

Case 2: A 40-year-old male with initial weight of 102.4kg (BMI 35kg/m^2) have been managing hypertension, type 2 diabetes, hyperlipidemia, non-alcoholic fatty liver disease with multiple medication. He received the intragastric balloon placement on April 18th, 2024 without prior pharmacotherapy. No significant procedural complications noted. Follow-up on June 5th, 2024 revealed weight reduction to 95.4kg (BMI 29.6kg/m^2), achieving total weight loss of 7kg (6.8% TWL). Initiated antiobesity medication due to slower weight loss progress.

Conclusion: In the short follow-up period, the procedure was safe, and significant weight loss outcomes was observed over three months. Given the multifaceted nature of obesity, various treatment modalities are necessary. Endoscopic therapies, alongside pharmacological and surgical options, are expected to advance as key pillars in the management of obesity.

PE 09-19 9. Therapeutics of Obesity and Metabolic Syndrome

Beneficial Effects of Limosilactobacillus fermentum-derived Metabolites on Hepatic Energy Metabolism in Streptozotocin and High-Fat Diet-induced Type 2 Diabetic Mice

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Background: Hyperglycemia-induced hepatic dysfunction is a major concern in type 2 diabetes mellitus (T2DM), which can be linked to disturbed energy metabolism, excessive lipid accumulation, inflammation, oxidative stress and cell death. Limosilactobacillus fermentum is well known for its potential role as a probiotic with anti-diabetic properties. Recently, numerous studies have reported that the effects of probiotics might stem from their metabolites, which are bioactive compounds produced by probiotics. In this study, we aimed to investigate the effects of L. fermentum-derived whole metabolites (LF) on hepatic energy metabolism in T2DM mice. Furthermore, specific metabolite of L. fermentum was administered as a single compound (LM) in T2DM mice, in order to identify which substance is particularly responsible for the beneficial effects among numerous metabolites derived from L. fermentum.

Method: T2DM was induced by high-fat diet (60% kcal) and streptozotocin (80 mg/kg BW i.p. injection, twice) in male C57BL/6 mice, whereas the mice in the normal control group (NC) were treated with control diet (10% kcal) and vehicle control buffer. After inducing T2DM (fasting blood glucose level ≥ 300 mg/dL), mice were randomly divided into four groups (n = 6-8 per group): diabetic control (DMC), 50 mg/kg BW of whole metabolites derived from L. fermentum (LF), 5 mg/kg BW of LM (LLM), and 20 mg/kg BW of LM (HLM). Fasting blood glucose (FBG) levels and hemoglobin A1c (HbA1c) levels were evaluated. The molecular mechanisms associated with insulin signaling, energy metabolism, inflammation, oxidative stress, and apoptosis were measured by western blot in hepatic tissue.

Results: FBG levels were reduced in LF and HLM group, while HbA1c levels were decreased in all treatment groups compared to those of DMC group. Moreover, increased hepatic lipid accumulation in T2DM mice was normalized by LF and LM administration in a dose-independent manner. At the molecular level, hepatic oxidative stress (catalase, NQO1, SOD2), inflammation (NF-kB) and apoptosis (p53, Bax, Bcl-2, Bcl-xL) were downregulated by both LF and LM supplementation regardless of dose, which could stem from enhanced insulin signaling (p-IRS, p-Akt) and energy metabolism (SIRT1, PGC1α) in T2DM mice.

Conclusion: This study demonstrated that LF and LM attenuated hyperglycemia-induced hepatic dysfunction by activating SIRT1/PGC1α signaling in T2DM mice. Thus, it can be deduced that both whole metabolites (LF) and single metabolite (LM) can exhibit ameliorative effects on T2DM-induced hepatic dysfunction. Taken together, LF and LM might serve as promising therapeutic intervention against T2DM-induced abnormal energy metabolism.

PE 09-20 9. Therapeutics of Obesity and Metabolic Syndrome

Ameliorative Effects of Bioconverted Plant Extract on Renal Inflammation via Regulation of SIRT1/PGC1α Pathway in High-Fat Diet and Streptozotocin-Induced Type 2 Diabetic Mice

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Background: Diabetic nephropathy is one of the diabetic complications and the leading cause of end-stage renal failure. The persistent hyperglycemic condition causes imbalanced energy metabolism and hyperinflammation in the renal tissue. Recently, bioconverted plant extracts have emerged as a novel therapeutic intervention for metabolic diseases including diabetes due to their enhanced bioavailability of its own metabolites. In this study, we aimed to investigate the effects of plant extract bioconverted by Limosilactobacillus fermentum (PBL) on hyperglycemia-induced renal inflammation in type 2 diabetic (T2D) mice.

Methods: T2D was induced by high-fat diet (60% kcal fat) and i.p. injection of streptozotocin (80 mg/kg BW, twice) dissolved in citrate buffer (pH 4.5) in male C57BL/6J mice, whereas normal control mice (NC) were treated with control diet (10% kcal fat) and i.p. injection of citrate buffer (pH 4.5). After inducing diabetes (fasting blood glucose level ≥ 300 mg/dL), diabetic mice were randomly divided into three groups: diabetic control (DMC), 50 mg/kg BW of metabolites of L. fermentum (LF), 50 mg/kg BW of plant extract bioconverted by L. fermentum (PBL) (n=5~6 per group). Treatment was administered via oral gavage for 15 weeks. Fasting blood glucose (FBG) levels were assessed weekly, whereas hemoglobin A1c (HbA1c) measurements and oral glucose tolerance test (OGTT) were conducted at the end of the experiment. Histopathological changes in renal tissue were examined using hematoxylin and eosin staining. The molecular mechanisms related to energy metabolism, inflammation and apoptosis were analyzed using western blotting in renal tissue.

Results: Supplementation of PBL as well as LF ameliorated hyperglycemia demonstrated by the levels of FBG and HbA1c and improved glucose tolerance represented by OGTT. Furthermore, administration of PBL as well as LF decreased glomerular area, indicating that PBL and LF could ameliorate T2D-induced abnormal morphological changes in diabetic renal tissue. However, only PBL supplementation showed increases in the renal protein levels of biomarkers associated with energy metabolism (SIRT1, PGC1α), while attenuating those related to inflammation (NF-κB, NLRP3, ASC, caspase-1, IL-1β) and apoptosis (p53, Bax, caspase-8, 9) in T2D mice.

Conclusion: PBL supplementation ameliorated hyperglycemia-induced renal inflammation via SIRT1/PGC1α pathway in T2D mice. Conclusively, PBL might be a more promising nutraceutical compared to LF in mitigating hyperglycemia-induced renal inflammation in T2D.

PE 09-21 9. Therapeutics of Obesity and Metabolic Syndrome

Human Origin Faecalibacterium prausnitzii Alleviates Symptoms of Obesity and Metabolic Disorders in Mice

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Background: Obesity and related metabolic issues are a growing global health concern. Recently, the discovery of new probiotics with anti-obesity properties has gained interest.

Method: In this study, four Faecalibacterium prausnitzii strains were isolated from healthy human feces and evaluated on a high-fat diet-induced mouse model for 12 weeks.

Results: The F. prausnitzii strains reduced body weight gain, liver and fat weights, and calorie intake while improving lipid and glucose metabolism in the liver and adipose tissue, as evidenced by regulating lipid metabolism-associated gene expression, including ACC1, FAS, SREBP1c, leptin, and adiponectin. Moreover, the F. prausnitzii strains inhibited low-grade inflammation, restored gut integrity, and ameliorated hepatic function and insulin resistance. Interestingly, the F. prausnitzii strains modulated gut and neural hormone secretion and reduced appetite by affecting the gut-brain axis. Supplementation with F. prausnitzii strains noticeably changed the gut microbiota composition.

Conclusion: In summary, the novel isolated F. prausnitzii strains have therapeutic effects on obesity and associated metabolic disorders through modulation of the gut-brain axis. Additionally, the effectiveness of different strains might not be achieved through identical mechanisms. Therefore, the present findings provide a reliable clue for developing novel therapeutic probiotics against obesity and associated metabolic disorders.

PE 09-22 9. Therapeutics of Obesity and Metabolic Syndrome

Associations between Dietary Patterns and Metabolic Syndrome

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Background: Metabolic syndrome (MetS) is a multifactorial cluster of metabolic disorders related to cardiovascular disease and type 2 diabetes mellitus. Diet and dietary patterns are significant factors in the development and management of MetS.

Methods: The associations between dietary patterns (i.e., high-carbohydrate [HCHO], high-fat [HF], and high-protein [HP] diets) and the prevalence of MetS according to sex in Koreans were examined using data from the Korean National Health and Nutrition Examination Survey, collected between 2018 and 2020. The study included data from 9,069 participants (3,777 men and 5,292 women).

Results: The percentage of participants with MetS was significantly higher in the HCHO diet group than in the normal diet, HF, and HP diet groups, and significantly lower in the HF diet group than in the normal diet group for both men and women. Women with HCHO diet were positively associated with elevated blood pressure and triglyceride levels based on a comparison with the normal diet group (p=0.032 and p=0.005, respectively). Men with HF diet were negatively associated with elevated fasting glucose levels based on a comparison with the normal diet group (p=0.014). Our findings showed that HCHO intake was strongly associated with a higher risk of MetS, especially elevated blood pressure and triglyceride levels in women, and HF diet was negatively associated with elevated fasting glucose levels in men.

Conclusion: Further prospective studies of the impact of dietary carbohydrate, fat, and protein proportions on metabolic health are needed. The optimal types and proportions of these dietary components as well as the underlying mechanisms through which suboptimal proportions can lead to MetS, should also be investigated.

PE 09-23 9. Therapeutics of Obesity and Metabolic Syndrome

Efficacy and Safety of WCFA19 (Weissella confusa WIKIM51) in Reducing Body Fat in Overweight and Obese Adults

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Background: WCFA19 (Weissella confusa WIKIM51), found during the fermentation of kimchi, is known for its inhibitory effects on body weight and body fat. This study looked at the impact of WCFA19 isolated from dandelion kimchi on weight loss in overweight and obese adults that are otherwise healthy

Method: This study was conducted as a multicenter, double-blind, randomized, placebo-controlled study with 104 overweight and obese subjects. Subjects were randomized evenly into the test group (WCFA19, 500 mg, n = 40) or control group (n = 34) for 12 weeks from 14 June 2021 to 24 December 2021. Effects were based on DEXA to measure changes in body fat mass and percentage

Results: Among the 74 subjects analyzed, WCFA19 oral supplementation for 12 weeks resulted in a significant decrease in body fat mass of 633.38 ± 1396.17 g ($p = 0.0066$) in overweight and obese individuals in the experimental group. The control group showed an increase of 59.10 ± 1120.57 g ($p = 0.7604$), indicating a statistically significant difference between the two groups. There was also a statistically significant difference ($p = 0.0448$) in the change in body fat percentage, with a decrease of 0.41 ± 1.22% ($p = 0.0424$) in the experimental group and an increase of 0.17 ± 1.21% ($p = 0.4078$) in the control group. No significant adverse events were reported.

Conclusion: Oral supplementation of 500 mg of WCFA19 for 12 weeks is associated with a decrease in body weight, particularly in body fat mass and percentage

Keywords: Lactobacillus fermentum; Weissella confusa WIKIM51; anti-obesity; kimchi; obesity; overweight; probiotics.

PE 09-24 9. Therapeutics of Obesity and Metabolic Syndrome

Selective CYP4A Inhibitor Reveals Potential in Treating Metabolic Dysfunction, Inflammation, and Fibrosis in Metabolic dysfunction-associated fatty liver disease(MAFLD)

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Background: Metabolic dysfunction-associated fatty liver disease (MAFLD) is identified by the presence of fatty liver combined with one or more conditions such as obesity, type Ⅱ diabetes, or another metabolic anomaly. These varied risk profiles impact the determination of the most effective treatment methods. Type Ⅱ diabetes (T2DM), a significant diagnosis for MAFLD, is the most common metabolic disorder. Despite the development of numerous drugs for these conditions, many have adverse side effects like hypoglycemia, weight gain, cardiotoxicity, and hepatotoxicity. Therefore, our goal was to discover new potential drugs without these side effects.

Methods: Through in silico screening, a potent CYP4A inhibitor was identified and subsequently tested in both in vivo and in vitro models. The effects of the inhibitor were quantified using fluorescence imaging for Nile Red staining, glucose uptake, and ROS production. Additionally, changes in gluconeogenesis and lipogenesis were analyzed using Western blotting. In vivo models utilized include the High Fat Diet (HFD) model, db/db mouse model, and ob/ob mouse model.

Results: We found that C1 and C2 reduce ectopic lipid accumulation, aberrant glucose metabolism, endoplasmic reticulum (ER) stress, oxidative stress, and insulin resistance in various in vitro and in vivo models of diabetes. Furthermore, they significantly reduced hepatic inflammation and fibrosis in a mouse model of nonalcoholic steatohepatitis (NASH). Using in vivo models, the effects of drug treatment were evaluated by measuring Food Intake, Glucose Tolerance Testing (GTT), and Insulin Tolerance Testing (ITT).

Conclusion: Based on these results, our study highlights C1 and C2 as promising CYP4A inhibitors with a diverse range of beneficial effects in both diabetes and NASH models, making them valuable candidates for further exploration in addressing metabolic dysfunction-associated fatty liver disease (MAFLD).

PE 09-25 9. Therapeutics of Obesity and Metabolic Syndrome

A Novel CYP4A inhibitors regulate Metabolic dysfunction-associated fatty liver disease (MAFLD)

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Background: Metabolic dysfunction-associated fatty liver disease(MAFLD) is contains a range of fatty liver changes from simple steatosis to Steatohepatitis and linked to metabolic syndrome. Recently, patients with type 2 diabetes mellitus(T2DM) has been proposed as a risk factor for the progressive form of MAFLD. Also, hepatic steatosis induced by lipid accumulation, is resulted in the development insulin resistance and T2DM. Recent drugs for hepatic steatosis and T2DM mostly target insulin but, it has lots of side effect like pancreas dysfunction. Therefore, it is essential to develop new therapeutic drugs to directly improve liver injury. In the previous study, Cytochrome P450 4A(CYP4A), known as an enzyme in lipid metabolism, were suggested a target of MAFLD.

Method: For the T2DM animal model, 8-week-old male C57BL/6N mice were fed an NCD or HFD (60% of energy derived from fat, Research Diets Inc, NJ, USA) for 12 weeks. C57BL/KsJ-db/db mice were used as a genetic model of T2DM. For the NASH model, 6-week-old male ob/ob mice were used and divided into groups; a methionine-choline deficient (MCD) diet (#A02082002B; Research Diets Inc, NJ, USA) to induce NASH and the control group with a standard diet. Each CYP4A inhibitors (5mg/kg/day) were injected intraperitoneally for 2 or 4 weeks.

Results: Targeting CYP4A binding site, drug candidates were found through in silico screening. The drug candidates were selected by CYP4A enzyme activity assay and we investigated their effect on hepatic steatosis and T2DM induced by palmitate and ER stress inducers in HepG2 cells. In addition, in T2DM mouse model, they improved hyperglycemia, hyperinsulinemia and hepatic steatosis as well. Then, it reduced the expression of ER stress and apoptosis markers in liver tissues. Also, they had the rescue effects on the MASH mouse model.

Conclusion: Together, novel CYP4A inhibitors that we discovered are effective for T2DM with MAFLD treatment.

PE 09-26 9. Therapeutics of Obesity and Metabolic Syndrome

Global Trends in the Clinical Development of MASH Treatment

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Background: Metabolic Dysfunction-Associated Steatohepatitis (MASH), previously known as Non-Alcoholic Steatohepatitis (NASH), has emerged as a significant global health concern. As the prevalence of obesity and metabolic syndrome continues to rise worldwide, so does the incidence of MASH. This study aimed to analyze current trends in the clinical development of MASH treatments globally, providing insights into the evolving therapeutic landscape.

Methods: We conducted a comprehensive review of ongoing and completed clinical trials for MASH treatments registered in major international databases, including ClinicalTrials.gov, EU Clinical Trials Register, and Japan's UMIN Clinical Trials Registry, from January 2010 to April 2024. Data were analyzed for trends in therapeutic approaches, geographic distribution, trial phases, and sponsor types. Additionally, we examined publication patterns in peer-reviewed journals to assess the dissemination of trial results.

Results: The analysis revealed a significant increase in MASH-focused clinical trials over the past decade, with a 300% rise in registered studies. Novel therapeutic approaches, including metabolic modulators, anti-fibrotic agents, and combination therapies, dominated the pipeline. North America and Europe led in trial numbers, accounting for 65% of all studies, but Asia showed the fastest growth rate, with a 450% increase since 2010. Phase II trials were most prevalent (45%), indicating a maturing field approaching later-stage development. Notably, there was a shift towards more industry-sponsored trials, now comprising 70% of all studies compared to 50% in 2010. Publication rates of trial results improved, with 60% of completed trials having published outcomes within two years of completion.

Conclusion: The clinical development landscape for MASH treatments is rapidly evolving, with diverse therapeutic strategies being explored globally. While significant progress has been made, particularly in advancing novel compounds to mid-stage trials, there remains a critical need for effective therapies to address this growing health burden. The increased industry involvement and improved result dissemination suggest a maturing field, potentially leading to new treatment options in the near future.

PE 09-27 9. Therapeutics of Obesity and Metabolic Syndrome

Identification of Potential Bioactive Phytochemicals for the Inhibition of Platelet-Derived Growth Factor Receptor β: Targeting Obesity and Metabolic Syndrome

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Background: Platelet-derived growth factor receptor beta (PDGFRβ) belongs to the receptor tyrosine kinase (RTK) protein family and affects glucose metabolism by modulating the function of insulin-responsive tissues. PDGFR-β signaling is crucial for the differentiation of precursor cells into adipocytes. It influences the development and expansion of adipose tissue by modulating the proliferation and differentiation of preadipocytes. Given its involvement in key processes related to obesity and metabolic syndrome, PDGFR-β is being investigated as a potential therapeutic target.

Method: This study aimed to identify potential PDGFRβ inhibitors through virtual screening of phy-tochemicals extracted from the IMPPAT database. The initial assessment involved applying the Lipinski rule-of-five to evaluate the physicochemical properties of the molecules. Subsequently, a comprehensive analysis encompassing binding affinity assessment, PAINS filter application, ADMET profiling, and PASS prediction was conducted.

Results: We identified Genostrychnine and Chelidonine exhibited remarkable affinity and specificity in their interactions with the PDGFRβ kinase domain. To gain insights into these interactions' temporal evolution and dynamics, all-atom molecular dynamics (MD) simulations and essential dynamics analysis were employed. These computational techniques provided valuable insights into the behavior and stability of the PDGFRβ-ligand complexes over time. Based on our findings, we propose that Genostrychnine and Chelidonine merit further investigation through in vivo and in vitro studies to evaluate PDGFR-β signaling to improve insulin sensitivity, reduce inflammation, and promote healthy adipose tissue function.

Conclusion: In conclusion, this study underscores the potential of Genostrychnine and Chelidonine as promising PDGFRβ inhibitors. Further experimental investigations are required to validate their efficacy and assess their therapeutic potential for PDGFRβ-related diseases, with a particular focus on obesity and metabolic syndrome management.

PE 09-28 9. Therapeutics of Obesity and Metabolic Syndrome

Time restricted feeding prevents the loss of rhythmicity in high fat diet induced obesity

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Background: Obesity is the most common problem in developing countries, which are the risk factors for the pathogenesis of diabetes, hypertension, cancer etc. It can be managed or cured by lifestyle modification. Time Restricted Feeding (TRF) is very important in today's scenario as changing the life pattern may protect from various diseases and improve quality of life.

Methods: Total 15 Wistar rats were included in our study and divided into two groups. Control group and High Fat diet (HFD) group which consist of six rats and nine rats respectively. HFD group was fed fatty diet for two months to developed obesity. These rats were shifted to TRF with HFD for three months, after which they were again put back on ad lib (24 hr feeding). These rats were sacrificed and samples collected. Body weight was measured monthly, with blood glucose, Insulin and lipid profile estimated after sacrifice.

Results: The body weight of HFD group were significantly increased and TRF with chow diet were significantly decreased as compared to control rats (p=0.0263) and (p= 0.0054) respectively. The level of HDL was reduced in rats fed with HFD whereas total cholesterol, TG a LDL were increased. TRF intervention with HFD diet reduced body weight, blood glucose level, TG and LDL and elevated the level of insulin, total cholesterol and HDL. Per1 and Bmal1 gene were up regulated in HFD group and after TRF intervention had reduced mRNA expression.

Conclusion: TRF is a potential behavioural intervention which is easily adaptable in lifestyle modification. TRF intervention can prevent and treat obesity and metabolic disorders.

PE 09-29 9. Therapeutics of Obesity and Metabolic Syndrome

Anti-atherosclerosis effect of Columbianadin against High Fat Diet induced atherosclerosis in rats via alteration of hyperlipidemia, inflammation and oxidative stress

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Background: Atherosclerosis is a medical condition characterized by the buildup of plaque inside the arteries. It is a progressive disease that typically develops over many years, and it can affect arteries throughout the body. In this study, we scrutinized the anti-atherosclerosis effect of columbianadin against High fat diet (HFD) induced atherosclerosis in rats.

Method: HFD were used for the induction of atherosclerosis in rats for 10 weeks and rats were received the oral administration of columbianadin (5, 10 and 15 mg/kg), respectively. The body weight, liver weight, lipid, antioxidant, cytokines, inflammatory and atherogenic index parameters were estimated. The mRNA expression of vascular cell adhesion molecule 1 (VCAM-1), Monocyte Chemoattractant Protein-1 (MCP-1) and Intercellular adhesion molecule-1 (ICAM1) were estimated.

Results: Columbianadin significantly (P<0.001) reduced the body weight and altered the level of organs such as liver and heart. Columbianadin significantly (P<0.001) altered the level of total cholesterol (TC), high density lipoprotein (HDL), triglyceride (TG), low density lipoprotein (LDL), very low-density lipoprotein (VLDL) and free fatty acids (FFAs), respectively. Columbianadin significantly (P<0.001) decreased the level of creatine kinase-MB (CK-MB), serum creatine kinase (CK), lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) levels. Columbianadin significantly altered the level of superoxide dismutase (SOD), malonaldehyde (MDA), catalase (CAT), glutathione (GSH), glutathione peroxidase (GPx) and glutathione S-transferase (GST); suppressed the level of tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β) interleukin-6 (IL-6) and interleukin-17 (IL-17); inflammatory parameters like prostaglandin, cyclooxygenase-2 and inducible nitric oxide synthase. Columbianadin also down-regulated the expression of TNF-α, IL-1β, IL-6, IL-17, ICAM1, VCAM-1 and MCP-1.

Conclusion: Collectively, we can say that Columbianadin exhibited the anti-atherosclerosis effect against HFD induced rats via alteration of hyperlipidemia, inflammation and oxidative stress.

Conclusion: Atherosclerosis, Columbianadin, Inflammation, Hyperlipidemia.

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Crocetin-Dextrin nano-formulation attenuates obesity-induced cardiac hypertrophy by alteration JAK2/STAT3-associated inflammation and oxidative stress

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Background: Cardiac hypertrophy has emerged as an independent and predictive risk factor for adverse cardiovascular events. Chronic low-grade inflammation and oxidative stress play a crucial role in the expansion obesity induced cardiac hypertrophy. In this experimental study, we fabricate the crocetin-dextrin nano-formulation (CDNF) and scrutinized the protective effect against obesity-induced cardiac hypertrophy by alteration JAK2/STAT3-associated inflammation and oxidative stress.

Methods: Crocetin-Dextrin nano-formulation was prepared the aqueous nano-emulsion of crocetin and dextrin. The primary cardiomyocytes and H9c2 cells were used for the invitro model. Male mice were fed with normal chow or high fat diet for 22 weeks for the induction of obesity and estimated the body weight, water and food intake. Oxidative stress parameters, cytokines, inflammatory and apoptosis parameters were estimated. The mRNA expression of Nppa, Mynh7 and Nppb were also estimated.

Results: Crocetin knockdown in H9c2 cells exacerbated PA-induced inflammatory responses and increased NOX4 expression. Conversely, pretreatment with exogenous crocetin mitigated PA-induced cardiomyocyte hypertrophy, reduced the up-regulation of inflammatory cytokines, and alleviated oxidative stress in both primary cardiomyocytes and H9c2 cells. CD-NF remarkably suppressed the body weight which was boosted in HFD induced obesity rodent. CD-NF altered the level of oxidative stress parameters like SOD, CAT, GSH, GPx; cytokines parameters viz., TNF-α, IL-1β, Il-6, IL-10, IL-17, IL-18; inflammatory parameters such as COX-2, iNOS, VEGF, NF-κB, respectively. CD-NF treatment significantly boosted the mRNA expression fo Nppb, Myh7 and Nppa. CD-NF treatment also altered the mRNA expression of JAK2 and STAT3.

Conclusion: We can conclude that CD-NF treatment exhibited the protective effect against obesity-induced cardiac hypertrophy by alteration JAK2/STAT3-associated inflammation.

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ANALYSIS OF FENUGREEK SEED EXTRACTS ON GLYCOSYLATED HAEMOGLOBIN IN PATIENTS WITH TYPE 2 DIABETES MILLITUS

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Background: The present study was planned to evaluate the effect of fenugreek seed extract on fasting & post-prandial blood glucose levels along with its effect on serum C-peptide levels & HbA1c levels.

Method: Both male & female participants with age of 25-60 years were recruited for the study. Patients with type-2 diabetes mellitus for <5 years were preferred for the evaluation. Patients were required to be on oral anti-diabetic treatment with no change in the treatment from last one month. those patients were selected who had HbA1c >7.5% & reported to have fasting plasma glucose not exceeding 180 mg/dL. Patient reported with diabetes other than type-2 diabetes mellitus were not included in the study.

Results: fenugreek seed extract caused significant change in blood sugar levels as compared to Placebo group. The decrease in sugar levels in Placebo group was due to concomitant anti-diabetic therapy. A significant decrease in HbA1c levels was observed as compared to respective baseline value. fenugreek seed extract caused significant reduction in fasting plasma sugar levels, reduction PP plasma sugar levels. fenugreek seed extract -treated group also showed reduction in concomitant anti-diabetic therapy. It was also found to be safe in patients with type-2 diabetes.

Conclusion: fenugreek seed extract when given as "an add on" to concurrent therapy of type-2 diabetes, was synergistic and effective in better management of type-2 diabetic patients, as compared to Placebo group, in which patients were on their routine allopathic diabetic medicine. fenugreek seed extract was safe in treating patients with type-2 diabetes mellitus.

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Potential Therapeutic Effects of Polysaccharide Derived from Ziziphus jujuba Mill on Nonalcoholic Fatty Liver Disease by in vitro and in vivo Approach

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Background: Non-alcoholic fatty liver disease (NAFLD) is a prevalent global health issue characterized by excessive fat accumulation in the liver, often leads to complications like obesity and diabetes, and in more severe cases, results in hepatic fibrosis, which involves excessive extracellular matrix protein deposition. Jujube (Ziziphus jujuba Mill.), a traditional food with recognized medicinal and nutritional value worldwide, has been found to exhibit a range of health-promoting effects. This study aimed to evaluate the anti-NAFLD effects of jujube derived polysaccharides (JP) using in vitro and in vivo models.

Methods: TGF-β1 (transforming growth factor- β) was used to induce fibrosis in human hepatic stellate cell line LX-2, followed by treatment with JP. Cell viability was assessed using the MTT assay, fibrosis-related gene expression was analyzed by RT-PCR, and protein levels were measured by Western blotting. Five-week-old male C57BL/6 mice were randomly divided into four groups: normal diet (ND), ND with 5% JP (N/JP), high-fat diet with high-fructose drinking water (HFHFD), and HFHFD with 5% JP (H/JP) for 17 weeks. Finally, basic parameters including body weight (B/W) and total energy intake were measured, body composition and liver histology were investigated.

Results: JP significantly attenuated liver fibrosis by decreasing the expression of fibrotic markers such as Tgf-β, Collagen Iα, Pdgfb and Timp1 through regulation of the TGF-β-mediated SMAD2/3/4 pathway in LX2 cells. In the NAFLD mouse model, JP supplementation significantly reduced B/W gain in the N/JP group compared to the ND group, while no significant difference was observed between the HFHFD and H/JP groups. Nevertheless, fat mass and overall adiposity were significantly decreased with JP supplementation compared to the HFHFD group, without affecting lean mass. Hematoxylin and eosin (H&E) staining of liver sections revealed substantial reductions in hepatic steatosis, inflammatory infiltration and liver cell injury in the H/JP group compared to the HFHFD group.

Conclusion: Based on the current data, JP exhibits protective effects against NAFLD in both in vitro and in vivo models by reducing fat accumulation, inflammation, and suppressing fibrosis, suggesting its potential therapeutic value for managing NAFLD. We are conducting tissue RT-PCR and multi-omics analyses, including microbiota profiling, liver RNA sequencing, and metabolite profiling to further elucidate the correlation and mechanisms by which JP exerts its anti-NAFLD effects.

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UPSPS's Role in Alleviating Obesity and Metabolic Syndrome: Transforming Seaweed Byproducts into Therapeutics

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Background: Undaria pinnatifida (UP), a brown seaweed (Phaeophycean), comprises various parts including a blade (lamina), midrib, sporophyll, and root-like structures. While UP is extensively studied for its nutritional and bioactive properties, its sporophylls, referred to as Undaria pinnatifida sporophyll (UPS), are often deemed a byproduct in the seaweed food industry. This study focuses on the upcycling of these byproducts.

Method: In this study, we unraveled UPS-derived Polysaccharide (UPSPS)'s protective mechanism on intestinal barrier inflammation in an intestine-mimicked co-culture model, additionally exploring its impact on the pathophysiology of a diet-induced obese (DIO) model and characterizing UPSPS's structure.

Results: UPSPS alleviated inflammation and enhanced gut permeability in the inflamed co-culture model by decreasing nitric oxide production and pro-inflammatory gene expression. In DIO mice, UPSPS administration resulted in significant reductions in body weight, liver and adipose tissue weight, blood glucose levels, triglyceride levels, and the number of crown-like structures in adipose tissue. Furthermore, UPSPS ameliorated obesity-induced dysbiosis and increased short-chain fatty acid levels. Structural analysis revealed that the major monosaccharides constituting UPSPS were identified as fucose (29.11%), galactose (27.52%), glucuronic acid (24.82%), mannuronic acid (7.00%), guluronic acid (6.33%), and mannose (2.02%). The polysaccharide has a molar mass of 2,496 Da and features a three-dimensional structure characterized as a long-chain polymer with a helical and layered spatial configuration.

Conclusion: UPSPS shows considerable promise in treating obese-metabolic syndrome, as confirmed through intestine-mimicked co-culture and DIO models. It effectively reduces inflammation, enhances gut permeability, and mitigates obesity-related metabolic disturbances. Additionally, advanced structural characterization techniques have uncovered the complex structure of UPSPS. Consequently, this study highlights the value of upcycling seaweed byproducts and facilitates in-depth application studies for treating metabolic syndrome and obesity-related disorders.

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Effects of Jeju Purple Jerusalem Artichoke Extracts on Adipocyte Differentiation and Immune Cell Response

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Background: This study investigates the dual role of Jeju purple Jerusalem artichoke extracts (PJAE) on both adipogenesis in 3T3-L1 adipocytes and splenocytes proliferation. Understanding how different compounds affect these processes can provide insights into its potential therapeutic applications.

Methods: Cell viability was assessed with the MTT assay. Anti-adipogenic effects of PJAE were measured using Nile red staining to quantify intracellular lipid accumulation. Additionally, splenocytes were treated with PJAE, and their proliferation was evaluated with the MTT assay in the presence and absence of Concanavalin A (ConA) and Phorbol 12-myristate 13-acetate (PMA)/Ionomycin.

Results: PJAE exhibited no cytotoxic effects on 3T3-L1 cells at concentrations up to 125 μg/mL and significantly diminished intracellular lipid accumulation in 3T3-L1 adipocytes at concentrations of 62.5 and 125 μg/mL compared to the control. While PJAE alone increased cell proliferation in splenocytes, its co-treatment with ConA or PMA/Ionomycin led to a concentration-dependent decrease in cell proliferation at higher concentrations (500 and 1000 μg/mL).

Conclusion: PJAE exhibited cell type-specific effects as not only significantly reducing lipid accumulation in 3T3-L1 adipocytes without cytotoxicity but also modulating splenocyte proliferation by enhancing proliferation alone while inhibiting proliferation when co-treated with ConA or PMA/Ionomycin. Thus, dual bioactivity of PJAE could be harnessed for the treatment of obesity and related metabolic disorders as well as for the potential role in immune modulation. Future studies are warranted to further elucidate the mechanisms underlying these effects and to explore their potential clinical applications.

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Maternal high-fat diet during pregnancy and lactation causes impairments in aminergic system and motor functions in rat offspring: protective effect of calcium

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Background: The present study aimed to examine the therapeutic efficacy of calcium (Ca) supplementation against the maternal high fat (HF) diet-induced perturbations in rat offspring's neurochemical and behavioral functions.

Method: To do this, we fed mother rats with HF and control diets from gestation day (GD) 6 to postnatal day (PND) 21 and stopped at weaning. We then supplemented Ca as 0.02% in drinking water to the HF diet-fed dams from GD 6 to PND 21.

Results: Our findings showed increased synaptosomal dopamine, epinephrine, and norepinephrine levels in the cortex, cerebellum, and hippocampus at PND 21, PND 45, and PND 60 age groups of offspring of HF diet-fed rats. In contrast, the synaptosomal serotonin levels and mitochondrial monoamine oxidase activity (MAO) decreased. Significant deficits were also observed in the open field and exploratory behaviors in the offspring of HF diet-fed rats. However, supplementation of calcium showed reversal effects against HF diet-induced alterations in the aminergic system and behavioral functions in HF diet-fed rats' offspring. The alterations in different brain regions indicate that the HF diet influences the aminergic system in a brain region-specific manner.

Conclusion: Our findings demonstrate that maternal HF diet consumption leads to persistent impairments in the aminergic system in the offspring, which may be associated with behavioral deficits, suggesting the therapeutic efficacy of calcium supplementation against HF diet-induced behavioral disorders.