The roles of purple sweet potato anthocyanins in optimizing dietary intervention of metabolic dysfunction-associated fatty liver disease

Syuma Adhy Awan¹,², I Dewa Nyoman Wibawa³, I Made Jawa³, I Wayan Weta¹, Gde Ngurah Indraguna Pinatih¹*, Agung Nova Mahendra⁴

ABSTRACT

Metabolic-associated fatty liver disease (MAFLD) is a multifactorial metabolic disorder with complex pathogenesis and a broad spectrum of disease. It is characterized by the accumulation of triglycerides (TG) in hepatocytes, which are associated with hepatic steatosis. Purple sweet potato (Ipomoea batatas L.) (PSP) tuber, is rich in anthocyanin contents. This review aims to discuss recent findings on the effects of purple sweet potato tubers and its potential therapeutic action on MAFLD. In various in vivo studies and limited clinical trials on patients, purple sweet potatoes have been shown to be beneficial not only in lipid metabolism but also in reducing liver fat deposition and insulin resistance. In addition to antioxidant, anti-inflammatory, and anti-hyperlipidemic effects, anthocyanins can be considered as important adjuvant therapeutic agents in the attenuation of inflammation, free radicals, insulin resistance, and hepatocyte injury.

Keywords: anthocyanins, purple sweet potato, dietary intervention, MAFLD.


INTRODUCTION

Metabolic-associated fatty liver disease, or metabolic dysfunction-associated fatty liver disease (MAFLD), was previously called non-alcoholic fatty liver disease (NAFLD).⁵ MAFLD is expected to become an economic burden in health control and prevention by 2030,⁵,⁶ as well as causing an increase in mortality among chronic liver disease cases.⁴ Currently, there is no single drug therapy that can effectively cure MAFLD.⁵,⁶ Several potential monotherapy agents have been studied widely, but have not provided an optimal response to the improvement of steatosis and its advanced forms.⁷-⁹ MAFLD management is aimed to reduce steatosis, liver injury, and sequelae due to metabolic and cardiovascular disorders.¹⁰

European Association for the Study of the Liver (EASL) guidelines with the European Association for the Study of Diabetes (EASD), the European Association for the Study of Obesity (EASO), the Latin American Association for the Study of the Liver (ALEH) and the American Association of Clinical Endocrinology (AACE) recommend the implementation of weight loss dietary interventions as a main line of fatty liver therapy.¹¹-¹³ However, its success is challenging because it is difficult to achieve and maintain weight loss.¹⁴

Dietary interventions are carried out through nutritional interventions, such as calorie restriction and modification of macronutrient composition (dietary restriction). Another dietary intervention is intermittent fasting.¹⁵-¹⁷ Calorie restriction can be achieved by reducing the total calorie intake to between 500 and 1000 kcal per day or by reducing the total daily calorie intake to around 1500-1600 kcal. Modification of the macronutrient composition is carried out by reducing the composition of carbohydrates (low carbohydrate diet) to less than 45%, or 130 grams, of total daily calories.¹⁸

The mechanism for the development of MAFLD involves many factors (the multiple-hit theory); chronic inflammation, excess free radicals, and insulin resistance are the main factors triggering the hepatic accumulation of fats and the development of MAFLD.¹⁹-²⁰ Several nutraceuticals such as anthocyanins which belong to polyphenol group have roles as antioxidants and anti-inflammatory agents in metabolic and chronic diseases,²¹-²³ and are expected to optimize the management and prevention of fatty liver disease.
Hepatic Steatosis
MAFLD is an etiology of chronic liver disease in both developed and developing countries, along with the increasing epidemic of obesity. The incidence in Western countries is found to range from 47–52% in high-risk groups such as those diagnosed with diabetes mellitus and obesity. The prevalence of MAFLD increases twofold with obesity in developing countries. In Asia, the prevalence of MAFLD is greater than 50% in diabetic patients and 50.7% in overweight and obese individuals. Once steatosis develops, the liver becomes more sensitive to various inflammatory stimuli, which can trigger non-alcoholic steatohepatitis (NASH). In the general population, the development of NAFL to NASH is relatively low, around 2-5%, but increases sharply > 25% in obesity, even increasing 70% to 90% in morbid obesity accompanied by type 2 diabetes mellitus. Patients with NASH may develop advanced fibrosis, cirrhosis and hepatocellular carcinoma.

MAFLD is defined as a clinical-pathological syndrome with a broad spectrum of liver damage and no history of excessive alcohol consumption. The spectrum of pathology ranges from benign steatosis (Benign, NAFL, Simple Steatosis), which is characterized by accumulation of triglycerides (TG) in hepatocytes, to non-alcoholic steatohepatitis (NASH). MAFLD was previously classified as simple macrovesicular steatosis (NAFL) if 5-10% intrahepatic fat accumulation was observed without changes in liver cell shape or hepatocyte injury, non-alcoholic steatohepatitis (NASH) or non-alcoholic steatohepatitis (SHNA) if additional liver injury was observed, and lobular inflammation with and without fibrosis. The most recent definition of MAFLD emphasizes the role of metabolic dysfuction as a major trigger for causative factors and overrides alcohol intake and other chronic liver diseases. The most recent criteria for the diagnosis of MAFLD are based on histology (biopsy), imaging, or blood biomarker evidence of fat accumulation in the liver (hepatic steatosis), plus one of the following three criteria: overweight or obesity, diabetes mellitus type 2 (DMT2), or evidence of dysregulation metabolic disorder defined by the presence of at least two metabolic risk abnormalities in non-obese (lean) individuals. Hepatic steatosis is assessed based on the percentage of fat in the hepatocytes. grade 0 (healthy, 5%), grade 1 (mild, 5%–33%), grade 2 (moderate, 34%–66%), and grade 3 (severe, >66%).

Natural History of MAFLD Development
MAFLD is a multifactorial metabolic disorder with complex pathogenesis and a broad spectrum of disease. The mechanism for the development of MAFLD is very dynamic, involving many factors (the multiple-hit theory). In obesity, mild degrees of chronic inflammation and oxidative stress are the initial molecular mechanisms of insulin resistance (IR) and the development of MAFLD. Insulin resistance causes an imbalance in lipid metabolism, resulting in increased hepatic glucose production and excess de novo lipogenesis (DNL), which worsens hepatic and systemic insulin resistance. Insulin resistance increases the accumulation of liver lipids to produce reactive oxygen species (ROS), triggering oxidative stress and increasing inflammation, depleting reserves of antioxidant molecules, and inhibiting the activity of antioxidant enzyme defenses such as glutathione (GSH) and superoxide dismutase (SOD). ROS and sustained inflammation result in hepatocyte injury, damaging cell membranes and liver cell DNA proteins, resulting in lipid peroxidation products such as malondialdehyde (MDA), mitochondrial dysfunction, and liver cell death. The bilateral relationship between hepatic steatosis and IR creates a vicious circle that contributes to the development of the disease, although it is still unclear whether steatosis is a cause or a consequence of IR.

Liver fat accumulation in obesity due to insulin resistance is the main cause of MAFLD, but the prevalence in non-obese or normal-weight individuals (lean) is quite large, ranging from 5–27% in the Asian population and 5–45% in non-Asian. Lean MAFLDs have metabolic abnormalities that have been previously linked to obesity. Ethnicity may be another factor in the development of MAFLD, although the proportion of people with and without fibrosis does not differ significantly. The prevalence of steatohepatitis in the Hispanic population with or without diabetes is the highest. Several genetic variants associated with hepatocyte triglyceride metabolism, such as patatin-like phospholipase domain-containing 3 (PNPLA3), increased LDL secretion, transmembrane 6 superfamily member 2 (TM6SF2), glucokinase regulator (GCKR), or hepatic acyl phosphatidylinositol chain remodeling membrane-bound O-domain-containing acyltransferase. Other factors that cause hepatic steatosis are drug use, total parenteral nutrition, and other health problems.

Vicious Cycle of Metabolic Pathways: Obesity, Inflammation, Insulin Resistance, De Novo Lipogenesis, and MAFLD Hepatic Lipotoxicity
Adipose tissue plays a role in energy homeostasis and inflammation, through the activation of the inflammatory pathways c-Jun N-terminal kinase (c-JNK) and nuclear factor kappa-B (NF-kB). The main mechanism of pathogenesis of steatosis or obesity of the liver involves an imbalance between lipogenesis, lipopogenesis de novo, lipolysis and a decrease in β-oxidation in liver cells. Disregulation of free fatty acid metabolism (FFA) between lipolysis and absorption in subcutaneous adipose tissue
leads to accumulation of ectopic fat (heart and skeletal muscles), hypoxia and chaos (dysfunction) of adipose tissue.\textsuperscript{60,61} Fat dysfunction accompanied by spillover of triacylglycerol, increased FFA circulation, leptin and decreased adiponectin forming intrahepatic fat accumulation (lipotoxicity of the liver) resulting in multi-organ insulin resistance.\textsuperscript{62–64}

Insufficient insulin brings excess circulating blood sugar into cells, further exacerbating the inflammatory process through activation of the immune response.\textsuperscript{65} Accumulation of TG triglycerides and hepatocyte cholesterol (lipid droplets) is a physiological protective response to lipotoxicity (simple steatosis).\textsuperscript{65,66} The development of NASH is triggered by the accumulation of metabolic products between fatty acids such as DAG and ceramide, which stimulate chronic inflammation and oxidative stress.\textsuperscript{67} Circulating FFAs also acts as a ligand for the TLR4 complex, known also to be associated with NLRP3 activation, which facilitate the cultivation of pro-inflammatory milieu.\textsuperscript{68}

Decreased adiponectin secretion, along with pro-inflammatory immune cells such as interferon (IFN)-γ+, type-1 helper T cells and CD8+ T cells contribute to insulin resistance.\textsuperscript{69–73} Involvement of immune cells in the inflammatory process is mediated by c-JNK and Inhibitor of kappa-B kinase beta (IκKβ) through NF-κB activation resulting in excessive production of pro-inflammatory cytokines such as TNF-α and IL-6.\textsuperscript{72} An increase in hepatic inflammatory cytokines due to an immune response ultimately triggers chronic inflammation and alters the histology of hepatocytes, establishing a characteristic histological marker of NASH.\textsuperscript{97,73}

Excess triglyceride production also reduces the synthesis of glucose transporters to the plasma membrane exacerbating insulin resistance.\textsuperscript{74} Increasing the amount of glucose and insulin induces the expression and activation of sterol regulatory element-binding protein 1 (SREBP-1c) and carbohydrate-response element-binding protein (ChREBP) in the liver, increases the expression of several lipogenic enzymes and increases hepatic FFA synthesis. FFA production in mitochondria activates peroxisome proliferator-activated receptors alpha (PPAR-α) via carnitine palmitoyltransferase-1 (CPT1), increasing the β-oxidation enzyme. Although mitochondrial β-oxidation is increased in obesity, eventually they are unable or exhausted to use all the FFAs that enter the liver due to insulin resistance.\textsuperscript{75,76} Increased saturated fat intake, de novo lipogenesis and lipolysis due to insulin resistance are the main factors, rather than simply due to the accumulation of triglycerides alone in simple steatosis.\textsuperscript{77} If this process continues to accommodate the formation of lipid peroxidation, it results in the release of hydroxoy free radicals, which injure hepatocytes by recruiting necro-inflammatory mediators, triggering a more severe inflammatory process and liver cell death.\textsuperscript{78,79}

Dysbiosis and impaired intestinal permeability on the other hand have an important role in the malfunctioning of the gut–liver axis, through activation of liver cell macrophages contributing to the development of low-grade chronic inflammation.\textsuperscript{80,81} In MAFLD, macrophage infiltration promotes the polarization of anti-inflammatory M2 to proinflammatory M1 phenotype.\textsuperscript{80,82}

The cross-talk of inflammatory response between obesity, insulin resistance and fatty liver is like a vicious cycle (depicted as Figure 1).

Figure 1. Proposed scheme of “vicious cycle” in MAFLD pathogenesis. Black arrows signify the main pathway, while red arrows signify additional inflammation pathway (modified from Polyzos et al and Nassir).\textsuperscript{66,83}

Current Diagnostic Criteria of MAFLD

The current definition of MAFLD emphasizes the role of metabolic dysfunction as a major causative factor and overrides alcohol intake and other chronic liver diseases. The latest proposed criteria for a positive diagnosis of MAFLD are based on histological (biopsy), imaging or blood biomarker evidence of fat accumulation in the liver (hepatic steatosis) plus one of the following three criteria, namely overweight or obesity, diabetes mellitus 2 (DMT2), or evidence of metabolic dysregulation as defined by the presence of at least two metabolic risk abnormalities in a non-obese (lean).\textsuperscript{40} In the case of non-obese/thin MAFLD there must be at least 2 abnormal metabolic risks including:\textsuperscript{84}

1. Waist circumference ≥ 102/88 cm in male/female Asian (or ≥ 90/80 in male/female Caucasian)
2. Blood pressure ≥ 130/83 mmHg or the use of specific drugs
3. Triglyceride level ≥ 150 mg/dL or the use of specific drugs

4. HDL level <40mg/dL in male and <50mg/dL in female or the use of specific drugs  
5. Prediabetes (fasting blood glucose level 100-125 mg/dL, or 2-hour postprandial blood glucose level jam 140-199 mg/dL, or HbA1c level that fall in the range of 5.7%-6.4%)  
6. Homeostasis model assessment of insulin resistance score ≥ 2.5  
7. Plasma high-sensitivity CRP >2mg/dL  

Management of MAFLD  
Short-term management of MAFLD aims to reduce steatosis, liver injury and improve the sequelae of metabolic and cardiovascular risks.5,10 Several potential monotherapy drug agents have been widely noted but have not provided optimal response to MAFLD and its advanced forms.5,7-9 Currently, there is no single intervention that has been proven to be fully effective in healing liver steatosis, and to optimize it, it is recommended to provide combination treatment.65 Some of the recommended drugs, if they work affect various pathways of disease pathogenesis, such as increasing insulin sensitivity, lowering lipid levels, as antioxidants and cytoprotective.86  

All MAFLD therapy guidelines “EASL-EASD-EASO Clinical Practice Guidelines for the management of nonalcoholic fatty liver disease” by “The European Association for the Study of The Liver (EASL)” in 2016; “Nonalcoholic fatty liver disease (NAFLD): Assessment and management by the National Institute for Health and Care Excellence (NICE)” in 2016; “AsiaPacific Working Party on NonAlcoholic Fatty Liver Disease guidelines” in 2017; “Italian Association for the Study of the Liver (AISF)”: “AISF position paper on nonalcoholic fatty liver disease (NAFLD): Updates and future directions” in 2017; “The diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance From the American Association for the Study of Liver Diseases” in 2018, and the American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings recommends lifestyle modifications for weight loss through dietary interventions (Dietary Interventions) and increased regular physical activity (exercises) as the main foundations of disease management.13 Medical and surgical interventions serve only as second-line or adjuvant treatments.87-90  

Dietary Interventions of MAFLD  
The role of dietary intervention in MAFLD is growing and focuses on low-carbohydrate diets and intermittent fasting.91-94 Dietary interventions were categorized based on modification of food composition (meal content) through nutrition interventions and based on meal timing through fasting interventions. Nutritional interventions (meal content) are carried out through various regimens: 1. Caloric restriction (CR), by reducing daily calorie intake by 15 to 40% without becoming malnourished. 2. Dietary restriction (DR), by limiting certain macronutrient sources, (e.g., meat protein). 3. Ketogenic diet (KD), by limiting carbohydrate sources to less than 10-15%. 4. Fasting-mimicking diet (FMD), reducing intake calories (~30% of energy needs) for five consecutive days before returning to normal eating cycles, FMD is done once a month or every 3 to 4 months per year.96  

Intervention fasting (meal timing) consists of 1. Periodic fasting (PF), fasting ≥ 2 times in a row followed by normal daily energy intake for at least 1 week, and 2. Intermittent fasting (IF) or intermittent fasting. IF is carried out for 24 hours of fasting or very low calorie intake (0% to 40% of energy requirements or 0 to 600 kcal per day) alternating with periods of eating according to daily energy needs (ad libitum). IF can be done by, regimen (5:2) fasting for 1 to 2 days per week (either sequentially or not sequentially) with a total caloric intake ranging from 0% to 40% or 0 to 600 kcal per day interspersed with 5 day periods eat according to daily energy needs. Regimen 2:1, 1 day of fasting followed by 2 consecutive days according to daily intake. Regimen 1:1, alternating fasting 1 day 0% to 40% total energy or 0 to 600 kcal followed by energy intake according to daily needs. Time-restricted feeding (TRF) regimen. Daily food consumption is limited to a 12 to 24 hour window (eg 16:8, 16 hour fast followed by an 8 hour eating window).17,95 Calorie restriction and periodic fasting are the main choices because they require easy access, inexpensive and low-risk modalities.96-97 In recent research, dietary interventions have been shown to improve serum transaminases and fatty liver in MAFLD.98-101 An eight-week modified alternate-day calorie restriction (MACR) fasting intervention showed a decrease in BMI, ALT and AST, and fatty liver.102 Randomized controlled trial studies provide interventions on a low-carbohydrate diet and intermittent fasting 5:2 for 12 weeks, effectively reducing steatosis and liver stiffness.103 Similar studies evaluating low-calorie diet interventions, in which the proportion of carbohydrate and lipid intake is limited to 50%-60% and 20%-25%, show improvement in NASH histology and fatty liver index.99,104,105 Musso et al106 and Fernandez et al107 evaluated the effects of dietary interventions and weight loss from eight randomized controlled studies on MAFLD, 5% weight loss improved fatty liver and 7% if greater correlated with improved MAFLD activity score (NAFLD Activity score).  

The Roles of Purple Sweet Potato Anthocyanins in MAFLD  
Chemical Structure of Anthocyanins  
Anthocyanins belong to the class of flavonoids with the main structure of anthocyanidins (aglycones) consisting of an aromatic ring A bonded to a heterocyclic ring C which contains oxygen, and bonded by a carbon bond to a third aromatic ring B.108 Anthocyanins are composed of aglycones (anthocyanidins) which are esterified with one or more sugar groups (glycones). The basic structure of anthocyanins consists of 2-phenylbenzopyrilium or flavylum.108 The main differences among anthocyanidins are the number of hydroxylated groups, the nature and number of sugars attached to their structure, the aliphatic or aromatic carboxylates attached to the sugar are mainly attached to the C-ring at position 3 or to the A-ring at position 5,7.109 The sugar group in anthocyanins varies, but mostly in the form of glucose, rhamnose, galactose
or arabinose. Flavonoids are found in six forms of anthocyanidins namely cyanidin (Cy), pelargonidin (Pg), peonidin (Pn), delphinidin (Dp), petunidin (Pt) and malvidin (Mv), with its distribution in nature is 50% Cy, 12% Pg, 12% Pn, 12% Dp, 7% Pt and 7% Mv, respectively. This was followed by 4 groups of anthocyanidin glycosides namely 3-mono-sides, 3-biosides, 3,5-diglycosides and 3-glycosides. Therefore, the largest form of anthocyanin found is cyanidin 3-glycosides.

Anthocyanin Antioxidant Activity

The antioxidant and anti-inflammatory activities of flavonoids depend on the configuration and the total number of hydroxyl groups. The configuration of the hydroxyl ring B determines ROS scavenging activity, further substitution of rings A and C weakens the scavenging effect of radicals on superoxide anions. The antioxidant activity of flavonoids depends on the configuration and the total number of hydroxyl groups. The configuration of the hydroxyl ring B is the most significant determinant of ROS scavenging activity, while ring substitutions A and C have little effect on superoxide anion radical scavenging.

Anthocyanin Anti-Inflammatory Activity

The role of Flavonoids as an anti-inflammatory works through the C2-C3 double bond (C-ring) and the hydroxyl group at the C3', C4', C5, and C7 positions of the A and B ring flavonoid frameworks, but changes in the configuration of the double bond at the C3 position of the C-ring reduces anti-inflammatory ability. Flavonoid anti-inflammatory activity is evident due to the C2-C3 double bond (C-ring) and the hydroxyl group at positions C3', C4', C5, and C7 of the flavonoid skeleton rings A and B, however changes in the configuration of the double bond at the C3 position of the ring -C reduces anti-inflammatory ability.

The Role of PSP Anthocyanins as Antioxidants, Antidiyslipidemic and Anti-inflammatory Agents

As antioxidants, PSP anthocyanins exert their effects via diverse action mechanisms. Anthocyanins suppress the nuclear factor kappa light chain enhancer of activated B cells (NF-κB) pathway, sterol regulatory element-binding protein 1 (SREBP-1c) by activating AMPK-activated protein kinase (AMPK), and upregulates peroxisome proliferator-activated receptor-α (PPAR-α), as well as nuclear factor erythroid 2-related factor 2 (Nrf2). Anthocyanins regulate lipid metabolism through AMPK activation, induces PPAR-α activity and reduces Srebp-1c expression. Sweet potatoes inhibit nuclear factor-κB increasing hepatic fatty acid oxidation, and attenuating the canonical pathway for the release of inflammatory cytokines. Anthocyanins have been shown to improve dyslipidemia, glucose tolerance and increase insulin sensitivity in MAFLD by increasing adiponectin. The main mechanism of anthocyanin extract in MAFLD is proven through suppressing lipid accumulation by downregulating lipogenesis factors, inhibiting activation of inflammatory pathways, suppressing oxidative stress through increasing antioxidants, and increasing β-oxidation to inhibit mitochondrial dysfunction.

The Role of PSP Anthocyanins in Insulin Resistance

Purple sweet potato (Ipomoea batatas) mitigates insulin resistance via multiple mechanisms. Purple sweet potato increases peripheral glucose uptake, prevents pancreatic β-cell apoptosis through stimulation of glucagon-like peptide-1 (GLP-1) and increases intracellular Ca2+ concentration triggering β-cell regeneration in the pancreas and improving insulin resistance. The cellular mechanisms of purple sweet potato phytoconstituents in improving hyperglycemia involve downregulation of TNF-α levels and p38 mitogen-activated protein kinase (p38 MAPK), a protein kinase involved in β-cell death. Excess TNF-α increases p38 phosphorylation, reduces the expression of Bcl-2 and Bax, as a regulator of β-cell apoptosis. Inhibition of the p38 pathway inhibits the decrease in Bcl-2 and Bax reduces blood glucose by increasing the role of endogenous anti-apoptotic Bcl proteins, such as Bcl-2 and Bcl-xL, suppressing the cell response to glucose. Therefore, PSP can be regarded as a promising natural product that has the potential to confer cytoprotection to pancreatic β-cells, while also mitigates insulin resistance.

Insulin resistance is also associated with ROS accumulation and diminished insulin biosynthesis, which are promising therapeutic target of purple sweet potato anthocyanins. Hyperglycemia-induced ROS accumulation in β cells activates c-Jun N-terminal kinase (JNK) pathway. The activation promotes translocation of pancreatic and duodenal homeobox-1 (PDX-1) to the cytoplasm, diminishing both PDX-1 activity and insulin gene expression. These events result in the inhibition of normal insulin biosynthesis process. Ipomoea batatas flavonoids have the capability to disinhibit the suppressed insulin biosynthesis by enhancing PDX-1 activity and upregulating Akt, thus improving not only insulin biosynthesis but also dyslipidemia as an additional bonus effect. Under the context of hyperglycemic state, acylated anthocyanins, ubiquitously present in dark-colored tubers such as purple sweet potato, are presumed to exert more powerful effects as energy metabolism regulators compared to their nonacylated counterparts.

The Potential Roles of PSP Anthocyanin as an Adjuvant Therapy for MAFLD

Purple sweet potato has the potential to prevent hepatocyte injury by mediating the transduction of various intracellular signaling as anti-inflammatory and antioxidant by: (1) inhibiting inflammation, via suppressing the degradation of IKK (IκB kinase complex) to release NF-κB into the nucleus; (2) increasing β-oxidation of fatty acids through upregulation of PPAR-α; (3) inhibiting lipogenesis by decreasing the downregulation of SREBP-1c expression through AMPK activation; and (4) enhancing endogenous antioxidant defense through the Nrf2 protein pathway, potentially downregulating Nox, and alleviating ER stress.

From various studies, anthocyanin extracts have been shown to play a role in metabolic diseases and MAFLD.
Several in vitro and in vivo studies have proven that PSP tubers reduce liver lipid accumulation in liver function biomarkers compared to the placebo and no adverse effects were found. Purple sweet potato also exert hepatoprotective effect in a human study. Purple sweet potato extract effectively improves fasting blood glucose level, glucose and insulin tolerance by suppressing reactive oxygen species (ROS) production and restoring glutathione (GSH) and antioxidant enzyme activity, similar to vitamin D. Purple sweet potato extract reverses insulin receptor substrate-1/phosphoinositide 3 kinase/protein kinase B (Akt) signaling defects protecting against HFD-induced hepatic insulin resistance through suppression of c-Jun-N-terminal kinase 1 and activation of I kappa B kinase β and translocation of nuclear factor-kappa B p65. Administration of purple sweet potato extract at a dose of 700 mg/kg/day to rats induced by a high-fat diet for 20 weeks reduced fatty liver, improved obesity and metabolic parameters. Purple sweet potato plays a role in regulating de novo lipogenesis improving insulin sensitivity by inhibiting the LXR-α receptor reducing SREBP-1c transcription and AMPK activation, while also conferring cytoprotective effect to hepatocytes.

CONCLUSION

Anthocyanin-rich purple sweet potato tubers have potential as a therapeutic agent in hepatic steatosis because they have significant antioxidant, anti-hyperlipidemic, anti-hyperglycemic, and anti-inflammatory effects. In various in vivo studies and limited clinical trials on patients, anthocyanins have been shown to be beneficial not only in lipid metabolism but also in reducing liver fat deposition and insulin resistance. Anthocyanins can be considered an important adjuvant therapeutic option for reducing inflammation, free radicals, insulin resistance, and hepatic steatosis in NAFLD.

ACKNOWLEDGMENT

We would like to acknowledge Prof. Dr. I Nyoman Adi Jaya Putra, MA (Department of English Language Education, UNDikal Pening) for his valuable comments on the early draft of this manuscript.

CONFLICT OF INTEREST

The authors declare that they have no any potential conflicts of interest.

FUNDING SOURCE

The authors received no specific grant from any funding agency.

ETHIC APPROVAL

Not applicable.

AUTHOR CONTRIBUTION

All authors contributed to all sequences of the study.

REFERENCES


REVIEW


