

Progress in Improving Metabolic Syndrome with Adzuki Bean

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Abstract:

Metabolic syndrome (MS) is a clinical condition characterized by the simultaneous onset of abdominal obesity, abnormal blood sugar levels, dyslipidemia, and hypertension. It significantly impacts overall health and exhibits an increasing prevalence with a decreasing age of onset. Metabolic syndrome affects approximately one quarter of the global population, posing a critical threat to human well-being as a major public health concern. Current approaches for prevention and management primarily rely on pharmaceutical interventions or lifestyle modifications; however, their effectiveness remains limited. In recent years, the concept of food-medicine homology has emerged as a novel theory that holds promise in alleviating metabolic syndrome. Adzuki bean, a widely cultivated legume rich in various nutrients and bioactive compounds, has been traditionally recognized in Chinese medicine for its beneficial effects on invigorating QI (vital energy), arming the middle (digestive system), strengthening the spleen (immune function), and eliminating dampness (excess moisture). Numerous studies have demonstrated that adzuki bean can effectively regulate blood sugar levels, lipid profiles, blood pressure while improving gut microbiota imbalances and exhibiting anti-obesity properties to some extent. As such, it can serve as an adjunct therapy for managing metabolic syndrome. Compared to conventional drugs used for this purpose, adzuki bean offers safer alternatives with diverse product options. These findings provide valuable theoretical foundations and practical references for preventing and treating diseases associated with metabolic syndrome.

Keywords: adzuki bean; metabolic syndrome; ameliorate disease; dietary therapy.

1. Introduction

Metabolic syndrome (MS) is a group of clinical syndromes characterized by hyperglycemia (diabetes or impaired glucose regulation), dyslipidemia (hypertriglyceridemia and/or low high-density lipoprotein cholesterol), hypertension, and obesity. MS can cause a variety of diseases, such as increased risk of diabetes, stroke, renal disease that is chronic and cardiovascular disease. As per the findings of a research report on the health and nutrition status of Chinese citizens, up to 39% of middle-aged individuals in China have metabolic syndrome [1]. Current research progress mainly focuses on the adjustment of lifestyle and the use of drugs, and the improvement of therapeutic sex lifestyle based on health education is particularly important, modern medicine can only treat each disease individually, but cannot cure MS as a whole [2].

Medicinal diet is the treasure of China, “Shen Nong” tasted all kinds of herbs in the past, opened up the source of food, and invented medicine, so there is „medicine and food homology“ said. In recent years, the drug and food homologous crops can be used as a new intervention for the integrated management of MS, and the drug and food

homologous crops have the characteristics of less adverse reactions, greater safety, high patient compliance, and long-term use. When used to its maximum potential, it might prevent MS from developing or postpone the illness’s course. Consuming beans or bean extracts can lower the risk of becoming overweight or obese, as seen by decreases in weight, fat, waist circumference, and hip circumference [3]. And beans also have many benefits in the prevention and control of obesity, cardiovascular disease, diabetes and cancer, so beans can be used as a reasonable food source for MS management.

A number of experimental data have demonstrated the potential of adzuki bean in controlling blood sugar, improving blood lipids, regulating blood pressure, reducing inflammation and stress, modulating intestinal flora, inhibiting adipocytes and combating obesity. However, there is currently a lack of comprehensive summarization in this field. Therefore, this article aims to review recent studies on the components of adzuki bean (especially polyphenols and proteins as well as polyphenols and saponins) used in the treatment of MS. This paper discusses the feasibility and potential advantages of utilizing adzuki bean intervention in MS management, summarizes key bioactive sub-

stances that exert pharmacodynamic effects, analyzes limitations found in both basic research and clinical studies, and explores future applications of adzuki bean extract. Ultimately, these findings provide a theoretical foundation for developing more effective intervention strategies for MS and other chronic diseases.

2. Study on adzuki beans improving metabolic syndrome

2.1 Lowering Blood sugar

Adzuki bean can improve type 2 diabetes mellitus (T2DM) by inhibiting the activity of α -glucosidase and related enzymes, regulating insulin signaling, improving pancreatic and liver function. It has been reported that increased intake of legumes in the dietary pattern of Chinese adults is positively associated with significantly lower levels of glycosylated hemoglobin (HbA1c) and a lower incidence of T2DM [4]. People with high soy consumption had a lower chance of getting diabetes than people with low soy consumption, according to a three-year investigation of over 200 individuals with type 2 diabetes [5].

Male KK-Ay mice with type 2 diabetes were subjected to a seven-week treatment regimen of adzuki bean hot water extract in an animal experiment, resulting in a significant reduction in their blood glucose levels. This reduction exhibited a positive correlation with the quantification of adzuki bean extract [6]. Alpha-glucosidase is an intestinal enzyme that separates complex carbohydrates into glucose. Red adzuki phenol extract has a greater inhibitory activity on Alpha-glucosidase than saponins on T2DM results [7]. The hydrolysis of small red protein using Alcalase and Flavourzyme enzymes yields a complex combination of bioactive peptides with potential anti-diabetic properties, making it suitable for the treatment of T2DM [8]. Another study showed that 400 mg/kg BW adzuki polysaccharides for 4 weeks in the treatment of diabetic mice showed that adzuki polysaccharides had a hypoglycemic effect similar to the oral hypoglycemic drug metformin, which may be due to the significant increase in insulin sensitivity through improving glucose homeostasis and the number of islet cells [9]. It was also found that *Insr*, *ir-1*, *Pi3k*, *Akt*, and *Glut-2* mRNA expressions were significantly increased, which proved that adzuki polysaccharide could activate PI3K/AKT signaling pathway in a dose-dependent manner to improve T2D [9].

A number of studies have shown that adzuki bean supplementation can improve the glycemic index of sick mice induced by high fat diet (HFD). After 12 weeks of adzuki bean powder intervention, fasting blood glucose, fasting serum insulin and OMA-IR index of male C57BL/6 mice on HFD were significantly reversed [10]. The detection

of related insulin conduction genes by ethanol extract of adzoko bean showed that the four insulin conduction genes *Pdk4* in rats fed the extract had lower levels, while *Irs2*, *Irs4* and *Sort1* levels were higher, indicating that Adzuki extract could enhance insulin signal transduction and promote glucose uptake [11].

The consumption of adzuki beans can also enhance pancreatic and liver function, thereby regulating blood sugar levels. Adzuki extract supplementation at a daily dose of 200 mg/kg body weight led to significant reductions in fasting blood glucose (FBG), serum insulin (FINS), insulin resistance, and the surface area of β cells in Langerhans islands in mice fed a HFD [12]. SOD is a commonly used index to evaluate oxidative stress in the body. Adding adzuki beans to HFD significantly reduced the level of SOD1 in mice, suggesting that red adzuki beans may reduce pancreatic resistance by reducing oxidative stress. Histological analysis showed that adzuki powder supplementation could reduce pancreatic damage caused by diabetes [13]. After Adzuki extract was added to HFD mice at 12 weeks, the activities of alanine aminotransferase and aspartate aminotransferase were significantly decreased, and the decreased activities of these two enzymes marked the improvement of liver function [14].

The main substances that play the role of sugar control are proteins, phenols and saponins. The protein contained in adzuki bean is mainly 7S globulin (78%), which has a high digestibility and can well reduce the glucose tolerance of diabetic KK-Ay mice [15,16]. The three oligopeptides WEMHA, FYPW and FYPTDW of adzuki bean have strong inhibitory activities of pancreatic lipase, cholesterol esterase and α -glucosidase [17]. Rutin (phenol) can dose-dependently inhibit the activity of α -glucosidase and promote glucose entry into cells [18]. Other studies have shown that rutin (Saponin) can also reverse the expression inhibition of *IRS2* after 73h of hyperglycemic stimulation and reduce glucose toxicity. By encouraging intestinal L cells to secrete GLP-1, the saponin centaurin-3-O-glucoside (C3G) can indirectly control islet cell insulin release. Additionally, it enhances glucose consumption and uptake as well as glycogen synthesis in hepatocytes, thereby promoting glucose metabolism. Moreover, C3G augments hepatocyte GLUT-1 expression through the activation of the WNT/ β -catenin signaling pathway, thus modulating PTP1B and p-IRS expression to enhance insulin sensitivity. Furthermore, quercetin (flavone) demonstrates a dose-dependent reduction in FBG and FINS levels [19].

2.2 Reverse dyslipidemia

Numerous findings indicate that adzuki beans are involved in blood lipid management as well. Animal experiments have shown that the concentrations of serum triglyceride

(TG) and low-density lipoprotein (LDL) total cholesterol (TC) in HFD mice were significantly reduced after 4-week intervention with adzuki polysaccharide extract, and 12-week intervention with 15% adzuki extract [14]. The same results also showed that treatment of C57BL/6 male mice with 30% adzuki bean hot water extract for 4 weeks and treatment of 3.5% adzuki bean hot water extract with 40% ethanol fraction for 2 weeks both reduced the plasma high density lipoprotein (HDL) and TG levels of male SD rats [20]. A human fat cell experiment also showed that different doses (250-750 $\mu\text{g/mL}$) of adzuki polyphenols or non-polyphenols could inhibit the glycerol phosphate dehydrogenase activity of human fat cells and significantly reduce the TG concentration in human fat cells [21].

Further studies have found that the main lipid lowering effects of adzuki bean are phenols (such as anthocyanins) and saponins (catechins, rutin, quercetin). Experiments have shown that anthocyanin (25 mg/kg) intervention can reduce TC level, reduce cholesterol content by up-regulating the expression of ABCA1 gene in mouse plasma, improve lipid metabolism and improve lipid disorders [22,23]. The addition of rutin can significantly reduce liver TC, TG levels and serum transaminase activity [24]. The 3-(3-hydroxyphenyl) propionic acid produced by quercetin after catabolic metabolism of intestinal bacteria can inhibit the expression of cell adhesion molecule E-selectin in human aortic endothelial cells by inhibiting the NF- κ B pathway, thereby reducing lipid residues, and dose-decreasing TC, TG and LDL-C [19,25].

2.3 Improving Blood Pressure

Adzuki bean extract upregulates NO production by stimulating eNOS and iNOS in the aorta and kidneys, leading to reduced systolic blood pressure. After two weeks of intervention with AE250 (200 mg/kg adzella extract) and AE500 (500 mg/kg Adzella extract) respectively, the systolic blood pressure of hypertensive mice showed a dose-dependent reduction [26]. The same research results showed that 0.8% or 0.9% adzpea extract mixed with feed could reduce systolic blood pressure of SHR [27]. Urinary NO_x excretion levels were significantly increased in hypertensive rats treated with adzuki bean polyphenol extract (ABE), suggesting that ABE may reduce blood pressure and inhibit the expression of eNOS and iNOS by promoting the production of NO. In ABE-treated hypertensive rats, the expression of vascular and glomerular protein-1 is up-regulated, which may reflect the protective effect of ABE on vascular and renal endothelial function and help maintain the stability of blood pressure [27].

The specific constituents of adzuki beans (specific monomers) that contribute to blood pressure improvement remain unclear in current studies.

2.4 Regulation of intestinal flora

Intestinal flora disturbance is also one of the risk factors for the development of MS, and the factors that induce MS overlap with those that affect intestinal flora homeostasis, including diet and lifestyle. Multiple studies have shown that supplementing with adzuki beans helps regulate the composition of the gut microbiota. Compared with high-fat foods, adzuki supplemented rich γ -Aminobutyric Acid (γ -GABA), inducing Firmicutes. Bacteroidetes and the two bacterial groups have been found to be associated with increased energy consumption. Notably, there were also significant changes in the abundance of Verrucomicrobia and Akkermansia. Among them, Bifidobacterium exhibited the most pronounced variation in abundance [28]. Furthermore, the polyphenol extract from red adzonia bean primarily reduces the overall content of short-chain fatty acids (SCFAs) by decreasing butyrate production, while also significantly lowering ammonia nitrogen concentration throughout the entire incubation period. These effects subsequently impact the composition of intestinal microflora [29].

It has been reported that 7S protein, which has the highest content in adzet bean, is also one of the effective factors. After the intervention of intestinal flora and SCFAs 7S protein in fermented samples, the extension region (ER) peptide of the protein subunit selectively inhibits the growth of intestinal gram-negative bacteria. At the same time, the production of SCFAs was significantly increased [30]. In vitro fermentation experiments also confirmed that the probiotic activity of polysaccharide water extract (RKBWEP) can promote the growth of intestinal probiotic *Lactobacillus plantarum* and *Lactobacillus fermentum* [31]. Proanthocyanidins are highly enriched in the feces of HFD mice after the intervention of red zoudou polyphenol, and protocatechuic acid can regulate the growth of specific intestinal flora and inhibit the growth of *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* [32].

2.5 Anti-Obesity

Adzuki bean and its extracts can promote the decomposition and synthesis of fat by influencing the expression of related genes and regulatory factors, such as lipolysis enzyme.

In vitro experiments, lipolysis could be significantly observed after 1mg/ml adzol extract was added to adipose cells, while the body weight, epididymal fat weight, perirenal fat weight, retroperitoneal fat weight and mesenteric fat weight of HFD mice were significantly reduced after adzol proteolysis was provided [10,33]. The mechanism may be that by improving lipolysis enzyme, the expression levels of lipolysis enzyme and its transcripts mRNA

in HFD mice increased in the same trend after adding 1g adjuvanto extract per 100g of diet for 12 consecutive weeks. Moreover, it was found that the mRNA expression levels of other fatty hydrolases Atgl, Hsl, Ppar- α , Cpt-1 α , Mcad and Acox in mice were significantly increased after intake of adzuki bean [34].

PPAR- γ and C/EBP- α are key regulators of lipogenesis and fatty acid oxidation pathways, PPAR γ can mediate lipid production, and C/EBP- β can initiate adipocyte differentiation by directly activating PPAR γ expression. Adzuki bean can inhibit the expression of PPAR- γ and C/EBP- α in the surrounding adipose tissue by activating the Wnt/ β -catenin pathway, which ultimately leads to the blockage of fat synthesis [35]. After feeding 1% adzuki bean hot water extract to male Fischer 344 rats for 4 weeks, activation of the Wnt/ β -catenin pathway was observed. Simultaneously, there was a notable rise in the expression levels of mouse receptor γ and CCAAT/enhancer binding protein α , which in turn prevented the development of 3T3-L1 adipocyte cells.

Intestinal flora can also enhance the increase in short-chain fatty acid content, inhibit hepatic cholesterol synthesis, and reduce blood lipid levels. This specific effect promotes the growth of beneficial bacteria such as Bifidobacterium lactobacillaceae and Lactobacillus, as well as increases the abundance of Firmicutes, Bacteroidetes, and Actinobacteria [36]. To achieve this, there is a reduction in the ratio of Firmicutes/Bacteroidetes (F/B) and metabolites derived from Lactobacillus along with tryptophan derivatives [10]. It has been reported that adzuki powder supplementation may induce changes in intestinal flora by regulating carbohydrate metabolism, lipid metabolism, sulfur metabolism, cysteine metabolism, and methionine metabolism [13]. Furthermore, 5% adzuki extract significantly reduces fat accumulation and high levels of triglycerides (TG) and lipopolysaccharides (LPS) in serum of mice induced with a HFD, alleviates liver function damage caused by HFD-induced conditions while restoring balance to the intestinal microflora imbalance [13]. Additionally, fermentation by *P. acidilactii* enhances fatty acid metabolism pathways along with biotin metabolism pathways and alkaloid biosynthesis pathways within adzuki beans [37].

In the process of combating obesity, the active constituents of red adzuki bean primarily consist of proteins, polyphenols, and saponins. The 7S protein, which has been reported to exhibit higher levels compared to average beans, elevates fibroblast cytokine 21 (FGF 21) levels in the postprandial circulatory system of mice while significantly reducing adipose tissue weight [38]. The anti-obesity effect of adzuki bean may be attributed to the inhibitory action of its flavonoids and saponins on α -glucosidase

and pancreatic lipase activity, as well as the promotion of lipolysis [32]. The 8-week proanthocyanidin intervention can reduce the accumulation of fat in rats, reduce the size of adipose tissue cells, and reduce liver fat deposition [39]. Four single flavones (catechin, Vitexin 4',-O-glucoside, quercetin-3-O-glucoside and quercetin-3-O-rutin) and six single saponins (Adzuki saponin i, ii, iii, iv, v and vi) extracted from Adzuki bean showed inhibitory effects on 3T3-L1 cell proliferation. Adzuki bean saponin II had the highest inhibitory effect (49.72%) [40].

3. Conclusion

Products with the same origin of medicine and food can be well used for long-term management of chronic diseases such as MS, and its research and application is a window for Chinese medicine to go international. Adzuki beans can improve metabolic syndrome in many ways, including lowering blood sugar, improving dyslipidemia, regulating blood pressure, alleviating intestinal flora disorders and anti-obesity. In general, the application of adzuki beans in the clinical adjuvant treatment of metabolic syndrome has broad prospects, but the current research still has certain limitations, such as a number of studies have shown that adzuki beans only play an auxiliary role, and most of them are animal and in vitro experiments, and how to better combine adzuki beans with human diet to improve metabolic syndrome has not been fully revealed. In the future, it can further carry out clinical research and exert therapeutic effect on the human body. At the same time, there are various kinds of adzuki beans, and it is still necessary to further screen and explore which adzuki beans contain the most abundant and effective active factors. In addition, it can also combine the development trend of adzuki bean food industry to produce adzuki bean health food to meet the needs of consumers, and better manage a number of other chronic diseases in addition to MS.

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