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Impact of soy isoflavones on the prevention and treatment of obesity

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Summary:

Introduction and purpose:

Currently, as the frequency of obesity is alarming, the role of many factors that could contribute in preventing and treating this condition are being researched, among them the certain food with beneficial health profiles - one of them is soybeans, specifically the isoflavones it contains. Populations that consume soy are known for lower risk of various disorders - among them obesity. The aim of this paper is to summarize the existing paper about the role of these bioactive components in the treatment of this condition. The search was conducted using PubMed and Google Scholarship databases.

Brief description of the state of knowledge:

Obesity is one of the leading challenges in today's healthcare as it leads to various chronic diseases that are fraught in consequences. Current knowledge is pointing into the association between composition of the soy isoflavones and the lower risk of obesity. Results of the studies indicate that patients affected with obesity could benefit from introducing soy isoflavones into their diet along with other necessary modifications.

Conclusions:

Soy isoflavones are potential agents in the holistic obesity treatment**.** Consumption of isoflavones merits further recognition as foregoing results of conducted studies are pointing to its possibly meaningful role. It is worth mentioning that consumption of soy isoflavones is not only an anti-obese factor, but also presents various other health benefits and when consumed rationally poses no risk to human's well being. We conclude that further studies would enable us to fully reveal the potential of those polyphenols.

Key words: soy isoflavones; obesity; health; NAFLD; prevention

1. Introduction

The soybean has been widely present in the Asian diet for thousands of years while residents of the other continents are slowly implementing this plant food to their diet as its health promoting qualities are gaining more attention worldwide [1]. Soy isoflavones are the bioactive components of the soybeans that demonstrate many health promoting effects. The attention those substances are gaining springs from their ability to bind to the estrogen receptors which as a result leads to weak estrogen-like effects [2]. Consumption of soy isoflavones is known to reduce the risk of cancers. Papers show that eating soybeans is linked with the lower risk of breast cancer [3]. The relationship between soy intake and prostate cancer was also evaluated and the conclusion showed that there is a significant interrelation between a diet rich in soy foods and the lower risk of prostate cancer [4]. Soy isoflavones are

recognized in the oncology department not only because of their anti-cancer, protective abilities, but also because of their properties in lowering the toxic effects of chemotherapy and raising its successfulness. This is achieved mainly because of one of the most potent isoflavones which can be found in soy-genistein [5]. Isoflavones have been also identified for their bone protecting effects. Their consumption enables the enhancement of bone metabolism and also lessens the bone resorption because of their impose on bone homeostasis and RANKL/RANK/OPG pathway [6].

Obesity is one of the main threats to human's health and its prevalence in populations is constantly rising. Defined as the immoderate fat accumulation in the body with the Body

Mass Index (BMI) rate > 30 kg/ m2 poses huge endangerment to human's health [7]. It contributes to the pathogenesis of many chronic disorders such as type 2 diabetes, dyslipidemia, hypertension, cardiovascular and neurodegenerative diseases [7,8].Association between soy isoflavones and obesity has also been recognized. Thus, we focus on this dependency in our paper.

2. Current state of knowledge

In the 2017 study, Akhlaghi et al. conducted a meta-analysis of 17 randomized controlled clinical trials related to the impact of soy isoflavones on obesity. Their results did not indicate a statistically significant effect of soy consumption on body weight. However, upon specifying certain groups, it was found that soy consumption may contribute to weight reduction in the following groups: obese individuals when the intake exceeds ≥ 40 g of soy protein every day, with a short duration from 1 up to 3 months. Additionally, soy was found to have a more favorable impact on weight compared to meat and protein. It was also observed that the use of isoflavones in women was associated with a reduction in BMI when taken in small doses and for a short period (2-6 months). This demonstrates the divers effec n body weight that products containing soy isoflavones may have. Therefore, the mechanism of action appears to be complex and challenging to predict [9]. In the study published by Ørgaard et al., where the authors attempt to summarize the knowledge regarding the impact of soy isoflavones on obesity, they describe ways in which consumption may influence adipose tissue through the regulation of adipogenesis. The structural similarity to the steroid structure

of E2 plays a key role here, leading to a reduction in lipogenesis. The interaction through peroxisome proliferator-activated receptors (PPAR) is also postulated. The authors emphasize that although in vitro studies show a noticeably positive impact of soy isoflavones on the proliferation of adipose tissue and it seems that there might be a potentially positive effect on adipose tissue in humans, this has not been unequivocally observed in human studies. As an explanation for this, the authors point to the transformations of soy isoflavones in the human digestive system and the possibly insufficient dose taken with food. It is also worth noting that increased intake of soy isoflavones can lead to numerous adverse effects [10]. Positive impact of soy isoflavones on obesity was also observed in the study published in 2021. The authors investigated the relationship between self-reported soy consumption and obesity. It was found that the reported increased consumption of soy was correlated with a lower occurrence of obesity and central obesity in the population residing in Shanghai, China. Furthermore, the study demonstrated that this correlation was particularly notable in postmenopausal women [11]. This confirms the findings from a study on rats, which showed the beneficial effects of genistein derived from soy on the amount of adipose tissue in female rats after ovariectomy, simulating the postmenopause [12]. Wang et al. also focused on the mechanisms of the influence of soy isoflavones on adipose tissue in their work. They highlight the pleiotropic and multiple pathways as potentially beneficial for patients with obesity [13]. In a 2019 study on rats, Luo et al. demonstrated that increased soy consumption in obese rats positively affected sperm quality and improved spermatogenic defects resulting from obesity [14]. Another study on rats focused on the influence of soy isoflavones through the AKT/mTORC1 pathway on adipose tissue in obese rats. In addition to reducing body weight, a decrease in lipogenesis and adipogenesis was noted [15]. Another rat study also confirmed the positive effect of soy isoflavones on the reproductive system of obese rats. It showed a positive impact on testosterone synthetase, which was disturbed due to obesity [16]. Soybeans seem to be useful also in improving the metabolic health of postmenopausal women. Findings indicate that soy protein intake is associated with blood lipids improvement and inversely proportional to obesity. Soy protein also promoted weight and fat loss in some obese animal models and its intake resulted in improved lipid distribution and insulin sensitivity and decreased blood sugar and insulin [17]. Whereas in vitro and animal studies indicated that soy protein and isoflavones can have a positive effect on body composition, human trials conducted by Liu et al. on postmenopausal Chinese women with mild hyperglycemia revealed mild but significant changes of body weight, BMI and body fat percentage after 6-month soy protein with isoflavones supplementation [18]. These results indicate that habitual soybean

intake may be beneficial not only for patients with metabolic syndrome, but also may take part in prevention of this disorder development. In another study the effect of diet, physical exercise and soy isoflavones extract consumption on leptin and other adipokines plasma levels in healthy obese postmenopausal women was investigated. After 6-months intervention, beneficial effects were observed - mean serum leptin and TNF-alpha levels were decreased, while mean serum levels of adiponectin were increased in soy isoflavones groups [19].

Metabolic syndrome

Visceral fat is one of the main known risk factors of cardiovascular diseases, which are the most common cause of death worldwide [20]. The excess of visceral fat results in insulin resistance, systemic inflammation and the specific features of the metabolic syndrome such as dyslipidemia, hyperglycemia, type 2 diabetes or hypertension [21]. Some findings link soybean-derived isoflavones and metabolic syndrome and suggest their potential to prevent and treat this disorder. The randomized controlled trial conducted on 26 subjects, who were consuming soybean-based food for 12 weeks, revealed improvement of the parameters related to metabolic syndrome in 13 of 26 patients. The weight loss and positive changes in atherogenic lipid markers levels such as total cholesterol (TC), low density lipoprotein (LDL-C), non-high density lipoprotein (non-HDL-C) and apoB were observed [22]. Improvement in the lipid profiles was also observed in another trial that sought to examine the effects of soy nut (soaked and roasted soybean) and soy protein intake in 75 women aged above 60 years with borderline metabolic syndrome. 12 weeks of nutritional intervention resulted in significant decrease in total TC, LDL-C, VLDL-C (very low density lipoprotein), apolipoprotein B10, insulin, HOMA-IR, malondialdehyde (MDA), an indicator of oxidation, levels in patients who received soy nut. In the comparison, soy protein intake was associated with decrease only in TC, insulin, MDA level. Therefore soy nut supplementation seems to more effective than soy protein intake. There were no changes in apolipoprotein AI, triglyceride (TG), high density lipoprotein (HDL-C), TG/HDL, C-reactive protein (CRP) and fibrinogen levels after intervention observed [23]. The cross-over study examining association between soy consumption, endothelial function and inflammation markers was conducted on postmenopausal women with the metabolic syndrome. The participants were divided into three groups: a control diet (Dietary Approaches to Stop Hypertension [DASH]), soy protein diet and or soy nut diet. The results showed that soy nut and soy protein intake may reduce the nitric oxide levels, which is responsible for vascular relaxation, by 9.8% and 1.7% in comparison to the control group. Furthermore, soy nut consumption was also associated with

reduction in the serum levels of E-selectin, which takes part in the induction of arteriosclerosis and lower inflammation-induced production of IL-18. In both soy nut and soy protein groups reduction in CRP levels was observed. These findings suggest that soy nut consumption may have a positive effect on reducing some markers of inflammation and increasing plasma nitric oxide levels [24]. The study conducted by Woo et al. aimed to compare soy protein to isoflavones intake in Koreans without metabolic syndrome. The incidence of metabolic syndrome was inversely correlated with soy protein and isoflavone consumption in women. In men correlation was not significant, but incidence of low-high-density lipoprotein cholesterol was lower both in men and women. Also abdominal obesity and elevated blood pressure were inversely related in women, while an inverse association of elevated triglyceride in men were observed [25]. These results indicate that habitual soybean intake may be beneficial for patients with metabolic syndrome but also may take part in prevention of this disorder development.

Non-alcoholic fatty liver disease

The hypolipidemic function of soy protein and isoflavones may be also used in non-alcoholic fatty liver disease (NAFLD), which is caused by excessive accumulation of lipids in the liver. While there is no direct pharmacological treatment of this disorder, dietary interventions and lifestyle modification play the major role in the prevention and treatment of NAFLD. The metaanalysis by Xiao et al. conducted that soy proteins and associated isoflavones intake may suppress the formation and accumulation of lipid droplets in the liver. The improvement in NAFLD-associated metabolic syndrome is mainly through modulation of transcription factors, sterol regulatory element-binding protein-1 and peroxisome proliferator-activated receptor-γ2 and expressions of their target genes involved in lipogenesis and lipolysis as well as lipid droplet-promoting protein, fat-specific protein-2. These findings were observed both in animal and human trials [26]. Lately, there was also a trial on obese rats conducted, that sought to examine the role of isoflavones levels in soy protein concentrate diets on NAFLD prevention. Whereas obese rats had significantly greater liver steatosis score than lean rats, both soy protein concentrate with low isoflavones and and soy protein concentrate with high isoflavones intake resulted in reduction in steatosis score compared to control group. Authors also suggested that soy protein concentrate with isoflavones consumption may protect against liver steatosis and these results are greater with a higher concentration of isoflavones [27].

3. Conclusion

Soy isoflavones effects on health promotion have been studied in recent years and researches investigated among others their obesity-preventing effect, blood glucose level reducing effect, anti-oxidative effect and disease preventing effect. It was determined that following a diet containing soy isoflavones is associated with weight reduction and may influence adipose tissue through the regulation of adipogenesis. Soy consumption also contributes to obesity prevention and obesity-related diseases such as metabolic syndrome and non-alcoholic fatty liver disease. Dietary interventions and lifestyle modification are the key strategies in the fight against these disorders. Therefore soy isoflavones intake may support different diet therapeutics interventions and appear to improve treatment outcome. Overall, further studies are required to explore the full potential of soy isoflavones as therapeutics for the prevention or treatment of these chronic diseases.

Author Contributions:

Conceptualization, K.W. and M.W.; methodology K.W; software, K.W.; check, M.W., K.W. and S.T.; formal analysis, S.T.; investigation, M.W.; resources, S.T; data curation, S.T.; writing - rough preparation, K.W. M.W. and S.T.; writing - review and editing, K.W. S.T and M.W.; visualization, S.T.; supervision, K.W.; project administration, M.W.

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Conflicts of Interest

The author declares no conflict of interest.

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