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POTENTIAL OF ISOTHIOCYANATE SULFORAPHANE FROM BROCCOLI TO COMBAT OBESITY AND TYPE 2 DIABETES: INVOLVEMENT OF NRF2 REGULATORY PATHWAY

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Biologically active food components are now considered to be remedies for the prevention and treatment of metabolic disorders of different etiology. The aim of this review was to analyze the current data on the application of isothiocyanate sulforaphane, found in broccoli and other cruciferous plants, for the treatment of T2DM, obesity, and their comorbidities with the presentation of established molecular, particularly dependent on NF-E2-related factor-2 (Nrf2), and signaling mechanisms of therapeutic effects.

K e y w o r d s: broccoli sprouts, sulforaphane, Nrf2, obesity, preventive health, type 2 diabetes mellitus, nutritional therapy.

According to the International Diabetes Federation, more than 400 million people worldwide suffer from diabetes mellitus, and 90% of these people belong to the category of patients with type 2 diabetes mellitus (T2DM) [1, 2]. This number is expected to rise to 500-640 million T2DM patients in the next few decades [2, 3]. Diabetes is characterized as a group of metabolic disorders and complications related to impaired metabolism of glucose and lipids [4]. An increase in blood glucose level due to insulin deficiency (type 1 diabetes mellitus) or the development of insulin resistance at high blood insulin levels (type 2 diabetes mellitus) is a characteristic feature of diabetes. The long-term persistence of hyperinsulinemia, hyperglycemia, and insulin resistance in T2DM leads to chronic damage to various tissues, such as the heart and skeletal muscle, blood vessels, eyes, kidneys, and nervous system [5]. T2DM-derived complications increase the risk of morbidity and mortality [6].

The WHO estimates that obesity has dramatically increased up to 1.9 billion people worldwide (https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight). Obesity is not only the excessive level of adipose tissue – it is now recognized as a low-grade sustained inflammatory state that causes oxidative stress in different organs. Oxidative stress develops as a result of an increase in the steady-state level of reactive oxygen species (ROS) which the antioxidant system cannot fully cope with [7]. Obesity-related inflammation and oxidative stress lead to many disorders including cardiovascular disease, metabolic syndrome, T2DM, and non-alcoholic fatty liver disease [8, 9]. Obesity and T2DM are usually tightly related.

Nuclear factor erythroid 2 (NF-E2)-related factor 2 (Nrf2), a basic leucine zipper transcription factor, activates the expression of genes involved in antioxidant defense and xenobiotic detoxification [7, 8]. Nrf2 molecules mainly reside in the cell cytoplasm by associating with kelch-like ECH-associated protein 1 (Keap1) and ubiquitin ligase cullin 3. Keap1 is a substrate adaptor protein for cullin 3, which facilitates the ubiquitination of Nrf2. The interaction of Nrf2 with Keap1 leads to the proteasomal degradation of Nrf2 [10]. Keap1 is a sensor for ROS: its oxidation by ROS prevents binding with Nrf2. This results in an increase in Nrf2 level, it translocates into the nucleus. As an activator, Nrf2 modulates the expression of a number of genes involved in glucose and lipid metabolism [8]. In the mouse liver, the constitutive activation of Nrf2 via Keap1 knockdown represses the expression of genes involved in gluconeogenesis and lipogenesis [11]. Moreover, this activation alleviates obesity, diabetes, and hepatic steatosis in mice on a high fat diet (HFD) [12].

HFD is being considered as a better strategy for the investigation, because it brings the development of the disease closer to common causes in humans (due to overeating and a sedentary lifestyle) and allows using functional foods for treatment [13].

The application of pharmacological Nrf2 activators, particularly sulforaphane (SFN, 1-isothiocyanate-4-methylsulfinylbutane), has been actively studied. Broccoli is one of the best and most promising SFN sources. Broccoli is a green vegetable rich in various bioactive phytochemicals [14, 15]. Sulforaphane is among the most attractive bioactive components of broccoli. SFN activates the transcription factor Nrf2, which, as noted above, is an important regulator of cellular redox homeostasis through its capacity to upregulate the expression of antioxidant defense proteins [16-18]. Sulforaphane interacts with the cytoplasmic Keap1 protein and prevents it from binding to Nrf2. Therefore, Nrf2 translocates into the nucleus and leads to the transcriptional activation of genes with the antioxidant response element in their promoters. The enhancement of the antioxidant network may inhibit the long-term complications of obesity and diabetes making SFN an effective preventive and moderating compound for these diseases [18, 19].

This paper aims to analyze current data on the usage of broccoli sprouts and sulforaphane preparations for the treatment of obesity, T2DM and their comorbidities with the presentation of established molecular mechanisms of therapeutic effects.

Sulforaphane in broccoli

Cruciferous vegetables of the family *Brassicaceae* (also called *Cruciferae*) such as broccoli, kale, cabbage, cauliflower, garden cress, bok choy, broccoli, Brussels sprouts, mustard plant and similar green leaf vegetables contain high amounts of glucosinolates. When the cells of these vegetables are breached, glucosinolates are released from the vacuole and are hydrolyzed by cytosolic myrosinase to isothiocyanates and glucose. Sulforaphane is an isothiocyanate formed due to the hydrolysis of glucosinolate glucoraphanin and is produced as a protective compound to prevent herbivores, particularly insects, from eating the plant (http://rave.ohiolink.edu/etdc/view?acc_num=osu1323373292), but it does not prevent eating of cruciferous vegies by slugs (VIL – personal observation). In both rodents and humans, glucoraphanin is also hydrolyzed to sulforaphane by gut microbiota-derived myrosinase, promoting SFN intestinal absorption [20]. The highest SFN levels were found in seeds and 3-day-old broccoli sprouts [21]. This raises a great interest in using broccoli sprouts as a functional food to prevent and attenuate certain diseases [22, 23].

Sulforaphane is a cytoprotective compound under oxidative stress. This effect is provided by its covalent interaction with Keap1, preventing Nrf2 from binding with Keap1 followed by undergoing proteasomal degradation. Consequently, Nrf2 enters the nucleus to induce the expression of Nrf2-regulated genes encoding antioxidant and other protective enzymes [24]. Specific cysteine residues of Keap1 are known to be modified by SFN due to which Keap1 acts as sensors to ROS and electrophilic compounds enabling the cell to respond to oxidative and electrophilic stress effectively through the activation of the Nrf2 pathway [25]. As Nrf2 activator, SFN has been reported to prevent oxidative damage [26, 27] and cardiovascular diseases [28]. Thus, SFN is considered as an indirect antioxidant due to the induction of Nrf2-dependent processes [29]. It has also been reported that SFN can affect epigenetic mechanisms through the inhibition of histone deacetylase and DNA methyltransferase [30]. The modulation of these mechanisms can influence the progression of various diseases including diabetes and obesity.

Due to the multiple health benefits, SFN itself and SFN-rich broccoli sprouts may be beneficial food supplements for the prevention and treatment of type 2 diabetes mellitus, obesity, and their comorbidities. This assertion is based on *in vitro* studies, animal models, and some clinical trials that are summarized in the Table. Generalized schemes of sulforaphane (SFN) treatment with effects on glucose and lipid metabolism are demonstrated in the Figure.

Sulforaphane and type 2 diabetes mellitus

Ignorance or poor health control of people with T2DM can lead to the progression of various complications. T2DM comorbidities affect different organs and systems of the body, causing diseases [31]. Sulforaphane has received wide attention as a compound that prevents T2DM and its complications via activation of Nrf2-dependent antioxidative pathways [32, 33].

Recently, the interplay between SFN and AMP-activated protein kinase (AMPK) has been reported in different systems to prevent T2DM and its comorbidities [34, 35]. It was reported that SFN prevented T2DM-induced renal lipotoxicity during diabetic

kidney disease via involving AMPK. AMPK-mediated activation of lipid oxidation and Nrf2-driven antioxidative function was observed in wild-type mice, but not in AMPKα2 knockout (KO) mice, although both groups were treated with SFN [36].

Nrf2 activation by SFN was demonstrated to be preventive against ferroptosis during diabetic cardiomyopathy [37]. This activation inhibited lipid peroxidation in HFD wild type and AMPKα2-KO mice. The authors found that ferroptosis led to the development of diabetic cardiomyopathy and suggested that this mechanism could be prevented by SFN treatment via AMPK-dependent Nrf2 activation.

SFN can prevent angiotensin II-induced cardiomyopathy via activation of Nrf2-mediated exogenous antioxidant defenses. That up-regulation and activation of Nrf2 by SFN is achieved partially through the Akt/GSK-3β/Fyn pathway [38].

A study of T2DM in male Wistar rats fed an HFD found that SFN supplementation reduced lipid accumulation in obese diabetic mice [39]. These results indicate that SFN could also be a potential therapeutic compound for T2DM-derived dyslipidemia.

Wang and colleagues used a T2DM mouse model to verify the protective function of SFN

Table. Protective effects of sulforaphane and broccoli sprouts in type 2 diabetes mellitus and obesity

T2DM		Obesity	
Pathway (if specified)	Effects	Pathway (if specified)	Effects
AMPK	↓Renal lipotoxicity during diabetic kidney disease [36] ↓Ferroptosis during diabetic cardiomyopathy [37] ↓Body mass, ↓hyperlipidemia [49]	*AMPK*	↓Body mass, ↓hyperlipidemia [49] ↑Glycerol release [74] ↑Browning of white adipose tissue, mitochondrial biogenesis [76]
Akt/GSK-3β/Fyn	↓Angiotensin II-induced cardiomyopathy [38]	*Nrf2/PGC-1α and MAPK*	↑Browning of white adipose tissue, mitochondrial biogenesis [76]
NF-kB	↓Serum insulin levels, ↑insulin sensitivity [48]	*Akt/p70s6k1/ Bad and ERK*	↑Apoptosis, adipocyte numbers were decreased [77]
Not specified		*PPAR*	↓Atherosclerosis, ↑insulin sensitivity [71]
Not specified	Lipid accumulation [39] ↓Inflammation, ↓oxidative damage, ↓apoptosis, ↓aortic fibrosis [40] ↑GSH/GSSG, ↓blood pressure [51] ↓Mitochondrial ROS production, ↓protein glycation [52] ↓Renal fibrosis, ↓inflammation, ↓oxidative stress markers during diabetic kidney disease [59] ↓TGF-b in hepatic cells [62] ↓Serum glucose and insulin levels, ↑Glutathione and superoxide dismutase [63] ↓Ceramide biosynthesis [64]		↓Adipogenesis, ↓lipid accumulation [74] ↓Expression of adipogenesis-related proteins, ↑expression of fatty acid oxidation proteins [75] ↓Fat absorption [78] ↓Activity of lipogenic enzymes, ↓expression of lipogenic enzyme genes [79,80] ↓Apolipoprotein B secretion [81] ↓Serum total cholesterol, ↓LDL, ↓TAG, ↑HDL [82] ↓Serum TAG, total cholesterol, and LDL levels, TAG/HDL ratio [83] ↓Total cholesterol, ↓LDL [84] ↓Body mass gain, ↓fat mass accumulation, ↑insulin sensitivity, ↑UCP1 level, ↑ browning in beige adipocytes [86]

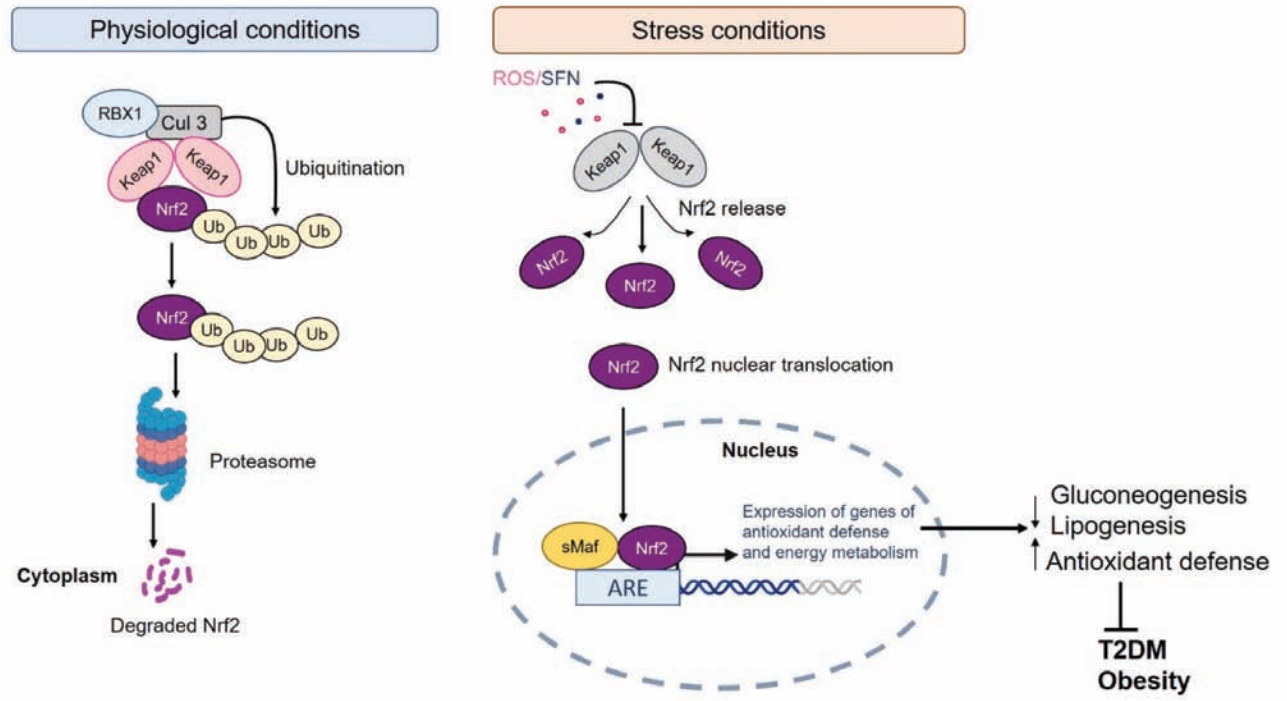

Figure. Generalized scheme of Nrf2 inactivation/activation during physiological conditions and stress conditions accompanied by ROS production or by sulforaphane (SFN) treatment with effects on glucose and lipid metabolism. Nrf2 protein is constitutively synthesized. Under physiological conditions, in the cytoplasm, Nrf2 is targeted for ubiquitinization and degradation via interaction with Keap1. Keap1 forms link between Nrf2 and Cul3 ligase, which catalyzes ubiquitination of Nrf2 followed by its proteasomal degradation. Under oxidative stress or SFN treatment, ROS and SFN modify specific cysteine residues in the Keap1 protein, making it unable to form complex with NrF2. Free Nrf2 is translocated into the nucleus, where it interacts with sMaf proteins and activates the expression of various genes controlled by the ARE. See the text for more details. Abbreviations: RBX1 – Ring-box 1 protein; Cul3 – Cullin-3 protein; Keap1 – Kelch like ECH associated protein 1; Nrf2 – NF-E2-related factor 2 protein; Ub – Ubiquitin protein; ROS – reactive oxygen species; sMaf – small Maf (musculoaponeurotic fibrosarcoma) protein; ARE – antioxidant response element protein; SFN – sulforaphane; T2DM – type 2 diabetes mellitus

against diabetic aortic damage [40]. Animals were treated with SFN for four months. The treatment with SFN prevented the progression of aortic fibrosis, inflammation, oxidative damage, apoptosis, and proliferation in T2DM mice.

Axelsson and colleagues found that SFN had no effects on insulin signaling and mitochondrial oxygen consumption in hepatoma cells during diabetic conditions [41]. For the study, the authors used broccoli sprout extract (BSE) in the form of a dried powder of an aqueous extract of broccoli sprouts. The powder contained high concentrations of the SFN precursor glucoraphanin. That study reported a reduction of glucose production and an improvement of glucose tolerance mediated by Nrf2 in mouse hepatocytes. These data suggest that BSE had a direct effect on gluconeogenesis rather than hepatic insulin sensitivity. Treatment of T2DM patients with SFN-containing broccoli sprout extracts showed that safety doses of BSE corresponding to 50-400 mmol SFN daily were required to achieve clinical effects [42-45].

Insulin resistance (IR) is the impaired ability of cells to increase glucose uptake due to insulin stimulation. In addition, IR is a characteristic feature of T2DM and a risk factor for metabolic and cardiovascular complications [46]. It was suggested that IR of adipocytes themself could be the main reason for the disturbance of carbohydrate metabolism, thus linking T2DM and obesity [47]. In T2DM patients, consumption of broccoli sprouts with a high content of sulforaphane decreased serum insulin levels. The

effect of SFN on IR may be related to the nuclear factor kappa-B (NF-kB) inflammatory pathway. This pathway has been known to be a key mediator in the development of IR and pathogenesis of T2DM and its complications. Inhibition of the NF-kB pathway by SFN increased insulin sensitivity [48].

Body weight gain and hyperlipidemia were suppressed under SFN treatment in HFD-fed mice [49]. The addition of SFN prevented HFD-induced oxidative stress by activating the AMPK/Nrf2 signaling pathway. Besides, the phosphorylation of AMPK was significantly decreased in the liver of HFD mice, and SFN treatment ameliorated the reduction of AMPK phosphorylation. Compared with the HFD group, the expression of three AMPK downstream genes, *Cpt1*, *Acc*, and *Fans*, also increased in the HFD within SFN group [49].

Hypertension in T2DM patients is a risk factor for the development of cardiovascular disease [50]. Supplementation of hypertensive rats with broccoli sprouts increased the ratio reduced/oxidized glutathione (GSH/GSSG) and improved endothelial-dependent relaxation of the aorta, resulting in a significant decrease in blood pressure [51]. This suggests that broccoli sprouts may affect cardiovascular diseases by decreasing the intensity of oxidative stress.

It is well known that inflammation can induce vascular endothelial damage. Sulforaphane has been found to inhibit this process via modulation of inflammatory signaling pathways mediated by p38 mitogen-activated protein kinases and c-Jun N-terminal kinases [52]. Activation of Nrf2 and upregulation of the expression of target genes were observed together with the suppression of vascular cell adhesion protein 1 under treatment with SFN [53,54].

Diabetic kidney disease is one of the main causes of human death from T2DM-derived complications [55]. Overproduction of ROS induced by hyperglycemia has been identified as a risk factor for the development of the disease [56]. Activation of Nrf2 may have therapeutic potential for preventing diabetic kidney disease, as suggested in several studies [57, 58]. Cui and colleagues tested this hypothesis by treatment of a diabetic mouse model with SFN 0.5 mg/kg body mass for 3 months. Such treatment prevented diabetes-induced renal fibrosis, inflammation, oxidative stress, which are markers of diabetic kidney disease, via upregulation of renal Nrf2 genes by SFN [59].

Fibrosis development in the liver and kidney can result from a diabetes-induced imbalance between the production and degradation of extracellular matrix structures, including collagen and fibronectin [60, 61]. Transforming growth factor beta (TGF-β) is a main profibrotic cytokine that contributes to the development of liver fibrosis. TGF-β could be inhibited by sulforaphane-induced activation of Nrf2 in hepatic cells [62]. In renal tubular cells, SFN prevented the profibrotic effects of hyperglycemia [59].

Oral administration of SFN exhibited protective effects against high-fat diet- or streptozotocin-induced type 2 diabetes in mouse models. These conclusions were drawn based on the observed decrease in fasting serum glucose levels and increase in serum insulin levels [63]. In this study, SFN increased the activities of glutathione peroxidase and superoxide dismutase in the liver of type 2 diabetic mice, suggesting that SFN improves the antioxidant capacity in the liver of these mice [63].

Treatment with SFN shows promise for recovering hepatic glucose homeostasis and improving insulin sensitivity. This statement was supported by both *in vitro* and *in vivo* studies that demonstrated the blocking ceramide biosynthesis through the downregulation of serine palmitoyltransferase long chain base subunit 3 gene expression [64].

Sulforaphane was shown to inhibit the NF-κB pathway, a key regulator of all inflammation responses, in the sciatic nerve of diabetic animals [65]. The molecular mechanism of NF-κB inhibition by SFN remains unspecified and requires further investigation. Direct SFN action on NF-κB signaling or indirect action through Nrf2/HO-1 upregulation were suggested as possible answers to that question [65, 66].

Reduction of c-Jun N-terminal kinase phosphorylation levels, inhibition of NF-κB and AP-1 signaling, and a decrease in levels of the inflammatory mediators (iNOS, COX-2, NO, and PGE2) and pro-inflammatory cytokines (TNF-α, IL-6, and IL-1β) were observed under SFN treatment [67].

In addition, the anti-inflammatory effects of SFN were demonstrated via modulation of the PI3K/AKT/GSK3β/Nrf-2 and NF-κB pathways in T-cells. *In vitro* and *in vivo* studies demonstrated suppression of T-cell mediated immune responses by inhibiting the GSK3β pathway, NF-κB suppression, and Nrf2 activation by SFN [68].

Sulforaphane and obesity

Many Nrf2 activators have been used to investigate the effects of Nrf2 on obesity and its comorbidities. Sulforaphane provides pharmacological Nrf2 activation, subsequently affecting adipocyte differentiation and preventing adipogenesis and lipid accumulation [69]. Nrf2 activation directly targets the expression of lipogenic genes such as peroxisome proliferator-activated receptor gamma (PPARG) [70]. Recent studies suggest that activation of PPARG might decrease atherosclerosis progression and increase insulin sensitivity [71].

AMPK is a regulator of energy and lipid metabolism [72]. Inactivation of AMPK stimulates lipid biosynthesis while activation of AMPK via phosphorylation inhibits lipogenesis by the inactivation of key metabolic enzymes involved in fatty acid and cholesterol synthesis, such as acetyl-CoA carboxylase (ACC) and hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR) [73].

Lee and colleagues suggested that SFN induces lipolysis [74]. They determined that glycerol release occurred in a dose-dependent manner to SFN treatment and suppression of AMPK and hormone-sensitive lipase.

The anti-obesogenic effect of broccoli sprout powder, mustard (*Sinapis alba* L.) seed powder was demonstrated through inhibition of adipocyte differentiation and reduction of their accumulation *in vitro* [75]. Levels of adipogenesis-related proteins (aP2, PPAR-γ, SREBP-1C, FAS, and C/EBP-α) were reduced, while the level of carnitine palmitoyltransferase, fatty acid oxidation enzyme, was increased [75].

Liu and colleagues investigated the browning of white fat tissue (WAT) and enhancing mitochondrial biogenesis [76]. An *in vitro* study demonstrated the association between the browning effect of SFN, increased mitochondrial biogenesis, and the Nrf2/PGC-1α and MAPK pathways. MAPK pathway was upregulated due to SFN treatment and the browning of WAT was increased at the late period of adipogenesis. They connected their findings with the upregulation of the AMPK and Nrf2 signaling pathways [76].

Fat accumulation could be prevented by the induction of apoptosis, thus reducing adipocyte numbers [77]. It was reported that SFN induced apoptosis in 3T3-L1 adipocytes. The authors suggested that the investigated process was accomplished via the mitochondria-induced apoptosis mechanism through the down- or up-regulation of Akt/p70s6k1/Bad and ERK pathways [77].

An *in vitro* study showed that isothiocyanates from broccoli bind with bile acids and reduce fat absorption [78]. Broccoli sprout extract inhibited the activity of lipoprotein lipase, diacylglycerol acyltransferases, fatty acid synthase, and acyl-CoA-cholesterol acyltransferase, which are key lipogenic enzymes, and also reduced the expression of their related genes [79, 80]. Indole glucosinolates can reduce apolipoprotein B secretion, a primary apolipoprotein of low-density lipoproteins (LDL) [81].

Decreasing levels of triacylglycerides (TAG) is the main objective of lipid-lowering therapies [80]. Administration of an ethanol extract of broccoli sprouts in two doses of 200 and 400 g/kg for 4 weeks in HFD-fed rats decreased levels of serum total cholesterol, LDL, TAG, and increased level of high-density lipoproteins (HDL) [82].

Trials with broccoli sprout powder in T2DM patients for four weeks resulted in an 18.7% decrease in serum TAG levels [83]. A nonsignificant decrease in serum levels of total cholesterol and LDL was also observed in that study. An atherogenic index of plasma (defined as the logarithm of the TAG/HDL ratio) is considered a direct determination of the lipoprotein particle size and the risk of atherosclerosis. A significant 52% reduction in this ratio was observed in patients treated with broccoli sprout powder [83].

Another trial was carried out with the consumption of fresh broccoli sprouts. One-week treatment was accompanied by a reduction in both total cholesterol and LDL in healthy subjects [84]. In contrast, ingestion of 10 g/day broccoli sprouts powder during 4 weeks of intervention in patients with hypertension had no effects on levels of LDL, total cholesterol, and HDL [85].

Nagata and colleagues showed that oral administration of the SFN precursor glucoraphanin mitigated body mass gain and attenuated fat mass accumulation in HFD-fed mice without affecting food intake [86]. Glucoraphanin supplementation improved systemic glucose tolerance and insulin sensitivity. Glucoraphanin acted against adiposity and hepatic steatosis by promoting energy utilization and preventing lipogenesis and oxidative stress in the liver. It increased levels of uncoupling protein 1 (UCP1) in white adipose depots and enhanced browning in beige adipocytes [86].

Conclusion and perspectives

Broccoli sprouts and their preparations hold promise as beneficial food supplements for the prevention and treatment of type 2 diabetes mellitus, obesity, and comorbidities. Evidence supporting these benefits is derived from *in vitro* studies, animal models, and clinical trials. Activation of Nrf2 by sulforaphane, a key component of broccoli sprouts, has been shown to reduce body mass without decreasing food intake. Positive effects include improved energy utilization, enhanced insulin sensitivity, and the prevention of lipogenesis and oxidative stress development. Despite these promising findings, several key aspects remain to be clarified. Most studies have been limited to a dose-response analysis, pharmacodynamics, and sulforaphane concentration measurements. Additionally, the duration of feeding with broccoli supplements is a critical factor that requires further investigation. While most studies have limited treatment duration to four weeks, which may result in the absence of effects, more prolonged treatment may yield more definitive results.

Further research should focus on determining the optimal doses and durations of broccoli supplementation. Extended studies with various doses and longer treatment periods are needed to provide more comprehensive information about the therapeutic effects of broccoli sprouts. Understanding these parameters will help to maximize the benefits and minimize the limitations currently observed in broccoli sprout supplementation for metabolic disorders. Moreover, further studies are necessary to uncover other potential benefits and key mechanisms of action of broccoli components, such as glucosinolates, polyphenols, vitamins, etc. A deeper understanding of the molecular pathways involved, including the role of sulforaphane and its interaction with other cellular mechanisms, will provide insights into how broccoli sprouts can be more effectively used in the prevention and treatment of metabolic disorders.

Conflict of interest. The authors have completed the Unified Conflicts of Interest form at http://ukrbiochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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ПОТЕНЦІАЛ ІЗОТІОЦІАНАТУ СУЛЬФОРАФАНУ З ХРЕСТОЦВІТИХ РОСЛИН У БОРОТЬБІ З ОЖИРІННЯМ ТА ЦУКРОВИМ ДІАБЕТОМ 2 ТИПУ: ЗАЛУЧЕННЯ РЕГУЛЯТОРНОГО ШЛЯХУ NRF2

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Метою цього огляду було проаналізувати поточні дані щодо застосування ізотіоціанату сульфорафану, знайденого в броколі та інших хрестоцвітих рослинах, для лікування цукрового діабету 2 типу, ожиріння та їх супутніх захворювань із представленням встановлених молекулярних, особливо залежних від NF-E2-пов'язаного фактора-2 (Nrf2), і сигнальних механізмів терапевтичних ефектів.

Ключові слова: проростки броколі, Nrf2, дієтотерапія, ожиріння, профілактика, сульфорафан, цукровий діабет 2 типу.

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