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[Research Summary Dossier]

SULPHORAPHANE & BLOOD SUGAR

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| SmarterNaturally Explains |

Sulforaphane & Blood Sugar

Sulforaphane is the bioactive form of a molecule called glucoraphanin, which is found naturally in some plants (most notably broccoli). When eaten, glucoraphanin is converted in our gut into sulforaphane, which then enters our cells and exerts several different metabolic effects. Together, these serve to boost our production of antioxidants, reduce inflammation and improve our cell's ability to function, produce energy and repair damage.

Due to the effects of sulforaphane in our cells, it has been extensively researched for its beneficial effects on human health across a range of different areas - including supporting people with diabetes. Studies indicate that increasing our exposure to sulforaphane (via adding more glucoraphanin to our diet) could help to both improve glycemic control - reducing elevated blood sugar down to healthier levels - and to mitigate many of the complications of diabetes, including cardiomyopathy, vascular complications, retinopathy, neuropathy, nephropathy and reproductive health complications.

> "In conclusion, sulforaphane could be used as a novel small molecule against Type-2 Diabetes."
>
> *Review: The improvement of sulforaphane in type 2 diabetes mellitus (T2DM) and related complications (Wang et al, 2022)*

Together, these effects make glucoraphanin a valuable nutrient for people either with or predisposed to diabetes (including those with prediabetes and type-1 diabetes) who are looking to improve their blood sugar and mitigate the impact of their condition on their wider health and wellbeing.

Summary of Research & Evidence

Improved glycemic control & lower blood sugar levels

Administering glucoraphanin/sulforaphane has been found to improve glycemic control through a variety of redundant and potentiating mechanisms which act together to lower blood sugar levels.[1,2,3,4,5]

The most important avenue by which this is achieved seems to be through boosting the effectiveness of insulin, achieved both through improving insulin sensitivity/reducing insulin resistance[6,7,8,9,10,11,12,13,14,15,16,17,18] (a major component of disease development in type 2 diabetes), and improving the health and function of the pancreas to drive increased insulin production.[5,19,20,21,22]

Alongside this, sulforaphane has also been found to alter the behavior of the liver (reducing its production and release of glucose into the bloodstream[23,24,25] and instead driving it to burn up glucose for energy[16]) and fat cells (converting them from inactive 'white fat' cells to metabolically-active 'brown fat' cells which burn up excess glucose[26,27]), as well as actually directly driving a healthier lipid profile & loss of excess fat.[6,16,28,29,30,31,32,33,34]

> "Collectively, the data revealed that broccoli and sulforaphane have the potential to reduce hyperglycemia, hyperlipidemia, insulin resistance and diabetes-induced oxidative stress."
>
> *Beneficial role of broccoli and its active ingredient, sulforaphane in the treatment of diabetes (Mohammed et al. Phytomed Plus. 2023)*

Overall, there is a scientific consensus that sulforaphane could play a valuable role in blood sugar management, and that supplementation with dietary sources rich in glucoraphanin is an exciting new approach for the management of type-2 diabetes.

Reduced risk and severity of diabetic health complications
(coming soon)

About SmarterNaturally

SmarterNaturally Soup is a unique delivery vector for glucoraphanin. It's made using a unique glucoraphanin-rich broccoli called GR-extra that was developed over decades, is backed by patented research from the Quadram Institute and clinical trials run with Norfolk NHS hospitals, supported by public research grants from Innovate UK.

Just one bowl of SmarterNaturally Super-Soup contains a once-weekly dose of glucoraphanin - the equivalent of eating 5 heads of raw broccoli or taking 14 tablets of a leading glucoraphanin supplement. This makes it the most powerful, convenient and cost-effective solution on the market for adding glucoraphanin to your diet.

Plus, being a natural, plant-based food rather than a pill means our SouperSoup is also rich in fibre and a range of key vitamins and minerals. This allows it to act as a healthy meal alternative that's been carefully formulated to be suitable for diabetics, as well as an effective delivery method for our active ingredient.

References

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2. The improvement of sulforaphane in type 2 diabetes mellitus (T2DM) and related complications: A review *(Wang et al. Trends Food Sci Tech. 2022)*
3. Potential Efficacy of Broccoli Sprouts as a Unique Supplement
4. Broccoli sprouts reduce oxidative stress in type 2 diabetes: a randomized double-blind clinical trial *(Bahadoran et al. Eur J Clin Nutr. 2011)*
5. Brassica oleracea Extracts Prevent Hyperglycemia in Type 2 Diabetes Mellitus *(Gupta et al. Prev Nutr Food Sci. 2022)*
6. Effect of broccoli sprouts on insulin resistance in type 2 diabetic patients: a randomized double-blind clinical trial *(Bahadoran et al. Int J Food Sci Nutr. 2012)*
7. The Effects of Aerobic-Resistance Training and Broccoli Supplementation on Plasma Dectin-1 and Insulin Resistance in Males with Type 2 Diabetes *(Saeidi et al. Nutrients. 2021)*
8. Sulforaphane alleviates high fat diet-induced insulin resistance via AMPK/Nrf2/GPx4 axis *(Zhang et al. Biomed Pharmacother. 2022)*
9. Sulforaphane Regulates Glucose and Lipid Metabolisms in Obese Mice by Restraining JNK and Activating Insulin and FGF21 Signal Pathways *(Tian et al. J Agric Food Chem. 2021)*
10. Sulforaphane Prevents Hepatic Insulin Resistance by Blocking Serine Palmitoyltransferase 3-Mediated Ceramide Biosynthesis *(Teng et al. Nutrients. 2019)*
11. Comparison of the effects of sulforaphane and pioglitazone on insulin resistance and associated dyslipidemia, hepatosteatosis, and endothelial dysfunction in fructose-fed rats (*Shawky et al. Environ Toxicol Pharmacol. 2019)*
12. Sulforaphane ameliorates glucose intolerance in obese mice via the upregulation of the insulin signaling pathway *(Xu et al. Food Funct. 2018)*
13. Glucoraphanin Ameliorates Obesity and Insulin Resistance Through Adipose Tissue Browning and Reduction of Metabolic Endotoxemia in Mice *(Nagata et al. Diabetes. 2017)*
14. Sulforaphane improves dysregulated metabolic profile and inhibits leptin-induced VSMC proliferation: implications toward suppression of neointima formation after arterial injury in western diet-fed obese mice *(Shawky et al. J Nutr Biochem. 2016)*
15. Broccoli Florets Supplementation Improves Insulin Sensitivity and Alters Gut Microbiome Population—A Steatosis Mice Model Induced by High-Fat Diet *(Zandani et al. Front Nutr. 2021)*
16. Broccoli microgreens juice reduces body weight by enhancing insulin sensitivity and modulating gut microbiota in high-fat diet-induced C57BL/6J obese mice *(Li et al. Eur J Nutr. 2021)*
17. Metabolic Effects of Sulforaphane Oral Treatment in Streptozotocin-Diabetic Rats *(de Souza et al. J Med Food. 2012)*
18. Sulforaphane ameliorates the insulin responsiveness and the lipid profile but does not alter the antioxidant response in diabetic rats *(de Souza et al. Food Funct. 2016)*
19. The protective effect of sulforaphane on type II diabetes induced by high-fat diet and low-dosage streptozotocin (*Tian et al. Food Sci Nutr. 2020)*
20. Broccoli (Brassica oleracea) Reduces Oxidative Damage to Pancreatic Tissue and Combats Hyperglycaemia in Diabetic Rats *(Suresh et al. Prev Nutr Food Sci. 2017)*
21. Sulforaphane Protects against High Cholesterol-Induced Mitochondrial Bioenergetics Impairments, Inflammation, and Oxidative Stress and Preserves Pancreatic β-Cells Function *(Carrasco et al. Oxid Med Cell Longev. 2017)*
22. Lipotoxic Stress Induces Pancreatic β-Cell Apoptosis through Modulation of Bcl-2 Proteins by the Ubiquitin-Proteasome System *(Litwak et al. J Diabetes Res. 2015)*
23. Could broccoli have a role in combating type 2 diabetes mellitus? *(Holmes et al. Nat Rev Endocrinol. 2017)*
24. Sulforaphane reduces hepatic glucose production and improves glucose control in patients with type 2 diabetes *(Axelsson et al. Sci Transl Med. 2017)*
25. Sulforaphane improves disrupted ER-mitochondria interactions and suppresses exaggerated hepatic glucose production *(Tubbs et al. Mol Cell Endocrinol. 2018)*
26. Sulforaphane induces adipocyte browning and promotes glucose and lipid utilization *(Zhang et al. Mol Nutr Food Res. 2016)*
27. The Protective Effects of Sulforaphane on High-Fat Diet-Induced Obesity in Mice Through Browning of White Fat *(Liu et al. Front Pharmacol. 2021)*
28. Potential effects of sulforaphane to fight obesity *(J Sci Food Agric. 2018)*
29. Glucoraphanin: a broccoli sprout extract that ameliorates obesity-induced inflammation and insulin resistance *(Adipocyte. 2018)*
30. The Effects of Aerobic-Resistance Training and Broccoli Supplementation on Plasma Dectin-1 and Insulin Resistance in Males with Type 2 Diabetes *(Saeidi et al. Nutrients. 2021)*
31. Broccoli sprouts powder could improve serum triglyceride and oxidized LDL/LDL-cholesterol ratio in type 2 diabetic patients: A randomized double-blind placebo-controlled clinical trial *(Bahadoran et al. Diabetes Res Clin Pract. 2012)*
32. Sulforaphane ameliorates lipid profile in rodents: an updated systematic review and meta-analysis *(Du et al. Sci Rep. 2021)*
33. Broccoli microgreens have hypoglycemic effect by improving blood lipid and inflammatory factors while modulating gut microbiota in mice with type 2 diabetes *(Ma et al. J Food Biochem. 2022)*
34. Dietary broccoli improves markers associated with glucose and lipid metabolism through modulation of gut microbiota in mice *(Zandani et al. Nutrition. 2021)*

Sulforaphane & Blood Sugar

Dossier of Supporting Evidence

SmarterNaturally's products are all made using GRextra - our unique super-broccoli which contains ~5x more glucoraphanin than traditional varieties of broccoli - as well as other bioactive molecules and polyphenols (including indole-3-carbinol/DIM, quercetin and kaempferol).

Glucoraphanin is a natural health-boosting molecule. When converted into its active form (called sulforaphane) in our gut, it has powerful effects on our metabolism, driving our body's natural anti-oxidant (Nrf2) and anti-inflammatory (anti-NFkB) responses to boost our health, as well as promoting cell resilience and survival through triggering heat-shock and other related pathways.

Through these pathways, there is now a growing body of evidence that these molecules can support the management of diabetes, both through helping to reduce elevated blood sugar down to healthier levels, and through mitigating the severity of secondary health complications of high blood sugar levels, which diabetics are at a far greater risk of suffering from.

Research studies have specifically linked glucoraphanin & sulforaphane to:

1. Improved glycemic control

Administering glucoraphanin/sulforaphane has been found to improve glycemic control through a variety of redundant and potentiating mechanisms, which act together to lower blood sugar levels both directly and indirectly (through boosting the effectiveness of the insulin pathway).

a. Improved insulin sensitivity and reduced insulin resistance

[REVIEW] Beneficial role of broccoli and its active ingredient, sulforaphane in the treatment of diabetes
Mohammed et al. Phytomed Plus. 2023 May;3(2):100431
(doi: 10.1016/j.phyplu.2023.100431)

“Collectively, the data revealed that broccoli and sulforaphane have the potential to reduce hyperglycemia, hyperlipidemia, insulin resistance and diabetes-induced oxidative stress… The present review confirms and encourages the inclusion of broccoli in the usual diet due to the high sulforaphane content.”

[REVIEW] The improvement of sulforaphane in type 2 diabetes mellitus (T2DM) and related complications: A review
Wang et al. Trends Food Sci Tech. 2022;129:397-407
(doi: 10.1016/j.tifs.2022.10.007)

“A variety of research has shown that sulforaphane could improve insulin resistance… In conclusion, sulforaphane could be used as a novel small molecule against T2DM.”

[REVIEW] Potential Efficacy of Broccoli Sprouts as a Unique Supplement for Management of Type 2 Diabetes and Its Complications
Bahadoran et al. J Med Food. 2013 May;16(5):375-82
(doi: 10.1089/jmf.2012.2559)

“Based on in vitro studies, animal models and some clinical trials, broccoli sprouts, a main source of bioactive components, especially sulforaphane, has been proposed as an effective supplement for diabetes management and prevention of its long-term complications.”

Effect of broccoli sprouts on insulin resistance in type 2 diabetic patients: a randomized double-blind clinical trial
Bahadoran et al. Int J Food Sci Nutr. 2012 Nov;63(7):767-71.
(doi: 10.3109/09637486.2012.665043)

Dosage = 5 or 10 g broccoli sprout powder per day for 28 days (~ 22.5 umol SFN/g)

- Human RCT, N=81 T2D patients
- "4-week supplementation 10 g/d BSP decreased fasting serum insulin & IR index."
- "It appears that the effect of broccoli sprouts on the improvement of hyperinsulinaemia and IR observed in this study is related to the antioxidant properties of bioactive components mainly SPN. SPN is an activator of transcription factor NF-E2-related factor-2, which is a potential regulator of the cellular redox homoeostasis through its capacity to induce the expression of enzymes that detoxify reactive oxygen species and other antioxidant proteins."
- "Enhancement of the endogenous antioxidant network inhibits stress-sensitive signalling pathways and consequently prevents IR and other long-term complications of diabetes"

The Effects of Aerobic-Resistance Training and Broccoli Supplementation on Plasma Dectin-1 and Insulin Resistance in Males with Type 2 Diabetes
Saeidi et al. Nutrients. 2021 Sep 9;13(9):3144.
(doi: 10.3390/nu13093144)

Dosage = 10g broccoli supplement /day for 12 weeks (~ 225 umol / 22.5 mmol/g SFN)

- Human RCT, N=44 T2D patients. 225 umol SFN /day for 12 weeks
- "We also measured improvements in insulin and HOMA-IR in the S (broccoli only) and TS (broccoli and exercise) groups when compared with their baseline levels, with the improvements caused by broccoli consumption similar to other studies."

Broccoli sprouts reduce oxidative stress in type 2 diabetes: a randomized double-blind clinical trial
Bahadoran et al. Eur J Clin Nutr. 2011 Aug;65(8):972-7.
(doi: 10.1038/ejcn.2011.59)

Dosage = BSP 10 g or 5 g/day for 28 days (estimated 22.5 umol SFN/g)

- Human RCT, N=81 T2D patients
- "In this study, the FBS was not the primary endpoint; however, it significantly decreased in both BSP groups"

Glyceamic and insulinaemic response to mashed potato alone, or with broccoli, broccoli fibre or cellulose in healthy adults
Ballance et al. Eur J Nutr. 2018 Feb;57(1):199-207.
(doi: 10.1007/s00394-016-1309-7)

Dosage = 360g broccoli florets or 8mg milled broccoli fibre for one meal before testing

- Human non-blind randomized crossover trial, n=13
- "The immediate glycemic response and insulinemic response to one serving of mashed potato eaten with two servings of broccoli were significantly lower than mashed potato eaten alone."

Sulforaphane alleviates high fat diet-induced insulin resistance via AMPK/Nrf2/GPx4 axis
Zhang et al. Biomed Pharmacother. 2022 Aug;152:113273.
(doi: 10.1016/j.biopha.2022.113273)

Dosage = 0.5 mg/kg SFN subcutaneously injected five times a week for 8 weeks

- "In this study, SFN was found to significantly reduce body weight, FBG, FINS and HOMA-IR index, and effectively improved insulin sensitivity in mice fed with HFD`'
- "By activating the vAMPK-Nrf2-GPx4 signaling cascade, SFN accelerated the clearance of ROS and reduced the accumulation of lipid peroxides MDA and 4-HNE to eventually restore impaired insulin signaling (inflicted by HFD-induced oxidative stress) to some extent, effectively reducing the extent of insulin resistance."

Sulforaphane Regulates Glucose and Lipid Metabolisms in Obese Mice by Restraining JNK and Activating Insulin and FGF21 Signal Pathways
Tian et al. J Agric Food Chem. 2021 Nov 10;69(44):13066-13079.
(doi: 10.1021/acs.jafc.1c04933)

Dosage = 10mg/kg SFN by oral gavage daily for 8 weeks

- (In mice) "Oral administration of metformin or SFN for 8 weeks resulted in significantly lower blood glucose concentrations at 60 and 120 min. Interestingly, the blood glucose concentrations in the HS (SFN) group were markedly lower than those in the PC (metformin) group at the time points of 60 & 120 min"
- "SFN regulated glucose and lipid metabolism by deactivating c-Jun N-terminal kinase (JNK) and blocking the inhibitory effect of the insulin signaling pathway. SFN also regulated glucose metabolism by alleviating fibroblast growth factor 21 (FGF21) resistance"

Sulforaphane Prevents Hepatic Insulin Resistance by Blocking Serine Palmitoyltransferase 3-Mediated Ceramide Biosynthesis
Teng et al. Nutrients. 2019 May 27;11(5):1185.
(doi: 10.3390/nu11051185)

Dosage = 0.5 or 5mg/kg SFN three times a week for 10 weeks via intraperitoneal injection

- (In mice) "We conclude that SFA recovers glucose homeostasis and improves insulin sensitivity by blocking ceramide biosynthesis through modulating SPTLC3"
- "The results showed that SFA dose-dependently increased glucose uptake and intracellular glycogen content by regulating the insulin receptor substrate 1 (IRS-1)/protein kinase B (Akt) signaling pathway in insulin-resistant HepG2 cells."

Comparison of the effects of sulforaphane and pioglitazone on insulin resistance and associated dyslipidemia, hepatosteatosis, and endothelial dysfunction in fructose-fed rats
Shawky et al. Environ Toxicol Pharmacol. 2019 Feb;66:43-54.
(doi: 10.1016/j.etap.2018.12.008)

Dosage = 0.5 or 5 mg/kg via oral daily administration for 44 days (day 16 to day 60)

- (In rats) "SFN showed insulin-sensitizing, hepatoprotective and vasculoprotective effects in fructose-fed rats, comparable to those exerted by PIO (piogliatazone). These effects could be explained on the basis of SFN mediated antioxidant and anti-inflammatory effects"

Sulforaphane ameliorates glucose intolerance in obese mice via the upregulation of the insulin signaling pathway
Xu et al. Food Funct. 2018 Sep 19;9(9):4695-4701.
(doi: 10.1039/c8fo00763b)

Dosage = 100 umol/kg SFN three times a week for 6 weeks

- (In mice) "In conclusion, our results support the notion that SFN acts as a promising agent to improve glucose tolerance through the up-regulation of insulin signaling mainly involving the IRS-1/Akt/GLUT4 pathway in the muscle"

Glucoraphanin Ameliorates Obesity and Insulin Resistance Through Adipose Tissue Browning and Reduction of Metabolic Endotoxemia in Mice
Nagata et al. Diabetes. 2017 May;66(5):1222-1236.
(doi: 10.2337/db16-0662)

Dosage = High fat diet containing 0.3% GR (containing 2.2% extract powder) for 14 weeks. Extract powder contained 135 mg GR/g or 0.31 mmol GR/g

- (In mice) "On NC (normal chow), blood glucose levels were not altered by glucoraphanin, but on the HFD, glucoraphanin-treated mice exhibited significantly lower fasted blood glucose compared with vehicle-treated controls"
- "Additionally, glucoraphanin significantly decreased plasma insulin concentrations in HFD-fed mice under both fasted and fed conditions, resulting in lower homeostatic model assessment-insulin resistance (HOMA-IR)"
- "In line with increased insulin sensitivity, insulin-stimulated Akt phosphorylation on Ser473 was enhanced by glucoraphanin in the liver, muscle, and epididymal WAT of mice fed the HFD"

Sulforaphane improves dysregulated metabolic profile and inhibits leptin-induced VSMC proliferation: implications toward suppression of neointima formation after arterial injury in western diet-fed obese mice
Shawky et al. J Nutr Biochem. 2016 Jun;32:73-84.
(doi: 10.1016/j.jnutbio.2016.01.009)

Dosage = 0.5 mg/kg SFN injected subcutaneously per day for 22 days (day 35 to day 57)

- "It is apparent that SFN-mediated decrease in plasma leptin may in part be accountable for the observed decrease in plasma insulin and improvements in HOMA-IR value (an index of insulin resistance) and glucose tolerance."

Brassica oleracea Extracts Prevent Hyperglycemia in Type 2 Diabetes Mellitus
Gupta et al. Prev Nutr Food Sci. 2022 Mar 31;27(1):50-62.
(doi: 10.3746/pnf.2022.27.1.50)

Dosage = 400 mg/kg of Brassica extract (unknown GR/SFN) orally for 42 days

- (In rats) "Significant improvement in blood glucose levels was observed in groups treated with 400 mg/kg of B. oleracea aqueous (32.31%), ethanol (19.62%), and petroleum ether (18.65%) extracts from days 0 to 7 (Table 1)."
- Furthermore, serum insulin level was restored to normal when treated with Brassica extracts (200 and 400 mg/kg)."

Broccoli Florets Supplementation Improves Insulin Sensitivity and Alters Gut Microbiome Population—A Steatosis Mice Model Induced by High-Fat Diet
Zandani et al. Front Nutr. 2021 Jul 28;8:680241.
(doi: 10.3389/fnut.2021.680241)

Dosage = High fat diet + 10% broccoli florets or stalks for 17 weeks (unknown GR/SFN)

- (In mice) "Broccoli florets addition to the HFD significantly reduced serum insulin levels, HOMA-IR index, and upregulated adiponectin receptor expression."
- "Modifications in diversity and in microbial structure of proteobacteria strains, Akermansia muciniphila and Mucispirillum schaedleri were also observed."

Broccoli microgreens juice reduces body weight by enhancing insulin sensitivity and modulating gut microbiota in high-fat diet-induced C57BL/6J obese mice
Li et al. Eur J Nutr. 2021 Oct;60(7):3829-3839.
(doi: 10.1007/s00394-021-02553-9)

Dosage = 0.4 ml 20g/kg broccoli microgreens juice orally daily for 8 weeks (weeks 2-10)

- "Our study indicated that [broccoli microgreens juice] enhanced insulin sensitivity by relieving inflammation, which may be a consequence of microbiome changes."

Metabolic Effects of Sulforaphane Oral Treatment in Streptozotocin-Diabetic Rats
de Souza et al. J Med Food. 2012 Sep;15(9):795-801.
(doi: 10.1089/jmf.2012.0016)

Dosage = 0.1, 0.25 or 0.5 mg/kg SFN via daily gavage for 3 days

- "Animals treated with SFN showed fasting glycemia, insulin sensitivity, and hepatic glycogen concentrations, similar to the control group (nondiabetic), and different from the diabetic group."

Sulforaphane ameliorates the insulin responsiveness and the lipid profile but does not alter the antioxidant response in diabetic rats
de Souza et al. Food Funct. 2016 Apr;7(4):2060-5.
(doi: 10.1039/c5fo01620g)

Dosage = 0.5 mg/kg SFN daily via intraperitoneal injection for 21 days

- "The improvement in the glycemia of the diabetic animals during the IRT suggests a synergistic effect of SFN and insulin."

b. Increased insulin production, through prevention and repair of pancreatic damage

The protective effect of sulforaphane on type II diabetes induced by high-fat diet and low-dosage streptozotocin
Tian et al. Food Sci Nutr. 2020 Dec 10;9(2):747-756.
(doi: 10.1002/fsn3.2040)

Dosage = 2mg/kg (LS group) or 10 mg/kg (HS group) SFN daily gavage for 8 weeks

- (In mice) “Overall, our results showed that SFN exerted its antidiabetic effect through easing NAFLD and repairing pancreas tissue in association with modulation of gut microbiota.”
- “the blood glucose of LS, HS, and PC groups was lower than DM group, it contributed to the protective effect of SFN on type II diabetes.”

Brassica oleracea Extracts Prevent Hyperglycemia in Type 2 Diabetes Mellitus
Gupta et al. Prev Nutr Food Sci. 2022 Mar 31;27(1):50-62.
(doi: 10.3746/pnf.2022.27.1.50).

Dosage = 400 mg/kg of Brassica oleracea aqueous extract (unknown GR/SFN) orally for 42 days

- (In rats) “The pancreatic β cells showed remarkable improvement in the ethanol and aqueous extract treated groups (Fig. 4H~4L) compared with the negative control group. Cellular regeneration was also observed in all treated groups at higher doses.”

Broccoli (Brassica oleracea) Reduces Oxidative Damage to Pancreatic Tissue and Combats Hyperglycaemia in Diabetic Rats
Suresh et al. Prev Nutr Food Sci. 2017 Dec;22(4):277-284.
(doi: 10.3746/pnf.2017.22.4.277)

Dosage = oral dose of 70.6 mg/kg of polyphenols in broccoli extract per week (calculated from the extract dose of 5ml/week)

- (In mice) “The freeze-dried BE-treated diabetic rats had decreased glucose levels.”
- “The results of this study indicated that BE reduced the STZ mediated hyperglycaemia and the STZ-induced oxidative injury to pancreas tissue.”

Sulforaphane Protects against High Cholesterol-Induced Mitochondrial Bioenergetics Impairments, Inflammation, and Oxidative Stress and Preserves Pancreatic β-Cells Function
Carrasco et al. Oxid Med Cell Longev. 2017;2017:3839756.
(doi: 10.1155/2017/3839756)

Dosage = 2 uM or 10 uM SFN for 6 h or 20 h

- (In vitro) “SFN, to the same extent as ES (another Nrf2 activator), prevented glucose-stimulated insulin secretion impairment in a pancreatic β-cell line exposed to cholesterol”

Lipotoxic Stress Induces Pancreatic β-Cell Apoptosis through Modulation of Bcl-2 Proteins by the Ubiquitin-Proteasome System
Litwak et al. J Diabetes Res. 2015;2015:280615.
(doi: 10.1155/2015/280615)

Dosage = 10 uM SFN for 2, 4, 8, or 24h

- (In vitro) “In conclusion, we found that the FFA palmitate inhibits the UPS, causing β-cell apoptosis, and that this effect could be reversed by activation of the proteasome."
- “Importantly, palmitate-induced β-cell death was prevented by SFN” (Palmitate is a free fatty acid)

c. Reduced hepatic glucose production

Could broccoli have a role in combating type 2 diabetes mellitus?
Holmes et al. Nat Rev Endocrinol. 2017 Aug;13(8):437
(doi: 10.1038/nrendo.2017.86)

- “Remarkably, sulforaphane suppressed hepatic glucose production and improved glucose tolerance by a similar magnitude as metformin.”

Sulforaphane reduces hepatic glucose production and improves glucose control in patients with type 2 diabetes
Axelsson et al. Sci Transl Med. 2017 Jun 14;9(394):eaah4477.
(doi: 10.1126/scitranslmed.aah4477)

Dosage = 0.5 to 10 uM SFN for 24h in-vitro; 5 or 10 mg/kg SFN daily via intraperitoneal injection for 14 days in rats; 0.5 or 10 mg/kg SFN daily via intraperitoneal injection for 4 weeks in mice; broccoli sprout extract (BSE) daily at 1.1 mg/kg SFN for 4 weeks in mice; oral BSE containing 150 uml SFN per dose once daily for 12 weeks in humans

- Human RCT, N=103 T2D patients
- “Sulforaphane suppressed glucose production from hepatic cells by nuclear translocation of nuclear factor erythroid 2–related factor 2 (NRF2) and decreased expression of key enzymes in gluconeogenesis”
- “Sulforaphane reversed the disease signature in the livers from diabetic animals and attenuated exaggerated glucose production and glucose intolerance by a magnitude similar to that of metformin.”
- “Sulforaphane, provided as concentrated broccoli sprout extract, reduced fasting blood glucose and glycated hemoglobin (HbA1c) in obese patients with dysregulated type 2 diabetes.”

Sulforaphane improves disrupted ER-mitochondria interactions and suppresses exaggerated hepatic glucose production
Tubbs et al. Mol Cell Endocrinol. 2018 Feb 5;461:205-214.
(doi: 10.1016/j.mce.2017.09.016)

Dosage = 3 uM SFN for 24h in vitro; 10 mg/kg SFN daily gavage for 4 weeks

- "Our study shows that SFN reduces glucose production in mouse hepatocytes.”
- (In mice) “SFN improved glucose tolerance and MAM integrity to a similar extent to that of metformin.”

d. Restored hepatic glucose metabolism

The protective effect of sulforaphane on type II diabetes induced by high-fat diet and low-dosage streptozotocin
Tian et al. Food Sci Nutr. 2020 Dec 10;9(2):747-756.
(doi: 10.1002/fsn3.2040)

Dosage = 2mg/kg (LS group) or 10 mg/kg (HS group) SFN daily gavage for 8 weeks

- (In mice) “We speculate that SFN may restore its glucose metabolism function by easing NAFLD which involved in enhancing of liver antioxidant ability and attenuating FGF21 resistance”
- “SFN was able to increase serum insulin level, enhance HOMA-β index, decrease fasting blood glucose and serum total cholesterol, triglyceride, low-density lipoprotein (LDL-C), fibroblast growth factor21 (FGF21) levels, ease NAFLD level, and repair the pancreas tissue.”

e. Increased glucose uptake by adipocytes and muscle cells

Sulforaphane induces adipocyte browning and promotes glucose and lipid utilization
Zhang et al. Mol Nutr Food Res. 2016 Oct;60(10):2185-2197.
(doi: 10.1002/mnfr.201500915)

Dosage = 0.2, 0.5, 1, 5, 10 uM SFN for 48h

- (In vitro) “these findings support the notion that browning of adipocytes triggered by SFN promotes glucose and lipid utilization in adipocytes, is favourable for improving of whole-body metabolic load, and therefore, may be considered as an appealing strategy for addressing obesity and obesity-related diseases.”

The Protective Effects of Sulforaphane on High-Fat Diet-Induced Obesity in Mice Through Browning of White Fat
Liu et al. Front Pharmacol. 2021 Apr 29;12:665894.
(doi: 10.3389/fphar.2021.665894)

Dosage = 10 mg/kg SFN daily via intraperitoneal injection for 30 days

- (In mice) “Our study suggests that SFN, as a nutritional factor, is a promising medicine in the battle against obesity and various metabolic disorders via promoting the browning of white fat and improving glucose metabolism.”
- "The SFN-treated mice showed remarkable improvement in glucose and insulin tolerance compared with vehicle control”

f. Improved insulin sensitivity through lipid profile modulation and weight loss

[REVIEW] Potential effects of sulforaphane to fight obesity
J Sci Food Agric. 2018 Jun;98(8):2837-2844
(doi: 10.1002/jsfa.8898)

“Thus the use of supplementation with natural compounds such as SFN, an isothiocyanate present in cruciferous vegetables such as broccoli and cauliflower, as an adjunct to lifestyle change can be a potentially effective way to treat obesity.”

[REVIEW] Glucoraphanin: a broccoli sprout extract that ameliorates obesity-induced inflammation and insulin resistance
Adipocyte. 2018;7(3):218-225
(doi: 10.1080/21623945.2018.1474669)

“Glucoraphanin acts against adiposity and hepatic steatosis by promoting energy utilization and preventing lipogenesis and oxidative stress in the liver.”

The Effects of Aerobic-Resistance Training and Broccoli Supplementation on Plasma Dectin-1 and Insulin Resistance in Males with Type 2 Diabetes
Saeidi et al. Nutrients. 2021 Sep 9;13(9):3144
(doi: 10.3390/nu13093144)

Dosage = 10g broccoli supplement per day for 12 weeks (approximately 225 umol SFN, or 22.5 mmol/g)

- Human RCT, N=44 T2D patients
- “Our study also reports improvements in the lipid profiles in the S, TP, and TS groups compared with their baseline levels; however, our study failed to improve lipid profiles, except for HDL-C, in the S group when compared to the CP group.”

Broccoli sprouts powder could improve serum triglyceride and oxidized LDL/LDL-cholesterol ratio in type 2 diabetic patients: A randomized double-blind placebo-controlled clinical trial
Bahadoran et al. Diabetes Res Clin Pract. 2012 Jun;96(3):348-54
(doi: 10.1016/j.diabres.2012.01.009)

Dosage = 5 or 10 g per day of broccoli sprout powder for 4 weeks

- Human RCT, N=81 T2D patients
- "After 4 weeks, BSP in dose of 10 g/d, significantly decreased serum triglycerides, OX-LDL/LDL ratio and AIP ($p < 0.05$ for treatment effect)"
- However, non-significant decreases in fasting blood glucose

Broccoli sprouts reduce oxidative stress in type 2 diabetes: a randomized double-blind clinical trial
Bahadoran et al. Eur J Clin Nutr. 2011 Aug;65(8):972-7.
(doi: 10.1038/ejcn.2011.59)

Dosage = BSP 10 g or 5 g/day for 28 days (estimated 22.5 umol SFN/g)

- Human RCT, N=81 T2D patients
- "Administration of BSP at doses of 10 g/d for 4 weeks induced improvement in lipid peroxidation in type 2 diabetes patients. These effects were seen with a decrease in plasma MDA (malondialdehyde) and OX-LDL."

Sulforaphane ameliorates lipid profile in rodents: an updated systematic review and meta-analysis
Du et al. Sci Rep. 2021 Apr 8;11(1):7804.
(doi: 10.1038/s41598-021-87367-9)

Dosage = Variable, most studies included featured from 0.5 mg up to 30 mg/kg of body weight per day via oral gavage or intraperitoneal or subcutaneous injection for between 3 and 16 weeks (one study used 1g/kg of diet)

- (In rodents) "In this updated meta-analysis, ten articles were utilized to assess SFN supplementation effects on body weight and lipid profile in preclinical animal models. Our analysis clearly demonstrates that SFN supplementation significantly decreased BW, LW, TC as well as LDL-C levels, apart from HDL-C."

Broccoli microgreens have hypoglycemic effect by improving blood lipid and inflammatory factors while modulating gut microbiota in mice with type 2 diabetes
Ma et al. J Food Biochem. 2022 Jul;46(7):e14145
(doi: 10.1111/jfbc.14145)

Dosage = 0.2 or 2 g/kg of broccoli microgreens via oral gavage daily for 8 weeks

- (In mice) “After treatment of broccoli microgreens, the blood lipid levels of mice decreased, especially in terms of TG and LDL-C levels.”

Brassica oleracea Extracts Prevent Hyperglycemia in Type 2 Diabetes Mellitus
Gupta et al. Prev Nutr Food Sci. 2022 Mar 31;27(1):50-62
(doi: 10.3746/pnf.2022.27.1.50)

Dosage = 400 mg/kg of Brassica oleracea aqueous extract (unknown GR/SFN) orally for 42 days

- (In rats) “Additionally, the plant extracts improved lipid profiles in a rat model with insulin resistance.”
- “Bodyweight was reduced ($P<0.05$) on the 45th day in groups treated with 400 mg/kg of ethanol extract, 100 mg/kg of aqueous extract, and metformin compared with the negative control group (Table 2).”

Dietary broccoli improves markers associated with glucose and lipid metabolism through modulation of gut microbiota in mice
Zandani et al. Nutrition. 2021 Oct;90:111240
(doi: 10.1016/j.nut.2021.111240)

Dosage = Diet with 10% by weight broccoli florets and stalks for 17 weeks (ad libitum access to food)

- (In mice) “This study provides new evidence regarding the benefits of broccoli stalks to improved glucose levels, insulin, and HOMA-IR index. Our results further suggest that broccoli stalks ameliorate fat oxidation by preserving liver AMPK activity and genes related to the process, while broccoli florets decrease fat mass and systemic triacylglycerol levels.”

Broccoli microgreens juice reduces body weight by enhancing insulin sensitivity and modulating gut microbiota in high-fat diet-induced C57BL/6J obese mice

Li et al. Eur J Nutr. 2021 Oct;60(7):3829-3839
(doi: 10.1007/s00394-021-02553-9)

Dosage = 0.4 ml 20g/kg broccoli microgreens juice administered by oral gavage daily for 8 weeks (from week 2 to week 10)

- “Furthermore, BMJ significantly enhanced insulin sensitivity and improved dyslipidemia”