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[SmarterNaturally Explains]

GRextra for WEIGHT LOSS

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GRextra for Weight Loss

Glucoraphanin is a natural molecule found in some plants - most notably broccoli. When these plants are eaten, glucoraphanin is converted into its active form - called sulforaphane - which is then absorbed by our gut. Sulforaphane then enters our cells and exerts several different metabolic effects, which together serve to boost our production of antioxidants, reduce inflammation, and improve our cell's ability to function, produce energy and repair damage.

GRextra is our super-strain of broccoli, which is a powerful source of sulforaphane.
For more details, including biological mechanisms of action, see our ***Guide to GRextra***

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 weight loss. Studies indicate that adding more sulforaphane to our diet could act through several different mechanisms to encourage the body to lay down less fat and burn up existing fat deposits as well as reducing appetite and food intake, leading to reduced body weight.

Adding more sulforaphane to our diet has also been shown in studies to help alleviate many of the negative consequences of obesity, including fatty liver disease, high cholesterol, and chronic inflammation.

> "Sulforaphane is a prime candidate (for) use against a preoccupying condition rampaging through mainly developed countries: obesity and its associated complications."
>
> *Review: Three in One: The Potential of Brassica By-Products against Economic Waste, Environmental Hazard, and Metabolic Disruption in Obesity (Castelão-Baptista et al, 2021)*

Together, these effects make glucoraphanin a valuable dietary nutrient for people looking to support their weight loss efforts and mitigate the impact of obesity on their health and wellbeing.

Summary of Research & Evidence

Below, we've summarised the key areas of research which are showing promising results for the potential of glucoraphanin & sulforaphane to support weight loss and mitigate the symptoms and complications of obesity, including:

1. Reduced body weight

Glucoraphanin/sulforaphane rich diets have been found, in both meta-analyses of animal studies,[1] and in epidemiological studies in humans,[2] to reduce body fat. Weight loss is achieved through numerous complementary pathways including:

- reducing the deposition of fat and the accumulation of fat cells[3,4,5,6,7,8,9,10]
- reducing appetite and food intake (through increasing responsiveness to the appetite suppressant hormone leptin)[11,12,13]
- promoting the burning of fat through increasing mitochondrial production[14] and driving the body to burn fats for energy[15,16]
- stimulating the conversion of inactive white fat to metabolically-active brown fat, promoting a higher base metabolic rate[17,18,19]
- supporting the gut microbiome to increase levels of good bacteria, which improves both fat and glucose metabolism,[20,21] further supporting weight loss

> "Treatment [with sulforaphane] reduces fat deposition in white adipose tissue and liver, decreases proliferation and differentiation of adipocytes, promotes white adipose tissue browning with an increase of energy expenditure, improves insulin sensitivity, reduces inflammation and decreases food intake."
>
> *Review: Mechanisms Underlying Biological Effects of Cruciferous Glucosinolate-Derived Isothiocyanates/Indoles: A Focus on Metabolic Syndrome (Esteve. Front Nutr. 2020)*

Through reducing fat deposition, suppressing appetite, promoting fat burning and browning, and increasing levels of good bacteria in the gut, these natural molecules can help to prevent weight gain and support weight loss.

2. Reduced insulin resistance

Administering glucoraphanin/sulforaphane in animal studies has been found to ameliorate glucose intolerance and insulin resistance,[13,22,23] via enhancing glucose uptake our of the blood and into muscles.[26]

This is supported by human studies which show that glucoraphanin/sulforaphane can support improved insulin sensitivity and healthier blood sugar levels, both in people who are overweight and diabetic,[24,25,26] as well as those of a healthy weight.[27]

> “Sulforaphane acts as a promising agent to improve glucose tolerance through up-regulation of insulin signaling.”
>
> *Sulforaphane ameliorates glucose intolerance in obese mice via upregulation of insulin signaling pathway (Xu et al, 2018)*

These natural molecules therefore offer promise to those wishing to lose weight, not just in terms of supporting fat loss but also in terms of preventing conditions associated with excessive body fat such as insulin resistance and diabetes.

(For more detail on the potential benefits of glucoraphanin/sulforaphane in diabetes, see our dedicated ‘Sulforaphane & Blood Sugar Explained’ document.)

3. Reduced inflammation

Being overweight is associated with chronic systemic inflammation, which drives a wide range of diseases and negative health impacts. Human, animal, and in vitro studies have indicated that as well as reducing body weight, liver fat, and ‘bad’ cholesterol levels, glucoraphanin/sulforaphane can soothe this chronic inflammation, through:

- reducing levels of pro-inflammatory molecules (such as IL-6 and C-reactive protein[28] and IL-1β and TNF-α in the blood[29]
- modulating the response of immune cells to suppress their production of pro-inflammatory molecules[32,33]
- reducing levels of harmful gut bacteria which release inflammation-inducing lipopolysaccharides (LPS)[18,20,21,27]
- increasing levels of good gut bacteria that promote gut integrity and prevent these harmful lipopolysaccharides (LPS) from entering the blood[20,21]

> “Sulforaphane modulates inflammatory responses in immune cells and may play a role in reducing systemic inflammation in obesity.”
>
> *Sulforaphane reduces pro-inflammatory response to palmitic acid in monocytes and adipose tissue macrophages (Williams et al, 2022)*

This means that these natural molecules can reduce the systemic inflammation caused by excess body fat and, therefore, reduce the risk of conditions associated with increased inflammation including cardiovascular disease, diabetes, and metabolic syndrome.

4. **Alleviation of metabolic non-alcoholic fatty liver disease (also known as hepatic steatosis)**

Animal and in-vitro studies have shown that glucoraphanin/sulforaphane both can prevent and reverse excessive fat build up in the liver (a condition commonly associated with obesity and commonly responsible for liver damage) by increasing energy expenditure and fat metabolism,[18] and preventing fat deposition in the liver.[2,30,31]

> "Notably, the anti-obesity agents sulforaphane and glucoraphanin prevent hepatic steatosis by increasing energy utilization and preventing lipogenesis and oxidative stress in the liver."
>
> *Impact of Glucoraphanin-Mediated Activation of Nrf2 on Non-Alcoholic Fatty Liver Disease with a Focus on Mitochondrial Dysfunction (Xu et al. Int J Mol Sci, 2019)*

Through preventing the development of a fatty liver, these natural molecules can help to minimise the destructive impact of obesity and promote healthy liver function.

5. **Healthier cholesterol levels**

Human trials have shown that administering glucoraphanin/sulforaphane results in reductions in 'bad' cholesterol (LDL) levels,[32,33] and increases 'good' cholesterol (HDL) levels[25] by promoting cellular metabolic activity and suppressing lipid and cholesterol synthesis.[24]

> "Evidence from two independent human studies indicates that consumption of high glucoraphanin broccoli significantly reduces plasma LDL-C."
>
> *Diet rich in high glucoraphanin broccoli reduces plasma LDL cholesterol: Evidence from randomised controlled trials (Armah et al. Mol Nutr Food Res, 2015)*

This indicates that through modulating lipid and cholesterol levels in the blood, these natural molecules may reduce the risk of cardiovascular events such as heart attacks that are associated with obesity and high 'bad' cholesterol levels.

About SmarterNaturally

GRextra is a unique delivery vector for glucoraphanin. It was developed over decades of research, is backed by patented research from the Quadram Institute and clinical trials run with NHS hospitals, supported by public research grants from Innovate UK.

We use it to create the most powerful, convenient and cost-effective solutions on the market for accessing the health benefits of sulforaphane. For example, SmarterNaturally SuperSoup contains a once-weekly dose of glucoraphanin - as much as 5 heads of raw broccoli or 14 tablets of a leading glucoraphanin supplement.

Our products are also rich in other nutrients, such as dietary fibre and Vitamins C & B6, calcium and folic acid, which help support our metabolism, bone health, energy production, the reduction of fatigue and our immune system - further boosting our health.

References

1. Sulforaphane ameliorates lipid profile in rodents: an updated systematic review and meta-analysis (Du et al. *Sci Rep.* 2021)
2. Bitter taste sensitivity, cruciferous vegetable intake, obesity, and diabetes in American adults: a cross-sectional study of NHANES 2013-2014 (Ma et al. *Food Funct.* 2023)
3. Chloroquine modulates the sulforaphane anti-obesity mechanisms in a high-fat diet model: Role of JAK-2/ STAT-3/ SOCS-3 pathway (Ashmawy et al. *Eur J Pharmacol.* 2022)
4. Anti-Obesogenic Effects of Sulforaphane-Rich Broccoli (Brassica oleracea var. italica) Sprouts and Myrosinase-Rich Mustard (Sinapis alba L.) Seeds In Vitro and In Vivo (Men et al. *Nutrients*. 2022)
5. Beneficial Effects of Broccoli (Brassica oleracea var italica) By-products in Diet-induced Obese Mice (Martins et al. *In Vivo.* 2022)
6. Sulforaphane attenuates obesity by inhibiting adipogenesis and activating the AMPK pathway in obese mice (Choi et al. *J Nutr Biochem.* 2014)
7. Comparative evaluation of Brassica oleracea, Ocimum basilicum, and Moringa oleifera leaf extracts on lipase inhibition and adipogenesis in 3T3-L1 adipocytes (Nallamuthu et al. *J Food Biochem.* 2022)
8. Comparative Effects of Sulforaphane and Allyl Isothiocyanate on 3T3-L1 Adipogenesis (Sakuma et al. *J Nutr Metab.* 2022)
9. Modulation of Adipocyte Differentiation and Proadipogenic Gene Expression by Sulforaphane, Genistein, and Docosahexaenoic Acid as a First Step to Counteract Obesity (Sakuma et al. *J Nutr Metab.* 2022)
10. Sulforaphane inhibits mitotic clonal expansion during adipogenesis through cell cycle arrest (Choi et al. *Obesity (Silver Spring).* 2012)
11. Sulforaphane reduces obesity by reversing leptin resistance (Cakir et al. *Elife.* 2022)
12. Sulforaphane improves leptin responsiveness in high-fat high-sucrose diet-fed obese mice (Shawky and Segar. *Eur J Pharmacol.* 2018)
13. 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)
14. Sulforaphane Mitigates High-Fat Diet-Induced Obesity by Enhancing Mitochondrial Biogenesis in Skeletal Muscle via the HDAC8-PGC1α Axis (Yang et al. *Mol Nutr Food Res.* 2023)

15. A web-based integrative transcriptome analysis, RNAseqChef, uncovers the cell/tissue type-dependent action of sulforaphane (Etoh et al. *J Biol Chem.* 2023)
16. Anti-obesity effect of sulforaphane in broccoli leaf extract on 3T3-L1 adipocytes and ob/ob mice (Ranaweera et al. *J Nutr Biochem.* 2022)
17. The Protective Effects of Sulforaphane on High-Fat Diet-Induced Obesity in Mice Through Browning of White Fat (Liu et al. *Front Pharmacol.* 2021)
18. Glucoraphanin Ameliorates Obesity and Insulin Resistance Through Adipose Tissue Browning and Reduction of Metabolic Endotoxemia in Mice (Nagata et al. *Diabetes*. 2017)
19. Sulforaphane induces adipocyte browning and promotes glucose and lipid utilization (Zhang et al. *Mol Nutr Food Res.* 2016)
20. Simulated Digestion and Fermentation In Vitro by Obese Human Gut Microbiota of Sulforaphane from Broccoli Seeds (Sun et al. *Foods.* 2022)
21. 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)
22. Sulforaphane ameliorates glucose intolerance in obese mice via upregulation of insulin signaling pathway (Xu et al. *Food Funct.* 2018)
23. 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)
24. 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)
25. 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)
26. Broccoli sprouts reduce oxidative stress in type 2 diabetes: a randomized double-blind clinical trial (Bahadoran et al. *Eur J Clin Nutr.* 2011)
27. 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)
28. Effects of long-term consumption of broccoli sprouts on inflammatory markers in overweight subjects (López-Chillón et al. *Clin Nutr.* 2019)
29. Sulforaphane reduces pro-inflammatory response to palmitic acid in monocytes and adipose tissue macrophages (Williams et al. *J Nutr Biochem.* 2022)
30. 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)
31. Brassica oleracea Var italica by-Products Prevent Lipid Accumulation and Cell Death in a Liver Cell Model of Lipid Toxicity (Castelão-Baptista et al. *Nutrients.* 2023)
32. Diet rich in high glucoraphanin broccoli reduces plasma LDL cholesterol: Evidence from randomised controlled trials (Armah et al. *Mol Nutr Food Res.* 2015)
33. Phase 1 study of multiple biomarkers for metabolism and oxidative stress after one-week intake of broccoli sprouts (Murashima et al. *Biofactors.* 2004)

Sulforaphane & Weight Loss

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 weight loss and the management of obesity, both through directly helping to burn up excess fat and reduce the body's propensity to lay down fat, and indirectly through mitigating the severity and symptoms of other secondary health conditions caused by obesity.

Research studies have specifically linked glucoraphanin & sulforaphane to:

1. Reducing body weight & adiposity

[REVIEW] Three in One: The Potential of Brassica By-Products against Economic Waste, Environmental Hazard, and Metabolic Disruption in Obesity
Castelão-Baptista et al. Nutrients. 2021 Nov 23;13(12):4194
(doi: 10.3390/nu13124194)

“A peculiarity of sulforaphane is that its antioxidant activity modulates lipid metabolism in hepatocytes, reducing lipid levels in cases of excessive accumulation, up-regulating mitochondrial gene expression, function, and mitochondrial biogenesis. These make sulforaphane a prime candidate (for) use against a preoccupying condition rampaging through mainly developed countries: obesity and its associated complications.”

[REVIEW] Mechanisms Underlying Biological Effects of Cruciferous Glucosinolate-Derived Isothiocyanates/Indoles: A Focus on Metabolic Syndrome
Esteve. Front Nutr. 2020 Sep 2;7:111
(doi: 10.3389/fnut.2020.00111)

“The results in animal and cell studies in relation to the MetS (metabolic syndrome) have shown that GLSs derivatives (ITCs and indoles) treatment reduces fat deposition in WAT (white adipose tissue) and liver, decreases proliferation and differentiation of adipocytes, promotes WAT browning with an increase of energy expenditure, improves insulin sensitivity, reduces inflammation and decreases food intake.”

[REVIEW] Glucoraphanin: a broccoli sprout extract that ameliorates obesity-induced inflammation and insulin resistance
Xu et al. 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.”

[REVIEW] Glucoraphanin: a broccoli sprout extract that ameliorates obesity-induced inflammation and insulin resistance
Martins et al. J Sci Food Agric. 2018;98:2837-2844
(doi: 10.1002/jsfa.8898)

“Nevertheless, the in vitro and in vivo studies conducted so far have shown that SFN has the potential to be used as an effective anti-obesity supplement.”

Bitter taste sensitivity, cruciferous vegetable intake, obesity, and diabetes in American adults: a cross-sectional study of NHANES 2013-2014
Ma et al. Food Funct. 2023 Oct 16;14(20):9243-9252
(doi: 10.1039/d3fo02175k)

Dosage = Observational study, cruciferous vegetable intake measured in g/day

- "Among participants who ate cruciferous vegetables, bitter tasters on average consumed 15.5 g (±7.0) grams less cruciferous vegetables per day compared to non-tasters."
- "Bitter tasters who did not eat cruciferous vegetable had a significantly higher likelihood of obesity as compared to non-tasters who ate cruciferous vegetable, which was not observed among bitter tasters who ate cruciferous vegetable. The results implied that bitter sensitive people may have a higher likelihood of obesity if they could not overcome their resistance to cruciferous vegetables; and that may consequently increase their risk of diabetes."
- "The multi-variates adjusted odds ratio of obesity was 1.29 (95% confident interval (CI): 0.76–2.17), 1.40 (95% CI: 0.90–2.18) and 1.68 (95% CI: 1.05–2.67) among bitter tasters who ate cruciferous vegetables, among non-tasters who did not ate cruciferous vegetables, and among bitter tasters who did not eat cruciferous vegetables, respectively, as compared with non-tasters who ate cruciferous vegetables."

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)

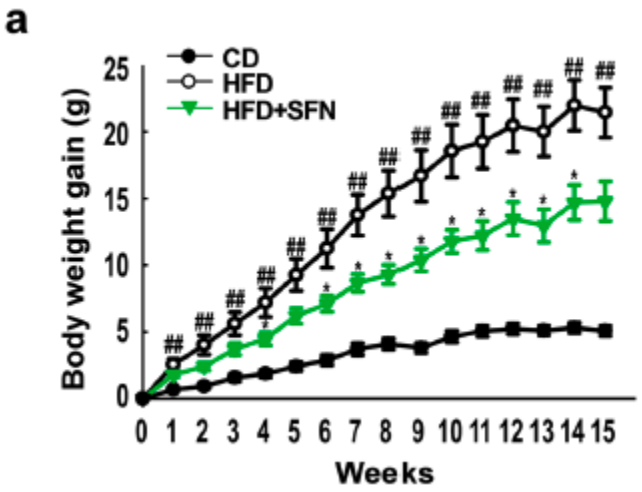
- "Sulforaphane reduced body weight (WMD: − 2.76 g, 95% CI: − 4.19, − 1.34) and liver weight (WMD: − 0.93 g, 95% CI: − 1.63, − 0.23) significantly in our ten trials."
- "This is the first meta-analytic study that summarizes the function of sulforaphane mono-treatment on lipid profile in rodents with metabolic syndrome."

Sulforaphane Mitigates High-Fat Diet-Induced Obesity by Enhancing Mitochondrial Biogenesis in Skeletal Muscle via the HDAC8-PGC1α Axis

Yang et al. Mol Nutr Food Res. 2023 Sep 29:e2300149
(doi: 10.1002/mnfr.202300149)

Dosage = 50 mg/kg orally administered every day for 15 weeks (equivalent to 4.05 mg/kg in humans)

- "Administration of SFN (50 mg kg−1 body weight (BW) day−1) reduced weight gain in HFD-induced obese mice (n = 21)"



- "Sulforaphane (SFN) inhibits histone deacetylase (HDAC)8 activity with high specificity."
- "PGC1α gene expression induced by HDAC8 inhibition may enhance mitochondrial biogenesis and consequently contribute to metabolic balance."
- "We found that HDAC8 inhibition by SFN increases PGC1α expression, consequently leading to changes in mitochondrial biogenesis in skeletal muscle of HFD-fed mice as well as in C2C12 myotubes."
- "These results suggest SFN as a beneficial anti-obesity agent providing new insight into the role of HDAC8 in the PGC1α-mediated mitochondrial biogenesis, which may be a novel and promising drug target for metabolic diseases."

A web-based integrative transcriptome analysis, RNAseqChef, uncovers the cell/tissue type-dependent action of sulforaphane
Etoh et al. J Biol Chem. 2023 Jun;299(6):104810
(doi: 10.1016/j.jbc.2023.104810)

Dosage = 5 mg/ml SFN via injection (duration not specified)

- "SFN treatment decreased the expression of a series of genes responsible for acetyl-CoA synthesis (such as Me1 and Acly), fatty acid synthesis from acetyl-CoA (Acaca and Fasn), fatty acid elongation and desaturation (Elovl6 and Scd1), and lipid deposition (Pparγ and Cidec)"
- "We found that SFN treatment in obese mice decreased BMAL1-target genes, such as Dbp and Bhlhe40 (Fig. 5D), which are important for the induction of PPARγ and SREBP-1c, which are key transcriptional factors involved in lipid metabolism"

Chloroquine modulates the sulforaphane anti-obesity mechanisms in a high-fat diet model: Role of JAK-2/ STAT-3/ SOCS-3 pathway
Ashmawy et al. Eur J Pharmacol. 2022 Jul 15;927:175066
(doi: 10.1016/j.ejphar.2022.175066)

Dosage = 0.5 and 1 mg/kg/day SFN orally for 6 weeks

- "On the other hand, SFN and/or CQ reduced BW, enhanced the OGTT and the glucose/lipid profile, and improved the histopathological picture to concur with previous studies"
- "In conclusion, our findings demonstrated that SFN, as a natural supplement, mediates its anti-obesity effect by suppressing the lipogenesis-related enzymes, inhibiting inflammatory mediators, and the inflammatory pathway JAK-2/STAT-3/SOCS-3, besides enhancing autophagy, as evidenced by the corrected lipid profile."

Anti-Obesogenic Effects of Sulforaphane-Rich Broccoli (Brassica oleracea var. italica) Sprouts and Myrosinase-Rich Mustard (Sinapis alba L.) Seeds In Vitro and In Vivo

Men et al. Nutrients. 2022 Sep 15;14(18):3814
(doi: 10.3390/nu14183814)

Dosage = BSP (broccoli sprout powder) at 150 mg/kg/day, MSP (mustard seed powder) at 15 mg/kg/day, MBP (mustard seed and broccoli seed powder mix) at 100 mg/kg/day administered orally for 12 weeks

- "When the BPA-induced (Bisphenol A; adipogenesis promoter) cells were treated with BSP (50 and 150 μg/mL) and MBP (25, 50, and 100 μg/mL) during the differentiation process, the lipid accumulation significantly decreased in mature cells by 47%, 46%, 40%, 33%, and 31%, respectively."
- "BSP and MBP inhibit adipocyte differentiation, reduce lipid accumulation in vitro, and significantly reduce body weight and epididymal adipose tissue mass in BPA-induced obese mice by reducing the expression of adipogenesis-related proteins (aP2, PPAR-γ, SREBP-1C, FAS, and C/EBP-) and increasing the expression of fatty acid oxidation proteins (CPT-1 and UCP-1)
- "In summary, our results suggest that BSP and MBP could be effective in the treatment and prevention of BPA-induced obesity."

Beneficial Effects of Broccoli (Brassica oleracea var italica) By-products in Diet-induced Obese Mice

Martins et al. In Vivo. 2022 Sep-Oct;36(5):2173-2185
(doi: 10.21873/invivo.12943)

Dosage = 0.67% or 1.34% broccoli flour as part of daily diet for up to 14 weeks (dose equivalent to human consumption of 150g broccoli three times a week)

- "In general, mice supplemented with BF had a lower body weight without altering their food intake. In agreement, BF supplementation reduced epididymal and retroperitoneal fat accumulation in mice fed the Western diet."
- "In conclusion, the use of broccoli by-products as a supplement may be a candidate to fight diet-induced obesity, reducing body weight and fat tissue accumulation."

Sulforaphane reduces obesity by reversing leptin resistance
Cakir et al. Elife. 2022 Mar 24;11:e67368
(doi: 10.7554/eLife.67368)

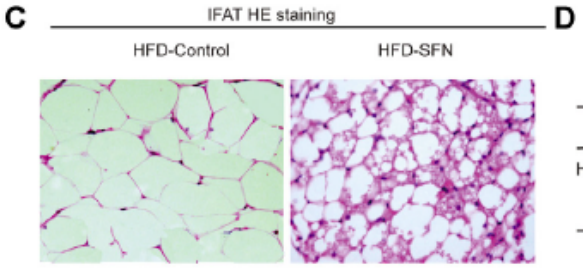
Dosage = 5 mg/kg SFN via daily intraperitoneal injection for 4 weeks

- "Here, we show that the natural isothiocyanate and potent NRF2 activator sulforaphane reverses diet-induced obesity through a predominantly, but not exclusively, NRF2-dependent mechanism that requires a functional leptin receptor signaling and hyperleptinemia."
- "Our findings argue for clinical evaluation of sulforaphane for weight loss and obesity-associated metabolic disorders."

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

- "Sulforaphane treatment substantially decreased the adipocyte size and body weight gain, and further prevented HFD-induced obesity through the browning of adipocytes via mitochondrial biogenesis and the activation of Ucp1 and Pgc1-α."
- "Sulforaphane reduced the lipid droplets and the size of adipose cell from IWAT and VWAT." (below)



Group	Average Cell size (μm²)	P value
HFD-Control	8802.5 ± 2899.1	*P* =0.0003
HFD-SFN	3543 ± 1640.1	

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 = 0.4ml 20 mg/kg bw broccoli microgreen juice via daily oral for 8 weeks

- "BMJ supplementation significantly reduced white adipose tissues (WAT) mass, the body weight and adipocyte size, and increased water intake in HFD-fed mice."
- "Compared with the HFD group, BMJ supplementation significantly increased the relative abundance of Bacteroidetes and decreased the ratio of Firmicutes to Bacteroidetes at the phylum level, and enriched Bacteroides_acidifaciens at the species level. These changes in the composition of gut microbiota are associated with the production of short-chain fatty acids (SCFAs), and reduced LPS levels, and had an obvious anti-inflammatory effect."

Sulforaphane suppresses obesity-related glomerulopathy-induced damage by enhancing autophagy via Nrf2

Lu et al. Life Sci. 2020 Oct 1;258:118153
(doi: 10.1016/j.lfs.2020.118153)

Dosage = 1mg/kg SFN administered intaperitoneally every other day for 3 months after obesity-related glomerulopathy had been established

- "Treatment with SFN reduced body weight, organ-associated fat weight, and urinary albumin/creatinine ratio in both the preventative and disease intervention regimens."

Sulforaphane improves leptin responsiveness in high-fat high-sucrose diet-fed obese mice

Shawkey and Segar. Eur J Pharmacol. 2018 Sep 15;835:108-114
(doi: 10.1016/j.ejphar.2018.07.050)

Dosage = 0.5 mg/kg SFN via subcutaneous injection every day for 22 days

- "The present findings demonstrate that in HFHS diet-fed obese mice, SFN treatment (0.5 mg/kg/day, s.c.) for ~2–3 weeks improves the responsiveness to exogenously administered leptin as revealed by temporal decreases in food intake and weight gain."

Anti-obesity effect of sulforaphane in broccoli leaf extract on 3T3-L1 adipocytes and ob/ob mice

Ranaweera et al. J Nutr Biochem. 2022 Feb;100:108885
(doi: 10.1016/j.jnutbio.2021.108885)

Dosage = SFN at a dose of 0.5 mg/kg body weight, GRN at a dose of 2.5 mg/kg body weight, BLE (broccoli leaf extract) at a dose of 50 and 500 mg/kg body weight every day

- "Overall results suggest that the SFN content in BLE exerts a potential anti-obesity effect by normalizing the expression of genes related to lipid metabolism, which are up- or down-regulated in ob/ob mice."
- "RNA sequencing analysis showed that up- or down-regulation of 32 genes related to lipid metabolism was restored to control level in both SFN and BLE-treated ob/ob mice groups."

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 = 0.3% GR powder containing 0.31 mmol/g GR fed with diet for 3 weeks

- "In the present study, we demonstrated that glucoraphanin, a stable precursor of the Nrf2 inducer sulforaphane, mitigated HFD-induced weight gain, insulin resistance, hepatic steatosis, oxidative stress, and chronic inflammation in mice."
- "Additionally, glucoraphanin lowered plasma LPS levels in HFD-fed mice, and decreased the relative abundance of Desulfovibrionaceae."

In Vitro Bioactivities of Commonly Consumed Cereal, Vegetable, and Legume Seeds as Related to Their Bioactive Components: An Untargeted Metabolomics Approach Using UHPLC-QTOF-MS(2)
Aloo et al. Antioxidants (Basel). 2023 Jul 27;12(8):1501
(doi: 10.3390/antiox12081501)

Dosage = NA, concentration of broccoli seed extract not specified

- "Remarkably, broccoli and red cabbage demonstrated substantial anti-glycation and lipase inhibitory potentials."
- "Plant-based inhibitors of α-glucosidase and pancreatic lipase have been shown to effectively inhibit the hydrolysis of carbohydrates and fats, which may lead to reduced release of sugar and triglycerides into the bloodstream and delayed absorption in the intestinal tract."
    - "For pancreatic lipase enzyme, broccoli seed extracts demonstrated the highest inhibition capacity, which did not differ significantly from red cabbage values."
- "Advanced glycation end products (AGEs) are a heterogeneous group of macromolecules that are formed by the nonenzymatic glycation of proteins, lipids, and nucleic acids. …Preventing the formation of these compounds is crucial in obesity and diabetes management as they are regarded as driving factors for the severity of these conditions."
    - "Broccoli and red cabbage possessed the highest inhibitory activities against AGEs formation. Their potent anti-AGEs did not significantly differ from those observed for the standard drug, aminoguanidine."
- "These results strongly support the anti-diabetic, anti-obesity, and anti-glycation potential of red cabbage, broccoli, and buckwheat seeds."

Sulforaphane induces lipophagy through the activation of AMPK-mTOR-ULK1 pathway signaling in adipocytes
Masuda et al. J Nutr Biochem. 2022 Aug;106:109017
(doi: 10.1016/j.jnutbio.2022.109017)

Dosage = In vitro cells treated with 10 or 100 μM SFN for 3h or 10 days; mice were administered 30 mg/kg SFN once before sacrifice via intraperitoneal injection

- "SFN was shown to induce lipophagy through the AMPK-mTOR-ULK1 signaling pathway in adipocytes, resulting in the reduction of LDs."
- "To our knowledge, this is the first study to demonstrate that dietary factors partially contribute to lipolysis through lipophagy in adipocytes."

Comparative evaluation of Brassica oleracea, Ocimum basilicum, and Moringa oleifera leaf extracts on lipase inhibition and adipogenesis in 3T3-L1 adipocytes
Nallamuthu et al. J Food Biochem. 2022 Jul;46(7):e14158
(doi: 10.1111/jfbc.14158)

Dosage = 0 to 1000 µl/ml broccoli leaf extract for up to 10 days

- "In cell culture studies, these plant extracts remarkably inhibited the intracellular triglyceride accumulation in 3T3-L1 cells and the effect was in the decreasing order of BO (*Brassica oleracea*; broccoli) > OB (*Ocimum basilicum;* basil) > MO (*Moringa oleifera;* moringa)"
- "The results revealed that the BO (*Brassica oleracea*; broccoli) extract had remarkable activity against adipogenesis in the 3T3-L1 Pre-adipocyte differentiation model as well as lipase inhibitory properties."

Comparative Effects of Sulforaphane and Allyl Isothiocyanate on 3T3-L1 Adipogenesis
Sakuma et al. J Nutr Metab. 2022 Jan 19;2022:8705163
(doi: 10.1155/2022/8705163)

Dosage = 0 to 100 µM SFN for 2 days

- "The results of the present study clearly showed that while both sulforaphane and allyl isothiocyanate inhibited adipocyte differentiation, sulforaphane was a much stronger inhibitor. This suggests that the anti-obesity effect of sulforaphane is greater than that of allyl isothiocyanate."

Modulation of Adipocyte Differentiation and Proadipogenic Gene Expression by Sulforaphane, Genistein, and Docosahexaenoic Acid as a First Step to Counteract Obesity
Valli et al. Oxid Med Cell Longev. 2018 Feb 7;2018:1617202
(doi: 10.1155/2018/1617202. eCollection 2018)

Dosage = 10, 25, 50 µM SFN for 4 days

- "All bioactive compounds markedly reduced lipid droplet formation compared to controls. GEN and sulforaphane were effective at the lowest concentration used for supplementation (10 µM)"
- "Our results evidence that all tested bioactives efficiently block adipocyte differentiation"

Sulforaphane and myricetin act synergistically to induce apoptosis in 3T3-L1 adipocytes

Yao et al. Mol Med Rep. 2018 Feb;17(2):2945-2951
(doi: 10.3892/mmr.2017.8235)

Dosage = 40 μM SFN and 100 μM myricetin (Myr) for 24h

- "In the present study, combined treatment of 3T3-L1 adipocytes with SFN and Myr decreased cell viability to a greater extent than the additive effect of each compound alone."
- "In conclusion, treatment with Myr and SFN combined was associated with synergistic pro-apoptotic effects in adipocytes."

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, and 10 μM SFN for 48 h

- "SFN was found to induce 3T3-L1 adipocytes browning based on the increased mitochondrial content and activity of respiratory chain enzymes"
- "Taken together, 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."

Sulforaphane induces apoptosis in adipocytes via Akt/p70s6k1/Bad inhibition and ERK activation

Yao et al. Biochem Biophys Res Commun. 2015 Oct 2;465(4):696-701
(doi: 10.1016/j.bbrc.2015.08.049)

Dosage = 40, 60, and 80 μM SFN for 24 h

- "Therefore, our findings clarified that SFN could induce 3T3-L1 adipocyte apoptosis via down-regulation of the Akt/p70s6k1/Bad pathway and up-regulation of the ERK pathway, suggesting SFN may be a promising agent for the treatment or prevention of obesity."

Sulforaphane induced adipolysis via hormone sensitive lipase activation, regulated by AMPK signaling pathway
Lee et al. Biochem Biophys Res Commun. 2012 Oct 5;426(4):492-7
(doi: 10.1016/j.bbrc.2012.08.107)

Dosage = 2.5, 5, 20 uM SFN for 24 h

- "Taken together, these results suggest that sulforaphane promotes lipolysis via hormone sensitive lipase activation mediated by decreasing AMPK signal activation in adipocytes."

Sulforaphane inhibits mitotic clonal expansion during adipogenesis through cell cycle arrest
Choi et al. Obesity (Silver Spring). 2012 Jul;20(7):1365-71
(doi: 10.1038/oby.2011.388)

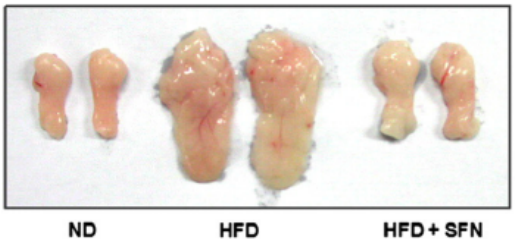
Dosage = 5, 10, and 20 uM SFN for 24-48 h

- "In conclusion, sulforaphane inhibits adipocyte differentiation by blocking clonal expansion via cell cycle arrest at the G0/G1 phase, which may be mediated by upregulation of p27 expression."

Sulforaphane attenuates obesity by inhibiting adipogenesis and activating the AMPK pathway in obese mice
Choi et al. J Nutr Biochem. 2014 Feb;25(2):201-7
(doi: 10.1016/j.jnutbio.2013.10.007)

Dosage =

- "In this study, sulforaphane markedly reduced the body weight of HFD-induced obese mice, and HFD plus SFN-fed mice showed a similar pattern of weight gain to the ND-fed group"
- "Effect of SFN on adipose tissues and liver in HFD-induced obese mice. (B) epididymal adipose tissue (below)"



2. Ameliorating symptoms and comorbidities associated with obesity

a. Metabolic-associated (non-alcoholic) fatty liver disease

[REVIEW] Impact of Glucoraphanin-Mediated Activation of Nrf2 on Non-Alcoholic Fatty Liver Disease with a Focus on Mitochondrial Dysfunction
Xu et al. Int J Mol Sci. 2019 Nov 25;20(23):5920
(doi: 10.3390/ijms20235920)

“Notably, the anti-obesity agents sulforaphane and glucoraphanin prevent hepatic steatosis by increasing energy utilization and preventing lipogenesis and oxidative stress in the liver. Moreover, they improve mitochondrial dysfunction.”

The protective effects of sulforaphane on high-fat diet-induced metabolic associated fatty liver disease in mice via mediating the FXR/LXRα pathway
Ma et al. Food Funct. 2022 Dec 13;13(24):12966-12982
(doi: 10.1039/d2fo02341e)

Dosage = 10 mg/kg SFN per day via oral gavage for 12 weeks

- “Our results showed that SFN not only improved the excessive accumulation of fat in the liver cells but also ameliorated liver and serum inflammatory and antioxidant levels.”
- “In addition, SFN can regulate bile-acid metabolism and fatty-acid synthesis by affecting their farnesoid X receptor (FXR)/liver X receptor alpha (LXRα) signaling pathway, ultimately alleviating MAFLD.”
- “In our experiment, we found that the gut microbiota composition of mice was improved after SFN intake, especially the ratio of Firmicutes to Bacteroidetes. The lower ratio of Firmicutes to Bacteroidetes was better for human health.”
- “The mice in the MAFLD group showed obvious weight gain, compared to that in the CN (control) group (Table 3, $P < 0.05$). Ingesting PPC (polyene phosphatidyl choline) and SFN significantly reversed this alteration (Table 3, $P < 0.05$).”

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

- "Our results indicated that SFN attenuated NAFLD, inflammation, oxidative stress, adipose tissue hypertrophy, and insulin resistance, as well as regulated glucose and lipid metabolism."

Brassica oleracea Var italica by-Products Prevent Lipid Accumulation and Cell Death in a Liver Cell Model of Lipid Toxicity
Castelão-Baptista et al. Nutrients. 2023 Feb 12;15(4):924
(doi: 10.3390/nu15040924)

Dosage = 1–10 µg/ml broccoli extract for 24 or 48 h

- "The extracts significantly decreased FFA-induced lipid accumulation in HepG2 cells either in a co-incubation or pre-incubation strategy"
- "Our study shows, in vitro, the potential of BBP extracts in reducing lipid accumulation in hepatic cells subjected to supraphysiological concentrations of fatty acids."
- "The effects identified highlight the therapeutic potential of BBPs for the prevention/treatment of NAFLD."

Sulforaphane suppresses the activity of sterol regulatory element-binding proteins (SREBPs) by promoting SREBP precursor degradation
Miyata et al. Sci Rep. 2022 May 24;12(1):8715
(doi: 10.1038/s41598-022-12347-6)

Dosage = 100 µM SFN for up to 24 h

- "Sterol regulatory element-binding proteins (SREBPs) are transcription factors that regulate various genes involved in cholesterol and fatty acid synthesis."
- "This study identifies SFaN as an SREBP inhibitor and provides evidence that SFN could have major potential as a pharmaceutical preparation against hepatic steatosis and obesity."

b. Cholesterol

Phase 1 study of multiple biomarkers for metabolism and oxidative stress after one-week intake of broccoli sprouts
Murashima et al. Biofactors. 2004;22(1-4):271-5
(doi: 10.1002/biof.5520220154)

Dosage = 100g fresh broccoli per day for 1 week

- "After 1 week treatment, improvement of lipid metabolism was observed."

"One week intake of broccoli sprouts significantly reduced total cholesterol and LDL cholesterol. Females had no significant reduction in total cholesterol but showed increased HDL cholesterol."

Diet rich in high glucoraphanin broccoli reduces plasma LDL cholesterol: Evidence from randomised controlled trials
Armah et al. Mol Nutr Food Res. 2015 May;59(5):918-26
(doi: 10.1002/mnfr.201400863)

Dosage = 400 g standard broccoli (6.9 umol/g GR) or 400 g high GR broccoli (21.6 umol/g GR) per week for 12 weeks

- "Evidence from two independent human studies indicates that consumption of high glucoraphanin broccoli significantly reduces plasma LDL-C."

c. Inflammation

Effects of long-term consumption of broccoli sprouts on inflammatory markers in overweight subjects
Lopez-Chillon et al. Clin Nutr. 2019 Apr;38(2):745-752
(doi: 10.1016/j.clnu.2018.03.006)

Dosage = 30g of broccoli sprouts daily for 70 days (roughly 51 mg or 117 µmol GR)

- "Adipose tissue is related to higher secretion of pro-inflammatory cytokines as TNF-a and IL-6 and elevated levels of these proteins have been described in overweight individuals"
- "In our study we observed a noticeable anti-inflammatory effect with the ingestion of broccoli sprouts, with a significant reduction by 38% and 59% in IL-6 and C-reactive protein concentrations, respectively."

Sulforaphane reduces pro-inflammatory response to palmitic acid in monocytes and adipose tissue macrophages
Williams et al. J Nutr Biochem. 2022 Jun;104:108978
(doi: 10.1016/j.jnutbio.2022.108978)

Dosage = 40 µM SFN for 3 hours

- "Sulforaphane was found to significantly reduce activation of the NLRP3 inflammasome in both peripheral blood monocytes and ATMs of obese individuals stimulated with combined palmitic acid and LPS, which suggests that sulforaphane could be used as a therapeutic strategy for reducing systemic inflammation in obesity."

d. Insulin resistance

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

Dosage = 100 μmol/kg SFN gavaged three times per week for 6 weeks

- "Our data showed that obese mice presented a marked insulin resistance and glucose intolerance as compared to control group, while SFN treatment exerted prominently protective effect."
- "Our results provided a basis for the use of SFN since it has important implications for the prevention of obesity-associated glucose intolerance and insulin resistance."

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 plus 10% broccoli florets or stalks for 17 weeks

- "Broccoli florets addition to the HFD significantly reduced serum insulin levels, HOMA-IR index, and upregulated adiponectin receptor expression."
- "Indeed, AdipoR1 and AdipoR2 were found to regulate insulin sensitivity in insulin target tissues, and are important in the pathophysiology of insulin resistance."

e. Arterial injury

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/day SFN via subcutaneous injection for 22 days

- “Using the mouse model of western diet-induced obesity, the present study demonstrates for the first time that subcutaneous delivery of SFN (0.5 mg/Kg/day) for ~3 weeks significantly attenuates neointima formation in the injured femoral artery [↓ (decrease) neointima/media ratio by ~60%; n = 5–8].”
- “This was associated with significant improvements in metabolic parameters, including ↓ weight gain by ~52%, ↓ plasma leptin by ~42%, ↓ plasma insulin by ~63%, insulin resistance [↓ homeostasis model assessment of insulin resistance (HOMA-IR) index by ~73%], glucose tolerance (↓ AUCGTT by ~24%), and plasma lipid profile (e.g., ↓ triglycerides).”

f. Alteration of gut microbiota

Simulated Digestion and Fermentation In Vitro by Obese Human Gut Microbiota of Sulforaphane from Broccoli Seeds
Sun et al. Foods. 2022 Dec 12;11(24):4016
(doi: 10.3390/foods11244016)

Dosage = Unknown concentration of extracted SFN for up to 24h

- "In vitro fermentation of SFN by gut microbes in obese patients results in alteration in constitution of microbiota and production of short chain fatty acids."
- "In obese human guts, the relative abundances of the beneficial genera including *Lactobacillus*, *Weissella*, *Leuconosto*, *Algiphilus* and *Faecalibacterium* significantly increased, whilst the detrimental genera, such as *Escherichia-Shigella, Klebsiella*, *Clostridium_sensu_stricto_1*, *Sutterella*, *Megamonas* and *Proteus* drastically declined."
    - "It has been reported that Algiphilus can produce succinic acid and a small amount of acetic and propionic acids, and that succinic acid can activate intestinal gluconeogenesis, imparting beneficial effects on blood sugar metabolism and obesity management"
    - "The genus Faecalibacterium is one of the most important bacteria in the human gut flora and one of the important producers of butyric acid, which has anti-inflammatory and protective effects on the digestive system from intestinal pathogens, particularly effective in obese patients"
- "These findings not only shed additional light on the mechanisms that underpin the health benefits of SFN, but also provide a potentially feasible revenue for ameliorating the symptoms of obesity by modifying the makeup of the gut microbiota."