

Sulforaphane... It's Not Just For Detox!

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Learning Objectives

- What is sulforaphane?
- Mechanism of action via the Nrf2 and Nfkb pathways
- Sulforaphane and inflammation
- Sulforaphane as a neuroprotective nutrient
- Sulforaphane's role as a potential detoxifier

Health Benefits of Cruciferous Vegetables

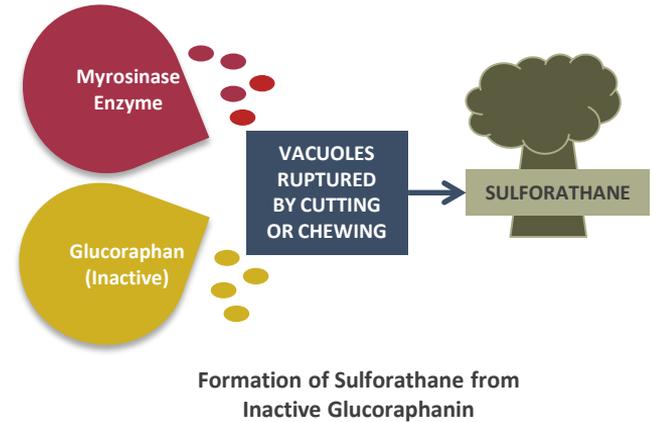
- Fruit and vegetable intake has long been recognized as an important part of a healthy diet
- Consumption of cruciferous vegetables such as broccoli, Brussels sprouts, cauliflower, and cabbage has been associated with a decreased risk of several chronic diseases, including:
 - Cardiovascular disease
 - Degenerative diseases
 - Certain cancers



1. Boddupalli S, Mein JR, Lakkanna S, James DR. Induction of phase 2 antioxidant enzymes by broccoli sulforaphane: perspectives in maintaining the antioxidant activity of vitamins a, C, and e. *Front Genet.* 2012;3:7.
2. James D, Devaraj S, Bellur P, Lakkanna S, Vicini J, Boddupalli S. Novel concepts of broccoli sulforaphanes and disease: induction of phase II antioxidant and detoxification enzymes by enhanced-glucoraphanin broccoli. *Nutr Rev.* 2012;70:654-665.
3. Tarozzi A, Angeloni C, Malaguti M, Morroni F, Hrelia S, Hrelia P. Sulforaphane as a potential protective phytochemical against neurodegenerative diseases. *Oxid Med Cell Longev.* 2013;2013:415078.

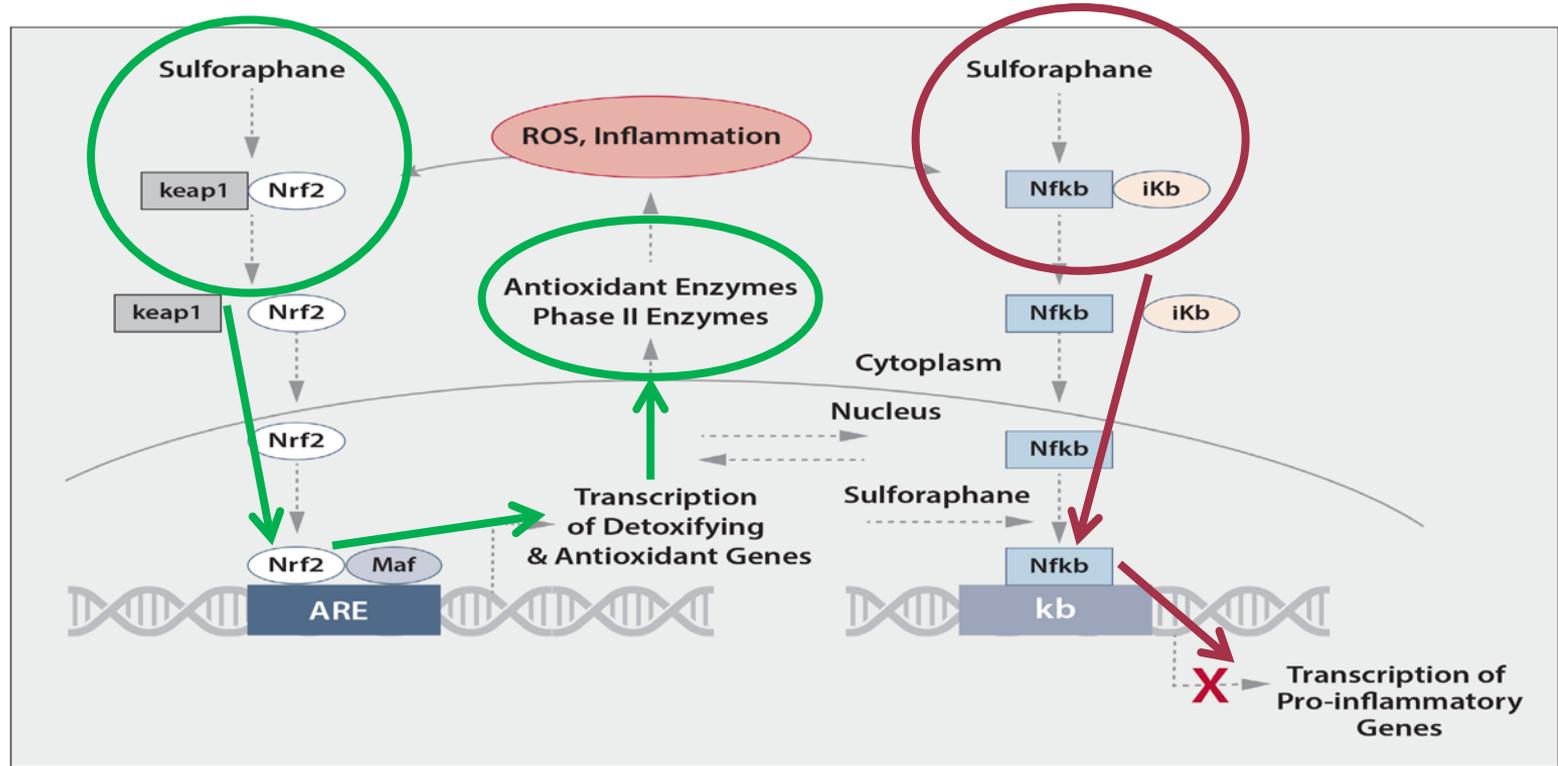
What Accounts for Broccoli's Health Benefits?

- Cruciferous vegetables such as broccoli accumulate significant concentrations of glucoraphanin (a glucosinolate)
- Glucoraphanin is converted *in vivo* to biologically active sulforaphane (an isothiocyanate). This conversion requires myrosinase enzyme
- Sulforaphane is the compound responsible for many positive health benefits associated with broccoli consumption



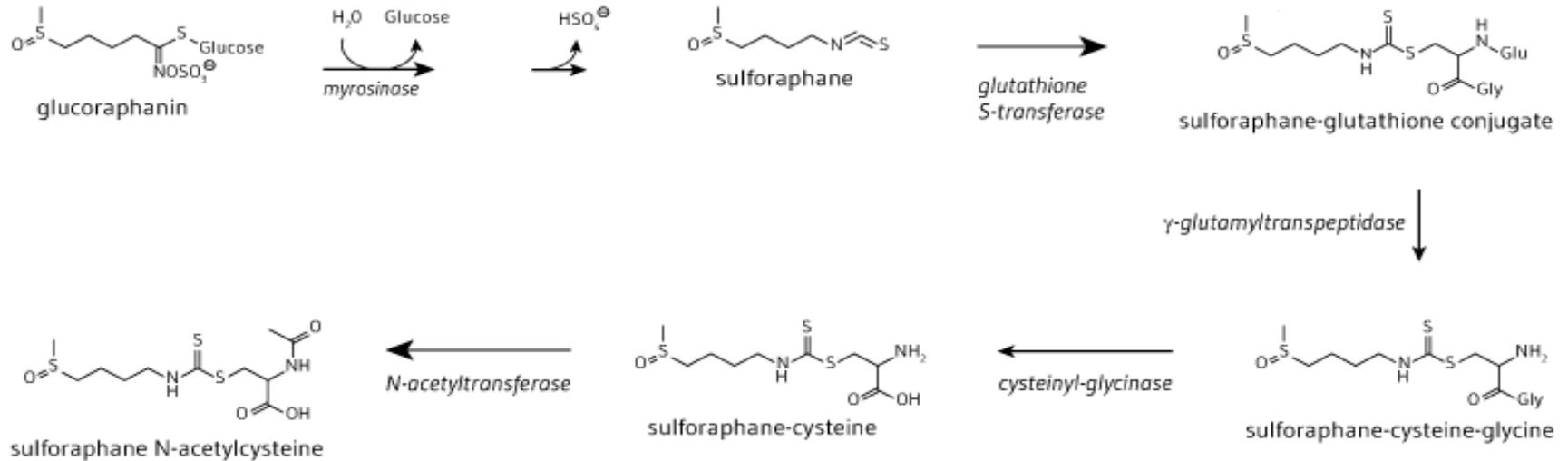
1. Egner PA, et al. Bioavailability of sulforaphane from two broccoli sprout beverages: results of a short term, cross-over clinical trial in Qidong, China. *Cancer Prev Res.* 2011; 4(3): 384-395

Mechanism of Action: Nrf2 and Nfkb Pathways



Keap1-kelch-like ECH-associated protein 1
Nrf2-nuclear factor erythroid related factor 2
ARE-antioxidant response element

Metabolism and Bioavailability of Glucoraphanin

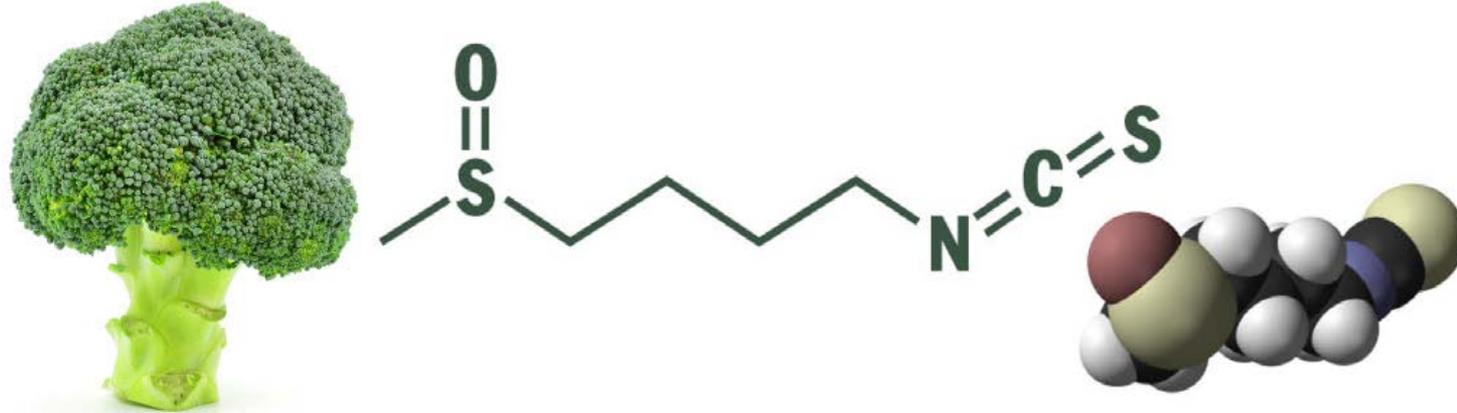


Key Takeaways

- Sulforaphane is a metabolite of glucoraphanin (a glucosinolate).
Glucoraphanin is hydrolyzed to sulforaphane by the enzyme myrosinase
- Myrosinase is released from plant cells by cutting or chewing and is denatured by sustained cooking
- Without **MYROSINASE**, sulforaphane cannot be produced
- Small amount of **MYROSINASE** is produced by the gut bacteria and can create some sulforaphane but the conversion capabilities vary from person to person

Did you know?

There are 1,545 sulforaphane articles cited on Pubmed



Sulforaphane's Role as a Potent **Therapeutic** Nutrient

- Inflammation
- Neurodegenerative Disease
- Metabolic Detoxification

Why Are We **Looking** at So Many Different Health Conditions?

Sulforaphane is a well-studied isothiocyanate due to its antioxidant, anti-inflammatory, and detoxification properties

Does Sulforaphane Help with Inflammation?

Sulforaphane and Inflammation

Objective: to evaluate the effects of broccoli sprouts powder (BSP) with high sulforaphane concentration on inflammatory markers.

Design:

- N=63 diabetic patients randomly assigned to 3 different treatment groups for 4 weeks and received either 40mg or 20mg sulforaphane or placebo
- Hs-CRP, IL-6, and TNF- α were measured at baseline and 4 weeks after treatment

Results:

Significant decrease in Hs-CRP and non-significant decrease in IL-6 and TNF- α observed in the 2 BSP groups.

Conclusion: high sulforaphane levels had favorable effects on inflammatory markers in T2DM. Further studies with longer duration and different doses are needed to confirm the effects of broccoli sprouts and its mechanisms.

1. Mirmiran P, et al. Effects of broccoli sprout with high sulforaphane concentration on inflammatory markers in type 2 diabetic patients: A randomized double-blind placebo-controlled clinical trial. *Journal of Functional Foods*. 2012: 4; 837-841

Sulforaphane and *H. Pylori*

Objective: to evaluate the efficacy of broccoli sprouts in reducing *H. pylori* infection in both the mouse model and human subjects

Design:

- Mice-fed sulforaphane-rich broccoli sprouts for 8 weeks
- Humans-48 *H. pylori*+ subjects with gastritis were randomized to receive placebo or 183mg of glucoraphanin/day for 8 weeks

Results:

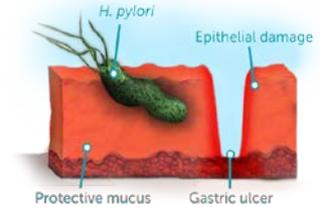
- Mice-reduced bacterial colonization and markers linked to an increased risk of gastric cancer
- Humans-significant drop in urease levels; decreased levels of serum pepsinogens 1 and 2

Conclusion: suggests that sulforaphane may have a direct antibacterial effect on *H. pylori* which results in reduced gastritis, as well as an indirect effect by increasing the cytoprotective phase 2 response. Therefore, it can be concluded that sulforaphane shows very promising as an antibacterial agent against *H. pylori* and as a dietary preventive agent against the development of gastric cancer.

1. Yanaka A, et al. Dietary sulforaphane-rich broccoli sprouts reduce colonization and attenuate gastritis in *Helicobacter pylori*-infected mice and humans. *Cancer Prev Research*. 2009;2:353-60

Sulforaphane and *H. Pylori*

Objective: to investigate whether a broccoli sprout extract containing sulforaphane inhibited the *H. pylori* infection density and produced an anti-oxidative effect on gastric mucosal damage



Design:

- 89 participants randomized in 3 groups and received a placebo capsule or a capsule containing 1000mcg sulforaphane 2x/day
- Urea breath test (UBT), ammonia, malondialdehyde (MDA) measured

Results:

- UBT and ammonia concentration were not statistically significant
- MDA concentrations significantly reduced in all subjects receiving sulforaphane capsules, irrespective of *H. pylori* infection ($P < 0.001$)

Conclusion: sulforaphane capsules did not inhibit the *H. pylori* infection density. However, sulforaphane capsules prevented lipid peroxidation in the gastric mucosa and may play a cytoprotective role in *H. pylori*-induced gastritis.

1. Chang YW, et al. The effects of broccoli sprout extract containing sulforaphane on lipid peroxidation and *Helicobacter pylori* infection in the gastric mucosa. *Gut and Liver*. 2015; 9(4); 486-493

Summary-Takeaways

- **Sulforaphane's anti-inflammatory properties are mediated by its potential to inactivate the pro-inflammatory Nfkb pathway**
- **These studies demonstrate significant reductions in inflammatory and oxidative markers with high sulforaphane concentrations**

Sulforaphane's Role as a Neuroprotective Nutrient

Sulforaphane and Parkinson's Disease in a Mouse Model

Objective:

to evaluate the effects of sulforaphane on behavioral changes and dopaminergic neurotoxicity in mice

Design:

Mice were treated with 5mg/kg of sulforaphane twice a week for four weeks

Results:

The increase in motor coordination were improved significantly by sulforaphane treatment. In addition, sulforaphane protected apoptosis via blocking DNA fragmentation and caspase-3 activation.

Conclusion:

These results suggest that sulforaphane may potentially be effective in slowing down the progression of PD by the modulation of oxidative stress and apoptotic machinery in the mouse model

1. Morroni F, et al. Neuroprotective effect of sulforaphane in 6-hydroxydopamine-lesioned mouse model of Parkinson's disease. *Neurotoxicology*. 2013; 36: 63-71

Sulforaphane and Autism

Objective: to assess and validate sulforaphane's effect on the core symptoms of autism spectrum disorder (ASD)

Design:

- 44 males with moderate to severe ASD were randomized to receive 9-27 mg/day sulforaphane or placebo daily for 18 weeks
- Behavior change was assessed using 3 different behavioral measurement tests

Results:

- After 18 weeks, participants receiving sulforaphane showed significant improvement in behavior for ABC (34%; $P < 0.001$); 17%; $P = 0.017$ for SRS; and CGI-1 ($P = 0.015 - 0.007$)
- After discontinuation of sulforaphane treatment, total scores on all scales rose towards pre-treatment levels

Conclusion: study is small but results are very promising for the nutritional support of autism. Larger scaled studies need to be conducted.

1. Singh K, et al. Sulforaphane treatment of autism spectrum disorder (ASD). PNAS. 2014; 111(43):15550-15555

Summary-Takeaways

- **These studies demonstrate sulforaphane as a promising plant-based agent in improving neurodegenerative conditions through its anti-oxidative properties**
- **More clinical studies with longer duration and higher doses of sulforaphane need to be conducted**

Sulforaphane: A Powerful Detoxifying Agent

Sulforaphane and Detoxification

Objective: to determine possible enhancement of detoxification of airborne pollutants (benzene, acrolein, crotonaldehyde) in China by a broccoli-sprout beverage.

Design:

- 291 healthy individuals were randomized to receive either a placebo or broccoli sprout beverage containing 262mg of glucoraphanin and 7mg of sulforaphane

Results:

- The urinary excretion of benzene was 54.7% higher in the broccoli sprout group compared to the placebo group
- The urinary excretion of acrolein was 21.7% higher in the broccoli sprout group than the placebo group
- The urinary excretion of crotonaldehyde was similar (only 2.0% higher) between the 2 groups

Conclusion: the key finding of the rapid excretion/detoxification of benzene and acrolein from the body was observed due to the high concentration of glucoraphanin and sulforaphane.

1. Egner PA, et al. Rapid and sustainable detoxification of airborne pollutants by broccoli sprout beverage: results of a randomized clinical trial in China. *Cancer Prev Res.* 2014;7(8); 813-23

Summary-Takeaways

- **Sulforaphane has been identified as the most potent inducer of phase 2 detoxification enzymes**
- **It is well established that sulforaphane-rich beverages provide higher and more consistent levels of sulforaphane than do glucoraphanin-rich beverages**

Safety

- No serious adverse effects of isothiocyanates in humans have been reported
- Other potential toxic effects reported in rodents have not been observed in humans

1. Okazaki K, et al. Enhancement of urinary bladder carcinogenesis by combined treatment with benzyl isothiocyanate and N-butyl-N-(4-hydroxybutyl)nitrosamine in rats after initiation. *Cancer Sci.* 2003;94(11):948-952.
2. Kumar G, et al. Isothiocyanates: a class of bioactive metabolites with chemopreventive potential. *Tumour Biol.* 2015;36(6):4005-4016

Pregnancy and Lactation

Although high dietary intakes of glucosinolates from cruciferous vegetables are not known to have adverse effects during pregnancy or lactation, there is no information on the safety of isothiocyanates or supplements containing high doses of glucosinolates and/or isothiocyanates during pregnancy or lactation in humans

Potential Drug Interactions

- Isothiocyanates are not known to interact with any drugs or medications
- However, the potential for isothiocyanates to inhibit various isoforms of the cytochrome P450 (CYP) family raises the potential for interactions with drugs that are CYP substrates

Further Research

- Majority of the studies have been conducted using animal models
- Need more long term studies to determine optimal dosing since amounts vary widely from study to study
- Preliminary research done on obesity, cholesterol, skin protection, etc.

Take Home Message

- Factors that alter cells, like oxidation, DNA-damaging chemicals, radiation and inflammation are fundamental to most chronic conditions
- Many studies have demonstrated that administration of sulforaphane or its precursors either as a supplement or via increased consumption of cruciferous vegetables may result in improved outcomes in a variety of chronic conditions due to its anti-inflammatory, and anti-oxidative properties
- To obtain sulforaphane's therapeutic benefits, consumption of cruciferous vegetables, especially raw broccoli sprouts, and/or supplements containing sulforaphane should be incorporated daily



Metagenics Institute