

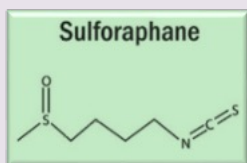
Broccoli, Glucoraphanin And Sulforaphane Unravelling



The health-promoting potential of sulforaphane, a biologically active compound derived from the broccoli plant is well documented.¹ In the early 1990s, scientists at Johns Hopkins University identified that sulforaphane is a potent Nrf2-mediated inducer of phase II detoxification enzymes. It was also identified that sulforaphane indirectly enhances cellular antioxidant capacity to reduce oxidative stress.¹⁻³ Since this early research, sulforaphane and its precursor, glucoraphanin, have been the subject of well over 125 human clinical studies and thousands of animal and laboratory studies.¹ This research spans a range of aspects including pharmacokinetics, pharmacodynamics, underlying mechanisms of action and therapeutic potential.^{1,2}

SUMMARY OF KEY POINTS

Sulforaphane - Actions



Combined findings across human, animal and laboratory research suggest that sulforaphane has several biological properties that may support health:¹⁻⁶

- Supports liver and cellular detoxification.
- Nrf2-mediated induction of phase II detoxification enzymes.
- Regulation of phase 1 enzyme activity.
- Modulates redox balance and indirect antioxidant.
- Induces the Keap1/Nrf2 pathway, important for several biological functions.
- Supports metabolism of oestrogen metabolites.
- Anti-inflammatory activity through suppression of NF-kappa B.
- Potential antimicrobial and neuroprotective properties.

Glucoraphanin – Precursor found in broccoli



- Broccoli is a rich source of glucoraphanin, the precursor to sulforaphane.²⁻⁵
- Glucoraphanin is chemically stable, but relatively inert.²⁻⁵
- Broccoli also contains myrosinase enzymes, which are segregated into separate plant cells to glucoraphanin.²⁻⁵
- When raw broccoli is damaged, cut or chewed, myrosinase enzymes and glucoraphanin interact. The enzymes hydrolyse glucoraphanin, resulting in conversion to the bioactive compound, sulforaphane.^{2,4,5}
- Glucoraphanin can also be converted to sulforaphane endogenously due to the enzymatic activity of myrosinase-containing intestinal bacteria.^{1,7-13}
- This is important as heat can denature the plant-based myrosinase enzymes. Broccoli is most often eaten cooked, not raw.^{11,12}

Supplemental use



- Sulforaphane is an unstable compound, especially at high temperatures and naturally has a bitter taste.¹⁴⁻¹⁷
- As such, supplements are generally standardised to glucoraphanin, the stable precursor, and often given without active myrosinase enzymes. This closely aligns with how nature segregates glucoraphanin from myrosinase into different plant cells to prevent premature enzymatic conversion to the unstable sulforaphane compound.²⁻⁵
- Endogenous conversion of supplemental glucoraphanin to the bioactive sulforaphane is then facilitated by the presence of myrosinase enzymes in gut bacteria.^{1,5,9,10} Several intestinal bacteria have been shown to produce myrosinase enzymes, including species from diverse genera such as *Lactobacillus*, *Bacillus*, *Enterobacter*, *Enterococcus*, *Lactococcus*, *Citrobacter*, *Lecleria* and *Companilactobacillus*.¹⁰
- Broccoli seeds are the richest source of glucoraphanin, followed by sprouts and then florets.²

Sulforaphane Review

Sulforaphane Actions

Sulforaphane, derived from broccoli is considered one of the most important phytonutrients identified to date.¹

Sulforaphane is regarded as a potent Nrf2-mediated inducer of phase II detoxification enzymes and supports detoxification processes. It also indirectly enhances cellular antioxidant capacity to reduce oxidative stress.³⁻⁵ Sulforaphane is recognised as the most potent naturally occurring inducer of the Keap1/Nrf2 pathway, which upregulates antioxidant and detoxification mechanisms, resulting in inhibition of inflammation. This pathway also plays an important role in immune function, mitochondrial health and certain neurological processes.¹ In addition, sulforaphane has been shown to reduce inflammation by suppressing NF-kappa B, which in turn downregulates expression of pro-inflammatory cytokines and mediators.^{6,8}

Sulforaphane can also aid in the detoxification of oestrogen metabolites, according to animal research. It has been shown to upregulate phase II detoxification enzymes and to contribute to a more favorable balance of oestrogen metabolites by increasing production of the 2-OHE1 oestrogen metabolite and decreasing production of 16α-OHE1, which is proliferative.¹ Sulforaphane may also help metabolism of xeno-oestrogens.¹

Furthermore, sulforaphane has been shown to induce apoptotic pathways, suppress cell cycle progression and inhibit angiogenesis in laboratory and animal research.⁵ It has also been shown to modulate the chemoprotective mechanism of cells by suppressing the phase 1 enzymes responsible for activation of carcinogens and activating phase II enzyme activity through the Nrf2 transcription factor.⁵ These properties have led to significant research interest into potential health applications for sulforaphane.^{1,3,5,18-23}

Sulforaphane has also been researched for its antimicrobial and neuroprotective properties, influence on cell signalling pathways and gene expression, as well as its potential benefit in various health disorders.^{2,5-9,22-24}

From Broccoli to Glucoraphanin to Sulforaphane

Broccoli contains glucoraphanin, a largely inert glucosinolate compound found naturally in chloroplast cells in broccoli plants, as well as in some other cruciferous vegetables. Glucoraphanin is the plant precursor of sulforaphane.²⁻⁵ Broccoli also contains myrosinase enzymes, which are physically segregated into different cellular compartments of the plant.^{2,5}

When the raw plant is damaged, cut, harvested, processed or chewed, the cells rupture and subsequently the myrosinase enzymes and glucoraphanin come into contact. This leads to enzymatic hydrolysis of glucoraphanin and conversion to the bioactive compound, sulforaphane.^{2,4-6} This process is part of the plant's natural defence mechanisms as the sulforaphane imparts the characteristic bitter taste to broccoli, which discourages animals, insects and other pests from eating the plant.^{2,5,10}

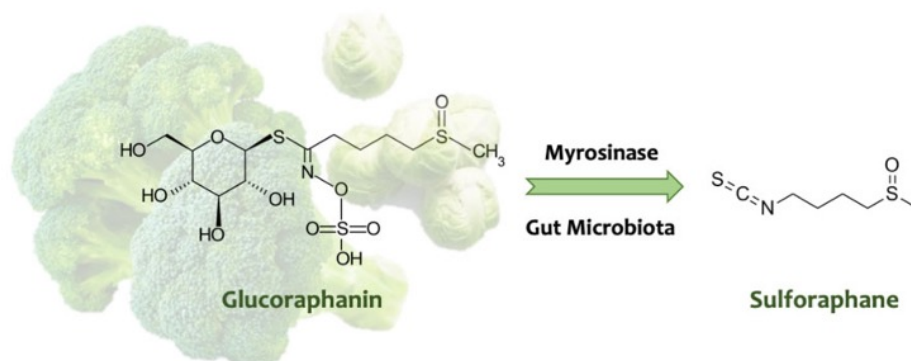
Intestinal Bacterial Conversion to Sulforaphane

When broccoli is eaten raw, the myrosinase enzymes naturally convert glucoraphanin to sulforaphane. When broccoli is cooked, however, the heat can denature the myrosinase enzymes and reduce their activity.^{11,12} Cruciferous vegetables, such as broccoli, are however, eaten cooked more often than raw. This has raised questions as to what other biological mechanisms exist that facilitate enzymatic conversion of glucosinolates, such as glucoraphanin, to bioactive isothiocyanates, such as sulforaphane.^{10,13}

Research has identified that some intestinal bacteria also produce myrosinase enzymes, which hydrolyse glucoraphanin to produce sulforaphane after ingestion. Several gastrointestinal bacterial species have been shown to produce myrosinase enzymes, including species from diverse genera such as *Lactobacillus*, *Bacillus*, *Enterobacter*, *Enterococcus*, *Lactococcus*, *Companilactobacillus*, *Citrobacter*, and *Leclercia*.¹⁰ These intestinal bacteria can also promote endogenous enzymatic conversion of other glucosinolates to isothiocyanates after ingestion.⁷⁻¹³

This finding has significance as it means that dietary cruciferous vegetables can still be metabolised to form bioactive compounds such as sulforaphane in the body. Therefore, even if cooking processes have deactivated the plant-based myrosinase enzymes, dietary consumption of vegetables such as broccoli can still provide potential health benefits.^{5,9,11,12}

Endogenous conversion of glucoraphanin²⁵



Supplemental Intake of Sulforaphane

As sulforaphane gains in scientific credibility and we learn more about its potential health benefits, it has become increasingly important to consider how to deliver quantifiable amounts in supplements and whether to give it in the form of broccoli, glucoraphanin or sulforaphane.²

Sulforaphane itself is a reactive unstable compound, especially at high temperatures.¹⁴⁻¹⁶ This presents challenges to standardising to sulforaphane. Standardising to broccoli also has potential challenges, as does the manufacturing processes involved in turning broccoli into a powder. An integral part of broccoli plant physiology is that glucoraphanin and myrosinase are kept in separate plant compartments to prevent enzymatic conversion to sulforaphane until it is chewed or chopped.^{2,5} Manufacturing processes to form broccoli powder may cause mechanical damage to cell walls and trigger glucoraphanin and myrosinase to interact and hydrolyse to the unstable sulforaphane prior to supplemental ingestion.

Taking these factors into account, many supplements are standardised to glucoraphanin. This provides a measurable quantity of the stable precursor. Broccoli seeds have been identified as having the highest concentration of glucoraphanin, followed by broccoli sprouts and then broccoli florets.² Research demonstrates comparable bioavailability and conversion efficiency for glucoraphanin sourced from seeds compared to glucoraphanin sourced from sprouts.²⁶

Supplemental glucoraphanin does not need to be given with supplemental myrosinase as it will be endogenously transformed to sulforaphane by the myrosinase enzymes present in some intestinal bacteria after ingestion.^{5,9-11} Separation of supplemental glucoraphanin and myrosinase enzyme activity closely aligns with how nature segregates glucoraphanin from myrosinase into different plants cells to prevent premature enzymatic conversion to the unstable sulforaphane compound.²⁻⁵

Research findings support use of supplements standardised to glucoraphanin as a means to achieve health benefits associated with bioactive, but unstable sulforaphane.

- In clinical research, a glucoraphanin-rich broccoli preparation has been shown to induce key phase II antioxidant enzymes more than double that of standard broccoli and demonstrated a >20-fold increase in phase II enzyme induction compared to water.²⁷
- Research has also reported that glucoraphanin-rich preparations can accelerate the detoxification and excretion of potentially harmful environmental contaminants.^{2,28}
- One study reported significantly increased excretion of glutathione-derived conjugates for both a glucoraphanin-rich (GRR) preparation and a sulforaphane-rich (SFR) preparation, with no significant differences reported between the effects of the two preparations.²⁸

In conclusion, sulforaphane has been identified as an important phytonutrient with detoxification antioxidant, anti-inflammatory and other health-promoting properties. Supplemental use shows promise for several clinical applications, with more research emerging on the scope of potential health benefits.

**References available on request.*