| SmarterNaturally Explains | GRextra for Longevity

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 <u>Guide to GRextra</u>

Due to the impact of sulforaphane in our cells, it has been extensively researched for its beneficial effects on human health across a range of different areas, and particularly with the challenges and progressive health conditions that become more common as we age.

Many age-related health conditions are linked to our metabolism - the chemical process that's constantly running inside every cell in our bodies to power our lives. It provides the energy we need to live, grow and thrive... but naturally becomes less efficient as we age. This internal ageing of our metabolism undermines our health and wellbeing at the most fundamental level, and has been linked to a wide range of health areas including:

- Weight loss & obesity
- Blood sugar & diabetes
- Cholesterol & heart health

- Brain health (e.g. dementia)
- Joint health (e.g. arthritis)
- Cancer

Excitingly, a huge and growing evidence base of independent research and clinical trials conducted over decades now indicates that adding a powerful source of sulforaphane to our diet could help to repair and reverse metabolic damage, slowing the internal process of ageing and restoring our metabolic health.

This in turn has a knock-on impact on our overall health and wellbeing, supporting improved longevity and better long-term health outcomes. In this new eta of metabolic medicine, your age in years is less important than your age on the inside - and focusing on our metabolic health can give us a better chance of staying well for longer and living our later lives to the full, unhindered by the many diseases of age that try to hold us back.

Weight loss & obesity

As we age and our metabolic health deteriorates, it becomes easier for us to put on weight. This has a huge impact on our health, and our ability to stay active and continue to live life to the full.

Studies indicate that sulforaphane can help to support weight loss efforts, which has a huge knock-on impact on wider areas of our health and wellbeing. This is achieved in four key ways:

- 1) Stimulating the body to lay down less fat^{1,2,3,4,5,6,7,8}, and instead encouraging the body to burn more fats for energy^{9,10}
- 2) Reducing appetite and food intake (through increasing responsiveness to the appetite suppressant hormone leptin)^{11.12,13}
- Promoting mitochondrial production¹⁴ and stimulating the conversion of inactive white fat to metabolically-active brown fat, which together lead to a higher base metabolic rate^{15.16.17}
- 4) Supporting the gut microbiome to increase levels of good bacteria, which improves both fat and glucose metabolism,^{18,19} further supporting weight loss.

"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)

In our citizen science programme, we've seen the positive effects of sulforaphane for supporting weight loss in validated by the experience of customers eating our super-broccoli regularly:

"Over the last year, my weight has gone down significantly with no pain whatsoever. It's quite remarkable really." **Alex, SmarterNaturally subscriber** "The weight definitely came off faster this time than it ever has before. It all just felt a little easier."

Robert, SmarterNaturally subscriber

Blood sugar & diabetes

High blood sugar becomes more and more common as we get older, and can lead to type-2 diabetes and a range of additional health complications, including sight loss, nerve problems, and a greater risk of heart attacks, stroke or kidney issues.

Studies indicate that sulforaphane can help to reduce blood sugar down to healthier levels, directly contributing to improved diabetic health and reducing the risk of developing the many health complications associated with high blood sugar. This is achieved in three key ways:

- Improving the effectiveness of insulin, both via improving insulin sensitivity/reducing insulin resistance^{20,21,22,23,24,25,26,27,28,29,30,31,32} (a major component of disease development in type 2 diabetes), and improving the health and function of the pancreas to drive increased insulin production^{5,33,34,35,36}
- 2) Altering the behaviour of the liver to reduce its production and release of glucose into the bloodstream^{37,38,39} and instead driving it to burn up glucose for energy¹⁶
- 3) Supporting weight loss, as outlined in the section on weight loss above

"In conclusion, sulforaphane could be an exciting novel small molecule to use against Type-2 Diabetes."

Review: The improvement of sulforaphane in type 2 diabetes mellitus (T2DM) and related complications (Wang et al, 2022)

In our citizen science programme, we've seen the positive effects of sulforaphane for supporting blood sugar validated by the experience of customers eating our super-broccoli regularly:

"While I'm sure it was a combination of things, I do think eating this soup has played a big role in bringing down my HbA1c and improving my diabetic health." **Anthony, SmarterNaturally subscriber** "I was kind of aware of the magical powers of brassicas, but this has been more effective than I was expecting! It's been a real game-changer for me." Glory, SmarterNaturally subscriber

Cholesterol & heart health

Heart disease is one of the biggest modern killers, with heart attacks and stroke often the first things that take us off our feet as we get older. High cholesterol levels and high blood pressure, both of which put us at a greater risk of a heart attack or stroke, are also incredibly common and can be tough to tackle.

Studies indicate that sulforaphane can help to support improved heart health, reducing the risk of major heart health events This is achieved in 4 key ways:

- 1. Lowering high cholesterol (LDL-C) back to healthier levels 40.41.42.43
- 2. Lowering high blood pressure down to healthier levels 44,45,46,47
- 3. Soothing inflammation within arteries and the heart through activation of the antioxidant NRF2 pathway^{48,49} and inhibition of pro-inflammatory pathways such as NFkB^{50,51,52}
- 4. Supporting weight loss, as outlined in the section on weight loss above

"Sulforaphane could contribute to the prevention of cardiovascular disease."

Sulforaphane Protects against Cardiovascular Disease via Nrf2 Activation (Bai et al, 2015)

In our citizen science programme, we've seen the positive effects of sulforaphane for supporting brain health validated by the experience of customers eating our super-broccoli regularly:

"My cholesterol level has dropped from 5.7 to 4 mmol/L, and the overall balance is much healthier too. So clearly this soup is doing me some good!" **Caroline, SmarterNaturally subscriber**

"My blood pressure has come down quite significantly over the last six months since I started eating this soup - it's now back in a really good range, which is brilliant." **Patrick, SmarterNaturally subscriber**

Brain health (e.g. dementia)

Keeping our body healthy is important, but keeping our brain healthy and working well for as long as possible is absolutely critical if we're to be able to keep living our lives to the full.

Studies indicate that sulforaphane can help to support improved brain health and help to slow and reduce the risk of developing neurodegenerative diseases such as Parkinson's or Alzhimer's, reducing the risk of dementia.

This is achieved by soothing inflammation within the brain through activation of the antioxidant NRF2 pathway, inhibition of pro-inflammatory pathways such as NFkB, and the triggering of HSP27, which are in turn linked to:

- 1. Reduced protein misfolding in the brain, 53, 54, 55, 56 which causes Alzhimers disease
- 2. Reduced oxidative stress in the brain leading to the protection of neurons from cell death, 57,58,59,60,61 which causes Parkinson's and other diseases of the brain
- 3. Improved recovery from acute brain damage caused by stroke or traumatic head injuries^{62,63,64,65}
- 4. Reduced symptoms in some psychological and psychiatric conditions, including autism spectrum disorder^{66,67,68,69,70,71,72,73} and schizophrenia^{74,75,76,77}

"Sulforaphane appears to be a promising compound with neuroprotective properties that may play an important role in preventing neurodegeneration."

Sulforaphane as a Potential Protective Phytochemical against Neurodegenerative Diseases (Tarozzi et al, 2013)

In our citizen science programme, we've seen the positive effects of sulforaphane for supporting brain health validated by the experience of customers eating our super-broccoli regularly:

"The most important thing is the improvement I've seen in the brightness of my head: I feel less fuzzy and woolly and brighter in my thinking and feeling." **Ed, SmarterNaturally subscriber**

Joint health (e.g. arthritis)

Arthritis is common as we age, but it can have a huge impact on our lives, causing chronic pain and preventing us from staying active and doing the things we love.

Studies indicate that sulforaphane can help to support improved joint health and help to slow or even prevent the progression of age-related joint diseases such as osteoarthritis and rheumatoid arthritis, improving mobility and quality of life. This is achieved in three key ways:

- 1) Soothing joint inflammation, helping to alleviate swelling and slowing down long-term damage to the joint^{78,79,80,81,82,83}
- 2) Protecting joint cartilage and linings from wear and damage which compromises joint function^{84,85,86,87,88,89,90,91,92}
- 3) Strengthening bones to support long-term joint health⁹³

"Previous studies have shown that a compound called sulforaphane, which is found naturally in broccoli, may protect against osteoarthritis."

A Dietary Intervention Trial To Examine The Protective Effect Of Broccoli Bioactives (Specifically Sulforaphane) On Osteoarthritis (BRIO study, ongoing)

In our citizen science programme, we've seen the positive effects of sulforaphane for supporting joint health validated by the experience of customers eating our super-broccoli regularly:

"After eating this soup for a year, I have definitely noticed my arthritis improving. My joints were often really sore, but now I'm in less pain and finding it easier to do more!" **Anita, SmarterNaturally subscriber**

Cancer

Cancer is the killer that needs no introduction. While nothing can completely protect us from developing cancer, every step we take to reduce our risk gives us a better chance of enjoying our later lives for longer, without having them stolen from us by the big C.

Studies indicate that sulforaphane can help to make our body less hospitable and more resistant to cancer cells, reducing our risk of developing serious and common cancers, and potentially slowing tumour growth, including for:

- 1. Prostate cancer^{94,95,96,97,98,99,100,101}
- 2. Breast cancer^{102,103,104}
- 3. Bowel cancer^{105,106,107}
- 4. Bladder cancer^{108,109,110}

"[Regular] dietary sulforaphane shows promise as a safe and effective anti-cancer strategy."

Multi-targeted prevention of cancer by sulforaphane (Clarke et al, 2008)

In our citizen science programme, we've seen the positive effects of sulforaphane for supporting prostate health validated by the experience of customers eating our super-broccoli regularly:

"My PSA was steadily rising, but I just got my latest test back and it's fallen back down lower than it's ever been. I was a bit confused until I realised I've been eating this soup regularly for a year now - it must be doing something good for my prostate!" **Sunil, SmarterNaturally subscriber**

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 for accessing the health benefits of sulforaphane - such as SmarterNaturally SuperSoup, which delivers ~5x more sulforaphane per portion than a normal broccoli - equivalent to 14 supplement tablets. 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.

An Answer for Everyone?

Because our metabolic health is utterly fundamental to our broader health and wellbeing, our super-broccoli and the active ingredients it contains can offer benefits to everyone, including:

- Those with specific health conditions or concerns

Repairing our metabolism is linked to healthier blood sugar and cholesterol levels, healthier blood pressure and a reduced risk of heart disease, offering a new hope to people struggling to control these essential aspects of their health. Learn more

- Those looking to stay well as they get older

Maintaining a healthy metabolism is linked to increased energy levels, slower progression of arthritis, a reduced risk of conditions of the brain (including Alzhimer's, Parkinson's and dementia) and a reduced risk of various forms of cancer (including breast and prostate cancer - two of the most common cancers in the UK). Learn more

- Those looking to maintain a healthy weight

A healthy metabolism can help to support weight loss efforts through encouraging the body to lay down less new fat whilst burning up existing fat reserves, and helping to regulate appetite so we feel full for longer. Learn more

- Those looking to recover from an accident, operation or health event

Traumas and treatments alike both take a huge toll on our body, and the hidden damage they cause to our metabolism can hold back our recovery. Fixing that damage helps us put a health scare behind us and get back to our best faster. Learn more

- Those looking to optimise their performance and recovery

Metabolic training is key for athletes looking to perform at their best, since greater metabolic fitness drives greater energy production and faster lactate clearance. This supports improved power and endurance during efforts and faster recovery, whilst protecting joints and organs from long-term damage. <u>Learn more</u>

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