

Phase II Detoxification and Sulforaphane

Detoxification has to be distinguished from purgative and diuretic effects. Most natural health products address the cleansing of the body via purgative and diuretic effects and by the stimulation of the liver. The usual European, and particularly Scandinavian, "cleansers" are nothing more than stimulators of the above effects. While this can be useful, true detoxification can only occur at the cellular level.

The body has designed an elaborate detoxification mechanism to deal with the thousands of toxins it is exposed to on a regular basis. These toxins come in the form of carcinogens, environmental pollutants (like pesticides, hormones and exhaust fumes), toxic pharmaceuticals, heavy metals, cigarette smoke, UV radiation and many others.¹⁻³ It is estimated that there are over 500,000 chemicals currently being used and up to 25% of these may be carcinogenic! Many of these chemicals contribute to other diseases including multiple chemical sensitivities, fibromyalgia, chronic fatigue syndrome, neurological diseases (like Alzheimer's, Parkinson's and MS), auto-immune diseases (like rheumatoid arthritis and lupus), diabetes and so on.^{1,3,4} Given the intensity of these exposures, an individual's ability to detoxify these harmful substances is now recognized as a key factor to maintaining overall health.

Phase I vs. Phase II Detoxification

Most detoxification reactions occur in the liver and to a lesser extent in the intestines and the skin. The detoxification process involves two steps termed phase I and phase II. In each step a family of around 20 enzymes is called into action.³ (see pages 6 and 7)

Phase I detoxification involves the well known cytochrome P450 enzymes that catalyze a variety of oxidation, reduction, hydrolysis and other reactions. The purpose of these enzymes is to make fat soluble toxins (called xenobiotics) more soluble by first "priming" these chemicals by incorporating an "active site" which will ultimately be acted upon by Phase II enzymes.^{5,6} By incorporating an active site the molecule becomes more reactive and therefore potentially more damaging to the tissues. It is essential that Phase II enzymes are activated quickly to eliminate the dangers of these phase I intermediates.³

Phase II reactions are also referred to as the "detoxification pathway" and involve the addition, or "conjugation" of various chemical molecules or groups to the Phase I intermediates. Examples of such groups are sulphhydryl groups (SH), methyl groups (CH₃), glutathione, glucuronide and so on. These groups make the xenobiotics more water soluble and therefore more easily excreted from the body. This is important since this ensures that toxins are not allowed to linger too long in the body.^{3,5,6} While the Phase I process can be a double-edged sword, Phase II reactions are widely regarded as being highly beneficial to health when stimulated.

Natural Stimulators of Phase II Enzymes

A number of phytochemicals can stimulate Phase II detoxification enzymes⁷, but none more so than sulforaphane, a component of various cruciferous vegetables like mustard, kale, bok choy, cabbage, cauliflower and especially broccoli sprouts. The cruciferous vegetables are a rich source of a group of compounds called glucosinolates that are rapidly converted by an enzyme called myrosinase into much more powerful compounds called isothiocyanates (ITC). Sulforaphane is one such compound.^{2,8}

Sulforaphane is the most widely studied ITC, both experimentally and clinically. Much of the pioneering work has been done in Baltimore at Johns Hopkins University by Paul Talalay and his group.¹ Sulforaphane has hundreds of studies worldwide attesting to its very powerful Phase II stimulating properties.



Figure 1. Cruciferous vegetables like broccoli are rich in compounds that promote phase II detoxification.

What are the Benefits of Sulforaphane?

1. Antioxidant

Free radicals or reactive oxygen species are created by toxins and carcinogens as well as by the body as a byproduct of various chemical reactions, especially in the mitochondria. These reactive species readily attack various tissues in the body causing disease and aging. Sulforaphane is a potent quencher of such species, acting by stimulating various enzymes and compounds that neutralize these reactive species effectively.^{2,4,9}

2. Anti-inflammatory

Inflammation is now considered the hallmark of a number of diseases like diabetes, allergies, cardiovascular disease and even obesity. Sulforaphane has an anti-inflammatory effect via a number of different mechanisms including the inhibition of COX 2 enzymes and NF-kappaB, a molecule associated with inflammation, and the promotion of Nrf2, a powerful molecule that inhibits inflammation.⁹ In a number of studies sulforaphane has been shown to clinically reduce inflammation and pain in osteo-arthritic patients as well as improving the repair of damaged cartilage.¹⁰

3. Lowers Blood Pressure

High blood pressure has been linked to high amounts of reactive oxygen species. Animal studies have demonstrated that sulforaphane significantly reduces blood pressure and improves other cardiovascular health conditions.¹¹

4. Anti-allergic Effects

Sulforaphane has been shown to reduce symptoms of allergies including sneezing, watery eyes, itchy and runny nose caused by a variety of allergens like different types of pollen, dust, diesel fuel etc. A recent human study showed that sulforaphane greatly increased antioxidant status of the patients and the authors suggested a potential application of sulforaphane in conditions like asthma.²

5. Anti-cancer Effects

Perhaps the most widely studied effect of sulforaphane for over 20 years is in the field of cancer research in a number of diverse species as well as variety of tissues like prostate, skin, colon, breast, uterine, ovarian, bladder, pancreas etc.^{1,5,6,12-15} No human studies are available due to the large number of subjects required, length of study (over 20-30 years) and the cost.

The anti-cancer effect is attributed to a number of mechanisms including the stimulation of phase II enzymes, apoptosis (cell suicide), cell cycle arrest (preventing replication), reduction of the spread of tumours (metastases) and the inhibition of blood supply to cancer cells (angiogenesis).¹³⁻¹⁶

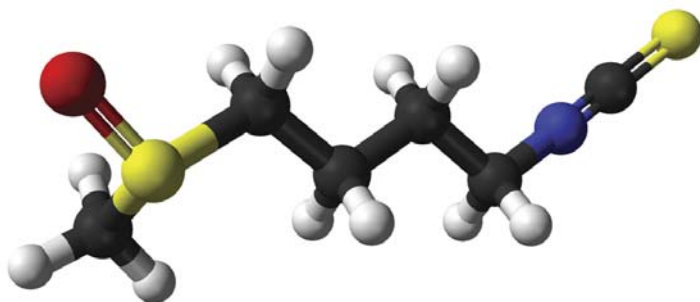


Figure 2. The chemical structure of Sulforaphane.

Detoxification at the Cellular Level

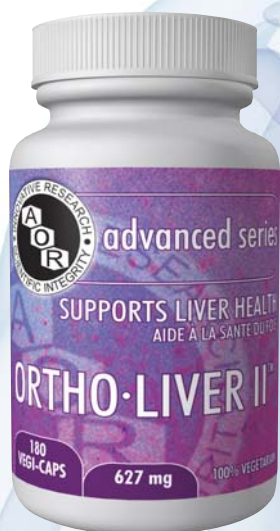
In conclusion, stimulation of Phase II detoxification enzymes promotes true detoxification of the body at the cellular level. Enhanced Phase II detoxification greatly assists the body in reducing the overall toxic burden as well as affording substantial health benefits in immune function, heart health, anti-inflammatory and anti-cancer effects. Sulforaphane is an exciting natural compound that is the most potent and widely studied Phase II detoxifier.

References

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