

DETOXIFYING GERONTOGENS TO REVERSE BIOLOGICAL AGE

We are used to attributing wrinkles, sunspots, and gray hairs - classic signs of aging - to the usual lifestyle suspects of UV exposure, chronic stress, and lack of sleep, but there is something else at play that we are losing site of: **Toxin Exposure and Toxic Burden**. The human "exposome" is defined as the milieu of toxins to which we are exposed across our lifetime, and this exposome can accelerate biological aging by influencing internal biological processes that drive deterioration of human health. In fact, certain toxins are such significant drivers of aging that they have been endowed with a specific name: "Gerontogens."¹ **"Gerontogens"** include air pollution (nitrogen dioxide and PM_{2.5}), smoking, lead, and aluminum, among many others.^{2,3,4}

Understanding proper detoxification may be the single most fundamental principle for healthy aging and longevity and supporting the body's detoxification system to clear gerontogens must be done before other anti-aging therapies as toxins become impediments to their success.

Our Unprecedented Exposure to Toxins and Their Effects on Aging

We live in an increasingly toxic world rife with chemical exposures of a magnitude that our bodies have never before experienced in human history. Emerging research suggests that certain toxins may adversely affect the course of biological aging. Examples include heavy metals, air pollution, BPA and BPA alternatives such as BPS and BPF, phthalates, microplastics, mycotoxins, and the herbicide glyphosate.

Our toxic burden taxes the body's antioxidant systems, which has been shown to drive biological aging by harming mitochondria, damaging cell and organelle membranes, draining NAD⁺ levels, interfering with healthy sirtuin and telomere function, and causing chronic cellular senescence and neuroendocrine dysfunction.^{5,6,7,8,9,10,11}

Which toxins disrupt our biochemistry?

- Acetaminophen, antibiotics, and heavy metals have been shown to actively disrupt mitochondrial energy production and increase production of reactive oxygen species (ROS).^{12,13}
- Particulate matter, pesticides, heavy metals, antibiotics, and non-native electromagnetic fields (EMFs) disrupt cell and organelle membranes, impairing cellular function.^{14,15,16,17}
- Metals like methylmercury and endogenous toxins like lipopolysaccharide (LPS) derived from Gram-negative gut bacteria can deplete NAD⁺ levels and block sirtuin activation, accelerating biological aging.^{18,19}

Understanding proper detoxification may be the single most fundamental principle for healthy aging and longevity. By regularly supporting the Nrf2 pathway, we can unload the body's toxic burden to set the stage for possibly slowing and even reversing the biological pace of aging.

Nrf2 for Healthy Aging

Nuclear factor erythroid 2-related factor (Nrf2) is a transcription factor, a protein that helps turn genes "on" or "off" by binding to sections of DNA. It resides in the cytosol of cells and, upon sensing oxidative stress, translocates to the nucleus, where it attaches to the promoter region of genes that encode critical elements of detoxification known as the antioxidant response element (ARE).

Nrf2-mediated activation of the ARE protects the body against oxidative stress and repairs DNA damage triggered by environmental toxins, influencing two critical drivers of aging. We like to think that the body has everything it needs to employ effective detoxification naturally, but ironically, toxin exposure and toxic burden impedes the body's natural ability to detox by interfering with Nrf2 signaling.

Because of this, we need to actively support Nrf2 with specific nutraceutical interventions.

A BETTER WAY TO SUPPORT DETOXIFICATION AND NRF2

Toxin exposure is a modifiable risk factor for aging, amenable to detoxification interventions that support the Nrf2 signaling pathway.²¹ Activation of Nrf2 supports glutathione synthesis, a cornerstone of detoxification. There are a variety of well-researched nutraceuticals that activate Nrf2 to facilitate detoxification, but many suffer from low bioavailability.

A successful detoxification program is an essential first step in a patient's longevity journey and hinges on '**biosynchronous activation™**', the concurrent delivery of key ingredients into the body using specific delivery technology to enhance bioavailability and elicit specific and powerful biochemical actions in a synchronized and timely way.

Biosynchronous Activation™ in detoxification is dependent on two critical factors:

1. Utilizing the right combination of Nrf2-upregulating and detoxification support compounds
2. Delivery technology to increase bioavailability and activation of ingredients

Nrf2 and Detoxification Compounds

Glutathione

Nrf2 regulates the synthesis of glutathione, the body's master antioxidant, and a vital detoxification molecule. Nrf2 regulates two enzymes involved in glutathione synthesis: Glutathione reductase and glutathione synthetase.^{22,23} Glutathione is needed for Phase I and Phase II of detoxification, in which chemicals are activated and then conjugated in preparation for elimination. A lack of glutathione availability slows down detoxification. The age-related decline in Nrf2 activity is one reason why glutathione synthesis, and possibly detoxification capacity, may decline with age.²⁴

Lipoic Acid

Lipoic acid is a sulfur-based compound that functions as an antioxidant in part through Nrf2 activation.²⁵ Upregulation of Nrf2 by lipoic acid protects against heavy metal toxicity.²⁶ Through its detoxifying and antioxidant effects, lipoic acid may reduce inflammation and oxidative stress during the aging process.

Milk Thistle

Milk thistle (*Silybum marianum*), a prickly plant from the Asteraceae (Daisy) family, has an extensive history of use in traditional Western herbalism for supporting the liver, the body's detox "hub." Milk thistle contains several bioactive phytochemicals that upregulate Nrf2 and support detoxification, including silymarin.²⁷ Flavolignan constituents of milk thistle have been shown to protect against a variety of chemical assaults, including arsenic, paraquat, and acrylamide, through Nrf2 bioactivation.²⁷

DIM

Diindolylmethane is a sulfurous phytochemical found in cruciferous vegetables such as broccoli, cauliflower, cabbage, and kale. It also upregulates Nrf2 activity, protecting against oxidative stress that advances biological aging.²⁸

Bitter Herbs

Bitter herbs can assist detoxification by stimulating bile flow and membrane proteins involved in Phase III detoxification, facilitating the movement of toxins out of cells, into bile, and out of the body via stool. Several bitter herbs also act on the Nrf2 pathway. For example, the bitter herb dandelion enhances bile flow and upregulates the Nrf2 antioxidant pathway.^{29,30} Myrrh, a resinous substance derived from the *Commiphora mukul* tree native to India, supports healthy bile flow by increasing the expression of the human bile salt export pump and enhances Nrf2 expression.³¹

NANOPARTICLE DELIVERY TECHNOLOGY FOR EFFECTIVE DETOXIFICATION

Nutrient cofactors and phytonutrients have the potential to support core detoxification pathways inside the body and clear the way for healthy aging. However, the poor bioavailability of many of these substances hinders cellular uptake and absorption creating an impediment to effective intracellular detoxification.

To maximally support detoxification, we must improve the bioavailability of these compounds. The delivery system in which we "package" nutrient cofactors and phytonutrients can make a remarkable difference in how these beneficial compounds

are processed by the body and used to support detoxification. Nanoparticle delivery systems, including liposomes and nanoemulsions, offer a solution to the bioavailability problem and support a more rapid and effective detoxification process.³³

Liposomes are tiny bi-layered lipid bubbles approximately the width of a single human hair made of the same fats – phospholipids – as our own cell membranes. The two phospholipid layers of a liposome form concentrically; the outer layer has hydrophilic “water-loving” phospholipid heads at the surface, allowing the particle to mix with water. The molecule’s core contains hydrophilic heads that face inward, allowing the liposome to carry water-soluble ingredients. Liposomal delivery systems can improve the bioavailability of water-soluble detoxification nutrients, including glutathione.³²

Nanoemulsions, on the other hand, are monolayered spheres that carry fat-soluble ingredients. They are composed of a single-layer membrane of phospholipid molecules with the hydrophilic head facing the outside and the hydrophobic tail on the inside. These droplets have a large surface area and volume and, like liposomes, significantly enhance the bioavailability of the therapeutic phytonutrients and vitamins they contain. As suggested by their structure, they work best for carrying fat-soluble ingredients such as vitamin D and carotenoids.³³

The structure of liposomes and nanoemulsions enables rapid and synchronized cellular absorption of these molecules across lipid membranes, avoiding the unpredictability of digestion, providing unparalleled support for intracellular detoxification. Rapid delivery of bioavailable detoxification ingredients through nanoparticle delivery systems supports *biosynchronous activation™*, creating effective and predictable detoxification protocols to remove gerontogens and other toxic elements clearing the way for healthy aging.

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