Detoxification Research Review

Environmental pollutants are ubiquitous in the air, drinking water, and food supply. Toxins in the environment include a wide range of compounds, such as heavy metals, organic pesticides, drugs, and industrial material. Exposure to environmental toxins has been associated with many types of cancers and syndromes characterized by fatigue, muscle weakness, and cognitive dysfunction. One of the most important biochemical processes attending to toxicant removal in our bodies is the biotransformation process, also called the detoxification system, which is comprised of Phase I, Phase II, and Phase III pathways. The detoxification system is highly dependent on nutrient support for optimal functioning.

Metagenics™

Genetic Potential Through Nutrition

The Role of Detoxification in the Prevention of Chronic Degenerative Diseases

HOW DO TOXICANTS AFFECT CHRONIC DEGENERATIVE DISEASES?

A growing body of literature suggests an association between toxicant exposure and the etiology of a number of chronic conditions, such as chronic fatigue syndrome (CFS), multiple chemical sensitivities (MCS), fibromyalgia (FM), and atherosclerosis.[1-4] Symptoms such as unremitting and debilitating fatigue, myalgias, arthralgias, and cognitive dysfunction are common amongst these syndromes. Moreover, a recent *New York Academy of Sciences* report indicates that individual response to toxicants is varied and is a primary factor in susceptibility to such conditions.[5]

Associations between environmental toxicant exposure with the development of many other chronic degenerative diseases have been reported as well (**Table 1**). Exposure to environmental toxicants can occur from air pollution, food supply, and drinking water, in addition to skin contact. For example, epidemiological studies have identified associations between prolonged exposure to pesticides through farming or drinking well water; proximity in residence to industrial plants, printing plants, or quarries; or chronic occupational exposure to manganese, copper, or a combination of lead and iron with symptoms of Parkinson's disease.[6] While the mechanisms of these toxic exposures are not known, an individual's ability to excrete toxins has been shown to be a major factor in disease susceptibility.[7,8]

Possibly the largest amount of research has focused on the implications of long-term toxin exposure and the risk of initiation and progression of a variety of cancers. Cancer is the third leading cause of death in children—succeeded only by injuries and violence—and the death rate is on the rise. For example, cancer death in children rose by 13% between 1973 and 1997 and, most notably, the incidence of non-Hodgkin's lymphoma and brain cancer in children rose by 30% and 21%, respectively, in the same time period.[9] Strong associations exist between these cancers and exposure to various toxins, including organochlorinated pesticides that have been shown to damage chromosomal DNA.[10-12]

Table 1. Common clinical symptoms and conditions associated with environmental toxicity

Abnormal pregnancy outcomes
Atherosclerosis
Broad mood swings
Cancer
Chronic fatigue syndrome
Chronic immune system depression
Contact dermatitis
Fatigue
Fertility problems
Fibromyalgia
Headaches
History of increasing sensitivity to exogenous exposures, odors, or medications
Joint pain
Kidney dysfunction
Learning disorders
Memory loss
Mineral imbalances (particularly zinc and calcium)
Multiple chemical sensitivities
Muscle pain and weakness
Nonresponsive or recurrent yeast infections
Panic attacks
Parkinson's disease
Tinnitus
Unusual responses to medications
Worsening of symptoms after anesthesia or pregnancy

WHAT ARE TOXINS, TOXICANTS, AND TOXIC SUBSTANCES?

The word "toxin" itself does not describe a specific class of compounds, but rather something that can cause harm to the body. More specifically, a *toxin* or *toxic substance* is a chemical or mixture that may injure or present an unreasonable risk of injury to the health of an exposed organism. Some definitions limit the use of the word "toxin" to poisonous compounds of animal or vegetable origin, and thus to avoid confusion, the Environmental Protection Agency (EPA) and other governmental organizations use the word "toxicant" to denote a toxin.[13] Each toxic substance has a defined *toxic concentration* or *toxic dose* at which it produces its toxic effect. However, most compounds referred to as environmental toxicants are damaging at low doses. A brief list of the most common classes of toxicants is provided below.

Industrial Chemicals and Combustion Pollutants. This is one of the largest categories of toxicants: virtually everyone is exposed to halogenated hydrocarbons, such as polychlorinated biphenyls (PCBs), at some level during an average day.[14] Volatile organic toxicants are a broad category of toxins that can include halogenated hydrocarbons. These toxicants are of particular concern because of their ability to become airborne.

Pesticides. Over 800 different chemicals belong to this class of toxicants. Many of the industrial chemicals are developed for their toxic effects on certain organisms and then sold as pesticides, insecticides, and herbicides. Although manufacturers of these agents try to make them selective for specific types of non-human organisms, absolute specificity is nearly impossible to achieve and most pesticides are in some way toxic to humans.[15]

Endocrine Disruptors. Common endocrine disruptors in the environment include phthalates found in plastics, PCBs, some pesticides, synthetic steroids in meat, and dichlorodiphenyltrichloroethane (DDT). Biologists have long noted problems with sterility and malformation of sex organs in many animal species that have been linked to the presence of these contaminants in the environment. It is important to note that not all estrogenically-active compounds are considered endocrine disruptors. For example, compounds such as isoflavones in soy and lignans from flaxseed are associated with health-promoting and estrogen-balancing activities and are considered selective estrogen receptor modifiers (SERMs) rather than endocrine disruptors.[16]

Toxic Metals. Toxic metals, including lead, mercury, cadmium, and arsenic, are ubiquitous in the environment and often have delayed effects because they accumulate in the body. For example, lead can be sequestered in the bone, replacing calcium, where it has a half-life of 62 years.[17] Consequences of lead toxicity include DNA damage, depressed immune system function, anemia, hypertension, kidney disease, and increased tooth decay.

Food Additives, Preservatives, and Drugs. The greatest toxin exposure by far is through oral intake. Foods, drugs, and water all contain toxic substances that move through the gastric system to the intestines where they can be absorbed. Drugs enter the body from more sources than just those consciously consumec. In fact, certain drugs—including growth hormones and antibiotics [??]—are considered one of the main contaminants of foods.

TOXIC LOAD AND STORAGE OF TOXICANTS

It is becoming apparent that toxin exposures cannot be considered individually, because humans are not exposed to individual toxins exclusively. Moreover, toxins can act in an additive manner if they exert their toxic effects through the same pathway(s). Even more concerning is the fact that many toxic substances are fat-soluble, so they can

sequester in tissues and remain there for many years. In this way, toxins can continue to accumulate so that body tissues are exposed to much higher doses than environmental concentrations would suggest are present.

HOW DOES THE BODY REMOVE TOXINS?

By far, the majority of toxins are lipid-soluble molecules. While water-soluble molecules are excreted through the urine, lipid-soluble molecules cannot directly enter into the urine and are instead attracted to the lipid in cell membranes. This attraction allows them to be transported inside of cells with ease, where they can sequester and exert their toxic effects.

In order to remove these diverse toxins, the body has a complex, integrated system designed to convert lipid-soluble toxins to water-soluble molecules, after which they can be directly excreted through renal or biliary routes. This system is called the detoxification or biotransformation system, including Phase I and Phase II metabolizing enzymes and Phase III transporters. First pass metabolism uses biotransformation reactions to convert lipid-soluble toxins to water-soluble molecules before they enter circulation. Drug metabolizing enzymes are predominantly expressed in liver, gastrointestinal tract, lungs, and kidney, although most cells have some detoxification capacity.

Biotransformation reactions occur in concert, working together to remove toxins. In brief, the detoxification system converts the lipid-soluble toxin to a water-soluble molecule by connecting (binding) the toxin to another molecule that is water-soluble (i.e., conjugation). This sounds like an easy, one-step process, but it is complicated by the fact that most toxins do not have a reactive site that will easily attach to the water-soluble moiety. Therefore, a reactive site must be made on the toxin before the water-soluble piece can be attached. This is accomplished by the Phase I enzymes.[18]

Phase I Bioactivation. Phase I reactions are catalyzed by a number of different enzymes, primarily from the cytochrome P450 (CYP450) superfamily of enzymes. Over 10 families of CYP450 enzymes have been identified in humans, and each of these contains several subfamilies. Phase I enzymes are localized to the cytosol of the cell and are regulated by receptor mediated gene transcription. CYP450s have broad specificity and use the reduced form of nicotinamide adenosine dinucleotide (NADH) as a cofactor in converting oxygen to a hydroxyl group on the lipid-soluble toxicant. The result of this reaction is the generation of a reactive site on the transformed toxicant. This reactive hydroxyl site is very much like that of a reactive oxygen species (ROS), and can readily bind to other molecules, such as DNA and proteins.

On occasion, the product from this part of the detoxification process becomes soluble in water after the addition of the hydroxyl group and can be directly excreted. This is the case with caffeine, which undergoes only Phase I activation before excretion. This direct, one-step excretion is not common, however, and most activated toxicants (*reactive intermediates*, see below) require conjugation with a larger, more water-soluble moiety to effectively alter their lipid characteristics.

Many dietary ingredients support CYP450 reactions, including niacin, which is required for generation of NADH. In addition, the activation reaction often generates ROS. Dietary antioxidants, therefore, may help protect tissue from damage that may occur by this reaction.[18,19]

Phase II Conjugation. One of the consequences of Phase I activation is that its product called a *reactive intermediate* is often more reactive—and potentially more toxic—than the parent molecule. Therefore, it is important that this molecule be converted to a non-toxic, water-soluble molecule at the site of production,

as soon as possible. Conjugation of the reactive intermediate to a water-soluble molecule is accomplished by Phase II conjugation enzymes, which consist of many enzyme superfamilies including sulfotransferases (SULT), UDP-glucuronosyltransferases (UGT), glutathione S-transferases (GST), and N-acetyltransferases (NAT).[19]

Conjugation reactions not only require the water-soluble moiety that will be attached to the toxicant—such as sulfate in the case of sulfation or glucuronic acid in the case of glucuronidation—but also use a large amount of energy in the form of adenosine triphosphate (ATP). In addition to energy repletion, Phase II reactions require an abundance of cofactors.[18] Multiple nutrients and phytonutrients may help support Phase II reactions (**Figure 1**).

Phase III Transport. Phase III enzymes are transmembrane-spanning enzymes that transport substrate out of the cell. The largest family of Phase II enzymes utilize energy from hydrolysis of ATP, and are called ATP binding cassette (ABC) transporters.[19] Toxic compounds may be exported from the cell directly, or undergo modification by Phase I and/ or Phase II enzymes, increasing hydrophilicity of the compound to facilitate excretion. Depending on the membrane localization of the transporter, toxic compounds or metabolites may be exported to the circulation for eventual elimination by the kidneys, or into the bile.[19]

THE ROLE OF ENERGY PRODUCTION AND OXIDATIVE STRESS IN TOXICITY

As can be seen by the above discussion, generation of ATP is vital for adequate biotransformation. Generation of adequate ATP requires healthy, nutrient-supported mitochondria. Unfortunately, many toxicants can inhibit mitochondrial function, which can lead to a decreased capacity to biotransform other toxins.[20] Production of ROS is also a consequence of energy production, and excess presence of these damaging molecules, called oxidative stress, is associated with toxicity.[21]

NUTRITIONAL SUPPORT FOR MITOCHONDRIAL FUNCTION

Nutrients that support mitochondrial function include the essential cofactors for energy production: thiamin, riboflavin, niacin, pantothenic acid, and magnesium. In addition, nutrients that help protect the body from oxidative stress, such as vitamins C and E, zinc, selenium, and copper, are also beneficial.[22,23]

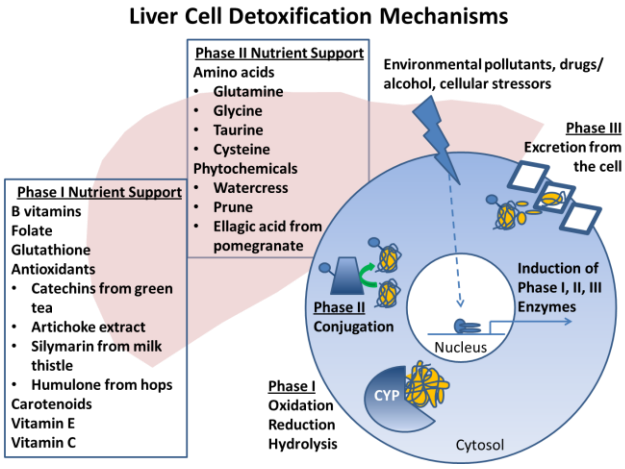

Figure 1. Detoxification occurs primarily in the liver, but also throughout the GI tract, kidneys, lungs, and brain. Nutrient support is vital for optimal functioning of cellular detoxification pathways.

DIET, DIGESTION, AND EXCRETION IN TOXICITY

Healthy digestion can have a profound effect on detoxification. Food intake is known to influence drug absorption by altering gastric emptying and intestinal transit, pH, and bile secretion.[24] In particular, toxins that are conjugated in the intestinal tract and during first pass metabolism in the liver are primarily excreted via bile, which requires healthy fecal production. Dietary fiber supports healthy excretion—which is important for removing biotransformed toxins—and has been shown to bind some toxins directly, thereby providing a route for their removal before significant absorption occurs.[25] In addition, adequate intake of water is essential to

maintaining healthy kidney function and promoting urinary excretion of toxins already in circulation.

In addition to support for excretion, overall nutrition influences biotransformation in many other ways. Support for energy production, as well as generation of new enzymes (protein production), are vital during detoxification. Therefore, adequate intake of carbohydrates, energy-supportive fats, and high quality protein are essential for providing protective mechanisms against toxic damage.[26]

Fats can be problematic, since many people consume too many unhealthy fats. Moreover, individuals undergoing toxic exposure may not efficiently absorb nutrients through the intestinal tract if they are also experiencing altered intestinal permeability. Therefore, provision of a highly bioavailable source of fats that can be used directly to support energy production is beneficial. The medium-chain triglycerides (MCTs) are fats that fit this profile.[27] Interestingly, olive oil, in contrast to sunflower, corn, or fish oil, was found to be protective against chemically-induced fibrosis in rats,[28] suggesting that it may also be a good source of fat for a detoxification program.

PHYTONUTRIENT SUPPORT FOR BALANCED DETOXIFICATION ACTIVITIES

The depletion or insufficiency of any cofactor needed in the detoxification process significantly increases susceptibility to toxicity. Phase I metabolizes a toxin, and Phase II conjugates a water-soluble group to the toxin, promoting its excretion in phase III. These activities work in concert and thus must be balanced. In particular, Phase II activities must be able to keep up with the Phase I generation of reactive intermediates, or an imbalance in the production of reactive substances occurs. When Phase I generates a reactive intermediate that is not immediately conjugated and removed, it can act as a ROS and bind DNA, proteins, and RNA, causing irreversible damage to a cell.

Nutrient support for all cellular detoxification activities is essential to achieving healthy, balanced, and complete detoxification. Many phytonutrients support detoxification systems through multiple mechanisms. Antioxidant activity supports Phase I specifically. Modulation of enzyme activity directly and induction of gene transcription of Phase I, II, and III enzymes are additional mechanisms of phytonutrient regulation of detoxification.

Some phytonutrients support Phase I activity, such as indole-3-carbinol from broccoli, which provides modest support for the CYP1A enzymes. Overactivation of Phase I is a concern, however, and is associated with high, continuous levels of toxins that are known to be particularly effective at inducing Phase I activities. For example, smoking (heterocyclic amines formed on charbroiled beef) and dioxins have all been shown to over-induce CYP1A enzymes, and even low doses of these compounds induce CYP1A much more effectively than the modest support provided by indole-3-carbinol.[29-31]

Phytonutrients that are particularly beneficial for Phase II activities include ellagic acid (found in pomegranate and many berries), catechins (from green tea and grapes), and glucosinolates (found in crucifers, such as watercress and broccoli).

Nutrients that serve as bifunctional modulators are often capable of inhibiting the Phase I enzymes when they are present at high levels, without inhibiting their entire production. For example, while ellagic acid can inhibit the induction of CYP1A by the mutagen benzo[a]pyrene, possibly by binding directly to the mutagen itself, it does not directly inhibit the constitutive, necessary activity of CYP1A.[32]

Many phytonutrients promote optimal balance of

detoxification systems via their ability to act as antioxidants and bind reactive intermediates and ROS from Phase I reactions. Therefore, nutrient modulators minimize damage caused by reactive intermediates, which may be one reason for the association between diets high in fruits and vegetables and reduced susceptibilities to diseases such as cancer.

Table 2. Clinical considerations for programs to support biotransformation

- Decrease exposure to toxins
- Provide nutritional support for biotransformation and conjugation reactions
- Provide nutritional support for energy production during detoxification programs
- Support endogenous antioxidant mechanisms for biotransformation and heavy metal detoxification
- Provide methyl donors to promote methylation pathways
- Support healthy digestion and excretion

WATER FASTING AND DETOXIFICATION

Water fasting can be detrimental to the body's ability to support detoxification. Fasting and alcohol both overinduce the CYP450E family of enzymes, leading to unbalanced detoxification.[26] In addition, fasting results in catabolism of muscle over fat, which is not beneficial to health. Fasting also results in a decreased intake of necessary cofactors that leads to a decrease in sulfation, glutathione, and glucuronidation conjugation cofactors. In animal models, fasting causes decreased glutathione levels and enhanced susceptibility to toxicity after toxin exposure.[33] Thus, the Phase II reactions are decreased and reactive intermediates remain in the body.

ADDITIONAL NUTRITIONAL SUPPORT FOR BIOTRANSFORMATION

Provision of macronutrients is extremely important in a detoxification program. Fasting has many adverse health effects, including decreased energy production, catabolism of lean tissue, overinduction of Phase I activities with a concomitant increase in oxidative stress, and decreased levels of Phase II cofactors. Detoxification is an energy-requiring process that puts a metabolic burden on the body. Instead of decreasing nutrient support, a focused, high-impact source of nutrients is essential. However, this source of nutrients should have a low allergy potential in order to decrease the body's burden of inflammation and potential allergen toxins.

An eight-week study in women with fibromyalgia demonstrated that a hypoallergenic, modified elimination diet supplemented with a phytonutrient-rich medical food produced increased elimination of heavy metals and improved fibromyalgia symptoms compared to a standard American diet supplemented with rice protein powder medical food.[34] An overall protein, carbohydrate, fiber, and fat nutrient base is important to maintaining healthy metabolism during a detoxification program.

Fiber. Fiber can benefit a detoxification program in many ways. Fiber supports intestinal mucosal cell barriers and colonic health, which decrease toxic burden on the body and provide a first line of defense to the system. Fiber promotes removal of the conjugated toxins that are excreted via bile and may decrease the absorption of some toxins. Most notably, some fibers have been shown to directly bind toxins, thereby helping to remove potentially damaging toxins. Fibers in rice bran have been shown to preferentially bind mutagens over wheat, corn, barley, or oat fibers.[25]

Protein. In addition to nutriture and fiber, a high quality protein that provides methionine and cysteine in a highly absorbable form, is also of benefit to Phase II conjugation since these amino acids can be used to generate the sulfation and glutathione cofactors. A high quality protein may also benefit those with toxic

mercury burdens, since mercury exposure is associated with the depletion of specific amino acids that are precursors to neurotransmitters.[35] Methionine is also a component of S-adenosylmethione (SAM), and is required for methylation.

N-Acetylcysteine (NAC) and Sodium Sulfate. Sulfate donors NAC and sodium sulfate are extremely important in a detoxification program. As a precursor of L-cysteine and reduced glutathione, NAC provides a source of sulfhydryl groups for cellular reactions and acts as a scavenger of free radicals to reduce oxidative stress.[36] Oral administration of NAC has been shown to increase the level of glutathione produced in the body. Glutathione is not only the cofactor for Phase II conjugation reactions but is also a major route for detoxification of heavy metals because of the ability of glutathione to act as a chelate for heavy metals.[17] Due to its support of glutathione production, cysteine—a principle factor in combating metal toxicity—becomes depleted in the presence of a toxic load of metals.[35] Provision of sulfate cofactors with 200 to 500 mg per day of NAC is suggested to support sulfation cofactor status and glutathione production.

Vitamin B_{12}, Folate, Methionine, and Choline. The methyl donors choline, methionine, and folate are called *labile methyls* because they are required for cellular metabolism and therefore need constant replenishment. The biologically active, natural form of folate is 5-methyltetrahydrofolate.[37]

Interestingly, dietary deficiency of labile methyls is the only nutrient deficiency known to be carcinogenic in itself.[38] Furthermore, CYP1A enzymes have been shown to be adversely induced in animals deficient of dietary labile methyls.[39] Choline is an essential nutrient;[40] and choline is particularly important for detoxification pathways. Choline deficiency has been shown to result in fatty liver and other liver diseases.[41, 42]

The importance of dietary labile methyls in health derives from their role in supporting balanced biotransformation by providing cofactors for Phase II conjugation reactions. Vitamin B_{12}, folate, and choline provide support for the homocysteine cycle, which drives remethylation of S-adenosylmethionine (SAM). SAM is a vital component not only of detoxification pathways, but also in biosynthesis and metabolic pathways throughout the body.[43]

Ellagic Acid. In animal studies, ellagic acid has been shown to significantly reduce tumor incidence in chemically-induced lung and liver tumorigenesis, protect from carbon tetrachloride liver damage, enhance glutathione production, and decrease lipid peroxidation.[44-46] Ellagic acid also may act directly against some metal toxicity (e.g., nickel) by chelating the metal and promoting its excretion, thereby providing protection from liver damage and oxidative stress.[47]

Ellagic acid promotes balanced detoxification via several mechanisms. It induces expression of glutathione synthesizing enzymes, glutathione-S-transferases, and other Phase II enzymes.[33,48,49] Reports that ellagic acid modulates CYP450 enzymes suggest a role for the compound in Phase I detoxification pathways as well. Ellagic acid has demonstrated direct binding to toxic substances such as benzo[a]pyrene-related compounds from air pollution, rendering them non-toxic and promoting their excretion.[32, 50]

Green Tea Catechins. A large body of literature studying the health benefits of catechins is available. These data suggest that catechins—a class of flavonoids found in high concentrations in green tea extracts—are bifunctional modulators that provide many beneficial activities, including induction of Phase I CYP450 enzymes and Phase II glucuronidation and glutathione conjugation enzymes.[51] Cell-based

assays demonstrated that catechins induce receptor-mediated gene expression of enzymes involved in metabolic detoxification.[52]

Interestingly, some catechins have been shown to induce Phase I activities while others selectively inhibit Phase I activities.[53-55] A cell-based study showed that catechins inhibited the over-induction of Phase I activities by a toxic substance, but were able to moderately induce Phase I activity themselves when the toxin was not present.[56] This capacity of catechins to regulate expression and activity of Phase I enzymes suggests that this natural compound is effective for supporting a balanced detoxification system.

Catechins are known to have antioxidant activity, and have demonstrated protection against anticancer drug-induced oxidative stress in rats.[57] The molecular structure of catechins enables these compounds to act as chelates, binding to reactive intermediates produced by Phase I that are not immediately conjugated by a Phase II reaction, which is another mechanism by which this class of flavonoids may promote balanced detoxification.

Prospective animal experiments have shown that green tea catechins possess anticarcinogenic and antimutagenic potential.[58,59] Epidemiological data suggest that catechins may be protective against many types of cancer in humans, while other data suggest that consumption of catechin-containing beverages, such as tea, is inversely associated with Parkinson's disease.[59,60] These activities have prompted the National Cancer Institute to investigate the potential of green tea extract containing catechins as a chemotherapeutic agent.[61]

One cup of tea contains between 100 to 200 mg catechins,[58] which is suggested to account for at least 90% of the observed beneficial effects of green tea.[56] Green tea catechins also have been shown to promote optimal intestinal microflora and pH and to support healthy bowel function—three qualities that further support optimal detoxification.[62]

Watercress Glucosinolates. Watercress (*Nasturtium officinale*), like other crucifers such as broccoli sprouts, contains high levels of glucosinolates. Glucosinolates are precursors to several bioactive isothiocyanates, including phenylethylisothiocyanate (PEITC). In humans, research has shown that glucosinolates can be effectively converted to PEITC by gut flora after consumption of watercress.[63, 64]

Watercress itself also contains particularly high levels of PEITC. PEITC from watercress has been shown to inhibit chemically-induced lung and colon carcinogenesis in rats and promote excretion of carcinogens in humans.[65-67] The proposed mechanisms of these activities include inhibition of select Phase I activities with concomitant induction of Phase II glucuronosyl transferases and glutathione S-transferases.[63,68,69] This bifunctional activity of watercress has been proposed as one of the reasons why crucifers have been shown to be chemoprotective in epidemiological data.[70]

Silymarin. Silymarin (from milk thistle) has been used in traditional medicine throughout the world as a hepatoprotectant, and recent studies demonstrate effective liver-protectant functions of silymarin.[71-73]

Randomized, controlled clinical trials have demonstrated a beneficial effect of 420 mg silymarin per day on indices of liver function in patients with various etiologies of acute hepatitis. Other studies have found similar benefits for patients with liver disease—including those exposed to toxic levels of industrial phenolics, such as toluene.[72,74] Silymarin has also been shown to increase serum glutathione and glutathione peroxidase in patients with liver disease and induce glutathione transferase

activity in animals.[72,75] Silymarin glycosides exhibit potent antioxidant activity, and therefore silymarin may act as a bifunctional modulator.[73,76]

Artichoke. Traditional medicine has long used artichoke extract (*Cynara scolymus*) as a hepatoprotectant, and several bioactives have been identified, including chlorogenic acid, cynarin, caffeic acid, and luteolin.[77,78] Results from cell-based studies suggest that artichoke has potent antioxidant activity and attenuates toxin-induced reduction of glutathione reserves.[79,80] Artichoke leaf extract administration for two weeks protected rats against oxidative stress-induced hepatotoxicity.[81]

Consumption of encapsulated artichoke extract has been shown to increase the absorption of these bioactives in humans, resulting in the production of beneficial metabolites such as ferulic acid.[82] Ferulic acid, chlorogenic acid, and cynarin provide strong antioxidant protection, which may account for some of their health-promoting activities.[77,78]

SUMMARY

Optimizing the body's ability to manage and excrete toxins is essential for optimal health. Several recent reviews have discussed targeted, nutrient-based detoxification intervention therapies for patients with CFS, FM, MCS, and Parkinson's disease, as well as in apparently healthy individuals.[83-87] [see notes about refs on last page]

Decreasing exposure to toxins is extremely important in all programs. Airborne toxins are of particular concern since, by entering through nasal passages, they can bypass the blood-brain barrier and travel through the olfactory nerve directly to the brain. However, minimizing toxin exposure is only one part of a successful strategy to decrease susceptibility to toxicity-related conditions. Low-allergy-potential, targeted nutrition that provides the full spectrum of cofactor precursors, support for excretion, and bifunctional inducers for balanced Phase I and Phase II biotransformation may promote balanced detoxification and optimal health throughout life.

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