

# **Detoxification:**

## **The Role of the Liver & Nutraceutical Support**







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In her 1962 groundbreaking book *Silent Spring*, Rachel Carson wrote: “For the first time in the history of the world every human being is now subjected to contact with dangerous chemicals, from the moment of conception until death.”

Of course humans have always been exposed to potentially harmful chemicals from plants and other sources, but Rachel Carson’s point is well taken. Modern living exposes all of us to an unprecedented number of chemicals on a daily basis. This includes environmental toxins such as heavy metals, pesticides, industrial compounds and chemical byproducts, medications, cosmetic additives, inorganic chemicals, etc. These chemical substances which are foreign to the biological system are referred to as “xenobiotics.”

The good news is that the body was designed to detoxify and excrete xenobiotics. The bad news is our bodies may not always be equipped to handle the volume of modern, environmental

pollutants and toxic substances. This problem may be exacerbated by the fact that the refining of many of our foodstuffs has caused them to provide considerably less of the nutrients that are essential to the detoxification process.<sup>1-2</sup>

### **Ramifications of toxic overload**

The ramifications of toxic overload can vary from one individual to another. One possible ramification is multiple chemical sensitivities

(MCS). MCS is a condition in which a person experiences various symptoms in response to being exposed to certain types of chemicals, primarily (but not limited to) those of petroleum and coal-tar derivation. The possible symptoms are many and may include headaches, fatigue, depression and an overall feeling of malaise and being sick.

MCS seems to develop after consistent, long-term exposure to certain chemicals at home or in the workplace. Eventually, the person develops intolerance to these chemicals, and starts suffering from MCS. For many MCS people, a sensitivity reaction will occur when exposed to even minute amounts of the offending chemicals which, in turn, can lead to severe symptoms characteristic of the MCS condition.<sup>3</sup> Of course an individual may suffer from toxic overload without having full-blown MCS. In fact, the most common symptom of toxic overload is probably fatigue. Other common symptoms include headache, muscle and joint pain, irritability, depression, mental confusion, gastrointestinal and/or cardiovascular irregularities, flu-like symptoms or allergic reactions including hives, stuffy or runny nose, sneezing and coughing.<sup>4-5</sup>

Furthermore, some researchers have suggested that toxic overload may contribute to autoimmune diseases including inflammatory and rheumatoid arthritis<sup>6-7</sup>, and neurological diseases such as Alzheimer’s and Parkinson’s.<sup>8</sup>

## **How to deal with toxic overload**

The question of how to deal with toxic overload has a multi-part answer which includes adapting to a healthier diet and reducing exposure to xenobiotics

The books *Multiple Chemical Sensitivity* by Gibson (2000, New Harbinger Publications, Inc.) and *Staying Well in a Toxic World* by Lawson (1993, The Nobel Press) provide good direction on how to do this.

Another part to the answer is to help your liver to become more proficient at detoxification. That’s what this article is really about. So now let’s have a brief overview on how the liver goes about detoxification.



## Detoxification by the liver

Water soluble toxins can pass through our bodies unchanged and be eliminated in the stool, sweat or urine. Fat soluble toxins, however, cannot be excreted without undergoing metabolic transformation (detoxification) in the liver so that they can become water soluble. Liver cells have sophisticated mechanisms to break down toxic substances. These include both endogenous (produced by the body) and exogenous (obtained from the environment; i.e., xenobiotics) substances. Every drug, chemical, pesticide and hormone, is broken down or metabolized via detoxification pathways in the liver called “phase 1” and “phase 2.”<sup>9-10-11</sup>

### Phase 1

Phase 1 utilizes cytochrome P450 enzymes produced in the liver. These enzymes initiate reactions that generally involve exposing or adding a “functional group” to the toxic molecule. This process of making the molecule more reactive is required as the first step in increasing its water solubility for excretion. Some chemicals are already highly reactive and they have functional groups, so they can bypass phase 1 and go right to phase 2. The majority, however, first need phase 1 activation.

Unfortunately, phase 1 does generate free radicals which mean that there is greater potential for oxidative damage at this time.<sup>12-13</sup>

### Phase 2

Phase 2 involves the coupling (attaching) or conjugation of a water soluble substance which is endogenously produced or sourced by the body, to the toxin. This makes the toxic molecule more water soluble and therefore less toxic. If the molecule is large, it is then excreted via the bile. Otherwise, it is excreted in the urine.<sup>14-15</sup>

*(There is even a phase 3 for detoxification<sup>16</sup>, but that won't be addressed in this article.)*

Now that we've briefly examined the process of liver detoxification, let's take a look at how we can use dietary supplements to support and promote liver detoxification.



## Amino acids and trimethylglycine

Certain amino acids are used in phase 2 as the water soluble substance that is conjugated (attached) to the toxic molecule. These amino acids include glycine, taurine, and glutamine. Clinically, supplementation with these amino acids has shown great benefit for patients with toxic overload, especially when body cleansing was undertaken contemporaneously.<sup>18</sup> Likewise, methyl groups also act as conjugating agents in phase 2.<sup>19</sup> Trimethylglycine (betaine) is a donor of methyl groups, and may be useful as such in biochemical reactions in the liver.<sup>20</sup>

## Milk Thistle

In herbal medicine, Milk Thistle (*Silybum marianum*) is arguably the premium liver herb. The active component in Milk Thistle is its flavonoids collectively called silimarin; and the majority of Milk Thistle-related research has been conducted on this component. Silimarin has long been recognized for its ability to benefit people with liver disorders, including hepatitis<sup>21-22-23-24</sup> and cirrhosis.<sup>25</sup>

Some toxic molecules pass through the glutathione conjugation pathway. A deficiency of this conjugating amino peptide can reduce the clearance of solvents from the bloodstream. Research shows that silimarin protects against glutathione depletion<sup>26</sup>, and increases liver glutathione status.<sup>27</sup> Since glutathione is one of the primary conjugating agents in phase 2, this is a significant contribution by Milk Thistle in supporting detoxification by the liver.<sup>28</sup>

In addition, Milk Thistle also provides liver protection by stabilizing liver cell membranes. It alters the structure of the outer cell membrane in such a way as to prevent the penetration of the liver by toxins into interior of the cell.

Milk Thistle also increases the regenerative ability of the liver and the formation of new liver cells. Further studies concluded that other actions of silimarin include preventing the recirculation

of toxins and regeneration of damaged liver cells. Other studies indicate that Milk Thistle may prevent liver damage from liver poisoning prescription medications.<sup>29-30</sup>

## Turmeric

Turmeric (*Curcuma longa*) is a bright yellow, ancient spice and a traditional remedy that has been used as a medicine, condiment and flavoring based on records dating back to 600 BC. Turmeric and its curcuminoids also exhibit strong antioxidant activity<sup>31</sup>, enhance cellular resistance to oxidative damage<sup>32</sup>, and enhance the body's natural antioxidant glutathione levels; which in turn aids the liver in detoxification.<sup>33</sup>

Turmeric has also been found to have hepatoprotective (i.e., liver-protective) properties against a variety of liver-toxic chemicals and drugs.<sup>34-35-36-37-38</sup>

## N-acetylcysteine

N-acetylcysteine (NAC) is the precursor to glutathione.<sup>39</sup> It stimulates glutathione synthesis and promotes liver detoxification; as well as acting as a powerful scavenger of free radicals.<sup>40-41</sup>

**Historically the most prevalent and well-accepted use of NAC has been as an antidote for acetaminophen (Tylenol®, paracetamol) poisoning.**<sup>42</sup>

The resultant liver toxicity is due to an acetaminophen metabolite that depletes the liver cells of glutathione and causes liver cell damage and possibly even death.

NAC has also been effective for heavy metal poisoning by gold, silver, copper, mercury, lead, and arsenic, as well as in cases of poisoning by carbon tetrachloride, acrylonitriles, halothane, paraquat, acetaldehyde, coumarin, and interferon.<sup>43</sup>

Since detoxification of mercury depletes glutathione, the use of NAC doubly makes sense.



## Green Tea

Green tea (*Camellia sinensis*) compounds increase both phase 1 and phase 2 enzyme activities.<sup>44</sup> Research shows that green tea may have liver protective properties.<sup>45-46-47-48</sup> In addition, green tea has been shown to block chromosomal (DNA) damage from chemicals in cigarette smoke.<sup>49</sup>

*Perhaps not surprisingly, green tea polyphenols are associated with a reduced risk of certain cancers in humans.<sup>50</sup> Other research has also shown an anticancer effect from these polyphenols <sup>51</sup>, including an inhibition of metastasis in skin cancer cells.<sup>52</sup>*





## Calcium D-glucarate

Another phase 2 pathway is the glucuronidation pathway. In this pathway, glucuronic acid is attached to certain toxins as well as hormones such as estrogen to facilitate their removal by excreting them via bile into the intestinal tract.

The problem is that beta-glucuronidase, a bacterial enzyme found in the intestines, can break the bond that attaches the glucuronic acid to the toxin.

Now the toxin can be reabsorbed back into the bloodstream, thereby contributing to the total toxic load on the liver; not a good thing. There is, however, a way to inhibit beta-glucuronidase from breaking the bond in the first instance. It involves D-glucarate, or calcium D-glucarate.

D-glucaric acid is a natural substance found in many fruits and vegetables such as apples, grapefruit, broccoli, and Brussels sprouts. Calcium D-glucarate is the calcium salt of D-glucaric acid typically used in dietary supplements. Calcium D-glucarate has been shown to inhibit beta-glucuronidase.<sup>53</sup> According to data released from the University of Texas M.D. Anderson Cancer Center, Calcium D-glucarate inhibited beta-glucuronidase by 57% in the blood, 44% in the liver, 39% in the intestines, and 37% in the lungs.<sup>54</sup> Such an inhibition of beta-glucuronidase may do much to protect the action of the glucuronidation pathway.

## Schizandra

In traditional Chinese medicine, Schizandra (*Schizandra chinensis*) is mainly used to treat cough and wheezing, spontaneous sweating, nocturnal emission, chronic diarrhea, insomnia and forgetfulness.<sup>55</sup> In Russia, it is regarded as an *adaptogen*.<sup>56</sup>

Research indicates that Schizandra can improve work performance, build strength, reduce fatigue, and increase endurance<sup>57-58</sup> ; all consistent with the effects of an adaptogen.

Schizandra also appears to have significant value for the liver. For example, it appears that the lignans in Schizandra protect the liver by activating the enzymes in liver cells that produce the antioxidant glutathione,<sup>59</sup> so this herb is beneficial for phase 2 detoxification reactions.

Furthermore, in-vitro (i.e., test tube) studies have shown that constituents of Schizandra decrease the mutagenicity of mutagenic toxin benzo(a) pyrene (BaP).<sup>60</sup> Schizandra also induces phase 1 detoxification enzymes<sup>61</sup> , yet has not been shown to cause any drug interactions. Schizandra's Studies from China indicate that Schizandra helped patients with chronic viral hepatitis.<sup>62-63</sup>

## Garlic

Garlic appears to induce both phase 1 and phase 2 enzymes.<sup>64-65</sup> In addition, aged garlic extract may increase the glutathione level and glutathione related enzymes which aid in detoxifying the body.<sup>66-67-68-69</sup>

Research has also suggested that garlic extract may help to protect the body from heavy metal poisoning.<sup>70</sup> When garlic extract was combined with red blood cells it prevented lead, mercury and aluminum from destroying them. Without the garlic extract, these heavy metals ruptured the red blood cells.

## Rosemary

Rosemary contains carnosol, an antioxidant that inhibits bioactivation of BaP and induces glutathione-S-transferase (a detoxification enzyme) and other important phase 2 enzymes.<sup>71-72</sup>

In a study<sup>73</sup> where mice were given Rosemary, the researchers concluded that liver activities of phase 2 liver enzymes were significantly increased, and that the results indicated that **components of rosemary extract have the potential to protect the liver and stomach from carcinogenic or toxic agents.**





## Conclusion

The dietary supplements discussed in this article are certainly not the only natural compounds capable of supporting and facilitating the liver's detoxification process. Compounds from citrus fruit and the Brassica or cruciferous group of vegetables (e.g., cabbage, Brussels sprouts, broccoli, etc.), as well as the dietary supplement alpha lipoic acid are some examples of other effective detoxifying agents.<sup>74</sup> Nevertheless, the compounds listed can be effective adjuncts to a program for detoxification.

Although the focus of this article is on the use of dietary supplements which may help promote liver detoxification, it should be understood that toxic overload should be treated with a comprehensive approach that also includes adapting to a healthier diet and reducing exposure to xenobiotics.

*Furthermore, since there can be side effects associated with a serious program of detoxification, it should generally be attempted with the help of a healthcare professional who is knowledgeable about the process.*



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