Highlights of The Body's Detoxification Processes

Introduction to the Detoxification Pathways

Detoxification in the body is often viewed as the removal of toxic or unneeded substances. While this is true, detoxification processes are more accurately described as highly coordinated metabolic processes which remove environmental toxin metabolites, as well as metabolites from daily consumption and biotransformation processes. These metabolic processes are operating throughout numerous body systems continuously, and concurrently. The liver, kidney, skin, respiratory, lymphatic and digestive systems are all key contributors for elimination. Proper function across these systems is crucial for optimal detoxification. Symptoms of increased burden from daily exposures can manifest as a constellation of symptoms in individuals, because so many body systems are involved in the detoxification process.

Detoxification Highlights

The Role of the Liver

The liver is a highly regenerative organ with over 500 known functions, including playing a significant role in the detoxification and elimination processes.[i] The liver essentially functions, in part, as an effective blood filter, able to process two liters of blood per minute. The liver is constantly receiving chemicals, gastrointestinal byproducts, medications, environmental toxins, and waste products from normal metabolic processes. Vitamins and minerals are also stored in the liver until needed.

There are two phases of detoxification commonly discussed in the liver. There are many nutrients required for the optimal function of these two phases (see table 2). These two phases are responsible for making lipophilic substances water soluble for excretion via the bile and stool, or through the urine. These phases require specific nutrients, enzymes, and cofactors.

Phase 1

Phase 1 of liver detoxification involves oxidation, reduction and hydrolysis reactions catalyzed by the complex cytochrome P450 monooxygenase enzyme system, and is the first step in biotransformation of medications and other substances.[iii] There are over 1,000 enzyme types, and individuals also possess genetic polymorphisms creating variability with metabolism with respect to CYP enzyme activity.[iv v] This system can be altered and influenced by nutrients, medications, foods and other substances, making this area a common interaction site, which has been a study extensively in the realm of drug interactions.

Oxidation, reduction and peroxidation reactions are taking place in the phase 1 processes. Hydroxyl, carboxyl and amino reactive groups are commonly added via these reactions which can increase the potential for reactive oxygen species formation, thereby increasing the risk of oxidative stress on surrounding tissues or cells.[vi] Toxic substances and unneeded metabolites must use the CYP enzyme system to be eliminated from the body if the substance is not water soluble enough to exit directly in the bile or urine. Substances that alter the enzyme activity via upregulating the CYP

enzyme creation, inducers, or by competing for the receptor sites, inhibitors, can drastically alter the ability of the toxin or metabolite to exit the body.

Numerous substances including drugs, nutrients and foods can play a key role in influencing the function of the phase 1 CYP enzymes system. Many substances can have both an inhibitory or inducing effect on the CYP enzyme system. *In vivo* studies suggest that certain bioactive compounds such as soy, curcumin, garlic, fish oil, rosemary, chicory and astaxanins act as CYP enzyme inducers.[6] Raspberries, blueberries, black currants, pomegranate, peppermint, and dandelion have demonstrated an inhibitory effect on CYP enzyme activity *In vivo*.[6] Numerous clinical studies have demonstrated inducing or inhibiting ability of various natural substances including cruciferous vegetables, teas, and quercetin containing foods (see table 1 for a more complete summary of the evidence).[6]

Phase 2

Metabolites from phase 1 move on to phase 2 detoxification unless the substance has been rendered water soluble enough to be eliminated.
Phase 2 renders the intermediary metabolites from phase 1 more polar, and more water-soluble. Through various conjugation processes the unneeded metabolites can be removed from the body via stool or urine. These phase 2 conjugations essentially join the metabolite from phase 1 onto a water-soluble group.[vii] Glucuronidation, sulfation, and glutathione and amino acid conjugation are the main phase 2 reactions. These conjugation reactions require a variety of amino acid and other nutrient cofactors.

Conclusions

Detoxification pathways in the body are complex and there is significant potential for interaction between drugs and nutrients on the various body systems, involved. Genetic polymorphisms and other individual pathophysiology may also provide strong influence on the function and efficiency of the detoxification processes.

Understanding how nutrients play a key role in the biochemical, metabolic and enzymatic biotransformation and detoxification reactions is crucial for developing whole food or nutritional supplement-based interventions to optimize the body's detoxification and elimination pathways. Novel evidence based therapies aimed at eliminating burden and supporting the various body systems involved in the metabolic and eliminatory processes offer great potential for improving health outcomes for individuals. More research is warranted on the systems and nutrients involved.

Table 1: Nutrient and Food Influences on Phase 1 Function[5]

Phase 1	
Bioactive Substance	**Influence**
Cruciferous Vegetables	Induction of CYP1A1, Clinical study, (500mg/d indole 3-carbinol)[viii] Induction of CYP1A2 Clinical study, (7-500g/d various vegetable sources)[bcdbii] Induction of CYP1B1, *In vivo* (25-250mg/kg indole-3-carbinol)[xiii] Inhibition CYP1A2, *In vivo* (2g/kg/d freeze dried kale drink)[xiv]
Resveratrol	Induction of CYP1A1, Clinical study, (1g/d resveratrol)[xv]
Tea (Green, black)	Induction of CYP1A1, CYP1A2 *In vivo (rat)*, (45mL/d green, 54mL/d black)[xvi] Inhibition CYP1A1, *In vivo* (20mg/kg theaflavins)[xvii]
Apiaceous vegetables	Inhibition of CYP1A2, Clinical study, (4g/kg vegetable sources carrot, celery, dill, parsley, parsnip)[9]
Quercetin	Inhibition of CYP1A2, Clinical study, (500mg/d)[xviii]
Daidzein	Inhibition of CYP1A2, Clinical study, (200mg BID)[xix]
Grapefruit	Inhibition of CYP1A2, Clinical study, (300mL/d juice)[xx]

Table 2: Liver Detoxification Phases and Key Nutrients[7]

Phase 1	
Reactions/Processes	**Nutrients Required**
Oxidation Reduction Hydrolysis Hydration Dehalogenation	Riboflavin Niacin Pyridoxine Folic acid B_{12} Glutathione Branch-chain amino acids Flavonoids Phospholipids
Phase 2	
Reactions/Processes	**Nutrients Required**
Sulfation Glucuronidation Glutathione conjugation Acetylation Amino acid conjugation Methylation	Glycine Taurine Glutamine *N*-Acetylcysteine Cysteine Methionine

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