Transformation and Elimination: The Detoxification System

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What toxins do we need to eliminate?

- Xenobiotics (environmental chemicals)
- Endobiotics (Steroid hormones or bilirubin)
- Drugs
- Sugar?

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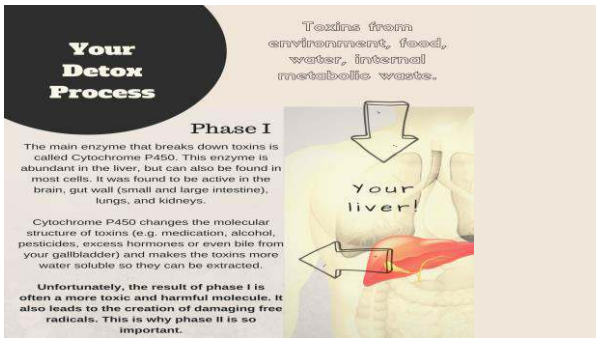

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Phase I

Adding a reactive group such as a hydroxyl, carboxyl, or an amino group through oxidation, reduction, and/or hydrolysis reaction

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Increase potential for oxidative damage within because of the resulting formation of reactive electrophilic species.

↓

react with intracellular nucleophilic substrates including DNA, lipids, and proteins.

(Associated with mutation and cancer development)

Munnia A, Giese RW, Polvani S, Galli A, Cellai F, Peluso MEM. Bulky DNA Adducts, Tobacco Smoking, Genetic Susceptibility, and Lung Cancer Risk. Adv Clin Chem. 2017;81:231-277. doi:10.1016/bs.acc.2017.01.006

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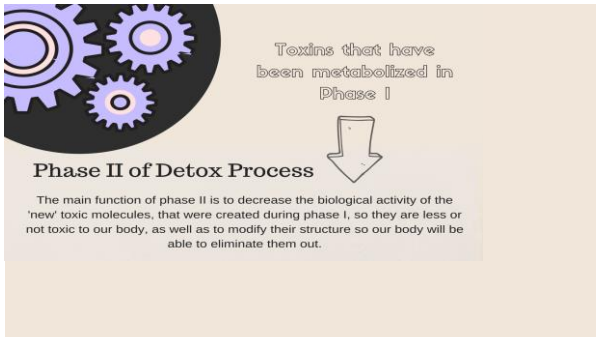

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Phase II Conjugation

- After toxin becomes hydrophilic due to CYP450 enzymes, its reactive site can be conjugate
- Several hydrophilic compounds are being transferred, by corresponding enzymes, including glucuronic acid (glucuronyl transferases), sulfate (sulfotransferases), glutathione (glutathione transferases), amino acids (amino acid transferases), an acetyl group (N-acetyl transferases), and a methyl group (N- and O-methyltransferases)

Xu C, Li CY, Kong AN. Induction of phase I, II and III drug metabolism/transport by xenobiotics. Arch Pharm Res. 2005;28(3):249-268. doi:10.1007/BF02977789

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Phase II Conjugation

- The process results in an increase in hydrophilicity of the compound, which should lead to better excretion through BM with the bile and/or urine.
- Influenced by genetic polymorphisms (the difference in DNA sequence between individuals or groups)

1. Xu C, Li CY, Kong AN. Induction of phase I, II and III drug metabolism/transport by xenobiotics. *Arch Pharm Res*. 2005;28(3):249-268. doi:10.1007/BF02977789
2. Ginsberg G, Guyton K, Johns D, Schimek J, Angle K, Sonawane B. Genetic polymorphism in metabolism and host defense enzymes: implications for human health risk assessment. Crit Rev Toxicol. 2010;40(7):575-619. doi:10.3109/10408441003742895

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Glutathione

An antioxidant produced in cells, composed mainly of cysteine, glutamate, and glycine

Produced in the cytosol and actively pumped into mitochondria

Essential for protecting cells from endogenous and exogenous reactive oxygen

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Importance to Glutathione

- ✓ Essential for protecting cells from endogenous and exogenous reactive oxygen species
- ✓ Regeneration of vit C and E
- ✓ Phase II detox: Neutralization of free radicals from phase I
- ✓ Important in transporting mercury out of cells
- ✓ Vital for mitochondria function and mtDNA

Pizzorno J. (2014). Glutathione!. Integrative medicine (Encinitas, Calif.), 13(1), 8–12.

9

Glutathione Depletion

- ✓ Associated with neurodegenerative, pulmonary, immune, cardiovascular, and liver diseases
- ✓ Associated with age related conditions, such as macular degeneration or cataract
- ✓ Associated with aging and loss of function
- ✓ Associated with lower activity of telomerase

1. Julius M, Lang CA, Gleiberman L, Harburg E, DiFranceisco W, Schork A. Glutathione and morbidity in a community-based sample of elderly. J Clin Epidemiol. 1994;47(9):1021-1026. doi:10.1016/0895-4356(94)90117-1
2. Pizzorno J. (2014). Glutathione!. Integrative medicine (Encinitas, Calif.), 13(1), 8–12.

10

Glutathione Depletion

- ✓ Associated with aging and loss of function
- ✓ Essential for cellular protection from free radicles that might lead to accelerated aging
- ✓ Associated with lower activity of telomerase

1. Julius M, Lang CA, Gleiberman L, Harburg E, DiFranceisco W, Schork A. Glutathione and morbidity in a community-based sample of elderly. J Clin Epidemiol. 1994;47(9):1021-1026. doi:10.1016/0895-4356(94)90117-1
2. Borrás C, Esteve JM, Viña JR, Sastre J, Viña J, Pallardó FV. Glutathione regulates telomerase activity in 3T3 fibroblasts. J Biol Chem. 2004;279(33):34332-34335. doi:10.1074/jbc.M402425200
3. Pizzorno J. (2014). Glutathione!. Integrative medicine (Encinitas, Calif.), 13(1), 8–12.

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Sugar Levels & Glutathione

- GSH levels were significantly reduced in patients with type 2 diabetes mellitus compared with patients with impaired glucose tolerance or normal subjects

Hakki Kalkan, I., & Suher, M. (2013). The relationship between the level of glutathione, impairment of glucose metabolism and complications of diabetes mellitus. Pakistan journal of medical sciences, 29(4), 938–942. https://doi.org/10.12669/pjms.294.2859

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Is Sugar A Toxicant? A Systematic Review

- *"High sugar intake may increase cancer risk by promoting insulin-glucose dysregulation, oxidative stress, inflammation, and body adiposity, but epidemiologic evidence is unclear."*
- *"8 of 15 studies on sugary foods and beverages, a 23-200% higher cancer risk was observed with higher sugary beverage consumption."*

Makarem N, Bandera EV, Nicholson JM, Parekh N. Consumption of Sugars, Sugary Foods, and Sugary Beverages in Relation to Cancer Risk: A Systematic Review of Longitudinal Studies. Annu Rev Nutr. 2018;38:17-39. doi:10.1146/annurev-nutr-082117-051805

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How to Increase Glutathione

- ✓ Reduce exposure to toxicity (depletes glutathione)
- ✓ limiting alcohol consumption and avoid smoking
- ✓ Supplementing with α-lipoic acid increases levels
- ✓ N-acetylcysteine (NAC) increases levels (Dosages: 600 to 2400 mg/d)

1. Khanna S, Atalay M, Laaksonen DE, Gul M, Roy S, Sen CK. Alpha-lipoic acid supplementation: tissue glutathione homeostasis at rest and after exercise. J Appl Physiol (1985). 1999;86(4):1191-1196. doi:10.1152/jappl.1999.86.4.1191
2. Pendyala L, Creaven PJ. Pharmacokinetic and pharmacodynamic studies of N-acetylcysteine, a potential chemopreventive agent during a phase I trial. Cancer Epidemiol Biomarkers Prev. 1995;4(3):245-251.

14

How to Increase Glutathione

- ✓ Significant increase in total and reduced GSH levels with sublingual GSH in comparison to oral GSH.
- ✓ Vitamin E levels in plasma increased only in sublingual GSH group
- ✓ Adequate levels require sufficient amount of amino acids

1. Schmitt, B., Vicenzi, M., Garrel, C., & Denis, F. M. (2015). Effects of N-acetylcysteine, oral glutathione (GSH) and a novel sublingual form of GSH on oxidative stress markers: A comparative crossover study. Redox biology, 6, 198–205. https://doi.org/10.1016/j.redox.2015.07.012

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Glutathione & Vitamin C

- ✓ 500 mg of vitamin C (L-ascorbate) per day for weeks 2-3 increased mean red blood cell glutathione levels by nearly 50% in comparison to placebo
- ✓ 2000-mg dosage provided the same results
- ✓ Levels reduced to baseline without vitamin C

Johnston CS, Meyer CG, Srilakshmi JC. Vitamin C elevates red blood cell glutathione in healthy adults. Am J Clin Nutr. 1993;58(1):103-105. doi:10.1093/ajcn/58.1.103

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Phase III Transportation & Elimination

Finally, the toxic molecules remaining from phase II are removed in two ways: Your kidneys urinate them and the second is through the gallbladder. You liver process toxins (phases I + II), attach them to the bile (gallbladder salts), and forward them to the gallbladder. When you eat a meal with fats, bile is secreted from your gallbladder into the intestine and you expel the bile and toxins in your stool.

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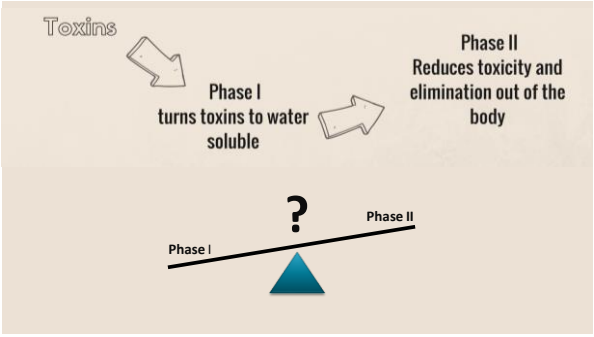

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FASTING: Pros and Cons

- Complete water fasting for 11 days showed reduction of oxidative stress, body weight and blood pressure
- Dietary restriction (DR) might up-regulation of phase II detoxification
- Cons: hunger sensation, fatigue, imbalanced sugar, difficulty to concentrate, dangerous with instable patients

1. Mojto V, Gvozdjakova A, Kucharska J, Rausova Z, Vancova O, Valuch J. Effects of complete water fasting and regeneration diet on kidney function, oxidative stress and antioxidants. *Bratisl Lek Listy.* 2018;119(2):107-111. doi:10.4149/BLL_2018_020
2. Wen, H., Yang, H. J., An, Y. J., Kim, J. M., Lee, D. H., Jin, X., Park, S. W., Min, K. J., & Park, S. (2013). Enhanced phase II detoxification contributes to beneficial effects of dietary restriction as revealed by multi-platform metabolomics studies. Molecular & cellular proteomics : MCP, 12(3), 575–586. https://doi.org/10.1074/mcp.M112.021352

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FASTING: Report Before, During, and After Ramadan Fasting

- No fluids or food from dawn to sunset for 30 days
- There was significant decrease in mercury, chromium, aluminum, manganese and cobalt levels in blood
- Significant decrease in lead, cadmium, mercury, aluminum and manganese hair levels
- Reduction in zinc and selenium as well

Saad, Khaled & Elnemr, Tarek. (2009). Effect of intermittent fasting on heavy metal detoxification. Mansoura journal of forensic medicine and clinical toxicology.

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What happens during fasting?

Studies show that during fasting, phase I activity may increase, which leads to the creation of potentially dangerous toxins. Furthermore, toxins might be released from fat tissue and other cells and will circulate within your body. To avoid this, we must provide large amounts of anti-oxidants, such as vitamin C, E and a variety of other nutrients like vitamin B2, B3, B6, and B12, folic acid, amino-acids, and flavonoids. andpromote phase II.

! Too many toxins or certain medications may inhibit the function of phase I and II, leading to over toxicity.

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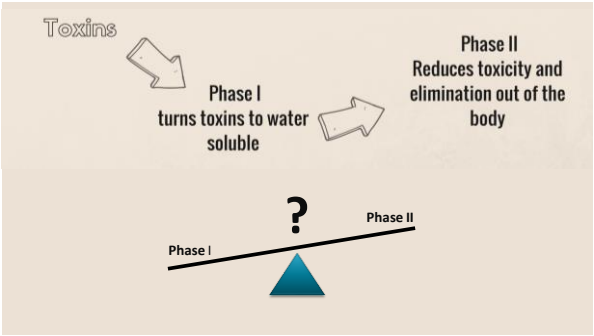

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Testing Liver Detox Pathway

(Hepatic Detox Profile)

A single, first morning void (FMV) urine collection

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Testing for Liver Detox Function

Hepatic Detox Profile; Urine

TOXIC EXPOSURE MARKERS	RESULT per creatinine		REFERENCE INTERVAL	PERCENTILE
D-Glucaric Acid (Phase I)	438	nM/mg	25 - 160	
Mercapturic Acids (Phase II)	67	µM/mM	36 - 80	

URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL
Creatinine	113	45 - 225

Measuring phase I
D-glucaric acid extraction in urine might indicate induction of cytochrome P-450 enzymes (phase I), however results of different studies are conflicting. Medication and liver diseases might increase D-Glucaric acid.

1. Gilbert, J. C., Scott, A. K., Galloway, D. B., & Petrie, J. C. (1974). Ethosuximide: Liver enzyme induction and D-glucaric acid excretion. British Journal of Clinical Pharmacology, 1(3), 249–252.
2. Kampf D, Roots I, Hildebrandt AG. (1980) Urinary excretion of D-glucaric acid, an indicator of drug metabolizing enzyme activity, in patients with impaired renal function. Eur J Clin Pharmacol. 18(3), 255-61.
3. Carrella, M., D'arienzo, A., Manzillo, G. et al. Digest Dis Sci (1978) 23: 18. https://doi.org/10.1007/BF01072570

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Hepatic Detox Profile; Urine

TOXIC EXPOSURE MARKERS	RESULT per creatinine		REFERENCE INTERVAL	PERCENTILE 2.5th	16th	50th	84th	97.5th
D-Glucaric Acid (Phase I)	430	nM/mg	25– 300					
Mercapturic Acids (Phase II)	67	µM/mM	36– 90					

URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD	-1SD	MEAN	+1SD	+2SD
Creatinine	113	45– 225					

Measuring phase I

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3. Carrella, M., D'arienzo, A., Manzillo, G. et al. Digest Dis Sci (1978) 23: 18. https://doi.org/10.1007/BF01072570

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URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD	-1SD	MEAN	+1SD	+2SD
Creatinine	113	45– 225					

Measuring Phase II

Urinary mercapturic acids, the products of interaction between glutathione transferase and toxicant metabolism, provide useful biomarkers of individual toxic exposure and absorption and metabolic processing.

1. Van Welie RT, van Dijck RG, Vermeulen NP, van Sittert NJ. (1992) Mercapturic acids, protein adducts, and DNA adducts as biomarkers of electrophilic chemicals. Crit Rev Toxicol, 22(5-6), 271-306
2. Mathias, P. I., & B'Hymer, C. (2016). Mercapturic acids: recent advances in their determination by liquid chromatography/mass spectrometry and their use in toxicant metabolism studies and in occupational and environmental exposure studies. Biomarkers : Biochemical Indicators of Exposure, Response, and Susceptibility to Chemicals, 21(4), 293–315. http://doi.org/10.3109/1354750X.2016.1141988

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URINE CREATININE	RESULT mg/dL	REFERENCE INTERVAL	-2SD	-1SD	MEAN	+1SD	+2SD
Creatinine	113	45– 225					

1. Creatinine concentrations can be used to determine whether the urinary sample is valid: too dilute (creatinine concentration < 30 mg/dL) or too concentrated (creatinine concentration > 300 mg/dL), another urine void should be collected.
2. High red meat intake -> higher urinary creatinine concentration
3. High creatinine concentrations might indicate dehydration, which changed the kidney's secretion, excretion, and/or reabsorption of the target chemical.

1. WHO 1996. Biological Monitoring of Chemical Exposure in the Workplace. Vol 1. Geneva:World Health Organization.
2. Lykken GI, Jacob RA, Munoz JM, Sandstead HH. (1980) A mathematical model of creatine metabolism in normal males--comparison between theory and experiment. Am J Clin Nutr. 33(12):2674-85
3. Barr, D. B., Wilder, L. C., Caudill, S. P., Gonzalez, A. J., Needham, L. L., & Pirkle, J. L. (2005). Urinary Creatinine Concentrations in the U.S. Population: Implications for Urinary Biologic Monitoring Measurements. Environmental Health Perspectives, 113(2), 192–200. http://doi.org/10.1289/ehp.7337

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Human and *in vivo* example nutrient **Inducers** of CYP1 enzymes.

Enzyme	Food, beverage, or bioactive compounds *Food sources in italics*	Type of study	Dosages used and references
	Cruciferous vegetables	Clinical	500 mg/d indole-3-carbinol [23]
	Resveratrol *Grapes, wine, peanuts, soy, and Itadori tea* [32]	Clinical	1 g/d resveratrol [28]: *note high dose used*
	Green tea	*In vivo*	45 mL/d/rat (avg. 150 g animal weight) green tea [33]
	Black tea	*In vivo*	54 mL/d/rat (avg. 150 g animal weight) black tea [33]
CYP1A1	Curcumin	*In vivo*	1,000 mg/kg/d/rat curcumin [35], or about 150 mg per rat per day

Hodges, R. E., & Minich, D. M. (2015). Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism*, *2015*, 760689. http://doi.org/10.1155/2015/760689

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Human and *in vivo* example nutrient **Inducers** of CYP1 enzymes.

Enzyme	Food, beverage, or bioactive compounds *Food sources in italics*	Type of study	Dosages used and references
	Turmeric, curry powder [34]		
	Soybean	*In vivo*	100 mg/kg soybean extract [7]
	Garlic	*In vivo*	30 to 200 mg/kg garlic oil [36]
	Fish oil	*In vivo*	20.5 g/kg fish oil [36]: *note high dose used*
	Rosemary	*In vivo*	Diet of 0.5% rosemary extract [37]
	Astaxanthin *Algae, yeast, salmon, trout, krill, shrimp*, and *crayfish* [38]	*In vivo*	Diets of 0.001–0.03% astaxanthin for 15 days [39]

Hodges, R. E., & Minich, D. M. (2015). Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism*, *2015*, 760689. http://doi.org/10.1155/2015/760689

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Human and *in vivo* example nutrient **Inducers** of CYP1 enzymes.

CYP1A2	Green tea	*In vivo*	45 mL/d/rat (avg. 150 g animal weight) green tea [33] Green tea (2.5% w/v) as sole beverage [40]
	Black tea	*In vivo*	54 mL/d/rat (avg. 150 g animal weight) black tea [33]
	Chicory root	*In vivo*	Diet of 10% dried chicory root [41]
	Astaxanthin *Algae, yeast, salmon, trout, krill, shrimp*, and *crayfish* [38]	*In vivo*	Diets of 0.001–0.03% astaxanthin for 15 days [39]
CYP1B1	Curcumin *Turmeric, curry powder* [34]	*In vivo*	Diet of 0.1% curcumin [35]
	Cruciferous vegtables	*In vivo*	25–250 mg/kg indole-3-carbinol [27]

Hodges, R. E., & Minich, D. M. (2015). Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism*, *2015*, 760689. http://doi.org/10.1155/2015/760689

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Human and *in vivo* example nutrient **inhibitors** of CYP1 enzymes.

Enzyme	Food, beverage, or bioactive compounds *Food sources in italics*	Type of study	Dosages used and references
CYP1A1	Black raspberry	*In vivo*	Diet of 2.5% black raspberry [8]
	Blueberry	*In vivo*	Diet of 2.5% blueberry [8]
	Ellagic acid *Berries, pomegranate, grapes, walnuts, and blackcurrants* [42]	*In vivo*	30 mg/kg/d ellagic acid [43] 400 ppm ellagic acid [8]
	Black soybean	*In vivo*	1 g/kg black soybean seed coat extract [44]: *note high dose used*
	Black tea	*In vivo*	20 mg/kg theaflavins [45]
	Turmeric	*In vivo*	Diet of 1% turmeric [46]
	Apiaceous vegetables	Clinical	4 g/kg apiaceous vegetables, including frozen carrots and fresh celery, dill, parsley, and parsnips [24]

Hodges, R. E., & Minich, D. M. (2015). Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism*, *2015*, 760689. http://doi.org/10.1155/2015/760689

Journal of Nutrition and Metabolism

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Human and *in vivo* example nutrient **inhibitors** of CYP1 enzymes.

	Quercetin *Apple, apricot, blueberries, yellow onion, kale, alfalfa sprouts, green beans, broccoli, black tea, and chili powder* [47, 48]	Clinical	500 mg/d quercetin [29]
CYP1A2	Daidzein *Soybean* [49]	Clinical	200 mg twice daily dosing of daidzein [49]
	Grapefruit	Clinical	300 mL grapefruit juice [50]
	Kale	*In vivo*	2 g/kg/d kale, as freeze-dried kale drink [51]
	Garlic	*In vivo*	100 mg/kg garlic oil [52]
	Chamomile	*In vivo*	Free access to 2% chamomile tea solution [53]
	Peppermint	*In vivo*	Free access to 2% peppermint tea solution [53]
	Dandelion	*In vivo*	Free access to 2% dandelion tea solution [53]
	Turmeric	*In vivo*	Diet of 1% turmeric [46]

Hodges, R. E., & Minich, D. M. (2015). Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism*, *2015*, 760689. http://doi.org/10.1155/2015/760689

Journal of Nutrition and Metabolism

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What do we learn from that chart?

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The effect of food and/or supplements on phase I detox is dose dependent

- Curcumin was inducing cytochrome P450 family 1 (CYP1A1) at 0.1% of the diet, while in higher amount (1% of diet) turmeric was inhibiting this function.

1. Bansal, S. S., Kausar, H., Vadhanam, M. V., Ravoori, S., Pan, J., Rai, S. N., & Gupta, R. C. (2014). Curcumin implants, not curcumin diet, inhibit estrogen-induced mammary carcinogenesis in ACI rats. Cancer prevention research (Philadelphia, Pa.), 7(4), 456–465. https://doi.org/10.1158/1940-6207.CAPR-13-0248
2. Thapliyal R, Maru GB. Inhibition of cytochrome P450 isozymes by curcumins in vitro and in vivo. Food Chem Toxicol. 2001;39(6):541-547. doi:10.1016/s0278-6915(00)00165-4

34

The same effect is also reported for members of the same food group.

For example, cruciferous vegetables can activate CYP1 enzymes, but animal studies show that kale is reported to inhibit CYP1A2.

1. Bansal, S. S., Kausar, H., Vadhanam, M. V., Ravoori, S., Pan, J., Rai, S. N., & Gupta, R. C. (2014). Curcumin implants, not curcumin diet, inhibit estrogen-induced mammary carcinogenesis in ACI rats. Cancer prevention research (Philadelphia, Pa.), 7(4), 456–465. https://doi.org/10.1158/1940-6207.CAPR-13-0248
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Inhibiting Phase I might lead to an increase in plasma levels of drugs and the concentration-time curve (AUC)

Yamasaki I, Yamada M, Uotsu N, Teramoto S, Takayanagi R, Yamada Y. Inhibitory effects of kale ingestion on metabolism by cytochrome P450 enzymes in rats. *Biomed Res*. 2012;33(4):235-242. doi:10.2220/biomedres.33.235

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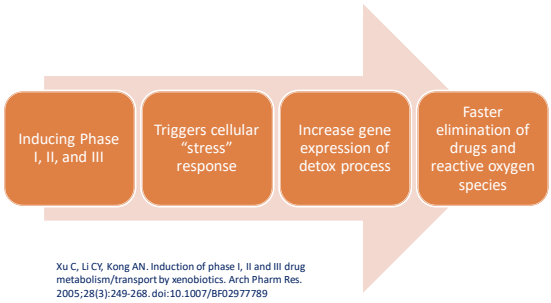

Xu C, Li CY, Kong AN. Induction of phase I, II and III drug metabolism/transport by xenobiotics. Arch Pharm Res. 2005;28(3):249-268. doi:10.1007/BF02977789

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With patients who are on prescription drugs, be careful when recommending food or supplements that might enhance or slow down the detox process

Yamasaki I, Yamada M, Uotsu N, Teramoto S, Takayanagi R, Yamada Y. Inhibitory effects of kale ingestion on metabolism by cytochrome P450 enzymes in rats. *Biomed Res*. 2012;33(4):235-242. doi:10.2220/biomedres.33.235

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Client 70yo female

- Chronic lower back and hip pain for over 10 years
- Tried treatments: Chiropractic, massages, pain medication, and several anti-inflammatory supplements
- Decrease in memory in last few years ("forgetting simple things every day. Gets worse and worse")
- General sensation of fatigue ("used to be more active")
- Occasional sensation of mild depression
- Chronic allergies and sinus congestion
- Occasional asthma attacks for over 25 years ("wakes up with difficulty to breath some nights")

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Toxic & Essential Elements; Hair — Heavy Metals Results

TOXIC METALS		RESULT ng/g	REFERENCE INTERVAL	PERCENTILE 68th / 95th
Aluminum	(Al)	2.2	< 7.0	
Antimony	(Sb)	0.013	< 0.050	
Arsenic	(As)	0.043	< 0.060	
Barium	(Ba)	0.05	< 2.0	
Beryllium	(Be)	< 0.01	< 0.020	
Bismuth	(Bi)	0.018	< 2.0	
Cadmium	(Cd)	0.012	< 0.050	
Lead	(Pb)	0.16	< 0.60	
Mercury	(Hg)	1.9	< 0.80	
Platinum	(Pt)	< 0.003	< 0.005	
Thallium	(Tl)	< 0.001	< 0.002	
Thorium	(Th)	< 0.001	< 0.002	
Uranium	(U)	0.010	< 0.060	
Nickel	(Ni)	0.04	< 0.30	
Silver	(Ag)	0.17	< 0.15	
Tin	(Sn)	0.12	< 0.30	
Titanium	(Ti)	0.22	< 0.70	
Total Toxic Representation				

High mercury can lead to poor memory, cognitive dysfunction, and neuromuscular disorders. Probably from dental fillings and fish.

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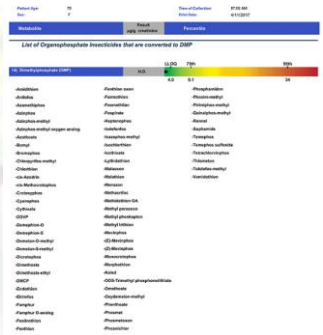
Results of measurement of 172 environmental toxins



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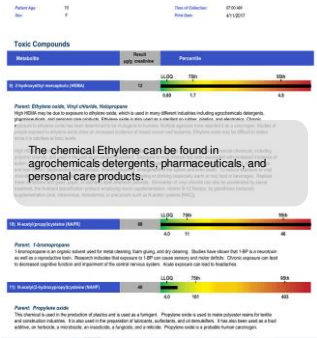

Results 172 toxins

Ethylene oxide causes damage to the central nervous system, (decline memory), liver (reduced toxic elimination), and hormonal system (thyroid, adrenal).

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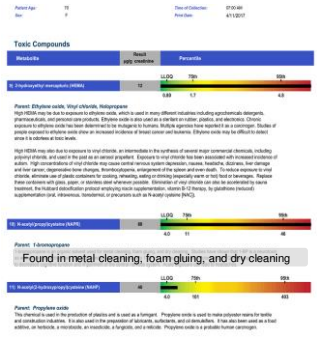

Results 172 toxins

Chronic exposure to 1-bromopropane can lead to decreased cognitive function and impairment of the central nervous system.

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Treatment protocol (detox):

1. Microgreen powder (Superfood by Amazing Grass): Organic fruits and vegetables powder with vitamins (e.g. B complex), minerals, fiber, and digestion enzymes to facilitate bowel movement and increase levels of nutrients.
2. Replace plastic containers with glass or stainless steel whenever possible.
3. Herbs: 2g twice a day of *Curcumin and Dan shen (Salvia Miltiorrhiza)* to support liver function to get rid of toxins.
4. Acupuncture to stimulate liver function (LI-11, GB-40)
5. Selenium 200mcg
6. Acetyl L-cysteine 600 to 1200mg TD (every 12 hours)
7. Vitamin C 500mg TD (every 12 hours)

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Results:

After three months, the client reported:

- ✓ Hip pain and lower back reduced
- ✓ No asthma attacks (from 3 weeks after treatment started)
- ✓ Congestion and allergies reduce significantly
- ✓ **Memory improved significantly**
- ✓ Energy improved and she started taking painting classes and work a few hours a week as substitute teacher.
- ✓ No abdominal bloating.
- ✓ Not taking any medication.

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Use of Food, Nutraceuticals, and Lifestyle as Medicine

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When should we support/stimulate phase II?

- Patients who have altered enzyme activity due to genetic predisposition
- Patients with high toxic load due to chronic exposure to environmental pollutants
- Patients with overactive phase I activity (turn to water soluble = more toxic)
- Patients with hormonal imbalance

Hodges, R. E., & Minich, D. M. (2015). Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. Journal of nutrition and metabolism, 2015, 760689. https://doi.org/10.1155/2015/760689

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Fiber Consumption & Heavy Metals

Children between the ages of 5 and 12 years received 15 g of pectin (PectaSol) in 3 divided dosages a day.

Blood serum and 24-hour urine excretion collection GFAAS analysis were performed on day 0, day 14, day 21, and day 28.

Results: A significant decrease in blood serum levels of lead (P = .0016; 161% average change) and a dramatic increase in 24-hour urine collection (P = .0007; 132% average change)

Zhao ZY, Liang L, Fan X, Yu Z, Hotchkiss AT, Wilk BJ, Eliaz I. (2008) The role of modified citrus pectin as an effective chelator of lead in children hospitalized with toxic lead levels.
Ther Health Med, 14(4):34-8.

49

Fiber Consumption & Heavy Metals

- ✓ Rice bran fiber can bind to PCBs, PCDFs, and PCDDs and was superior to other dietary fibers, including corn, wheat bran, spinach, Hijiki, sweet potatoes, and burdock fibers.
- ✓ Effectiveness of binding appears to be related to the content of lignin.

Sera N, Morita K, Nagasoe M, Tokieda H, Kitaura T, Tokiwa H. (2005) Binding effect of polychlorinated compounds and environmental carcinogens on rice bran fiber. J Nutr Biochem, 16(1):50-8.

50

Alpha Lipoic Acid & Metal Chelation

- Powerful antioxidant activity
- To support antioxidants such as vitamins E and C, and reduced glutathione.
- Metal-chelating activity
- It is readily absorbed from the gut and crosses cellular and blood-brain membrane barriers
- Dosage: 200-600 mg/day

• Rooney, JP. (2007) The role of thiols, dithiols, nutritional factors and interacting ligands in the toxicology of mercury. Toxicology, 234(3):145-56.
• Pande M, Flora SJ. (2002) Lead induced oxidative damage and its response to combined administration of alpha-lipoic acid and succimers in rats.Toxicology. 177(2-3), 187-96.

51

Flaxseed & Heavy Metals

- Breast cancer is considered as one of the most common cancers with the highest number of deaths worldwide. (WHO: in 2012 more than 1.68 million of women were diagnosed with breast cancer worldwide. Approximately 521,000 died.)
- Flaxseeds has an antioxidant and antitumorigenic functions with approximately 100 times more lignans than other foods.
- Flaxseed has was found to inhibit cancer cells.

- World Health Organization (WHO). (2015) Fact Sheet No. 297: Cancer. Available from: http://www.who.int/mediacentre/factsheets/fs297/en/
- Nesbitt, PD., Thompson, LU. (1997) Lignans in homemade and commercial products containing flaxseed. Nutr Cancer, 29(3), 222-7.
- McCann SE, Edge SB, Hicks DG, Thompson LU, Morrison CD, Fetterly G, Andrews C, Clark K, Wilton J, Kulkarni S. A pilot study comparing the effect of flaxseed, aromatase inhibitor, and the combination on breast tumor biomarkers.

52

Flaxseed & Heavy Metals

- Lignans are phytoestrogens that bind to estrogen receptors, as they have a very similar chemical structure as to an estrogen molecule.
- Ligans might relieve the symptoms of menopause and can balance the effects of estrogen in the body.
- Caution with the use of soluble fiber in patients with high cadmium levels. (3)
- In contrast to the protection provided by insoluble fiber, flax seed consumption might increase intestinal absorption of cadmium and retain (3)

1. Lucas EA, Wild RD, Hammond LJ, Khalil DA, Juma S, Daggy BP, Stoecker BJ, Arjmandi BH (2002) Flaxseed improves lipid profile without altering biomarkers of bone metabolism in postmenopausal women.. J Cln Endocrinol Metab. 87(4):1527-32.
2. McCann SE, Edge SB, Hicks DG, Thompson LU, Morrison CD, Fetterly G, Andrews C, Clark K, Wilton J, Kulkarni S. A pilot study comparing the effect of flaxseed, aromatase inhibitor, and the combination on breast tumor biomarkers.
3. Nutr Cancer. 2014; 66(4):566-75.MG, Milbradt BG, Alves E, Dietrich T, Kemerich DM, Hausen BS, Duarte FA, Flores EM, Dressler VL, Emanuelli T. (2011) Effect of wheat bran and flaxseed on cadmium effects and retention in rats. Hum Exp Toxicol. 30(8), 981-91.

53

Selenium & Glutathione activity

A cellular study, published in the Archives Biochemistry Biophysics, deficiency of selenium leads to 93% reduction in the activity of enzyme glutathione peroxidase in liver cells.

According to the U.S. Centers for Disease Control, "Selenium deficiency does not usually cause illness. Rather, it can make the body more susceptible to illnesses caused by other nutritional, biochemical, or infectious stresses."

Baker RD, Baker SS, LaRosa K, Whitney C, Newburger PE. Selenium regulation of glutathione peroxidase in human hepatoma cell line Hep3B. Arch Biochem Biophys. 1993 Jul;304(1):53-7.

54

Selenium & Glutathione activity

- Study of 103 local residents in Wanshan, China, who were suffering from elevated mercury levels due to history of extensive mercury exposure from mercury mining.
- Selenium supplementation: 100mcg organic selenium-enriched yeast vs nonselenium-enriched yeast.
- **Selenium yeast product increased mercury excretion and decreased oxidative stress-related biomarkers in their urine.**

Li YF, Dong Z, Chen C, Li B, Gao Y, Qu L, Wang T, Fu X, Zhao Y, Chai Z. (2012) Organic selenium supplementation increases mercury excretion and decreases oxidative damage in long-term mercury-exposed residents from Wanshan, China. Environ Sci Technol. 46(20), 11313-8.

55

Selenium is abundant in vegetables, fruits, and nuts (very high in Brazil nuts).

In cases of arthritis, thyroid conditions, autoimmune diseases, or digestion problems, Recommended to take 200mcg of selenium daily.

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Curcumin is derived from the rhizomes (underground stems) of the plant Curcuma longa.
Curcumin has powerful antioxidant and anti-inflammatory properties, is the most active constituent of turmeric.

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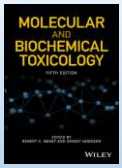

Curcumin reduced nephrotoxic, oxidative, histopathological and residual impacts of a toxic heavy metals such as lead

Ahmed, A. Y., Gad, A. M., & El-Raouf, O. M. (2017). Curcumin ameliorates diclofenac sodium-induced nephrotoxicity in male albino rats. Journal of Biochemical and Molecular Toxicology, 31(10). doi:10.1002/jbt.21951

58

Curcumin & Liver Function

Administration of curcumin reduced hepatic injury that was induced by dietary Aflatoxin B1.

Administration of curcumin prevented a decrease in levels of antioxidant ability (glutathione peroxidase, catalase, and glutathione), and an increase in lipid peroxidation (MDA). It also prevented damage to DNA.

Zhang, N., Qi, M., Zhao, L., Zhu, M., Guo, J., Liu, J., & ... Sun, L. (2016). Curcumin Prevents Aflatoxin B_1 Hepatoxicity by Inhibition of Cytochrome P450 Isozymes in Chick Liver. Toxins, 8(11)

59

Curcumin & Detox Pathway

Several foods appear to act as both inducers and inhibitors. The effect might be dose dependent or altered by the isolation of bioactive compounds derived from food.

Curcumin at 0.1% of the diet has been shown, in animals, to induce CYP1A1,(1) while a diet of 1% turmeric was inhibitory.(2)

1. Bansal, S. S., kausar, H., Vadhanam, M. V., Ravoori, S., Pan, J., Rai, S. N., & Gupta, R. C. (2014). Curcumin Implants, not Curcumin Diet Inhibits Estrogen-Induced Mammary Carcinogenesis in ACI Rats. Cancer Prevention Research (Philadelphia, Pa.), 7(4), 456–465. http://doi.org/10.1158/1940-6207.CAPR-13-0248
2. Thapliyal R., Maru G. B. (2001) Inhibition of cytochrome P450 isozymes by curcumins in vitro and in vivo. Food and Chemical Toxicology. 39(6), 541–547. doi: 10.1016/S0278-6915(00)00165-4.

60

Curcumin & Liver Function

Recommended dosage: 300mg to 1000mg twice a day.

Zhang, N., Qi, M., Zhao, L., Zhu, M., Guo, J., Liu, J., & ... Sun, L. (2016). Curcumin Prevents Aflatoxin B_1 Hepatoxicity by Inhibition of Cytochrome P450 Isozymes in Chick Liver. Toxins, 8(11)

61

Milk Thistle & Detox Pathways

Animal studies show that consumption of Milk Thisle (Silybum Marianum) resulted in

- ✓ Higher levels of glutathione in liver cells,
- ✓ Decreased oxidative stress,
- ✓ Stimulate or inhibit phase I detoxification pathways,
- ✓ Stimulate phase II detoxification pathways. (Post-White & Ladas, 2007)

Post-White J, Ladas EJ, Kelly KM. (2007) Advances in the Use of Milk Thistle (Silybum marianum). Integrative Cancer Therapies, 6(2), 104-109. doi:10.1177/1534735407301632. Retrieved from http://journals.sagepub.com/doi/abs/10.1177/1534735407301632?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

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Cruciferous Vegetables & Inflammation

Indole-3-Carbinol (I3C) inhibited expression of proinflammatory cytokines, such as interleukin-6 (IL-6).

Cruciferous vegetables, including broccoli, cauliflower, cabbage, brussels sprouts, rutabaga/swede, turnip, and watercress.

Chang, H.-P., Wang, M.-L., Hsu, C.-Y., Liu, M.-E., Chan, M.-H., & Chen, Y.-H. (2011). Suppression of inflammation-associated factors by indole-3-carbinol in mice fed high-fat diets and in isolated, co-cultured macrophages and adipocytes. International Journal of Obesity (2005), 35(12), 1530–1538. http://doi.org/10.1038/ijo.2011.12

63

Cruciferous Vegetables & Detoxification

Indole-3-carbinol (I3C)increases **phase II enzyme glutathione S-transferase**.

Iwona B, Monika O, Jolanta C. Effect Of Indole-3-carbino on Detoxification Enzymes and Lipid Metabolism. Medicina Veterinaria 1(2) 2002, 5-11

64

Cruciferous Vegetables & Cancer

Indole-3-Carbinol (I3C) I3C shows efficacy for the prevention of breast, endometrial, and cervical cancers.

1. Shertzer HG, Senft AP. The micronutrient indole-3-carbinol: implications for disease and chemoprevention. Drug Metabol Drug Interact. 2000; 17(1-4):159-88.
2. Rogan EG. The natural chemopreventive compound indole-3-carbinol: state of the science. In Vivo. 2006 Mar-Apr; 20(2):221-8.

65

Beets & Glutathione Peroxidase

- ✓ Beets contains bioactive agents (betaine and polyphenols), which was found to significantly increase the levels of enzymatic antioxidants glutathione peroxidase and superoxide dismutase in the liver. (1)
- ✓ consumption of red beet (Beta vulgaris L.) leaf significantly increases levels of antioxidants (glutathione and β-carotene) and the activities of antioxidant enzyme (glutathione peroxidase) in plasma and liver. (2)

1. Váli, L., Stefanovits-Bányai, É., Szentmihályi, K., Fébel, H., Sárdi, É., Lugasi, A., . . . Blázovics, A. (2007). Liver-protecting effects of table beet (Beta vulgaris var. rubra) during ischemia-reperfusion. Nutrition, 23(2), 172-178. doi:10.1016/j.nut.2006.11.004 Retrieved from http://www.nutritionjrnl.com/article/S0899-9007(06)00394-7/fulltext
2. Lee, J. H., Son, C. W., Kim, M. Y., Kim, M. H., Kim, H. R., Kwak, E. S., ... Kim, M. R. (2009). Red beet (Beta vulgaris L.) leaf supplementation improves antioxidant status in C57BL/6J mice fed high fat high cholesterol diet. Nutrition Research and Practice, 3(2), 114–121. http://doi.org/10.4162/nrp.2009.3.2.114

66

Berries

Significantly increased the expression of Nuclear Factor Erythroid 2 (NF-E2), a transcription factor that plays a role in regulating the body's **detoxification and antioxidant system** by promoting or enhancing portion of genes associated with phase II detoxification

Kavitha K, Thiyagarajan P, Rathna Nandhini J, Mishra R, Nagini S (2013) Chemopreventive effects of diverse dietary phytochemicals against DMBA-induced hamster buccal pouch carcinogenesis via the induction of Nrf2-mediated cytoprotective antioxidant, detoxification, and DNA repair enzymes. Biochimie, 95(8), 1629-39. Retrieved from https://www-ncbi-nlm-nih-gov.uws.idm.oclc.org/pubmed/20382588/

67

Silymarin (Milk Thistle)

Consumption of silymarin can increase elimination of toxins.

Animal studies show that consumption of silymarin resulted in higher levels of glutathione in liver cells, decreased oxidative stress, stimulate or inhibit phase I detoxification pathways, and stimulate phase II detoxification pathways.

Post-White J, Ladas EJ, Kelly KM. (2007) Advances in the Use of Milk Thistle (Silybum marianum). Integrative Cancer Therapies, 6(2), 104-109. doi:10.1177/1534735407301632. Retrieved from http://journals.sagepub.com/doi/abs/10.1177/1534735407301632?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

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Green Tea Extract

Strong antioxidant activity.

Administration of green tea can increase in the activities of antioxidant and phase II enzymes in skin, small intestine, liver, and lungs.

Dosage: 100-200mg daily

Khan SG, Katiyar SK, Agarwal R, Mukhtar H. (1992) Enhancement of antioxidant and phase II enzymes by oral feeding of green tea polyphenols in drinking water to SKH-1 hairless mice: possible role in cancer chemoprevention. Cancer Res, 52(14), 4050-2. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/1617681

69

Yoga & Detox Pathways

✓ Regular practice of yoga significantly increased both levels of Reduced glutathione level and total antioxidant status in comparison with physical exercise training.

1. Post-White J, Ladas EJ, Kelly KM. (2007) Advances in the Use of Milk Thistle (Silybum marianum). Integrative Cancer Therapies, 6(2), 104-109. doi:10.1177/1534735407301632. Retrieved from
2. Sinha S, Singh SN, Monga YP, Ray US. (2007) Improvement of glutathione and total antioxidant status with yoga. J Altern Complement Med, 13(10), 1085-90. doi: 10.1089/acm.2007.0567. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/18166119

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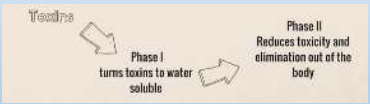
Detox: Promoting Phase II

Glutathione (GSH) and glutathione S-transferases (GSTs) has a significant role in the detoxification of xenobiotics.



Findlay V.J., Townsend D.M., Tew K.D. (2006) Glutathione and Glutathione S-Transferases in Drug Resistance. In: Teicher B.A. (eds) Cancer Drug Resistance. Cancer Drug Discovery and Development. Humana Press

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In vivo example nutrient **inhibitors** of glutathione S-transferases (GSTs).

Enzyme	Food, beverage, or bioactive compounds *Food sources in italics*	Type of study	Dosages used and references
	Apiaceous vegetables	Clinical	1 tsp fresh dill weed, 0.5 cups of fresh celery, 3 tbsp. fresh parsley, 1.25 cups of grated parsnips, and 0.75 cups of frozen carrots [116]
GSTs	Quercetin *Apple, apricot, blueberries, yellow onion, kale,* and *alfalfa sprouts, green beans, broccoli, black tea,* and *chili powder* [47, 48]	*In vivo*	2 g/kg quercetin [126]: *note high dose used*
	Genistein (liver GSTs) *Fermented soy* (e.g., *miso, tempeh*) containsup to 40% bioavailable genistein, versus 1% or less in other soy products [125]	*In vivo*	1.5 g/kg genistein [123]: *note high dose used*

Hodges, R. E., & Minich, D. M. (2015). Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism*, *2015*, 760689. http://doi.org/10.1155/2015/760689

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In vivo example nutrient **inducers** of glutathione S-transferases (GSTs)

Enzyme	Food, beverage, or bioactive compounds *Food sources in italics*	Type of study	Dosages used and references
	Cruciferous vegetables	Clinical, observational	Approximately 5 and 10 servings/d of cruciferous vegetables including frozen broccoli, cauliflower, fresh cabbage (red and green), and fresh radish sprouts [114] >9.1.2 g/d cruciferous vegetables [115] 4.5 cups of cruciferous vegetables/d, including 0.5 cups of radish sprouts, 1 cup of frozen cauliflower, 2 cups of frozen broccoli, and 1 cup of fresh cabbage [116] 300 g/d cooked Brussels sprouts [117]
	Allium vegetables	Clinical	3 tbsp fresh chives, 1.33 cups of fresh leeks, 1 tsp garlic, and 0.5 cups of fresh onion [118]
	Resveratrol	Clinical	1 g/d resveratrol [120]; none high dose used
	Grapes, wine, peanuts, soy, and *Arabidopsis* [122]		
	Citrus	Observational, in vivo	>78 g/d citrus [123] 20 mg limonoid mixture every 2 days [124]
	Garlic	*In vitro*	30 to 200 mg/kg garlic oil [125] 80 and 200 mg/kg garlic oil 5 times weekly [126]

Hodges, R. E., & Minich, D. M. (2015). Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism*, *2015*, 760689. http://doi.org/10.1155/2015/760689

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In vivo example nutrient **inducers** of glutathione S-transferases (GSTs)

Enzyme	Food, beverage, or bioactive compounds *Food sources in italics*	Type of study	Dosages used and references
GSTs	Fish oil	*In vivo*	20.1 g/kg fish oil [128]; none high dose used
	Black soybeans	*In vivo*	1 g/kg black soybean seed coat extract [86]
	Purple sweet potato	*In vivo*	100 and 200 mg/kg anthocyanin extract from purple sweet potato [129]
	Curcumin	*In vivo*	Diet of 2% curcumin [130]
	Green tea	*In vivo*	Equivalent of 4 cups (1200 mL each) of green tea [131]
	Rooibos tea	*In vivo*	Rooibos tea as sole beverage, concentration 4 g tea leaves/100 mL water steeped for 30 minutes [132]
	Honeybush tea	*In vivo*	Honeybush tea as sole beverage, concentration 4 g tea leaves/100 mL water steeped for 30 minutes [132]
	Ellagic acid (Berries, pomegranate, grapes, walnuts, and Mirabelle plums) [92]	*In vivo*	30 mg/kg/d ellagic acid [92]
	Rosemary	*In vivo*	20 mg/kg carnosic acid 3 times weekly [133]
	Ghee (clarified butter)	*In vivo*	19.5 mg CLA (conjugated linoleic acid)/g fat [134]
	Cinnamon (Isolate: GSTs) *Fermented soy (e.g., miso, tempeh) contains up to 40% less soluble genistein versus 3% or less in other soy products* [135]	*In vivo*	1.5 g/kg genistein [122]; none high dose used

Hodges, R. E., & Minich, D. M. (2015). Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *Journal of Nutrition and Metabolism*, *2015*, 760689. http://doi.org/10.1155/2015/760689

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Glutathione

Glutathione is made from three amino acids: glycine, cysteine and glutamic acid.

It is a potent free radical and reactive oxygen species scavenger, critical for the regeneration of other antioxidants and for phase II detoxification.

Sen C.K. Redox signaling and the emerging therapeutic potential of thiol antioxidants. Biochem. Pharmacol. 1998;55:1747–1758.
Meister A. Glutathione, ascorbate, and cellular protection. Cancer Res. 1994;54:1969s–1975s.

75

Glutathione Depletion & Disease

"The most well-known conditions associated with GSH depletion include neurodegenerative diseases pulmonary diseases, liver diseases, immune disorders, cardiovascular diseases, as well as the aging process itself."

Schmitt, B., Vicenzi, M., Garrel, C., & Denis, F. M. (2015). Effects of N-acetylcysteine, oral glutathione (GSH) and a novel sublingual form of GSH on oxidative stress markers: A comparative crossover study. Redox Biology, 6, 198–205. http://doi.org/10.1016/j.redox.2015.07.012

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Absorption of Glutathione

Randomized, double-blinded, placebo-controlled trial of orally administered GSH (500 mg twice per day of 98% reduced glutathione) in healthy, adult humans showed **no significant change** in biomarkers of lipid peroxidation, DNA adduct formation or glutathione status

Allen, J., & Bradley, R. D. (2011). Effects of Oral Glutathione Supplementation on Systemic Oxidative Stress Biomarkers in Human Volunteers. Journal of Alternative and Complementary Medicine, 17(9), 827–833. http://doi.org/10.1089/acm.2010.0716

77

What would be the best form of Glutathione (GSH)?

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Sublingual form of Glutathione (GSH) was superior to oral GSH.

Schmitt, B., Vicenzi, M., Garrel, C., & Denis, F. M. (2015). Effects of N-acetylcysteine, oral glutathione (GSH) and a novel sublingual form of GSH on oxidative stress markers: A comparative crossover study. Redox Biology, 6, 198–205. http://doi.org/10.1016/j.redox.2015.07.012

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Vitamin C & Glutathione

- Mean red blood cell glutathione rose nearly 50% ($P < 0.05$) after the 500mg period compared with baseline.
- Consumption of 2,000mg of vitamin C did not significantly change the levels of glutathione in RBC.

Johnston, CS., Meyer, CG., Srilakshmi JC. (1993) Vitamin C elevates red blood cell glutathione in healthy adults. Am J Clin Nutr. 58(1), 103-5.

80

N-Acetylcysteine & Liver Function

1. N-acetyl-cysteine (NAC) is an effective chelator of toxic elements.
2. NAC was used to increase intracellular glutathione levels.

1. Giampreti, A., Lonati, D., Ragghianti, B., Ronchi, A., Petrolini, V. M., Vecchio, S., & Locatelli, C. A. (2016). N-Acetyl-Cysteine as Effective and Safe Chelating Agent in Metal-on-Metal Hip-Implanted Patients: Two Cases. Case Reports in Orthopedics, 2016, 8682737. http://doi.org/10.1155/2016/8682737
2. Yim CY, Hibbs JB Jr, McGregor JR, Galinsky RE, Samlowski WE. (1994) Use of N-acetyl cysteine to increase intracellular glutathione during the induction of antitumor responses by IL-2. J Immunol. Jun 15;152(12):5796-805.

81

N-Acetylcysteine & Liver Health

- NAC might be useful in improving liver health in patients with liver disease.
- 600 mg of NAC TD resulted in a significant decrease of serum alanine aminotransfrase after three months in patients with non-alcoholic fatty liver disease.

Khoshbaten, M., Aliasgarzadeh, A., Masnadi, K., Tarzamani, M. K., Farhang, S., Babaei, H., … Najafipoor, F. (2010). N-Acetylcysteine Improves Liver Function in Patients with Non-Alcoholic Fatty Liver Disease. Hepatitis Monthly, 10(1), 12–16.

82

Toxic Elimination: Sweating

- Many toxic elements appeared to be preferentially excreted through sweat.
- Sauna and exercise might be a beneficial therapy in detox protocol.
- Sweating might lead to loss of minerals.

Genuis, S. J., Birkholz, D., Rodushkin, I., & Beesoon, S. (2011). Blood, urine, and sweat (BUS) study: monitoring and elimination of bioaccumulated toxic elements. Archives Of Environmental Contamination And Toxicology, 61(2), 344-357. doi:10.1007/s00244-010-9611-5

83

According to a study published in the Journal of Environmental and Public Health, perspiration stimulated the extraction of arsenic, cadmium, lead and mercury. The study showed that mercury levels reduced and normalized with repeated saunas. (Sears, Kerr, & Bray, 2012)

1. Sears, M. E., Kerr, K. J., & Bray, R. I. (2012). Arsenic, Cadmium, Lead, and Mercury in Sweat: A Systematic Review. Journal of Environmental and Public Health, 2012, 184745. http://doi.org/10.1155/2012/184745 Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3312275/

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Nutritional Deficiencies & Detox

Nutritional deficiencies might lead to toxic accumulation.

1. Animals studies reported that calcium deprivation enhanced absorption of lead and cadmium.
2. Supplementation of magnesium and zinc reduced absorption of cadmium.
3. Supplementing with 1,200mg of Ca reduced lead mobilization from maternal bones during pregnancy and lactation, thus provided protection for the newborn and infant.

1. Van Barneveld AA, Van den Hamer CJ. (1985) Influence of Ca and Mg on the uptake and deposition of Pb and Cd in mice. Toxicol Appl Pharmacol, 79(1), 1-10.
2. Matović V, Buha A, Bulat Z, Dukić-Ćosić D. (2011) Cadmium toxicity revisited: focus on oxidative stress induction and interactions with zinc and magnesium. Arh Hig Rada Toksikol. 62(1), 65-76
3. Ettinger, A. S., Lamadrid-Figueroa, H., Téllez-Rojo, M. M., Mercado-García, A., Peterson, K. E., Schwartz, J., ... Hernández-Avila, M. (2009). Effect of Calcium Supplementation on Blood Lead Levels in Pregnancy: A Randomized Placebo-Controlled Trial. Environmental Health Perspectives, 117(1), 26–31. http://doi.org/10.1289/ehp.11868

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Testing for Micronutrients Levels

Micronutrient testing (SpectraCell or Cell Science)

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Nutritional Deficiencies – My SpectraCell Results

Other Vitamins				
Vitamin D3 (Cholecalciferol)	67			>50%
Vitamin A (Retinol)	73		Borderline	>70%
Vitamin K2	35		Borderline	>30%
Minerals				
Calcium	39		Borderline	>38%
Manganese	56		Borderline	>50%
Zinc	50			>37%
Copper	59			>42%
Magnesium	57			>37%
Carbohydrate Metabolism				
Glucose-Insulin Interaction	54			>38%
Fructose Sensitivity	38		Borderline	>34%
Chromium	50			>40%

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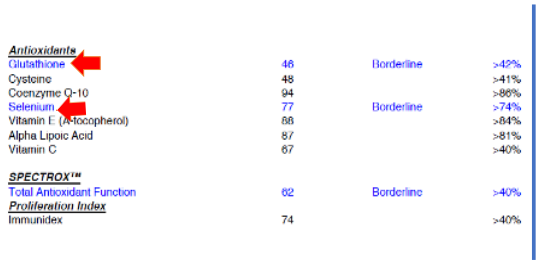
Nutritional Deficiencies – My SpectraCell Results



Antioxidants			
Glutathione	46	Borderline	>42%
Cysteine	48		>41%
Coenzyme Q-10	94		>86%
Selenium	77	Borderline	>74%
Vitamin E (A-tocopherol)	88		>84%
Alpha Lipoic Acid	87		>81%
Vitamin C	67		>40%
SPECTROX™			
Total Antioxidant Function	62	Borderline	>40%
Proliferation Index			
Immunidex	74		>40%

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Summary of Important Nutrients to Support Detox

Tal Cohen, DAOM, MS-HNFM

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Supporting Detox Pathway I

- including Vitamins A, C, E
- A broad spectrum of B vitamins (Riboflavin B2, Niacin B3, Pyridoxine B6)
- Folic Acid
- Glutathione
- Selenium
- Flavonoids (barriers, cabbage, beans, onions,)
- Phospholipids (sunflower seeds, eggs)

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Supporting Detox Pathway II

Nutrients for Glutathione and other phase II support:

- Vitamin B6+B12 (methylation)
- Magnesium (at least >500mg)
- Selenium
- Vitamin C
- Silymarin
- Glycine
- N-Acetylcysteine
- Folate
- Alpha-lipoic acid

Healthy function of Phase II requires several amino-acids, such as glycine, arginine, glutamic, methionine and therefore it is recommended to supplement with a clean for form of protein shake, if possible.

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Supporting Detox Pathways

- ✓ Maintain a diet full of nutrients, e.g. Mediterranean Diet
- ✓ Ensure absorption of food in patients with digestion problems, e.g. low HCL might need support with meals.
- ✓ Avoid high alcohol
- ✓ Consume more organic food, if possible (at least the "dirty dozen")
- ✓ Minimize medication use. Use lifestyle and nutritional medicine when possible.
- ✓ Support bowel movements: 80% heavy metals come out in stool. Some toxic metabolites also coming out via bile.

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Supporting Detox Pathways

- ✓ Use nutritional powders, e.g. Amazing Grass by SuperFood
- ✓ Green tea catechins induce phase II enzymes and glutathione S-transferase
- ✓ Silybum marianum promotes the production of glutathione in the liver and stimulate elimination of waste. (1)
  Dosage: 300mg twice a day (80% silymarin) up to 3,000mg TD
- ✓ Stress management: e.g. yoga sessions two to three times a week to alleviate stress and increase levels of Reduced glutathione.. (2)

1. Post-White J, Ladas EJ, Kelly KM. (2007) Advances in the Use of Milk Thistle (Silybum marianum). Integrative Cancer Therapies, 6(2), 104-109. doi: 10.1177/1534735407301632. Retrieved from
2. Sinha S, Singh SN, Monga YP, Ray US. (2007) Improvement of glutathione and total antioxidant status with yoga. J Altern Complement Med, 13(10), 1085-90. doi: 10.1089/acm.2007.0567. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/18166119

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Remember that every detox must start with reduction of exposure to chemicals

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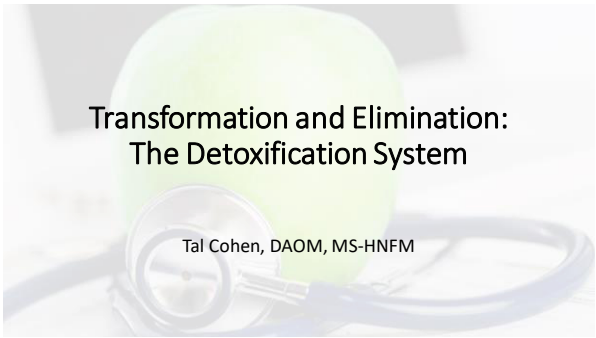

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