



new

4ENVIRO

One box to address the effects
on environmental pollution



Exposure to environmental toxicants is ongoing
= accumulation and amplification toxicants affect
metabolism, gut health & immunity

Landscape of environmental chemicals

- Chemicals are innocent until proven guilty.
- No requirements to prove safety before coming to the market. Slow or inexistent regulations + many Agencies. The different Agencies in charge are not communicating.



Obesogens

Chemicals that directly or indirectly increase obesity through disruption of metabolic, hormonal or development processes: pesticides, flame retardants, bisphenols, PFAS, phthalates, arsenic, dioxins.



How to guard against environmental toxicants?

1 _ **Lifestyle changes** to lower the burden of toxicity

2 _ **Dietary management** and **nutritional support** are strongly advised

Dietary management & nutritional support



PHASE 1 Biotransformation

Cytochrome enzymes activate toxicants. Toxicants are prepared for conjugation in phase 2.

→ **Vit B Cofactors**
induce cytochrome enzymes phase 1



PHASE 2 Conjugation

Activated toxicants are conjugated with endogenous molecules to form water-soluble compounds.

Phase 2 enzymes are in charge, toxins are neutralized and prepared for elimination.

→ **Broccoraphanin** – as a sulforaphane precursor – empowers phase 1 and phase 2
→ **EGCG green tea extract & Trans-Resveratrol**, both induce specific conjugation enzymes: Glutathione-S-Transferase & UDP-glucuronosyltransferase (UGT)



PHASE 3 Elimination

Active elimination of conjugated toxicants via bile, stool and urine.

+ Probiotics lower intestinal absorption of toxicants

Oishi, Kenji, et al. "Effect of probiotics, Bifidobacterium breve and Lactobacillus casei, on bisphenol A exposure in rats." Bioscience, biotechnology, and biochemistry 72.6 (2008): 1409-1415.

Zhai, Qixiao, et al. "Oral administration of probiotics inhibits absorption of the heavy metal cadmium by protecting the intestinal barrier." Applied and Environmental Microbiology 82.14 (2016): 4429-4440.

Abdel-Megeed, Rehab M. "Probiotics: a promising generation of heavy metal detoxification." Biological trace element research 199.6 (2021): 2406-2413.



4ENVIRO

Prepacked sachets containing 4 pills for daily administration to protect from environmental toxicity.

[Product sheet](#) and [references](#) on the following pages.

Complementary recommendations



Butyflam®

Research based delivery of bio-active Butyrate

> [Product sheet and references](#) on page 8 and 9



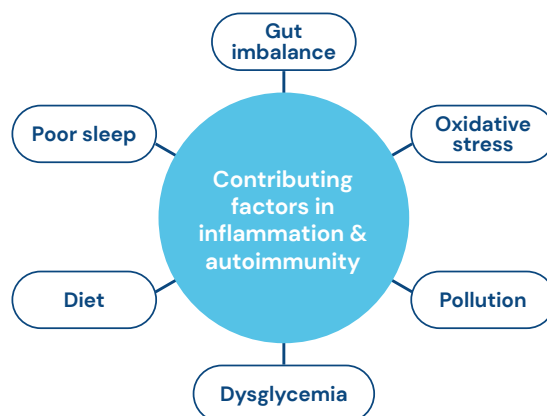
Tri-Fortify®

Liposomal delivery has been used to enhance the GSH status

> [Product sheet and published research](#) on page 10 and 11

Butyflam & autoimmunity

- Only **30%** of autoimmunity is **genetic**.
- **Gut dysbiosis & pollution** are strongly linked.
- **Halogenated chemicals** alter Iodine uptake & directly interfere with Thyroid function.
- **Faecalibacterium prausnitzii colon bacteria** are most affected by environmental pollution.
- Butyflam® **turns on T reg cells** to support self-tolerance & address auto-immunity.



Torres-Sánchez, Alfonso, et al. "Exploring Next Generation Probiotics for Metabolic and Microbiota Dysbiosis Linked to Xenobiotic Exposure: Holistic Approach." *International Journal of Molecular Sciences* 23.21 (2022): 12917.



4Enviro

The majority of environmental toxicants are lipophilic, they accumulate in bone matrix and adipose tissue. 4Enviro strongly empowers our protection + our detoxification system:

1_Broccoraphanin activates nrf2 and our enzymes responsible for detoxification phase II

2_Cofactor B Complex are the bio-activated enhancers of our Cytochrome enzymes in phase I

3_AO Defense induces both enzymes Glutathione-S-Transferase and UDP-Glucuronyl-Transferase, responsible for conjugation in phase II

4_Probiotic strongly reduces intestinal absorption of toxicants

indication	Protection against environmental toxicity	
dosage	1 sachet 30 min. before breakfast + 1 sachet during breakfast	
packaging	4 pills in prepacked sachets for daily administration One month per box	
composition (amount per 2 sachets)	<p>Broccoraphanin 300 mg</p> <p>Co-Factor B Complex:</p> <p>Vitamin B2 (as riboflavin) 200 mg</p> <p>Vitamin B3 (as nicotinamide) 100 mg</p> <p>Vitamin B5 (as D-Calcium pantothenate) 92 mg</p> <p>Vitamin B1 (as thiamin HCl) 63 mg</p> <p>Pyridoxal-5-phosphate (as coenzym B6) 20 mg</p> <p>Biotine 5 mg</p> <p>MTHF (Bio-active Folate) 1,62 mg</p> <p>AO Defense:</p> <p>Japanese knotweed dry extract (Polygonum cuspidatum) 210 mg</p> <p>(Natural Trans-Resveratrol)</p> <p>Green tea extract (Camillia sinensis) (50% EGCG) 200 mg</p> <p>Grape skin extract (Vitis vinifera) 140 mg</p> <p>Grape seed dry extract (Vitis vinifera) 100 mg</p> <p>Probiotic: Lactobacillus acidophilus DDS-1, L-Rhamnosus, L-Rhamnosus (type B, Bifidus), Steptococcus Lactis, Bifidobacterium Longum, Bifidobacterium Bifidum, Steptococcus Thermophilus 550 mg</p>	

References

4Enviro



Michnovicz J. J., Bradlow H. L. Induction of estradiol metabolism by dietary indole-3-carbinol in humans. *Journal of the National Cancer Institute*. 1990;82(11):947–949. doi: 10.1093/jnci/82.11.947.

Horn T. L., Reichert M. A., Bliss R. L., Malejka-Giganti D. Modulations of P450 mRNA in liver and mammary gland and P450 activities and metabolism of estrogen in liver by treatment of rats with indole-3-carbinol. *Biochemical Pharmacology*. 2002;64(3):393–404. doi: 10.1016/S0006-2952(02)01190-5.

Chow H. H. S., Garland L. L., Hsu C. H., et al. Resveratrol modulates drug- and carcinogen-metabolizing enzymes in a healthy volunteer study. *Cancer Prevention Research*. 2010;3(9):1168–1175. doi: 10.1158/1940-6207.CAPR-09-0155.

Walters D. G., Young P. J., Agus C., et al. Cruciferous vegetable consumption alters the metabolism of the dietary carcinogen 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) in humans. *Carcinogenesis*. 2004;25(9):1659–1669. doi: 10.1093/carcin/bgh164.

Chow H. H. S., Garland L. L., Hsu C. H., et al. Resveratrol modulates drug- and carcinogen-metabolizing enzymes in a healthy volunteer study. *Cancer Prevention Research*. 2010;3(9):1168–1175. doi: 10.1158/1940-6207.CAPR-09-0155

Navarro S. L., Peterson S., Chen C., et al. Cruciferous vegetable feeding alters UGT1A1 activity: diet- and genotype-dependent changes in serum bilirubin in a controlled feeding trial. *Cancer Prevention Research (Phila)* 2009;2(4):345–352. doi: 10.1158/1940-6207.capr-08-0178

Saracino M. R., Bigler J., Schwarz Y., et al. Citrus fruit intake is associated with lower serum bilirubin concentration among women with the UGT1A1*28 polymorphism. *Journal of Nutrition*. 2009;139(3):555–560. doi: 10.3945/jn.108.097279

Navarro S. L., Chang J. L., Peterson S., et al. Modulation of human serum glutathione S-transferase A1/2 concentration by cruciferous vegetables in a controlled feeding study is influenced by GSTM1 and GSTT1 genotypes. *Cancer Epidemiology Biomarkers and Prevention*. 2009;18(11):2974–2978. doi: 10.1158/1055-9965.epi-09-0701.

Wark P. A., Grubben M. J. A. L., Peters W. H. M., et al. Habitual consumption of fruits and vegetables: associations with human rectal glutathione S-transferase. *Carcinogenesis*. 2004;25(11):2135–2142. doi: 10.1093/carcin/bgh238.

Lampe J. W., Chen C., Li S., et al. Modulation of human glutathione S-transferases by botanically defined vegetable diets. *Cancer Epidemiology Biomarkers and Prevention*. 2000;9(8):787–793.

Nijhoff W. A., Mulder T. P. J., Verhagen H., van Poppel G., Peters W. H. M. Effects of consumption of brussels sprouts on plasma and urinary glutathione S-transferase class- α and π in humans. *Carcinogenesis*. 1995;16(4):955–957. doi: 10.1093/carcin/16.4.955

Sinha, R., Sinha, I., Calcagnotto, A., Trushin, N. Oral supplementation with liposomal glutathione elevates body stores of glutathione and markers of immune function. *Eur J Clin Nutr*. 2018 Jan;72(1):105–111.

Xie Y., Zhao Q. Y., Li H. Y., Zhou X., Liu Y., Zhang H. Curcumin ameliorates cognitive deficits heavy ion irradiation-induced learning and memory deficits through enhancing of Nrf2 antioxidant signaling pathways. *Pharmacology Biochemistry and Behavior*. 2014 doi: 10.1016/j.pbb.2014.08.005.

Soetikno V., Sari F. R., Lakshmanan A. P., et al. Curcumin alleviates oxidative stress, inflammation, and renal fibrosis in remnant kidney through the Nrf2-keap1 pathway. *Molecular Nutrition & Food Research*. 2013;57(9):1649–1659. doi: 10.1002/mnfr.201200540.

He H. J., Wang G. Y., Gao Y., Ling W. H., Yu Z. W., Jin T. R. Curcumin attenuates Nrf2 signaling defect, oxidative stress in muscle and glucose intolerance in high fat diet-fed mice. *World Journal of Diabetes*. 2012;3(5):94–104. doi: 10.4239/wjd.v3.i5.94.

Farombi E. O., Shrotriya S., Na H. K., Kim S. H., Surh Y. J. Curcumin attenuates dimethylnitrosamine-induced liver injury in rats through Nrf2-mediated induction of heme oxygenase-1. *Food and Chemical Toxicology*. 2008;46(4):1279–1287. doi: 10.1016/j.fct.2007.09.095.

Zhang Z., Wang S., Zhou S., et al. Sulforaphane prevents the development of cardiomyopathy in type 2 diabetic mice probably by reversing oxidative stress-induced inhibition of LKB1/AMPK pathway. *Journal of Molecular and Cellular Cardiology*. 2014;77:42–52. doi: 10.1016/j.yjmcc.2014.09.022.

Boddupalli, Sekhar et al. "Induction of phase 2 antioxidant enzymes by broccoli sulforaphane: perspectives in maintaining the antioxidant activity of vitamins a, C, and e." *Frontiers in genetics* vol. 3 7. 24 Jan. 2012, doi:10.3389/fgene.2012.00007

Hodges RE, Minich DM. Modulation of Metabolic Detoxification Pathways Using Foods and Food-Derived Components: A Scientific Review with Clinical Application. *J Nutr Metab*. 2015;2015:760689. doi:10.1155/2015/760689

Institute for Functional Medicine. *Textbook of Functional Medicine*. Boulder, Colo, USA: Johnston Printing; 2006.

Ullrich V. Cytochrome P450 and biological hydroxylation reactions. *Topics in Current Chemistry*. 1979;83:67–104. doi: 10.1007/bfb0019663.

Danielson P. B. The cytochrome P450 superfamily: biochemistry, evolution and drug metabolism in humans. *Current Drug Metabolism*. 2002;3(6):561–597. doi: 10.2174/1389200023337054.

Paine A. J. Hepatic cytochrome P-450. *Essays in Biochemistry*. 1981;17:85–126.

Chen Q., Zhang T., Wang J. F., Wei D. Q. Advances in human cytochrome P450 and personalized medicine. *Current Drug Metabolism*. 2011;12(5):436–444. doi: 10.2174/138920011795495259.

General references related to the impact of pollution

Huang, Qiansheng, and Qionghua Chen. "Mediating Roles of PPARs in the Effects of Environmental Chemicals on Sex Steroids." *PPAR research* vol. 2017 (2017): 3203161. doi:10.1155/2017/3203161

Janesick, Amanda, and Bruce Blumberg. "Minireview: PPAR γ as the target of obesogens." *The Journal of steroid biochemistry and molecular biology* vol. 127,1–2 (2011): 4–8. doi:10.1016/j.jsbmb.2011.01.005

Patel, Jessal J et al. "PPAR agonists stimulate adipogenesis at the expense of osteoblast differentiation while inhibiting osteoclast formation and activity." *Cell biochemistry and function* vol. 32,4 (2014): 368–77. doi:10.1002/cbf.3025

Navas-Acien, Ana, et al. "Arsenic exposure and prevalence of type 2 diabetes in US adults." *Jama* 300.7 (2008): 814–822.

Tseng, Chin-Hsiao, et al. "Long-term arsenic exposure and incidence of non-insulin-dependent diabetes mellitus: a cohort study in arseniasis-hyperendemic villages in Taiwan." *Environmental health perspectives* 108.9 (2000): 847–851.

Ettinger, Adrienne S., et al. "Maternal arsenic exposure and impaired glucose tolerance during pregnancy." *Environmental health perspectives* 117.7 (2009): 1059–1064.

Clair, Heather B et al. "Liver Disease in a Residential Cohort With Elevated Polychlorinated Biphenyl Exposures." *Toxicological sciences : an official journal of the Society of Toxicology* vol. 164,1 (2018): 39–49. doi:10.1093/toxsci/kfy076

Kharrazian, Datis. "The potential roles of bisphenol A (BPA) pathogenesis in autoimmunity." *Autoimmune diseases* 2014 (2014).

Kindgren, Erik, Carlos Guerrero-Bosagna, and Johnny Ludvigsson. "Heavy metals in fish and its association with autoimmunity in the development of juvenile idiopathic arthritis: a prospective birth cohort study." *Pediatric Rheumatology* 17 (2019): 1–9.

Domingo, José L., and Martí Nadal. "Human exposure to per-and polyfluoroalkyl substances (PFAS) through drinking water: A review of the recent scientific literature." *Environmental research* 177 (2019): 108648.

Zhang, Limin et al. "Perfluorooctane sulfonate alters gut microbiota–host metabolic homeostasis in mice." *Toxicology* vol. 431 (2020): 152365. doi:10.1016/j.tox.2020.152365

Lamichhane, Santosh, et al. "Impact of exposure to per-and polyfluoroalkyl substances on fecal microbiota composition in mother–infant dyads." *medRxiv* (2022): 2022–12.

Wang, Wei, et al. "Perfluoroalkyl substances exposure and risk of polycystic ovarian syndrome related infertility in Chinese women." *Environmental pollution* 247 (2019): 824–831.



Butyflam Coated

Butyrate is a short-chain fatty acid produced by the intestinal bacteria through fermentation of non-digestible fibers. Butyflam Coated delivers bio-available levels of butyrate in our intestines to guarantee immune tolerance and avoid excessive inflammation or auto-immune reactions.

indication	Neuroinflammation Immune modulating (T reg + IL-10 anti-inflammation) Remodeling intestinal barrier function
dosage	3 x 2 caps per day
packaging	180 coated caps per container
composition (amount per 6 caps)	Butyrate – 3000 mg

References

Butyflam Coated



- Donohoe, Dallas R., et al. "Microbial regulation of glucose metabolism and cell-cycle progression in mammalian colonocytes." *PloS one* 7.9 (2012).
- Donohoe, Dallas R., et al. "The microbiome and butyrate regulate energy metabolism and autophagy in the mammalian colon." *Cell metabolism* 13.5 (2011): 517–526.
- Sanderson, Ian R. "Short chain fatty acid regulation of signaling genes expressed by the intestinal epithelium." *The Journal of nutrition* 134.9 (2004): 2450S–2454S.
- Arpaia, Nicholas, et al. "Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation." *Nature* 504.7480 (2013): 451–455.
- Chang, Pamela V., et al. "The microbial metabolite butyrate regulates intestinal macrophage function via histone deacetylase inhibition." *Proceedings of the National Academy of Sciences* 111.6 (2014): 2247–2252.
- Vinolo, Marco AR, et al. "Suppressive effect of short-chain fatty acids on production of proinflammatory mediators by neutrophils." *The Journal of nutritional biochemistry* 22.9 (2011): 849–855.
- Usami, Makoto, et al. "Butyrate and trichostatin A attenuate nuclear factor κ B activation and tumor necrosis factor α secretion and increase prostaglandin E2 secretion in human peripheral blood mononuclear cells." *Nutrition research* 28.5 (2008): 321–328.
- Kim, Ha-Jung, et al. "Clinical efficacy and mechanism of probiotics in allergic diseases." *Korean journal of pediatrics* 56.9 (2013): 369.
- Marchix, Justine, Gillian Goddard, and Michael A. Helmrath. "Host-gut microbiota crosstalk in intestinal adaptation." *Cellular and molecular gastroenterology and hepatology* 6.2 (2018): 149–162.
- Cao, Anthony T., et al. "Th17 cells upregulate polymeric Ig receptor and intestinal IgA and contribute to intestinal homeostasis." *The Journal of Immunology* 189.9 (2012): 4666–4673.
- Keubler, Lydia M., et al. "A multitier model: colitis lessons from the interleukin-10-deficient mouse." *Inflammatory bowel diseases* 21.8 (2015): 1967–1975.
- Wilson, Mark S., et al. "Colitis and intestinal inflammation in IL10^{-/-} mice results from IL-13R α 2-mediated attenuation of IL-13 activity." *Gastroenterology* 140.1 (2011): 254–264.
- Matt, Stephanie M., et al. "Butyrate and dietary soluble fiber improve neuroinflammation associated with aging in mice." *Frontiers in immunology* 9 (2018): 1832.
- Bourassa, Megan W., et al. "Butyrate, neuroepigenetics and the gut microbiome: can a high fiber diet improve brain health?" *Neuroscience letters* 625 (2016): 56–63.
- Huuskonen, Jari, et al. "Regulation of microglial inflammatory response by sodium butyrate and short-chain fatty acids." *British journal of pharmacology* 141.5 (2004): 874–880.
- Roda, Aldo, et al. "A new oral formulation for the release of sodium butyrate in the ileo-cecal region and colon." *World Journal of Gastroenterology: WJG* 13.7 (2007): 1079.

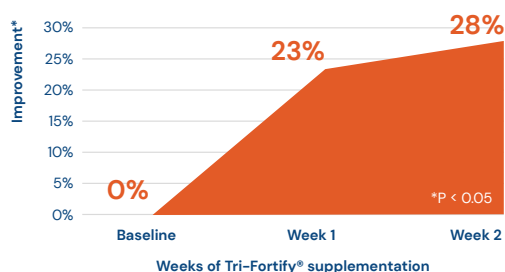
Tri-Fortify Watermelon® or Orange®



indication	Detoxification with glutathione in high bioavailable formulation Powerful antioxidant on tissue level and brain level Natural Killer Cell support	
dosage	1 teaspoon (1 pack) per day, away from food	
packaging	236 ml per tube or 20 packs per box	
composition (based on 1 teaspoon = 5 cc or 1 pack)	Glutathione Liposomal Vitamin C	450 mg 50 mg

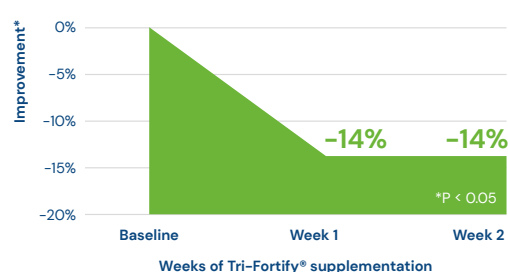
Glutathione levels

Increase in red blood cell levels (Erythrocytes)



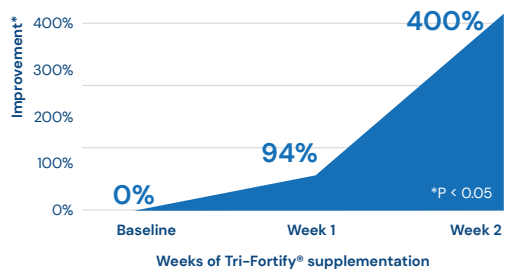
Oxidative stress markers

Oxidized / Reduced GSH

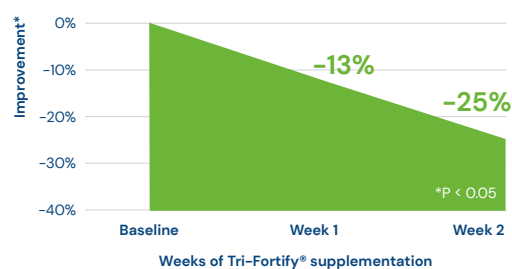


Immune function

Natural Killer Cell activity



Lipid Peroxidation (Reduced Cellular Membrane Oxidation)



Published research : Sinha, R., Sinha, I., Calcagnotto, A., Trushin, N. Oral supplementation with liposomal glutathione elevates body stores of glutathione and markers of immune function. Eur J Clin Nutr. 2018 Jan;72(1):105-111.

Tri-Fortify Watermelon® or Orange®



Research on liposomal glutathione

Clinical research presented at the 2015 ILADS medical conference demonstrated **red blood cell absorption, increased natural killer cell function & reduced oxidative stress**.

This study, conducted at Penn State University, measured the glutathione. The product is formulated to promote healthy intracellular glutathione levels and natural killer cell function.

Healthy patients with glutathione levels at the low end of the normal range were included in the study. The patients were divided into two groups, one taking one serving (450 mg) per day and the other taking two servings (900 mg) per day. Both groups performed fairly close to one another so the results shown below are the combined impact, with a p-value of <0.05.

Research results

After two weeks of daily oral liposomal glutathione supplementation:

- **Red blood cell levels** (erythrocytes) increased 28% over the baseline.
- **Natural Killer Cell function** increased by 400% over the baseline.
- **Oxidative stress**, (as measured by lipid peroxidation) decreased by 25%

Published research : Sinha, R., Sinha, I., Calcagnotto, A., Trushin, N. Oral supplementation with liposomal glutathione elevates body stores of glutathione and markers of immune function. Eur J Clin Nutr. 2018 Jan;72(1):105-111.

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