DETOXIFICATION: ENVIRONMENTAL TOXINS

The incidence of chronic disease and ill health is increasing across all age groups globally, with the concentration and number of toxic compounds in the environment having been identified as an important contributing factor.[1] Primary exogenous environmental toxins include heavy metals, persistent organic pollutants, solvents and plasticisers.[1] It is estimated that over 60,000 different chemicals are now in use, with 6.5 billion pounds of chemicals released into the air per year in the US alone.[1] A growing body of research indicates that excessive exposure to environmental toxins results in metabolic damages and significant disruption to body functions, with many strong correlations being shown between toxic load and disease burden.[1]

Table 1: Key environmental toxins

Toxic heavy metals	Toxic heavy metals are major environmental pollutants, mostly due to industrialisation, with lead, mercury, cadmium and arsenic being the most important metal toxins for human health. Toxic metals can affect health in a variety of ways including increased production of free radicals and oxidative stress, enzyme poisoning, direct DNA damage, endocrine disruption and mitochondrial or cell wall damage.[1]
Persistent organic pollutants (POPs)	Persistent organic pollutants (POPs) are compounds designed for specific chemical, physical or biological effects, as well as for resistance to environmental degradation. Examples include pesticides, herbicides and industrial chemicals.[1] Polychlorinated dibenzo-para-dioxins (dioxins) and polychlorinated dibenzofurans (furans) and dioxin-like polychlorinated biphenyls (PCBs) also fall under this broader category.[2] POPs are lipophilic in nature and bio-accumulate in human and animal tissue and bio-magnify in food chains, thus increasing their concentration and toxicity in the environment.[1] Toxic manifestations of POPs are often seen in the liver and other organs.[1] POPs have also been shown to interfere with blood sugar regulation, cause DNA and mitochondrial damage, trigger epigenetic changes, promote inflammation and disrupt methylation pathways.[1]
Bisphenol A (BPA) and phthalates	Bisphenol A (BPA) is an industrial component commonly used in the synthesis of polycarbonate plastics, epoxy resin and other polymer materials and is ubiquitous in the environment due to its mass production and widespread applications.[4] BPA can enter the body via the digestive and respiratory tract and through the skin. BPA is regarded as an endocrine disruptor and has oestrogen-like and anti-androgen effects, causing damage to different tissues and organs, including the reproductive, immune, neuroendocrine, hepatic and renal systems.[3] Phthalates are chemicals used to make plastics more flexible and as solubilising agents for fragrances in health and beauty products.[4] The primary source of exposure to phthalates are found in the dust of homes, personal care products, solid plastic products used in the home and plastic-covered foods.[1] Phthalates have been associated with infertility, low testosterone, allergies, autism, mood disorders, reduced cognition, diabetes and obesity.[4]

Organic solvents and volatile organic compounds (VOCs)	Organic solvents are carbon-based substances capable of dissolving or dispersing one or more other substances. Many classes of chemicals are used as organic solvents, including aliphatic hydrocarbons, aromatic hydrocarbons, amines, esters, ethers, ketones and nitrated or chlorinated hydrocarbons.[4] Organic solvents can be carcinogens, reproductive hazards and neurotoxins.[4] Volatile organic compounds (VOCs), including toluene, benzene, styrene and xylene, are produced commercially from coal and petroleum sources. They are rapidly absorbed via inhalation, skin and oral ingestion, and are distributed in the blood and fatty tissues, including the brain.[4] VOCs are associated with an increased risk of neurological, respiratory and reproductive disorders, as well as damage to liver function.[1,4] Styrene is produced from ethylbenzene and then used in numerous manufacturing processes, including the production of polystyrene as well as several other commonly used substances.[4]

Strategies to support detoxification of environmental toxins

Supporting detoxification from environmental toxins is a continual process and depends on an individual's health as this influences their ability to detoxify and eliminate toxins.[1]

Toxins are expelled from the body through a variety of organ systems and supporting these can aid in detoxification, or reduce the damaging effects of environmental toxins:[1]

- The liver is the primary organ for detoxifying lipophilic chemicals and metabolises and supports excretion of many potentially harmful environmental contaminants.[1]
- The gastrointestinal (GI) system is the primary avenue by which the external environment, including toxins, antigens and xenobiotics interact with the body, and can potentially enter into circulation.[1] Increasing the excretion of fat via stools has been shown to be an effective way of eliminating toxic load.[1] The gastrointestinal tract also plays a vital role in maintaining immune homeostasis and houses the largest number of immune cells in the body.[7]
- The kidneys are another important organ for toxin elimination to aid urinary excretion.[1]
- Antioxidant support is also important as environmental toxins increase the pro-oxidant load, escalating the risk of oxidative damage to cells, leading to greater risk of disease, both acute and chronic.[1]

Figure 1: Management of environmental toxin exposure

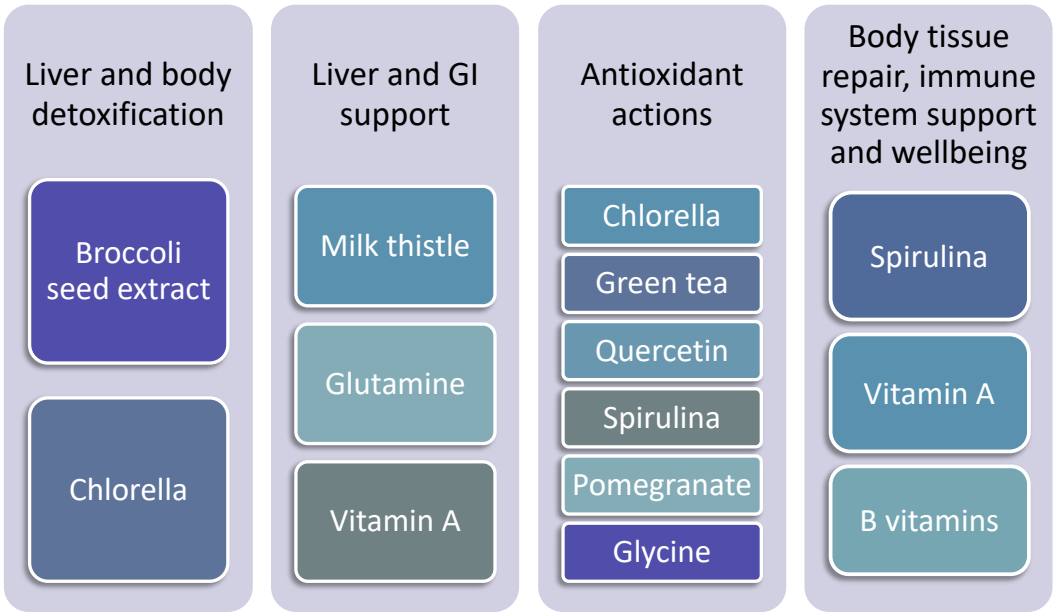

Table 2: Reducing the health impact of environmental toxins

Nutrients	Actions and evidence
Broccoli seed extract	• Broccoli seed extract supports liver detoxification pathways and a healthy liver function. Broccoli contains glucoraphanin, a potent natural inducer of phase II detoxification enzymes, as well as being an indirect, long-acting antioxidant.[8,9] Glucoraphanin is subsequently enzymatically transformed to sulforaphane, in the GI tract by myrosinase-producing gut bacteria.[8] • Sulforaphane helps to balance phase 1 and phase II detoxification.[8] It regulates phase 1 CYP450 enzymes activity and increases the action of phase II enzymes, such as glutathione-S-transferase to support the glucuronidation pathway.[8,9]. Sulforaphane also supports natural defences against oxidative stress via indirect mechanisms.[8,9]
Chlorella	• Chlorella is a source of chlorophyll, and numerous other nutrients, fibre, vitamins D2, B6, B12, folate and vitamin K, as well as iron, copper and magnesium.[9,10] Chlorella is also naturally rich in antioxidants including beta-carotene, ascorbic acid, alpha-tocopherol and zeaxanthin.[9,10] • Human research has reported that chlorella supplementation (6.3 g daily) increases plasma levels of vitamin C, alpha-tocopherol and improves antioxidant enzyme activity.[11] • Chlorella supports immune system function. In a 12-week placebo controlled human study, chlorella supplementation (5 g daily) provided beneficial immunostimulatory effects that increased natural killer cell activity and elevated levels of gamma-interferon, interleukin-12 and interleukin 1β.[10,12] Chlorella also supports body detoxification of several environmental toxins: • Chlorella supplementation (6 g daily) may be effective in reducing dioxin levels, including dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), based on the findings of a small placebo-controlled study conducted in pregnant women.[13] The findings of another two small studies suggest that chlorella may reduce maternal transfer of dioxins to infants during breast-feeding.[14,15] Chlorella has also been shown to significantly inhibit gastrointestinal absorption of dioxins and promote their excretion in animal models.[10] • Chlorella has been shown to reduce levels of heterocyclic amines (HCA), according to a small human study.[16] Based on animal research, it appears that the chlorophyll constituent of chlorella traps heterocyclic amines and polycyclic aromatic hydrocarbons and promotes their elimination.[10] • Chlorella may have protective effects against acute hepatic injury caused by the solvent, carbon tetrachloride.[10] • Chlorella may also chelate and promote excretion of heavy metals, such as mercury.[10]
Glutamine	• Glutamine is the primary amino acid for intestinal cells and plays a key role in supporting gastrointestinal repair, regeneration of intestinal mucosa and intestinal barrier integrity.[1,17-19] • Glutamine has been shown to promote enterocyte proliferation, regulate intercellular tight junction integrity and intestinal barrier function, suppress pro-inflammatory signalling pathways, and protect cells against apoptosis and cellular stresses during normal and pathologic conditions.[1,17] Glutamine also contributes to detoxification of ammonia and systemic acid-base balance.[17] • Experimental models suggest that a healthy intestinal barrier function may help to reduce intestinal absorption of toxic metals such as arsenic, cadmium, lead and mercury and mitigate their toxicity.[19] Glutamine depletion may however result in increased intestinal permeability.[20]
Glycine	• Glycine is an amino acid that may contribute towards reducing oxidative stress as it plays an important role in balancing the redox reactions in the human body.[9,21] • Glycine has been shown to have a protective effect against both lead and cadmium toxicity in animal models, which was attributed to its antioxidant effects.[21]

Green tea	• Green tea is a source of antioxidants, with green tea constituents having been shown to increase endogenous antioxidant defenses (SOD, CAT, GSH), help reduce free radicals and protect against damage caused by oxidative stress.[9, 22-26] • A review of 16 RCTs concluded that green tea supplementation improves total antioxidant capacity and increases antioxidant status in adults.[22] It has been proposed that this may decrease the risk and progression of chronic diseases related to higher levels of oxidative stress.[22] Green tea and its constituents may have protective properties against environmental pollutants: • Green tea has been shown to reduce markers of oxidative stress in smokers,[27] and to have protective actions against nicotine, a volatile alkaloid that is the primary toxic component of cigarettes.[25] • Green tea may protect against lead and cadmium toxicity due to the antioxidant activity of its active constituents - catechins.[25,28] Preliminary research suggests that catechins inhibit cadmium absorption and reduce their effect on bone health, as well as having protective effects against lead-induced damage to their liver cells.[28] Green tea may also have metal-chelating actions.[25] • Green tea and its constituents have been shown to have protective actions against para-nonylphenol, and deltamethrin (a synthetic insecticide).[25] • Green tea has been shown to protect against benzene-induced toxicity and oxidative stress in human research.[29] • Epigallocatechin gallate (EGCG) from green tea may also help eliminate toxic load by inhibiting pancreatic lipase activity, which increases faecal fat excretion and thereby elimination of fat-soluble toxicants.[1]
Milk thistle	• Milk thistle is traditionally used in Western herbal medicine to support liver function, as a liver protectant and to help relieve digestive disturbances.[30] • Therapeutic actions are attributed to silymarin, which is a complex of flavonolignans, of which silybin is the most active component.[9] Silymarin is reported to have hepatoprotective, gastroprotective, renal protective, antioxidant, anti-inflammatory and immunomodulatory effects and to enhance liver detoxification and support liver regeneration.[1,9,31] • The antioxidant actions of silymarin protect the liver from the free radical damage produced during metabolism of alcohol and other toxins.[32,33] Milk thistle also increases synthesis of glutathione, helps prevent glutathione depletion in the liver and increases the rate of liver tissue regeneration.[1] According to animal research, milk thistle and its constituents may protect the liver, kidneys and other organ systems against several environmental toxins:[33] • Silibinin has been shown to reduce metal-induced organ damage caused by arsenic, cadmium, mercury and lead.[33] These effects are attributed to its metal-chelating and antioxidant effects.[33] • Silymarin has been shown to have protective effects against pesticides such as malathion, an organophosphate insecticide and paraquat, a toxic herbicide that causes oxidative stress and is associated with human morbidity.[33] Silymarin has been shown to provide both protective and curative effects against immunotoxicity caused by chlorpyrifos, an organophosphorus insecticide.[34] • Silymarin appears to reduce hepatotoxicity induced by the organosulfur toxin, thioacetamide.[35] • Silymarin has been shown to protect against the hepatotoxic effects of the solvent, carbon tetrachloride.[33] • Silymarin has been shown to have hepatoprotective actions against bisphenol A (BPA).[36] • *In vitro* research has also reported that silymarin has protective effects against other environmental toxins including benzo(a)pyrene.[37,38]

Pomegranate	• Pomegranate has demonstrated antioxidant activity in human, animal and *in vitro* studies.[9] • Pomegranate hulls are also a source of ellagic acid. Preliminary research suggests that ellagic acid may have protective actions against several environmental toxins associated with an increased risk of reproductive damage including phthalates, arsenic and polychlorinated biphenyl.[25]
Quercetin	• Quercetin is a flavonoid with significant antioxidant properties and has the ability to scavenge highly reactive oxygen species and inhibit lipid peroxidation.[39-41] • Quercetin is also known to have anti-inflammatory properties, which is attributed in part to the interplay between oxidative stress and inflammation.[39] Reactive oxygen species (ROS) are involved in the occurrence of oxidative stress, as well as in the promotion of inflammatory processes via activation of transcription factors such as NF-κB and activator protein (AP)-1 which induce the production of cytokines such as TNF-alpha. Consequently, scavenging ROS can prevent both the occurrence of oxidative stress and help reduce inflammation.[39] Quercetin has potential to help address environmental toxins based on animal and *in vitro* research: • Quercetin attenuates reproductive toxicity induced by the organic pesticide lambda cyhalothrin.[42] • Quercetin has been shown to ameliorate oxidative stress caused by bisphenol-A (BPA) and consequent damage to various body systems and tissues.[40,43] • Quercetin is a natural chelator of heavy metals.[26,41] Research reports that quercetin scavenges free radicals induced by arsenic exposure when given alone or in combination with a thiol chelator.[26] Research suggests quercetin may help to complex with and remove cadmium,[41] and combat cadmium-induced neurotoxicity [41,44] and renal toxicity.[45] • *In vivo* studies have shown that quercetin has antioxidant and hepatoprotective activity against acute hepatic injury caused by tertiary butyl hydrogen peroxide.[41]
Spirulina	• Spirulina has antioxidant, anti-inflammatory and immunomodulatory properties, and has been described as a functional food.[9,46,47] It is a rich source of nutrients which support general health as well as body tissue repair. Spirulina is a source of proteins, complex carbohydrates, polysaccharides, lipids, polyunsaturated fatty acids, minerals and vitamins A, B-complex, E, K and beta-carotene, carotenoids, chlorophyll, and phycobiliproteins including C-phycocyanin, allo-phycocyanin and phycoerythrin.[9] • Spirulina supports the innate immune system and promotes activity of natural killer cells and has also been shown to improve growth of beneficial intestinal microbiota.[47,49] Spirulina has been shown to increase concentrations of immunoglobulin A (IgA) in the gastrointestinal tract and improve GI defences, as well as to inhibit IgE-mediated histamine release and production of TNF-alpha.[9,47,48] Spirulina has also been shown to have prebiotic activity.[50] • Clinical research reports that spirulina prevents skeletal muscle damage under conditions of exercise-induced oxidative stress, stimulates production of antibodies and regulates expression of cytokine-encoding genes to induce immunomodulatory and anti-inflammatory responses.[46] • Spirulina may help protect against detrimental health effects of environmental and occupational toxins due to its anti-inflammatory, antioxidant, metal-chelating and immunomodulating actions.[9, 47,49] • In a human study, spirulina (250 mg) plus zinc (2 mg), twice daily for 16 weeks, increased urinary excretion of arsenic and reduced chronic arsenic poisoning. In this study, the combination of spirulina and zinc removed 47% of arsenic from scalp hair.[51] In another small human study, spirulina (10 g daily) prevented arsenic-induced cellular toxicity in a population exposed to drinking water contaminated with arsenic, with 60% of participants in the spirulina treatment group showing improvements.[52] • Spirulina may reduce the toxic effects of heavy metals due to its antioxidant activity.[49,53,54] In animal studies, spirulina has been shown to reduce the effects of metal toxicity on male reproductive health,[25,55] as well as to ameliorate arsenic-induced damage to female reproductive health.[56]

	• Spirulina has been shown to remove chromium, cadmium, nickel, copper, lead and other metal ions from contaminated water. The mechanism involves adsorption of the heavy metal to the surface of the blue-green algae, followed by transport into the algal cell.[9,57,58] • Spirulina reduced the effects of the insecticide, bifenthrin and benzo(alpha)pyrene on male reproductive health in animal models.[25] • Spirulina has protective actions against carbon tetrachloride and the insecticide, deltamethrin, in animal studies.[49]
Vitamin A	• Vitamin A supports the health and function of the immune system.[9,59] Retinoic acid is required to maintain sufficient levels of natural killer cells, and may increase the production of cytokines, such as interleukin 1 (IL-1). Additionally, B lymphocyte growth, differentiation and activation are dependent on retinol.[9] • Vitamin A also supports mucous membrane integrity,[9] which supports immune defence mechanisms.[60] The mucosal innate immune system acts as both a physical and an immunological barrier, playing a key role in protection against pathogens and other toxins.[60] • Laboratory studies have shown that many contaminants, including polychlorinated biphenyls (PCBs), polychlorinated dibenzo-para-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), can disrupt vitamin A physiology and alter the distribution of its essential metabolites.[61] • Vitamin A influences cell growth and proliferation.[9,62] Retinoic acid has been shown to inhibit oestrogen-induced proliferation of many cell types *in vitro* and in animal research, especially relating to BPA.[62] Retinoids are stored in the liver where they help to initiate xenobiotic elimination of BPA.[62]
Vitamin B6	• Vitamin B6 supports numerous biological functions which play a key role in maintaining good health.[59] • Vitamin B6 deficiency may enhance sensitivity towards cadmium and lead toxicity. Conversely, supplementation may reduce toxicity of these heavy metals, according to human and animal studies.[28] • Increased intake of vitamin B6 (pyridoxine) and other B-group vitamins has been reported to significantly increase urinary arsenic excretion, according to the findings of a large study conducted in a population experiencing chronic exposure to arsenic through contaminated water.[63] • Vitamin B6 also plays a central role in endogenous redox reactions through its effects on the glutathione peroxidase system and may indirectly help reduce oxidative stress.[64]
Vitamin B9 (folate)	• In adults exposed to arsenic, folic acid or folate supplementation reduces blood arsenic concentration and improves urinary arsenic excretion, according to the findings of a Cochrane review.[65] • Arsenic methylation reduces the risk of arsenic toxicity. Folate plays a critical role in methylation reactions, and low folate status, whether due to poor dietary intake or genetic variations, impedes arsenic methylation and urinary excretion and exacerbates or increases the risk of arsenic toxicity.[65] • Low folate levels are also associated with increased plasma homocysteine levels, which is a risk factor for cardiovascular disease and cognitive impairment.[9,66] Some evidence suggests that exposure to toxic heavy metals such as lead, cadmium and mercury increases plasma homocysteine levels.[66]
Vitamin B12	• Vitamin B12 is required for homocysteine metabolism.[9,66] Re-methylation of homocysteine to methionine requires folate and the active methylcobalamin form of vitamin B12 as a cofactor.[66] • Evidence suggests that raised homocysteine levels may lead to impaired endothelium-dependent vasodilation due to reduced nitric oxide activity, vascular endothelial cell damage, increased oxidation and the deposit of low-density lipoproteins (LDL) in arteries, increased platelet adhesiveness and activation of the clotting cascade.[9] • Some evidence showed that exposure to the toxic heavy metals lead, cadmium and mercury may interfere with homocysteine metabolism, resulting in increased plasma homocysteine levels.[66] It has been recommended that in subjects exposed to excessive heavy metals, homocysteine levels should be monitored and managed, such as through use of folate and vitamin B12 supplementation.[66]

**References available on request*