



The Health Implications of Plastic Bioaccumulation and the Potential to Enhance Biotransformation Using Herbal Medicine and Nutritional Supplements

Carina Harkin*

University College Cork (UCC), Ireland

Abstract

Plastic is ubiquitous with recent studies having highlighted that plastic is in bottled and tap water and food products including honey, sugar and beer. The 3 to 10 tonnes are estimated to fall on Paris per year. Plastic has recently been shown to be a vector for heavy metal contamination and to cross the Blood Brain Barrier (BBB). Global concern regarding the health implications is mounting, with the World Health Organization (WHO) having conducted a risk assessment review of plastics. Whilst knowledge gaps exist, we remain to eat, drink and inhale plastic without knowing what harm it is potentially causing. This paper discusses the scale of global microplastic contamination, the sources and routes of microplastic contamination including inhaling and ingesting plastics, and the potential health implications of plastic bioaccumulation. Biotransformation research into is a relatively new field in the early stages of evolution. This paper looks at how plastic is biotransformed and the potential pharmacognostical approaches that have the potential to maximize plastic biotransformation. This paper discusses what is known about how plastic is biotransformed by Phase I cytochrome P450 enzyme group modification and Phase II glutathione, sulphation, glucuronidation and glycine conjugation pathways, and the importance of supporting endogenous antioxidants to assist plastic biotransformation. The paper specifically discusses what is known about how ingested plastics including Phthalates and Bisphenol-A (BPA), and inhaled plastics, including dioxins and furans are biotransformed by these processes and what herbal medicine and nutritional supplementation may maximize plastic biotransformation and address plastic bioaccumulation.

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*Correspondence:

Carina Harkin, University College Cork (UCC), Cara Health, Galway, 24 Waterlane, H91VH9X, Ireland, Tel: 00353 834 735 746;

E-mail: info@carahealth.com

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Keywords: Plastic bioaccumulation; Plastic biotransformation; Microplastic; Nanoplastic; Microplastics in drinking-water; Microplastic exposure and impacts on human health; Complementary and Alternative Medicine (CAM); Herbal medicine; Nutritional supplements; Pharmacognosy

Abbreviations

Acetyl-Co A: Acetyl Coenzyme A; ALS: Amyotrophic Lateral Sclerosis; ADHD: Attention Deficit Hyperactivity Disorder; BPA: Bisphenol-A; BBB: Blood Brain Barrier; CDG: Caclium D-Glucarate; CAT: Catalase; CDC: Centers for Disease Control and Prevention; CD: Cluster of Differentiation; CoA: Coenzyme A; CAM: Complementary and Alternative Medicine; CuZn-SOD: Copper-Zinc SOD; CYP450: Cytochrome P450; DDT: Dichlorodiphenyltrichloroethane; DINP: Diisononyl phthalate; DIDP: Diisodecyl Phthalate; EDCs: Endocrine Disrupting Chemicals; FSAI: Food Safety Authority of Ireland; GSH: Glutathione; GPx: Glutathione Peroxidase; GR: Glutathione Reductase; GST: Glutathione S-Transferase; GST family: Glutathione S-Transferases; GMIT: Galway Mayo Institute of Technology; GnRH: Gonadotropin-Releasing Hormone; HSE: Health Service Executive; HPA: Hypothalamic-Pituitary Axis; LGBTQI: Lesbian, Gay, Bisexual, Transgender, Queer or Questioning and Intersex; bZIP: Leucine Zipper; Mn-SOD: Manganese SOD; MFO: Mixed-Function Oxidase Enzyme; NAC: N-acetylcysteine; NHANES: National Health and Nutrition Examination Survey; NATs: N-Terminal Acetyl Transferases; NDDs: Neurodevelopmental Disorders; NDGs: Neurodegenerative Diseases; Nrf2: Nuclear Factor Erythroid-2-Related Factor 2; PCOS: Polycystic Ovary Syndrome; POPs: Persistent Organic Pollutants; PTS: Persistent Toxic Substances; PAHs: Polycyclic Aromatic Hydrocarbons; PCBs: Polychlorinated Biphenyls; PETE: Polyethylene Terephthalate; SAM-e: S-Adenosyl-L-Methionine; SFN: Sulforaphane; SOD: Superoxide Dismutase; TcR: T-Cell Receptor; TCDD: Tetrachlorodibenzo-p-Dioxin; TEQ: Toxic Equivalent; T2D: Type 2 Diabetes; US: United States; UDP: Uridine Diphosphate; UDPGA: Uridine

Diphosphate Glucuronic Acid; UGT: UDP Glucuronosyltransferase; WHO: World Health Organization

Introduction

Plastic is a crude oil product a non-renewable energy source

The largest global consumer of oil is the United States (US) military, consuming 100 million barrels of oil per year [1,2]. Regardless of the ever increasing abundance of evidence of fossil fuelled climate change and billions in subsidies for alternative technologies, global oil consumption will reach 100 million barrels per day, double what it was 50 years ago, with no sign of abating [3]. The US alone uses 330 million barrels of oil per year in plastics production alone, three times the US military use [4].

The scale of microplastic contamination is staggering

An estimated 8 million tons of plastic enters our oceans each year. Microplastics are omnipresent in sea waters, from deep sea ocean sediments to the polar caps [5].

Microplastics contain and absorb toxic chemicals

Microplastics are a vector for heavy metal contamination from the marine environment [6,7]. Microplastics attract harmful pathogenic bacteria in sewage and contain and absorb toxic chemicals. More than 50 Persistent Organic Pollutants (POPs), in particular Polychlorinated Biphenyls (PCBs) and Polycyclic Aromatic Hydrocarbons (PAHs) are found in the five most common types of plastic [8]. POPs are also called Persistent Toxic Substances (PTS) [9].

Plastic in tap water globally

Billions of the global populations are drinking water contaminated by plastic particles with 83% of samples found to be polluted. The US contamination rate was the highest at 94%. The next highest rates were found in Lebanon and India. The lowest contamination rates at 72% were found in Germany, France and the UK. Each 500 ml sample was found to contain on average 4.8 plastic fibers in the US and 1.9 plastic fibers in Europe [10,11]. In 2017 an Irish study sampling tap and well water found microplastic contamination present in a small amount; "We don't know what the health impact is and we should follow the precautionary principle so we can find out what the real risks are," said Dr. Anne Marie Mahon marine microplastic scientist from Galway-Mayo Institute of Technology (GMIT) [12].

Plastic in bottled water globally

The Orb study (Orb Media is a US based non-profit journalism organization) tested 259 bottles from 19 locations in 9 countries. Eleven different brands were found to contain on average 325 plastic pieces of microplastic in every liter of water. Nile red dye was used to fluoresce the particles of plastic in the water. This technique was developed by Dr. Andrew Mayes of University of East Anglia. Nestle Pure Life was found to have the highest levels of microplastic contamination with as many as 10,000 pieces of microplastic per liter. Only 17 of the 259 plastic water bottles tested were free of plastic [13]. The contamination is thought to be in part derived from the packaging and bottling processes [14]. Polypropylene plastic, the same plastic used to make bottle caps was the most common plastic piece found. Polypropylene (recycling number 5) is considered a safe non-leaching plastic. The study was not published in a journal, nor has been peer reviewed. A second unrelated study of stuff study in the US looked at 19 bottled water brands and found plastic pieces to be widely distributed. Bottled water was found to have twice the

amount of microplastic than tap water [15].

Plastic water bottles

Plastic water bottles are made from Polyethylene Terephthalate (PETE recycling code 1). This symbol is normally also found in soft drinks. PETE does not contain BPA or phthalates but studies have found that the Endocrine Disrupting Chemical (EDC) antimony, a toxic phthalate 'plasticizer' used to make plastics flexible, leaches from PET bottles placed in the heat for prolonged periods of time [16]. Reusable plastic drinking water bottles are or more generally now, were made from polycarbonate (recycling code 7). Polycarbonate is manufactured from BPA [17]. Investigations show in some cases, BPA-free PETE containers might leach estrogen-like chemicals [18].

Sources of Environmental Microplastic

Washing acrylic, polyester and nylon

Plastic derived, acrylic, polyester and nylon persist in the environment. Synthetic clothing set to landfill breaks down to plastic microfiber pollution that contaminates ground and surface water. The estimates are that one truck load of clothes goes to landfill every second and one truckload of plastic enters the sea every second. Scientists estimate that plastic will outweigh fish in the sea by 2050 [19]. Acrylics are by far the most polluting with the average load of household washing shedding 750,000 microplastic fibers per load. This is 5 times greater than is shed by polyester cotton. Drying synthetics in clothes dryer vents microplastic into the air [20,21].

Burning plastics

Burning plastics releases endocrine disrupting cancer causing dioxins and furans the most toxic chemicals known to humankind [22].

Human sludge

A 2017 study for the Environmental Protection Agency (EPA) co-written by Dr. Anne Marie Mahon from the Marine from the Freshwater Research Centre, Galway-Mayo Institute of Technology (GMIT) identified sludge spreading and the washing of plastic by the recycling industry as significant sources of environmental microplastic. Estimates are that at least a billion microplastic fibers are spread on Irish farmland annually [23].

Plastic in teabags

A recent study estimated that steeping one plastic containing teabag in 95°C water temperature releases 11.6 billion microplastic fibers and 3.1 billion nanoplastic fibers into each cup of tea. The composition of particles released was found to be nylon and PETE matching the original teabags. Scientists conducted a toxicity assessment which showed that exposure to the plastic particles leaching from the teabags caused harmful behavioral and developmental health effects and that these were dose-dependent [15]. Non-biodegradable plastic containing teabags have been added to the municipal compost for decades.

Extent of Plastic Contamination in Food and Air

Plastic in beer, salt and well water

German scientists tested 24 beer brands, honey and sugar and discovered microplastic fibers were found in all those tested. The study concluded the average person is ingesting 5,800 particles of plastic annually, with largest proportion (88%) of this contamination being attributed to tap water consumption [10].

The 3 and 10 tons of plastic fibers fall on Paris per year

Microplastics and nanoplastic fibers in our sea evaporate to provide a source of both outdoor and indoor air pollution. A study examining microplastic atmospheric fallout estimated an annually fallout of between 3 and 10 tons of microplastic on Paris [24].

Evidence of Plastic in Humans

Biomonitoring programs

Biomonitoring human studies are evolving and useful for investigating exposure to phthalates, BPA and other chemicals. The US Center for Disease Control and Prevention (CDC) conducts a yearly National Health and Nutrition Examination Survey (NHANES). One of the objectives of the NHANES is to assess the number of POPs detected in high concentrations in the population. NHANES results indicate it is common for people to have low and high concentrations of a number POPs. In relation to plastic POPs the NHANES study measures [25];

- Serum dioxins, furans and PCB
- Urinary phthalates and BPA

One NHANES study found 91 POPs analyzed in blood samples and concluded that one tenth of the US population may have ≥ 10 POPs each at concentrations in the top decile [26].

Plastic in human stools

Nine different plastics have been found in all human stools tested [27].

Latest cause for concern

Nanoplastic passes the BBB in fish: Science has shown that nanoparticles or nanoplastic passes the Blood Brain Barrier (BBB) in fish resulting in behavioral disorders and brain damage [28]. Most of the information we understand about the detrimental health effects of come from studies conducted in fish. The WHO is only just now looking into the health effects of plastics in humans. The WHO launched a health review on microplastic in drinking water to review the very scarce evidence which they described as scarce, to highlight evidence gaps, establish an agenda for research and allow for a more informed and thorough risk assessment.

Endocrine Disrupting Chemicals (EDCs) and Human Health

EDCS include organochlorine pesticides, PCBs, BPA, phthalates, dioxins and furans [29]. Nearly 800 EDCs have the capacity to interfere with hormone receptors, hormone synthesis and hormone conversion. The three strands of evidence that give rise to concerns over EDCs include a high incidence and increasing rates of endocrine related disease in the population, numerous observations of endocrine-related sequelae in the fauna and laboratory tests linking EDCs with detrimental human health outcomes [30].

EDC diseases and disorders

Infertility in males and females: BPA can interfere with the hypothalamic-pituitary-ovarian/testicular axis (HPA), to increase hypothalamic Gonadotropin-Releasing Hormone (GnRH) secretion and promote pituitary proliferation [31].

Low sperm count: Up to 40% of young males have a low sperm count.

Genital malformations: Cryptorchidism and hypospadias in

baby boys. Sharp increase in children born with intersex variation IV: Ambiguous genitalia, hermaphrodite, pseudohermaphroditism etc.

Sharp increase in the incidence of gender dysphoria, transgender and gender neutral: It must be noted that Lesbian, Gay, Bisexual, Transgender, Queer or Questioning and Intersex (LGBTQI) existed pre-industrial revolution.

Precocious puberty in young girls: This is a risk factor for breast cancer.

Adverse pregnancy outcomes: Including premature birth and low birth weight.

Neurobehavioral disorders:

- Cognitive, motor and sensory deficits.
- Neurological Impairments (NIs) including neuropathies.
- Neurodevelopmental Disorders (NDDs) including Attention Deficit Hyperactivity Disorder (ADHD) and autism.
- Neurodegenerative Diseases (NDGs) including Parkinson's and Alzheimer's disease, and Amyotrophic Lateral Sclerosis (ALS).
- POPs, BPA and phthalates exposure is associated [32].

Hormone dependent tumors: Including breast, endometrial, ovarian, prostate, testicular and thyroid.

Metabolic disorders:

- Polycystic Ovary Syndrome (PCOS).
- Metabolic syndrome: Evidence shows that EDCs may contribute to the evolution of the obesity pandemic and metabolic disorders including Type 2 Diabetes (T2D). Lipophilic POPs are linked to T2D [33,34].

Atopic disorders: Phthalates and BPA exposure are linked to the pathogenesis of allergies, asthma and atopic dermatitis [35].

Lowered vaccine response

A Faroe Island study, where diets may include PCB contaminated whale blubber, on the vaccine response of two birth cohorts, suggested that PCB exposure may reduce the immune response to childhood immunizations [36]. Another study on the vaccine response of Dutch preschool children measured humoral immunity by antibody levels for mumps, measles, and rubella after primary vaccination and found that prenatal PCB exposure measured as a higher dioxin Toxic Equivalent (TEQ) was associated with an increased number of lymphocytes, T cells, and Cluster Of Differentiation (CD) CD8+ (cytotoxic), CD4+ (memory), T-Cell Receptor (TcR) and CD3(+)(activated) T cells and lower antibody levels to mumps and measles at preschool age [37].

Health implications of microplastic according to the WHO

It was recently widely reported that the WHO report referred to found no evidence of a current danger from microplastic [38]. It must be noted that WHO report is about microplastic in drinking water only. Microplastic is as previously described universal. The WHO report in fact identified knowledge gaps and made recommendations in respect to monitoring and management of microplastic in the environment in order to better assess health risks posed to humans and to better inform appropriate management actions [39].

Microplastic Mitigation

BPA and phthalates and dioxin-like PCBs are ingested plastic toxins. Dioxins and furans are inhaled plastic toxins produced when plastic is burned. Dioxins, furans and dioxin like PCBs are abbreviated names for a family of chemicals with similar toxicity and shared chemical characteristics. Dioxins and furans are also known as Tetrachlorodibenzo-P-Dioxin (TCDD). TCDD was the contaminant in Agent Orange, the notorious herbicide used during the Vietnam War [40].

Mitigate environmental exposure

Mitigation strategies include avoiding drinking water in plastic bottles and using an end stage water filtration unit to filter public drinking water supplies. Avoiding plastic incineration will also mitigate exposure. Phthalates are most typically found in industrial solvents and lubricants, additives in the textile industry, in pesticides, floorings, roofing, wall coverings, cables, clothing, packaging materials, personal-care products and toys [41]. BPA is used in the manufacture of epoxy and polycarbonate plastic resins. Products derived from BPA are commonly used in safety equipment, protective coatings inside tin cans and as composites and sealants in dentistry. BPA exposure primarily results from the ingestion of contaminated food [42].

Plastic Biotransformation

Measuring the burden of human exposure

BPA-glucuronide has terminal half-life of <6 h, is rapidly excreted in urine and can be used as a biomarker of exposure to BPA. Exposure to these phthalates can be assessed using custom synthesized reference standards of specific oxidized metabolites of Diisononyl Phthalate (DINP) and Diisodecyl Phthalate (DIDP). Phthalates are quickly metabolized and excreted in urine [43].

What happens after exposure?

After ingestion, nanoplastic reaches the systemic blood circulation, distributes to a variety of body compartments and penetrates cells [44]. Plastic too large to pass through the gut wall still present a risk to human health as it is a vector for hydrophobic POPs and EDCs of a smaller molecular size that are capable of penetrating cells [45].

Understanding biotransformation of plastic

Research into human biotransformation and elimination systems is relatively new and continues to evolve.

Phase I and II Liver Detoxification Pathways

Liver detoxification is a misnomer as Phase I and II liver detoxification pathways also occur in kidney, intestine, lung, skin, prostate, and brain. In medical terminology toxicity is referred to as bioaccumulation and detoxification is referred to as biotransformation. Very little attention is being paid to human exposure to environmental chemicals and POPs. Many toxic chemicals are fat-soluble, making them difficult to excrete. The P450 enzyme system turns lipophilic toxins into hydrophilic chemicals that are then able to be readily excreted in urine, bile and sweat. In the event that fat lipophilic toxins are not made hydrophilic, lipophilic chemicals have a high affinity for fat tissues and cell membranes and can accumulate. These lipophilic toxins may be stored for years and released during times of exercise, stress or fasting [46].

Bisphenol A

Accumulation of BPA induces cytochrome P450 (CYP450) enzyme activities [47]. In humans BPA is mainly metabolized by CYP2C and inhibits CYP17 activity [48]. BPA is rapidly metabolized by glucuronidation conjugation [49]. BPA is also metabolite of sulphation and glutathione conjugation [50]. Transferases including sulfotransferases, Glutathione-S-Transferases (GSTs) are also involved in BPA conjugation [51]. A fraction of absorbed BPA may distribute to body storage site (s) such as adipose tissue, followed by a slow, low-level release of BPA into the bloodstream [43].

Phthalates

Phthalates undergo a series of phase I hydrolysis and phase II conjugation reactions and are subsequently excreted in feces and urine [52]. Phthalates induce CYP450 specifically CYP4 enzymes [53,54]. Phthalates are a metabolite of glucuronidation, glycine and sulphation conjugation [55-57].

Dioxins, Furans and dioxin-like PCBs

People vary in capacity to eliminate TCDD. The elimination rate is much faster at higher than lower levels [58]. TCDD induces a number of CYP450 enzymes systems [59]. Accumulation of POPs, dioxins and furans induce cytochrome P450 enzyme systems [59-61]. Dioxins, furans and PCBs are metabolites of either glucuronidation or sulphate conjugation, mainly in the liver and excreted in the bile or urine [62]. Dioxins undergo glutathione sulphation, glucuronidation and glycine conjugation phase II reactions [40,63-65].

Phase I Modification

Phase I reactions occur in the liver and are catalyzed by CYP450 Mixed Function Oxidase enzyme (MFO) chemical reactions including oxidation, reduction, hydrolysis, cyclization, decyclization (cyclization and decyclization have no relevance in plastic biotransformation) and hydroxylation. MFO enzymes inhabit hepatocytes membranes.

Modification pathways involve

- Oxidation is process of being oxidized (combining chemically with oxygen/rust).
- Reduction involves gaining of electrons by one atom involved in reaction.
- Hydrolysis involves a chemical breakdown of a compound due to a water reaction.
- Hydroxylation involves introduction of a hydroxyl group (-OH).

Induction of Phase I (over activity)

Certain metabolites of Phase I reactions are readily excreted. Many Phase I products are not rapidly eliminated and undergo subsequent Phase II reactions. If not adequately supported or when excessive POPs exist, Phase I is induced producing high levels of damaging free radicals. In cases whereby these reactive molecules are not readily metabolized by Phase II conjugation this can result in damage to proteins, RNA, and DNA. Phase I can turn a nontoxic molecule into a toxic (mutagenic/carcinogenic) molecule hence contribute to early ageing and cancer pathogenesis [66,67].

Phase II Conjugation

In the hepatocytes, toxic metabolites undergo biotransformation

and are conjugated using Glutathione (GSH), sulphate, glucuronic acid or glycine. These reactions are catalyzed by a large group of broad-specificity transferases, the most important being glutathione S-transferases (GSTs). Phase II conjugation reactions transform a fat soluble toxin into water-soluble chemical that can be excreted in bile, urine and sweat.

Major Phase II detoxification conjugation pathways include

Glutathione (GSH): Co-factor: Glutathione and endogenous antioxidants; Glutathione S-Transferase (GST), Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx), Glutathione Reductase (GR) and Catalase (CAT) [68]. The Glutathione S-Transferases (GST family) are activated through cysteine, glutamic acid and glycine to make glutathione. BPA, dioxins, furans and PCBs undergo glutathione conjugation [50,63].

Sulphation: Co-factor: 3'-phosphoadenosine-5'-phosphosulfate (endogenously synthesized) Sulphation renders a xenobiotic less active but sometimes activates xenobiotics. Sulphation is involved in detoxification and hormone regulation. BPA, phthalates, dioxins, furans and PCBs undergo sulphation conjugation [50,56,57,62,64].

Glycine conjugation: Co-factor: Glycine is catalyzed by glycine N-acyltransferase. Glycine conjugation is an important metabolic pathway which allows for maintenance of sufficient Coenzyme A (CoA) levels. Phthalates, dioxins, furans and PCBs undergo glycine conjugation [56,57,65].

Glucuronidation: Co-factor: Uridine Diphosphate (UDP), UDP-Glucuronic Acid, Uridine Diphosphate Glucuronic Acid (UDPGA). β -glucuronidase breaks the chemical bonds formed during the detoxification processes, thus allowing the recirculation of toxins [69]. BPA, phthalates, dioxins, furans and PCBs undergo glucuronidation conjugation [40,49,55,56,70].

Phase II conjugation pathways not associated with plastic biotransformation

Methylation: Co-factor: S-Adenosyl-L-Methionine (SAM-e). Heavy metals, arsenic, mercury, cadmium and DNA/RNA are biomethylated [71].

Acetylation: Co-factor: Acetyl-CoA (Acetyl Coenzyme A). N-Terminal Acetyltransferases (NATs) catalyze N-terminal Acetylation. NATs act as both onco-proteins and tumour suppressors in human cancers [72].

Pharmacognostical objectives: Inhibit CYP450, Induce conjugation.

Andrographis/Chuan Xin Lian/King of the bitters andrographis paniculata: Contains the diterpenolactones andrographolide, 14-deoxy-11-dehydroandrographolide, 14-deoxy-11-oxoandrographolide, 5-hydroxy-7,8,2',3'-tetramethoxyflavone, neoandrographolide, paniculide-A, paniculide-B and paniculide-C inhibit CYP450 [73].

Bupleurum/Chai Hu Bupleurum falcatum: Contains saikosaponins which inhibit CYP450, specifically CYP1A2, CYP2C9 and CYP3A4. The flavonoids and steroids, rutin, isoquercetin, isorhamnetin, quercetin, β -sitosterol, α -spinasterol, daucosterol and α -spinasterol glucoside inhibit CYP450 specifically CYP3A4 [73,74].

Burdock/Nui Bang Zi Arctium Lappa: Contains lignans lappaol

F, diartigenin and arctigenin which inhibit CYP450 [73].

Centella/Ji Xue Cao Centella asiatica: Contains triterpenes madecassic acid, brahmic acid and asiatic acid which inhibit CYP450 [73].

Eleutherococcus/Ci Wu Jia Eleutherococcus senticosus: Contains glycans eleutherans A, B, C, D, E, F, and G and eleutheroside C which inhibit CYP450 [73].

Scut Baic/Huang Qin Scutellaria baicalensis: Contains iridoid glycosides baicalein, wogonin and oroxylin which inhibit CYP450 [73].

Inhibit Phase I and Induce Phase II

Milk thistle Silybum marianum: Contains flavonolignans silymarin, silybin A, silybin B, isosilybin A, isosilybin B, silychristin, isosilychristin, silydianin, and one flavonoid taxifolin which significantly inhibit CYP450 [75,76]. Silymarin restores depleted GSH to assist in glutathione conjugation [77]. Milk thistle is rich in phytochemicals that can modulate UDP-Glucuronosyltransferase (UGT) Phase II enzymes [78].

Globe artichoke/Yang Ji Cynara scolymus: Contains the flavonoid luteolin which inhibits CYP450 specifically CYP 3A4 and CYP3A5 [79]. Contains the hydroxycinnamic acid cynarin which promotes glucuronidation conjugation. Artichoke is a formidable antioxidant thus inhibiting toxin-induced glutathione reserve depletion [80].

Barberry/Fu Niu Berberis vulgaris: Contains the benzyloquinoline alkaloid berberine which inhibits CYP450 [81]. Berberine specifically increases endogenous antioxidants, Glutathione Peroxidase (GPx) and Superoxide Dismutase (SOD), both Copper-Zinc SOD (CuZn-SOD) and Manganese SOD (Mn-SOD) to assist glutathione conjugation [82].

Turmeric/Jiang Huang Curcuma longa: Contains the diaryl heptanoid curcumin which inhibits CYP450 whilst inducing Phase II [83,84]. Curcumin assists glutathione conjugation by restoring toxin-induced depleted GSH reserves [85]. Curcumin induces nuclear factor-erythroid-2-related factor 2 (Nrf2), a leucine zipper (bZIP) protein that regulates expression of antioxidant proteins thereby protecting against oxidative damage triggered by injury and inflammation [86]. Nrf2 regulates Phase-II enzymes. Curcumin modulates Phase I and Phase II enzymes [87].

Supplements

N-Acetylcysteine: N-Acetylcysteine (NAC) is a precursor to L-cysteine that results in GSH elevation biosynthesis. NAC increases GSH conjugation and is a powerful antioxidant/free radical scavenger [88].

Caclium D Glucarate: Caclium D-Glucarate (CDG) inhibits β -glucuronidase, therefore enhances glucuronidation conjugation [89]. CDG is in cruciferous vegetables or vegetables from the Brassicaceae family.

Sulforaphane: Sulforaphane (SFN), an isothiocyanate found in cruciferous vegetables inhibits CYP450 and induces Phase II [90].

Hesperidin: Hesperidin, a flavanone found in citrus fruits (oranges, lemons, pomelo), inhibits CYP450 and induces Phase II [91].

Grapefruit: Grapefruit contains the compound naringenin which inhibits CYP450 and induces Phase II [54].

Conclusion

As the awareness of microplastic contamination grows, so too does global concern regarding the health implications. While reproductive and developmental abnormalities linked to EDC exposures in fauna are documented, the human health effects associated with full exposure of the whole gamut of endocrine-disrupting chemicals in the environment is yet to be determined, with the WHO report identifying knowledge gaps. While some in the medical fraternity dismiss detoxification as quackery, bioaccumulation exists and is measurable. Research on human biotransformation and elimination systems and pharmacognostical approaches that support biotransformation of POPs, more specifically PCBs, BPA, phthalates, dioxins and furans, is urgently needed. In addition, mitigation strategies should be widely encouraged. CAM therapists who specialize in bioaccumulation and biotransformation may have a valuable role to play in detoxifying harmful EDCs in human beings. Further research into this area is warranted and the results and applications of this research have the potential to reduce endogenous EDCs and POPs in humans and thus, have the potential to lead to improved global health outcomes.

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