MOSAIC DIAGNOSTICS
Formerly Great Plains Laboratory

HOW THE BODY METABOLIZES ENVIRONMENTAL TOXICANTS

Review 95 references at MosaicDX.com/resource/how-the-body-metabolizes-environmental-toxicants-metabolite-chart

PHTHALATES

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
1-5. Phthalates	1-5. Diethylphthalates Di-n-butyl Phthalate (DBP) Di(2-ethylhexyl) Phthalate (DEHP)	Yes	**1.9-3.5 hours** for most metabolites.[1]	***Phase I:*** Undergoes hydrolysis to form monoester phthalates, catalyzed by CES1 and CES2.[2] Then, it undergoes oxidative metabolism in the liver via CYP2C9, CYP2C19, and CYP3A4.[2] ***Phase II:*** Metabolites are conjugated with glucuronic acid and excreted via urine.[3]	**Sweating** can help facilitate elimination.[3] May negatively impact **mitochondrial** function and the human **microbiome**[4,5] (may consider **Organic Acid Test (OAT)** and **Comprehensive Stool Analysis (CSA)**). Supporting microbiome with **probiotics** may decrease toxicity.[5]

BISPHENOLS

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
6. Bisphenol A (BPA)	6. Bisphenol A (BPA)	Yes	Oral exposure: 4.4-8.4 hrs [6] Dermal exposure: 11.1-30.2 hrs [7]	***Phase I:*** involves CYP450, specifically SPY3A4 [11] ***Phase II:*** Primarily involves conjugation reactions, including glucuronidation (UGTs) and sulfation (SULTs).[9,10]	
7. Bisphenol S (BPS)	7. Bisphenol S (BPS)	Yes	6.8-7.9 hours	***Phase I:*** CYP3A4 and 2C9 are involved in hydroxylation but phase 2 is the primary metabolic pathway of BPS.xi ***Phase II:*** Glucuronidation and sulfation of BPS facilitate detoxification and excretion via urine.[12] These metabolites are generally considered inactive (related to endocrine disruption) compared to the parent compound.[13]	

VOC'S

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
8. Xylene	8. 2-3-4-Methylhippuric acid (2,3,4-MHA)	Yes	**Rapid initial phase: about 1 hour. Slower phase: 20-58 hours depending on the tissue.**	**Phase I:** Involves methyl hydroxylation in the liver via CYP2E1 to form MHA.[14] Then, excreted via urine.[15]	Absorbed primarily through **inhalation,** with about **60% retained in the lungs.**[16] Can cause **mitochondria damage** and deplete **glutathione** (may consider **OAT**).[17]
9.Styrene/ Ethylbenzene	9. Phenylglyoxylic Acid (PGO)	Yes	**1-10 hours**	***Styrene Phase I:*** Oxidation via **CYP2E1** to form **styrene-7,8-oxide (SO)**.[18] Then converted by **mEH** to form **phenylglyoxylic acid, mandelic acid**, and **hippuric acid**. ***Styrene Phase II:*** SO undergoes **glutathione (GSH)** conjugation to form **PGO**.[19] ***Ethylbenzene:*** Hydroxylation by **CYP2E1**, mainly, but can also go through **CYP1A2** and **CYP2B6** to a lesser degree.[20]	Variability in **CYP2E1** activity for ethylbenzene metabolism may be due to **genetic polymorphisms** and environmental factors.[9] **Mandelic** and **Hippuric** acids are intermediates of Styrene's breakdown in the body. (may consider OAT).[21]
10. Benzene	10. N-Acetyl Phenyl Cysteine (NAP)	Yes	**8 hours**	***Phase I:*** Oxidation of benzene to benzene oxide (BO) via CYP2E1. BO can be further metabolized through several pathways.[22] ***Phase II:*** GSH conjugation results in formation of NAP.[23]	**Green tea** can decrease oxidative stress from exposure.[22] **Broccoli sprouts** can enhance detoxification.[23] Can be stored in bone marrow, causing a decrease in **red blood cells and anemia**.[24]
11. Acrylonitrile (ACN)	11. N-Acetyl (2-Cyanoethyl) Cysteine (NACE)	Yes	**3-18 hours**	***Phase I:*** Oxidation through ACN to CNEO via CYP2E1 and then further degrade to cyanide.[25] ***Phase II:*** ACN conjugates with glutathione to form NACE and excreted via urine.[26]	**Fasting** may enhance CYP2E1-mediated oxidative metabolism of ACN and decrease liver GSH levels, potentially increasing the toxicity of exposures.[27]
12. 1-bromopropane (1-BP)	12. N-Acetyl (Propyl) Cysteine (NAPR)	Yes	**6-8 hours**	**1-BP** Undergoes two pathways: CYP450-mediated oxidation and GSH conjugation. ***Phase I:*** CYP2E1 oxidation leads to formation of 1-bromo-2-propanol and bromoacetone. ***Phase II:*** Conjugate with GSH to form various mercapturic acids including NAPR.[30]	Elimination can be accelerated with **GSH (reduced)** oral, IV, transdermal or **N-acetylcysteine (NAC)** supplementation. Observed effects on neurotransmitter metabolites (**DOPAC, HVA**, and **5HIAA**)[32] (may consider **OAT**).
13. 1,3 butadiene	13. N-Acetyl (3,4-Dihydroxybutyl) Cysteine (NADB)	Yes	**Variable; few minutes - few hours**	***Phase I:*** Oxidation by CYP2E1 and 2A6 (at increased concentrations) to form epoxide, diepoxybutane, and epoxybutane diol. ***Phase II:*** Several transformations involving GSH conjugation, forming mercapturic acids to be excreted via urine.[31]	Inhalation is the predominant route of exposure; with **half exhaled** and the other half metabolized via liver and excreted in urine.[32] **GSTT1 polymorphisms** influence metabolism and detoxification.[33]
14. Ethylene Oxide (EO), Vinyl Chloride (VC)	14. 2-Hydroxyethyl Mercapturic Acid (HEMA)	EO: somewhat more hydrophilic, VC: Yes	**EO: 42-84 minutes; VC: 1-2 days**	***EO Phase I:*** Metabolized by CYP2E1 in liver, then undergoes hydrolysis by epoxide hydrolase. ***EO Phase II:*** Conjugation with GSH mediated by Glutathione S-transferase (GST).[34] ***VC Phase I:*** Also metabolized by CYP2E1 to form CEO and CAA, and undergoes hydrolysis. ***VC Phase II:*** GSH conjugation.[35 36]	**EO** can convert to ethylene glycol, then to **oxalic acid** (may consider **OAT**).[37, 38] **VC** can cross the placenta and enter the **fetus**.[30]

PARABENS

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
15-18. Parabens	**15-18. Methylparaben (MeP) Ethylparaben (EtP) Propylparaben (PrP) Butylparaben (BuP)**	Yes	Depends on the specific type of paraben but ranges from **7.7-20.3 hrs**[41] **MeP: 12.2 hrs, EtP: 12.0 hrs, Prp: 9.3 hrs.**[42]	**Phase I:** Parabens undergo hydrolysis by carboxylesterases (CES1 mainly in the liver and CES2 is more active in the skin).[43 44] **Phase II:** Primarily undergo glucuronidation via UGTs.[45]	

PESTICIDES

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
19. Atrazine Mercapturate	**19. Atrazine Mercapturate**	Yes	**12 hrs**[46]	***Phase I:*** Involves CYP450, particularly CYP1A2, leading to the formation of various metabolites.[47] ***Phase II:*** Key enzymes in phase II are GST, specifically the pi class GST (hGSTP1-1).[48]	hGSTP1-1 catalyzes the conjugation of atrazine with glutathione, forming atrazine mercapturate, which is then excreted.[48]
20. 2,4-Dichlorophenoxyacetic Acid (2,4-D)	**20. 2,4-Dichlorophenoxyacetic Acid (2,4-D)**	No, but chemical modifications can increase its lipophilicity	**11.6 hours from plasma and 17.7 hours for urinary excretion.**	Metabolism of **2,4-D** is minimal and largely excreted as the unchanged parent compound – about **82% unchanged** and **12% is excreted as a conjugate.**[49]	**2,4-D** can form reactive metabolites, such as **2,4-D-CoA**, which can covalently bind to proteins, potentially contributing to **hepatotoxicity**. This binding occurs through the formation of **2,4-D-S-acyl-glutathione (2,4-D-SG)** thioester and covalent adducts with human serum albumin.[50]
21. Pyrethroids	**21. 3-Phenoxybenzoic Acid (3PBA)**	Yes	**5-8 hours with 88% excreted in urine within 24 hrs of exposure.**	***Phase I:*** Undergo extensive metabolism in humans through hydrolysis and oxidation. **CES1** and **CES2** play a role in hydrolysis.[51] Many **CYP450** enzymes, but especially **CYP2C19**, exhibit highest intrinsic clearance of pyrethroid metabolites.[52] ***Phase II:*** Metabolites formed in Phase I reactions, such as **3PBA,** may undergo further conjugation with amino acids, sulfates, and sugars.[53]	**Pyrethroids** have the ability to influence **glucose metabolism** and lipid oxidation.[54] (may consider **OAT**)
22. Organophosphates (OPs)	**22. Diethylphosphate (DEP)**	Yes	**Depends on type of organophosphate but can vary between 18 hours - 7 days.**	**Bioactivation:** Involves oxidative desulfuration to form **oxon metabolites** – potent AChE inhibitors. Key CYP enzymes involved are **CYP2B6, 2C19, and 1A2.**[55] Detoxification: Involves dearylation of OPs to form inactive metabolites. **CYP2C19 and 3A4** significantly contribute to this pathway, but **2C19** is involved in detoxification of **chlorpyrifos** and **diazinon**, converting them to non-toxic metabolites.[56]	**Lactobacillus rhamnosus** may help decrease toxic OP pesticide exposure by passive binding.[57] **Lactobacillus casei** may decrease OP-induced cytotoxicity.[58] **Paraoxonase 1 (PON1)** is involved in the hydrolysis of certain OPs. Polymorphisms in this enzyme can increase susceptibility to toxicity.[59] **PON1** can be upregulated by **pomegranate juice**.[60]

OTHER

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
23. Triphenyl Phosphate (TPHP)	**23. Diphenyl Phosphate (DPP)**	Yes	**7.6 days**	***Phase I:*** TPHP undergoes O-dearylation to form DPP and hydroxylation to produce mono- and dihydroxylated metabolites with CYP1A2 and 2E1 playing a significant role.[61] ***Phase II:*** hydroxylated metabolites undergo conjugation, such as glucuronidation, to form glucuronide conjugates to be more water-soluble.[62]	
24. Acrylamide	**24. 2N-Acetyl (Carbomethyl) Cysteine (NAE)**	No	**2.5 hours for initial phase and longer second phase extending up to several days.**	**Glutathione Conjugation:** acrylamide + GSH forms NAE, which is then excreted in the urine. This accounts for the majority of acrylamide metabolism (75-86%).[63] **Oxidation to Glycidamide:** this is done via CYP2E1. Glycidamide is considered a more reactive and potentially genotoxic metabolite. [64]	The relative contribution of these pathways can vary based on individual factors such as genetic polymorphisms in **CYP2E1** and **GSTs**, as well as external factors like diet and exposure levels.[65] GSH precursors such as NAC and methionine have been shown to protect against the cytotoxicity of AA and other metabolites.[66]
25. Perchlorate	**25. Perchlorate (PERC)**	No	**8 hours**	Perchlorate is not metabolized in the human body. Instead, it is absorbed and excreted largely unchanged. [65] It competitively inhibits the sodium-iodide symporter in the thyroid gland, blocking iodide intake (which is essential for thyroid hormone synthesis). [66]	In breastfed infants, there is evidence suggesting **bifidobacteria** in the gut may reduce perchlorate via perchlorate reductase.[69]
26. Oxybenzone	**26. Oxybenzone (OBZ)**	Yes	**1.5 - 2 days[70]**	***Phase I:*** oxybenzone (BP-3) is primarily metabolized by CYP450 enzymes through hydroxylation and demethylation, producing BP-1 and BP-8.[71] ***Phase II:*** the hydroxylated metabolites are conjugated with glucuronic acid or sulfate, making them more water-soluble for excretion.[72]	Oxybenzone is a common ingredient in sunscreens and other personal care products. Its lipophilicity facilitates its penetration through skin and subsequent systemic absorption.[73]

Visit **MosaicDX.com/Test/TOXDetect-Profile** for references.