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. Various Metabolites	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.[4] May negatively impact **mitochondrial** function and the human **microbiome**[5,6] (may consider **Organic Acid Test (OAT)** and **Comprehensive Stool Analysis**) Supporting microbiome with **probiotics** may decrease toxicity.[7]

VOC'S

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
6. Xylene	6. Methylhippuric acid (2,3,4-MHA)	Yes	In the terminal phase for most metabolites, half-lives are from **30-38.5 hours**, and in the slow phase are about **20 hours**.[8,9]	***Phase I:*** Involves methyl hydroxylation in the liver via CYP2E1 to form MHA.[10] Then, excreted via urine.[11]	Absorbed primarily through inhalation, with about 60% being **retained in the lungs**.[12] Can cause **mitochondria** damage and deplete **glutathione**.[13] (may consider **OAT**)
7. Styrene/ Ethylbenzene	7. Phenyl-glyoxylic Acid (PGO)	Yes	**Styrene's** half-life in blood **62-82 minutes**.[14] **Ethylbenzene's** half-life from the first hour after exposure is **0.5 hours**.[15]	***Styrene Phase I:*** Oxidation via CYP2E1 to form styrene-7,8,-oxidate (SO).[16] Then converted by mEH to form phenylglyoxylic acid, mandelic acid, and hippuric acid.[16] ***Styrene Phase II:*** SO undergoes glutathione (GSH) conjugation to form PGO.[17] ***Ethylbenzene:*** Hydroxylation by CYP2E1, mainly, but can also go use CYP1A2 and CYP2B6 to a lesser degree.[16,18]	Variability in CYP2E1 activity for ethylbenzene metabolism may be due to **genetic polymorphisms** and environmental factors.[16] **Mandelic** and **Hippuric** acids are intermediates of Styrene's breakdown in the body.[19] (may consider **OAT**)

VOC'S

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
8. Benzene	8. N-Acetyl Phenyl Cysteine (NAP)	Yes	**8 hours** [20]	***Phase I:*** Oxidation of benzene to benzene oxide (BO) via CYP2E1. BO can be further metabolized through several pathways.[21] ***Phase II:*** GSH conjugation results in formation of NAP.[22]	**Green tea** can decrease oxidative stress from exposure.[23] **Broccoli sprouts** can enhance detoxification.[24] Can be stored in the bone marrow, causing a decrease in **red blood cells** and **anemia**.[25]
9. Acrylonitrile (ACN)	9. N-Acetyl (2-cyanoethyl) Cysteine (NACE)	Yes	**148 days** [26]	***Phase I:*** Oxidation through ACN to CNEO via CYP2E1 and then further degrade to cyanide.[27] ***Phase II:*** ACN conjugates with glutathione to form NACE and excreted via urine.[28]	**Fasting** may enhance CYP2E1-mediated oxidative metabolism of ACN and decrease liver GSH levels, potentially increase the toxicity of exposures.[29]
10. 1-bromo-propane (1-BP)	10. N-Acetyl (Propyl) Cysteine (NAPR)	Yes	**2-9 hours** and is highly dependent on P450 and GSH pathways.[30]	1-BP undergoes 2 metabolism pathways: CYP450-mediated oxidation and GSH conjugation.[31] ***Phase I:*** CYP2E1 oxidation leads to formation of 1-bromo-2-propanol and bromoacetone.[31] ***Phase II:*** Conjugate with GSH to form various mercapturic acids including NAPR.[31]	Elimination can be accelerated with **GSH** (reduced) oral, IV, Transdermal or **N-acetylcysteine** (NAC) supplementation.[32] Observed effects on various neurotransmitter metabolites **(DOPAC, HVA, and 5HIAA)**.[33] (may consider **OAT**)
11. 1,3 butadiene	11. N-Acetyl (3,4-dihydroxybutyl) Cystein (NADB)	Yes	**2-6 days** [34]	***Phase I:*** Oxidation by CYP2E1 and 2A6 (at increased concentrations) to form epoxybutene, diepoxybutane, and epoyxybutane diol.[35] ***Phase II:*** Undergoes several transformations involving GSH conjugation, leading to formation of mercapturic acids to be excreted via urine.[35]	Inhalation is the predominant route of exposure; with half **exhaled** and the other half metabolized via liver and excreted in the urine.[36] **GSTT1 polymorphisms** have been shown to influence metabolism and detoxification.[37]
12a. Ethylene oxide (EO), Vinyl chloride (VC)	12a. 2-Hydroxyethyl Mercapturic Acid (HEMA)	EO: somewhat more hydrophilic: Yes	**EO: 42 minutes** [38] **VC: 4 minutes -4 hours,** depending on dose and route of exposure.[39,40]	***EO Phase I:*** Metabolized by CYP2E1 in liver, then it undergoes hydrolysis by epoxide hydrolase.[41] ***EO Phase II:*** Conjugation with GSH mediated by Glutathione S-transferase (GST).[41] ***VC Phase I:*** Also metabolized by CYP2E1 to form chloroethylene oxide (CEO) and chloroacetaldehyde (CAA) and undergoes hydrolysis[42,43,44] ***VC Phase II:*** GSH conjugation.[42,43,44]	**EO** can be converted to ethylene glycol, and then be further metabolized to **oxalic acid** during the hydrolysis phase.[45] (may consider **OAT**) **VC** can cross the placenta and enter the **fetus**.[43]

VOC'S

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
12b. MTBE/ETBE	12b. 2-Hydroxy-isobutyric Acid (2HIB)	Yes	**2-19 hours** [46,47]	***Phase I:*** Metabolized through oxidative pathways mediated by CYP2A6.[48] Primary metabolic pathway involves conversion of MTBE to tert-butyl alcohol (TBA) and formaldehyde, and ETBE to TBA and acetaldehyde with CYP dependent demethylation.[49] Then, oxidation of TBA forms 2-HIB (and 2-methyl1,2-propanediol) to be excreted in urine.[50] ***Phase II:*** Other metabolites may go through additional glucuronide conjugation.[51]	Accelerated metabolism of TBA occurs with **oral exposure** compared to other routes of exposure.[51] Has been found in **fatty tissue** and **breast** milk of patients.[49]
12c. Acrolein	12c. 3-hydroxy-propylmercapturic acid (3-HPMA)	Moderately lipophilic	**10 hours** [52]	Primary metabolism via conjugation with GSH, leading to formation of GSH-acrolein adducts, which are then converted to mercapturic acid metabolites and excreted in urine.[53]	Can also undergo **Michael Addition Reactions** with nucleophiles such as **ascorbic acid** to be then further metabolized via the aldo-keto reductase enzymes (particularly AKR7A1) to form less toxic alcohols.[54] Can directly decrease **GSH** levels in the buccal cavity; sublingual GSH may be beneficial after recent exposures.[52] Can be converted to **malonic acid** by aldehyde dehydrogenase.[55] (may consider **OAT**)
12d. Propylene Oxide (PO)	12d. N-acetyl (2, hydroxypropyl) cysteine (NAHP)	Yes	**8 hours** during the rapid phase, and **5.3 days** in the slow phase.[56] Note, there is very limited data in humans.	***Phase I:*** Hydrolyzed via epoxide hydrolase (EH) in microsomes.[57] ***Phase II:*** GST in the cytosol. Both occurring primarily in the liver.[58]	**Glutathione** or **NAC** supplementation may accelerate detoxification.[58]

PESTICIDES

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
13. 2,4-Dichloro-phenoxyacetic acid (2,4-D)	13. 2,4-Dichloro-phenoxyacetic acid (2,4-D)	No, but chemical modifications can increase its lipophilicity	**11.6 hours** from plasma and **17.7 hours** for urinary excretion.[59]	Metabolism of 2,4-D is minimal and is largely excreted as the unchanged parent compound – about 82% unchanged and 12% is excreted as a conjugate.[60]	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.[61]
14. Pyrethroids	14. 3-Pheno-xybenzoic acid (3PBA)	Yes	**5-7 hours** [14]	***Phase I:*** Undergo extensive metabolism in humans through hydrolysis and oxidation. CES1 and CES2 play a role in hydrolysis.[64] Many CYP450 enzymes, but especially CYP2C19, exhibit highest intrinsic clearance of pyrethroid metabolites.[65] ***Phase II:*** Metabolites formed in phase I reactions, such as 3PBA, may undergo further conjugation with amino acids, sulfates, and sugars.[66]	Pyrethroids have the ability to influence **glucose metabolism**, and **lipid oxidation**.[67] (may consider **OAT**)
15. Multiple Organopho-sphates (OPs)	15. Diethyl-phosphate (DEP) and Dimethyl-phosphate (DMP)	Yes	Depends on type of organophos-phate but can vary between **3-30 hours**.[68,69]	***Bioactivation:*** involves oxidative desulfuration to form oxon metabolites – potent AchE inhibitors. Key CYP enzymes involved are CYP2B6, 2C19, and 1A2.[70] ***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.[71]	***Lactobacillus rhamnoses*** may help decrease toxic OP pesticide exposure by passive binding.[72] *Lactobacillus casei* may decrease OP induced cytotoxicity.[73] **Paraoxonase 1 (PON1)** is involved in the hydrolysis of certain OPs. Polymorphisms in this enzyme can increase susceptibility of toxicity.[74] PON1 can be upregulated by **pomegranate** juice.[75]

OTHER

PARENT COMPOUND	METABOLISM OF PARENT COMPOUND	LIPOPHILIC? YES/NO	HALF-LIFE	METABOLISM IN HUMANS	ADDITIONAL DETAILS
16. Triphenyl Phosphate (TPHP)	16. Diphenyl Phosphate (DPP)	Yes	The data in humans is lacking, but has been shown to be **1-2 days** in other animals.[76]	***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.[77] ***Phase II:*** Hydroxylated metabolites undergo conjugation, such as glucuronidation, to form glucuronide conjugates to be more water-soluble.[78]	**Cruciferous** vegetables, **quercetin**, green and black **teas**, **chicory root**, and **Astaxanthin** can all enhance CYP1A2 activity.[79]
17. Acrylamide	17. N-Acetyl (carbomethyl) Cysteine (NAE)	No	**3-4 hours** for initial phase and **10 hours** in the second phase.[80,81]	***Phase I:*** Oxidation to glycidamide is done via CYP2E1. Glycidamide is considered a more reactive and potentially genotoxic metabolite.[82] ***Phase II:*** Glutathione conjugation occurs with Acrylamide + GSH and forms NAE, which is then excreted in the urine. This accounts for the majority of acrylamide metabolism (75-86%).[83]	Contribution of these pathways can vary based on individual factors such as **polymorphisms** in CYP2E1 and GSTs, and external factors like **diet** and **exposure levels**.[84] GSH precursors such as **NAC** and **methionine** have been shown to protect against the cytotoxicity of the metabolites.[85]
18. Perchlorate	18. Perchlorate (PERC)	No	**8 hours** [86]	Perchlorate is not metabolized in the human body. Instead, it is absorbed and excreted largely unchanged.[87] It competitively inhibits the sodium-iodide symporter in the thyroid gland, blocking iodide intake (which is essential for thyroid hormone synthesis).[88]	In breastfed infants, evidence suggests **bifidobacteria** in the gut may decrease perchlorate via perchlorate reductase.[89]
19. Bisphenol S (BPS)	19. Bisphenol S (BPS)	Yes	**6-7 hours** [52]	***Phase I:*** CYP3A4 and 2C9 are involved in hydroxylation but phase 2 is the primary metabolic pathway of BPS.[91] ***Phase II:*** Glucuronidation and sulfation of BPS facilitate detoxification and excretion via urine.[92] These metabolites are generally considered inactive (related to endocrine disruption) compared to the parent compound.[93]	Studies have found increased levels of **neurotransmitters**, and **intestinal inflammation** markers, after exposures.[94] (may consider **OAT** and **CSA**) Bisphenol A, which is a very similar analog to BPS (both with 2 phenol groups on each side of a sulfonyl group) has been shown to be excreted through sweat; sauna therapy may be beneficial in elimination.[95]