

Table S3-1. Compound Discoverer processing settings for generating isotonitazene putative metabolites

Isotonitazene	
Phase I reactions	Deethylation ($-2C -5H \rightarrow +H$) Deisopropylation ($-3C -7H \rightarrow +H$) Desaturation ($-2H \rightarrow \emptyset$) Dihydrodiol formation ($\emptyset \rightarrow +2H +2O$) Nitro-reduction ($-2O \rightarrow +2H$) Oxidation ($\emptyset \rightarrow +O$) Oxidative deamination to alcohol ($-2H -N \rightarrow +H +O$) Oxidative deamination to ketone ($-3H -N \rightarrow +O$) Reduction ($\emptyset \rightarrow 2H$)
Phase II reactions	Acetylation ($-H \rightarrow +2C +3H +O$) Cysteine conjugation ($-H \rightarrow +3C +6H +N +2O +S$) Cysteine-Glycine conjugation ($-H \rightarrow +5C +9H +2N +3O +S$) Glucuronide conjugation ($-H \rightarrow +6C +9H +6O$) Glutathione conjugation ($-H \rightarrow +10C +16H +3N +6O +S$) Methylation ($-H \rightarrow +C +3H$) Sulfation ($-H \rightarrow +H +3O +S$)
Max number of dealkylations	3
Max number of phase II reactions	2
Max number of all steps	5
Adducts	$[M+H]^+$ $[M-H]^-$

Table S3-2. Compound Discoverer processing settings for generating metonitazene putative metabolites

Metonitazene	
Phase I reactions	Demethylation ($-C -3H \rightarrow +H$)
	Deethylation ($-2C -5H \rightarrow +H$)
	Desaturation ($-2H \rightarrow \emptyset$)
	Dihydrodiol formation ($\emptyset \rightarrow +2H +2O$)
	Nitro-reduction ($-2O \rightarrow +2H$)
	Oxidation ($\emptyset \rightarrow +O$)
	Oxidative deamination to alcohol ($-2H -N \rightarrow +H +O$)
	Oxidative deamination to ketone ($-3H -N \rightarrow +O$)
	Reduction ($\emptyset \rightarrow 2H$)
Phase II reactions	Acetylation ($-H \rightarrow +2C +3H +O$)
	Cysteine conjugation ($-H \rightarrow +3C +6H +N +2O +S$)
	Cysteine-Glycine conjugation ($-H \rightarrow +5C +9H +2N +3O +S$)
	Glucuronide conjugation ($-H \rightarrow +6C +9H +6O$)
	Glutathione conjugation ($-H \rightarrow +10C +16H +3N +6O +S$)
	Methylation ($-H \rightarrow +C +3H$)
	Sulfation ($-H \rightarrow +H +3O +S$)
Max number of dealkylations	3
Max number of phase II reactions	2
Max number of all steps	5
Adducts	$[M+H]^+$
	$[M-H]^-$

Table S3-3. Compound Discoverer processing settings for generating etodesnitazene putative metabolites

Etodesnitazene	
Phase I reactions	Deethylation ($-2C -5H \rightarrow +H$) Desaturation ($-2H \rightarrow \emptyset$) Dihydrodiol formation ($\emptyset \rightarrow +2H +2O$) Oxidation ($\emptyset \rightarrow +O$) Oxidative deamination to alcohol ($-2H -N \rightarrow +H +O$) Oxidative deamination to ketone ($-3H -N \rightarrow +O$) Reduction ($\emptyset \rightarrow 2H$)
Phase II reactions	Acetylation ($-H \rightarrow +2C +3H +O$) Cysteine conjugation ($-H \rightarrow +3C +6H +N +2O +S$) Cysteine-Glycine conjugation ($-H \rightarrow +5C +9H +2N +3O +S$) Glucuronide conjugation ($-H \rightarrow +6C +9H +6O$) Glutathione conjugation ($-H \rightarrow +10C +16H +3N +6O +S$) Methylation ($-H \rightarrow +C +3H$) Sulfation ($-H \rightarrow +H +3O +S$)
Max number of dealkylations	3
Max number of phase II reactions	2
Max number of all steps	5
Adducts	$[M+H]^+$ $[M-H]^-$

Table S3-4. Compound Discoverer processing settings for generating metodesnitazene putative metabolites

Metodesnitazene	
Phase I reactions	Demethylation ($-C -3H \rightarrow +H$) Deethylation ($-2C -5H \rightarrow +H$) Desaturation ($-2H \rightarrow \emptyset$) Dihydrodiol formation ($\emptyset \rightarrow +2H +2O$) Oxidation ($\emptyset \rightarrow +O$) Oxidative deamination to alcohol ($-2H -N \rightarrow +H +O$) Oxidative deamination to ketone ($-3H -N \rightarrow +O$) Reduction ($\emptyset \rightarrow 2H$)
Phase II reactions	Acetylation ($-H \rightarrow +2C +3H +O$) Cysteine conjugation ($-H \rightarrow +3C +6H +N +2O +S$) Cysteine-Glycine conjugation ($-H \rightarrow +5C +9H +2N +3O +S$) Glucuronide conjugation ($-H \rightarrow +6C +9H +6O$) Glutathione conjugation ($-H \rightarrow +10C +16H +3N +6O +S$) Methylation ($-H \rightarrow +C +3H$) Sulfation ($-H \rightarrow +H +3O +S$)
Max number of dealkylations	3
Max number of phase II reactions	2
Max number of all steps	5
Adducts	$[M+H]^+$ $[M-H]^-$