ShinyTPs: Curate transformation products from text mining results

Emma H. Palm, Parviel Chirsir, Jessy Krier, Emma L. Schymanski

Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101036756.

>300 000 compounds and mixtures

Wang et al. Environ. Sci. Technol. 2020, DOI:10.1021/acs.est.9b06379

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Transformation products

Lack analytical standards

Few reference spectra

Scattered transformation reaction information

Wang et al. Environ. Sci. Technol. 2020, DOI:10.1021/acs.est.9b06379

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Transformation reaction data sources

Transformation reaction data sources

PubChem Atrazine (Compound)

9.7 Transformations

31 items View More Rows & Details

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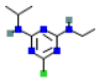
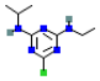
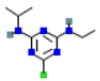
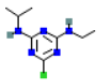
Predecessor	Predecessor Name	Successor	Successor Name	Transformation	Enzyme	Evidence DOI
	atrazine		6-deisopropyl atrazine	Environmental		10.1021/acs.est.1c0046
	atrazine		deethylatrazine	Environmental		10.1021/acs.est.1c0046
	atrazine		2-hydroxyatrazine	Environmental		10.1021/acs.est.1c0046
	Atrazine		Ammeline	Mammalian metabolism		10.5281/zenodo.3827

Krier et al. Environment International, 2022, DOI: 10.1016/j.envint.2021.106885

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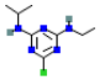
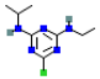
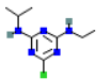
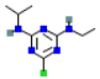
	atrazine		6-deisopropyl atrazine	Environmental		10.1021/acs.est.1c0046
	atrazine		deethylatrazine	Environmental		10.1021/acs.est.1c0046
	atrazine		2-hydroxyatrazine	Environmental		10.1021/acs.est.1c0046
	Atrazine		Ammeline	Mammalian metabolism		10.5281/zenodo.38274

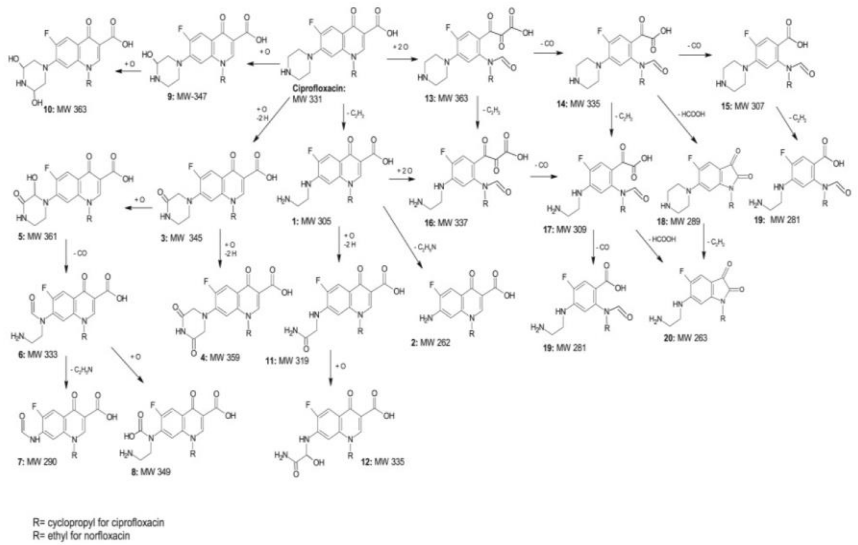
ELSEVIER

Water Research

Volume 46, Issue 16, 15 October 2012, Pages 5235-5246

Spectroscopic study of degradation products of ciprofloxacin, norfloxacin and lomefloxacin formed in ozonated wastewater

Chen Liu [a b c], Venkateswarlu Nanaboina [b], Gregory V. Korshin [b], Wenju Jiang [c]



Liu et al. Water Research, 2012, DOI: [10.1016/j.watres.2012.07.005](https://doi.org/10.1016/j.watres.2012.07.005)

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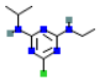
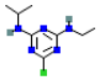
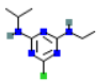
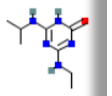
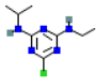
	atrazine	
	atrazine	
	atrazine	
	Atrazine	

PubChem C.I. Direct Brown 95 (Compound)

6 Pharmacology and Biochemistry

6.1 Metabolism/Metabolites

Benzidine derived azo dyes may be degraded metabolically in the gut or liver in man to free benzidine or monoacetylbenzidine. /Benzidine derived azo dyes/

IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: https://monographs.iarc.fr/ENG/Classification/index.php, p. V29 326 (1982)

▸ Hazardous Substances Data Bank (HSDB)

Rhesus monkeys excreted an average of 1.25% benzidine plus monoacetylbenzidine of the benzidine moiety in Direct Brown 95 in the urine after receiving two different doses by gavage, whereas gavage with pure benzidine yielded 1.45%.

IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work). Available at: https://monographs.iarc.fr/ENG/Classification/index.php, p. V29 326 (1982)

▸ Hazardous Substances Data Bank (HSDB)

Caution is also indicated by preliminary results from the NIOSH field studies showing that humans working with these same dyes /Direct Black 38, Direct Brown 95, and Direct Blue 6/ also excrete higher than expected levels of benzidine in their urine. Both laboratory and field studies indicate that these benzidine derived dyes can be metabolized to benzidine, which is present in the urine of animals and humans.

Zenz, C. Occupational Medicine-Principles and Practical Applications. 2nd ed. St. Louis, MO: Mosby-Yearbook, Inc, 1988., p. 710

▸ Hazardous Substances Data Bank (HSDB)

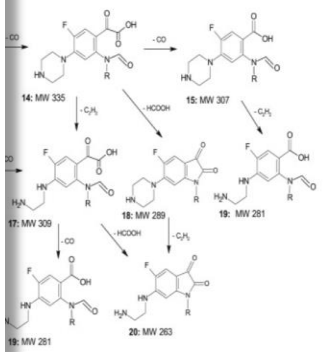
Water Research

Pages 5235-5246

tion products of

lomefloxacin

rshin [b], Wenju Jiang [c]



Krier et al. Environment International, 2022, DOI:10.1016/j.envint.2021.106885

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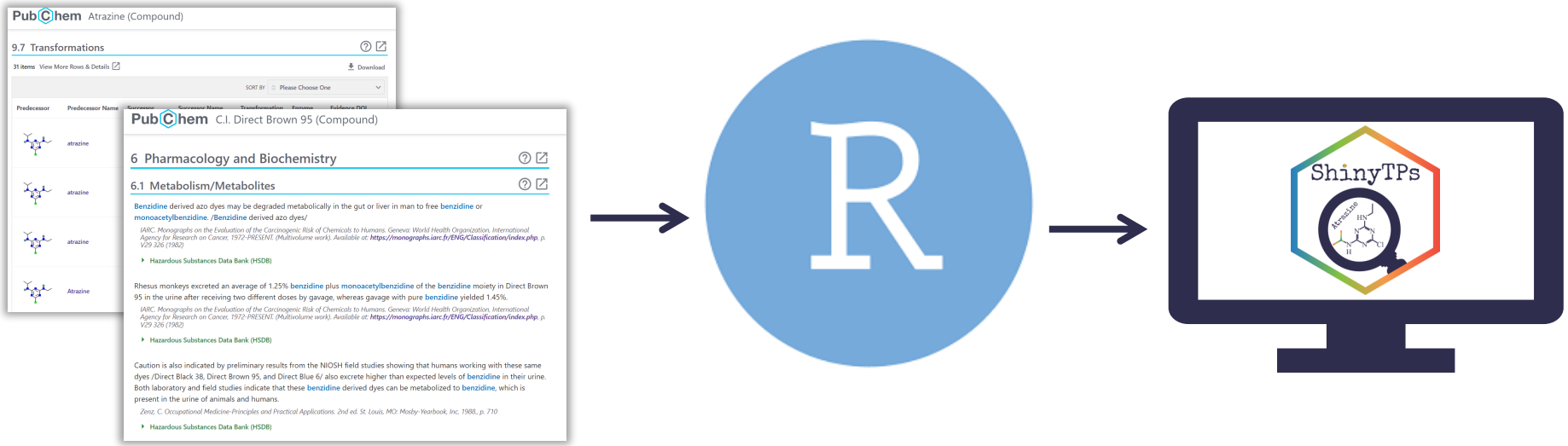
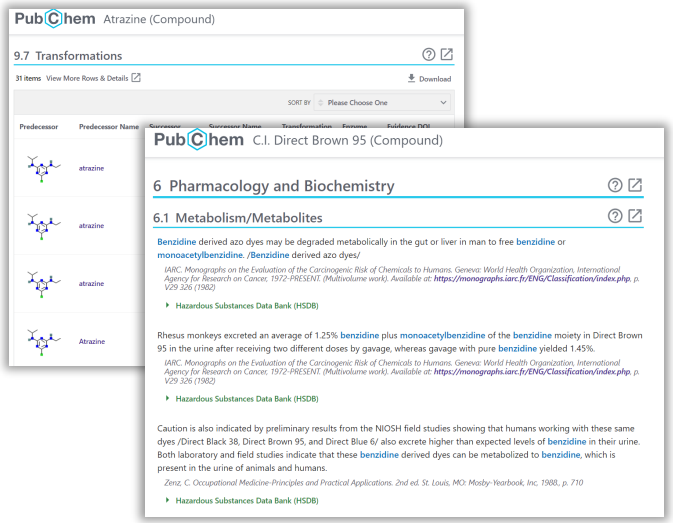
Building ShinyTPs



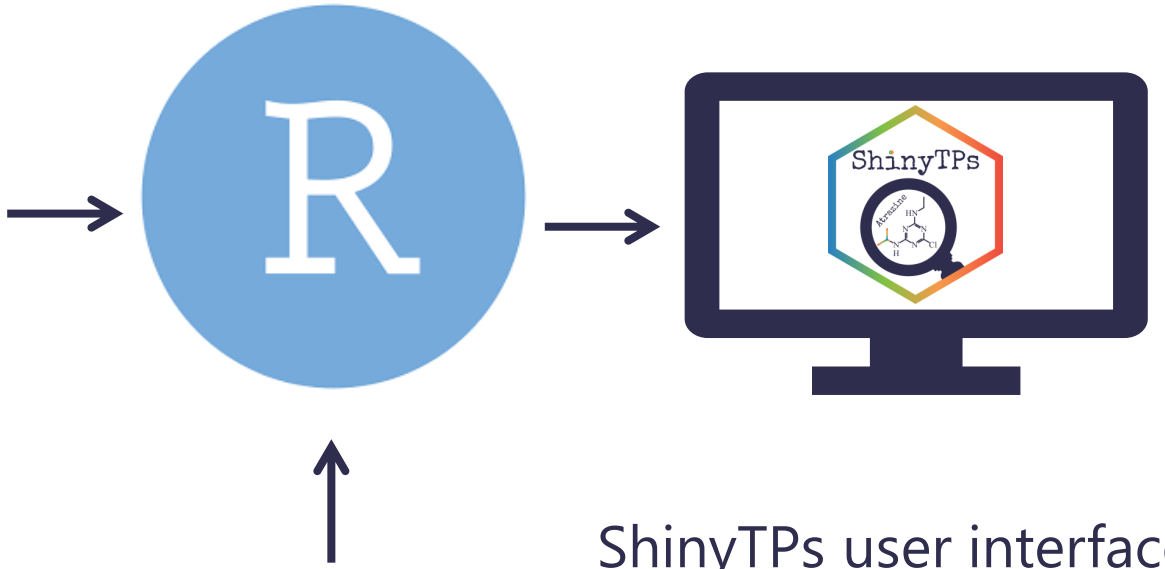
Data sources

ShinyTPs user interface

Building ShinyTPs



Data sources



ShinyTPs user interface

Name	SMILES	CID
Direct Brown 95	C1=CC(=CC=...	135585372
Atrazine	CCNC1=NC(=...	2256
...	...	...

User input file

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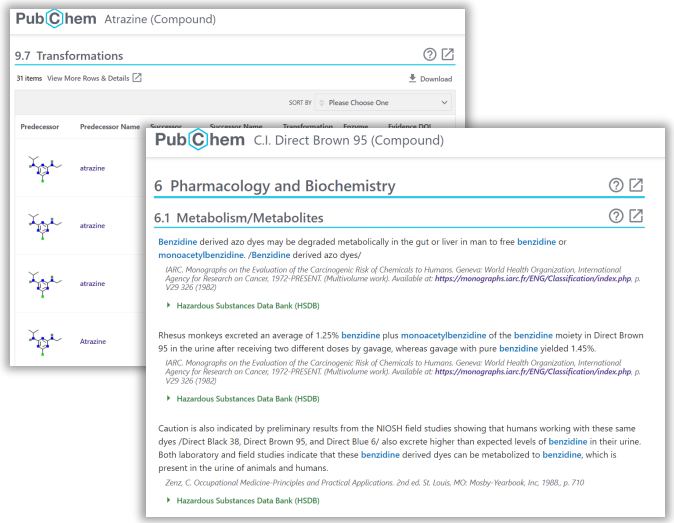
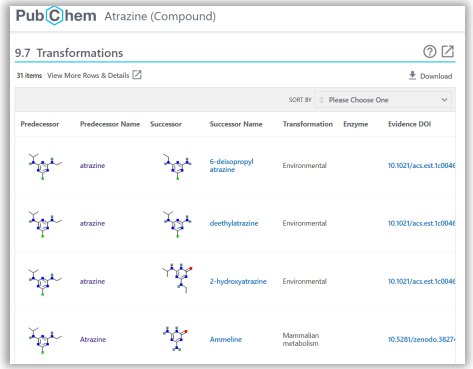
Building ShinyTPs



Data sources



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...	...	...

User input file

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LeadMine text mining

PubChem Acyclovir (Compound)

8.6 Metabolism/Metabolites

Acyclovir is metabolized partially to **9-carboxymethoxymethylguanine** and minimally to **8-hydroxy-9-(2-hydroxyethoxymethyl)guanine**. In vitro, acyclovir also is metabolized to **acyclovir monophosphate**, diphosphate, and **triphosphate** in cells infected with herpes viruses, principally by intracellular phosphorylation of the drug by virus coded **thymidine** kinase and several cellular enzymes.

American Society of Health-System Pharmacists 2013; Drug Information 2013. Bethesda, MD. 2013, p. 769

▸ Hazardous Substances Data Bank (HSDB)

LeadMine text mining

PubChem Acyclovir (Compound)

8.6 Metabolism/Metabolites

Acyclovir is metabolized partially to 9-carboxymethoxymethylguanine and minimally to 8-hydroxy-9-(2-hydroxyethoxymethyl)guanine. In vitro, acyclovir also is metabolized to acyclovir monophosphate, diphosphate, and triphosphate in cells infected with herpes viruses, principally by intracellular phosphorylation of the drug by virus coded thymidine kinase and several cellular enzymes.

American Society of Health-System Pharmacists 2013; Drug Information 2013. Bethesda, MD. 2013, p. 769

▸ Hazardous Substances Data Bank (HSDB)

LeadMine text mining

PubChem Acyclovir (Compound)

8.6 Metabolism/Metabolites

Acyclovir is metabolized partially to 9-carboxymethoxymethylguanine and minimally to 8-hydroxy-9-(2-hydroxyethoxymethyl)guanine. In vitro, acyclovir also is metabolized to acyclovir monophosphate, diphosphate, and triphosphate in cells infected with herpes viruses, principally by intracellular phosphorylation of the drug by virus coded thymidine kinase and several cellular enzymes.

American Society of Health-System Pharmacists 2013; Drug Information 2013. Bethesda, MD. 2013, p. 769

▸ Hazardous Substances Data Bank (HSDB)

LeadMine text mining

PubChem Acyclovir (Compound)

8.6 Metabolism/Metabolites

Acyclovir is metabolized partially to 9-carboxymethoxymethylguanine and minimally to 8-hydroxy-9-(2-hydroxyethoxymethyl)guanine. In vitro, acyclovir also is metabolized to acyclovir monophosphate, diphosphate, and triphosphate in cells infected with herpes viruses, principally by intracellular phosphorylation of the drug by virus coded thymidine kinase and several cellular enzymes.

American Society of Health-System Pharmacists 2013; Drug Information 2013. Bethesda, MD. 2013, p. 769

▸ Hazardous Substances Data Bank (HSDB)

LeadMine text mining

PubChem Acyclovir (Compound)

8.6 Metabolism/Metabolites

Acyclovir is metabolized partially to 9-carboxymethoxymethylguanine and minimally to 8-hydroxy-9-(2-hydroxyethoxymethyl)guanine. In vitro, acyclovir also is metabolized to acyclovir monophosphate, diphosphate, and triphosphate in cells infected with herpes viruses, principally by intracellular phosphorylation of the drug by virus coded thymidine kinase and several cellular enzymes.

American Society of Health-System Pharmacists 2013; Drug Information 2013. Bethesda, MD. 2013, p. 769

▸ Hazardous Substances Data Bank (HSDB)

Using ShinyTPs

~/PhD/ShinyTPs - Shiny

http://127.0.0.1:6255 | Open in Browser | Publish

ShinyTPs

Menu | About | PubChem Transformations | Transformations by compound | **Transfomration reaction curration** | Unidentified compound names

Select a input compound

C.I. Direct Brown 95

Select a transforamtion product CID

7111

Select an entry

1

Please add the transformation type if specified in the text

Please add the enzyme if specified in the text

Please add the biosystem if specified in the text

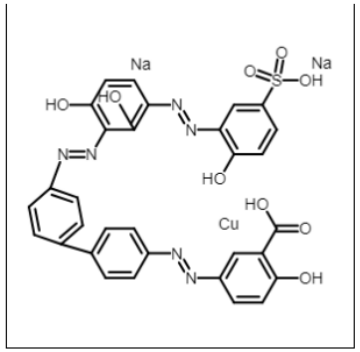
Is the compound a precursor or TP?

Transformation product

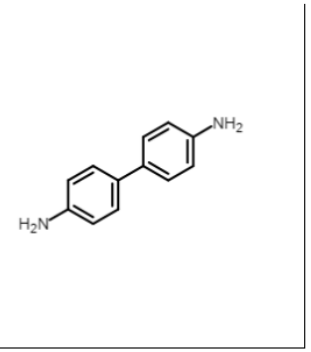
Comment

Input_compound	source_ID	cids	LeadMine_CID	Input_SMILES	LeadMine_SMILES
C.I. Direct Brown 95	5082	135585372	7111	C1=CC(=CC=C1C2=CC=C(C=C2)N=NC3=C(C=CC(=C3[O-])N=NC4=C(C=CC(=C4)S(=O)(=O)[O-])[O-])O)N=NC5=CC(=C(C=C5)O)C(=O)[O-].[Na+].[Na+].[Cu+2]	C1=CC(=CC=C1C2=CC=C(C=C2)

Input compound structure



Potential parent or TP structure



Text in HSDB:

Benzidine

derived azo dyes may be degraded metabolically in the gut or liver in man to free benzidine or monoacetylbenzidine. /Benzidine derived azo dyes/

Using ShinyTPs

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ShinyTPs

Menu | About | PubChem Transformations | Transformations by compound | Transfomration reaction curration | Unidentified compound names

Select a compound

Select a input compound

C.I. Direct Brown 95

- Propylene glycol alginate
- Folic Acid
- Allopurinol
- C.I. Direct Brown 95
- 1,2,3-Benzotriazin-4(3H)-one
- Orange I
- 2-Isopropyl-6-methyl-4-pyrimidone
- Clozapine

Please add the enzyme if specified in the text

Please add the biosystem if specified in the text

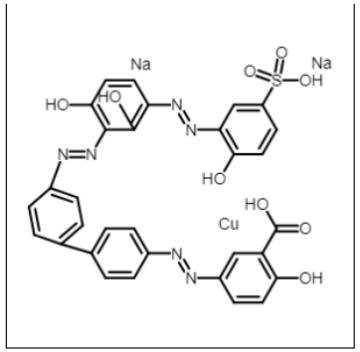
Is the compound a precursor or TP?

Transformation product

Comment

Input_compound	source_ID	cids	LeadMine_CID	Input_SMILES	LeadMine_SMILES
C.I. Direct Brown 95	5082	135585372	7111	C1=CC(=CC=C1C2=CC=C(C=C2)N=NC3=C(C=CC(=C3[O-])N=NC4=C(C=CC(=C4)S(=O)(=O)[O-])[O-])O)N=NC5=CC(=C(C=C5)O)C(=O)[O-].[Na+].[Na+].[Cu+2]	C1=CC(=CC=C1C2=CC=C(C=C2)

Input compound structure



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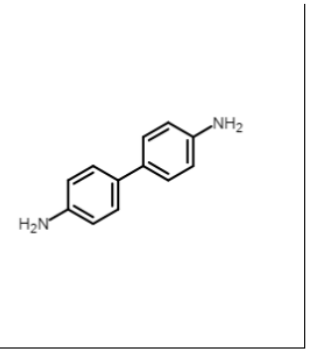

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C.I. Direct Brown 95

Select a transforamtion product CID

7111

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Is the compound a precursor or TP?

Transformation product

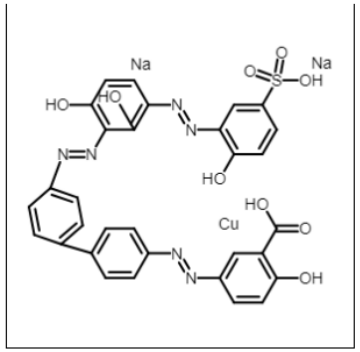
Comment

Input_compound	source_ID	cids	LeadMine_CID	Input_SMILES	LeadMine_SMILES
C.I. Direct Brown 95	5082	135585372	7111	C1=CC(=CC=C1C2=CC=C(C=C2)N=NC3=C(C=CC(=C3[O-])N=NC4=C(C=CC(=C4)S(=O)(=O)[O-])[O-])O)N=NC5=CC(=C(C=C5)O)C(=O)[O-].[Na+].[Na+].[Cu+2]	C1=CC(=CC=C1C2=CC=C(C=C2)

Text mined CID

Entry number

Input compound structure



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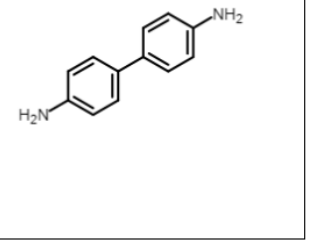

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Menu | About | PubChem Transformations | Transformations by compound | Transfomration reaction curration | Unidentified compound names

Select a input compound: C.I. Direct Brown 95

Select a transforamtion product CID: 7111

Select an entry: 1

Please add the transformation type if specified in the text

Please add the enzyme if specified in the text

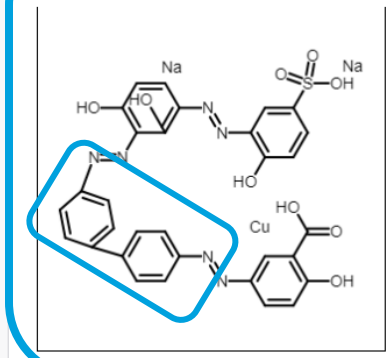
Please add the biosystem if specified in the text

Is the compound a precursor or TP?: Transformation product

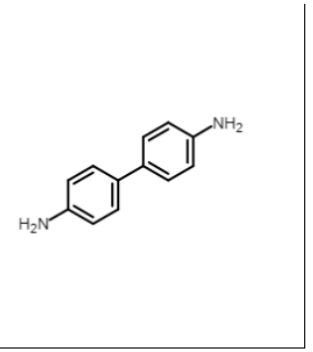
Comment

Input_compound	source_ID	cids	LeadMine_CID	Input_SMILES	LeadMine_SMILES
C.I. Direct Brown 95	5082	135585372	7111	C1=CC(=CC=C1C2=CC=C(C=C2)N=NC3=C(C=CC(=C3[O-])N=NC4=C(C=CC(=C4)S(=O)(=O)[O-])[O-])O)N=NC5=CC(=C(C=C5)O)C(=O)[O-].[Na+].[Na+].[Cu+2]	C1=CC(=CC=C1C2=CC=C(C=C2)

Input compound structure



Potential parent or TP structure



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Select a input compound: C.I. Direct Brown 95

Select a transforamtion product CID: 7111

Select an entry: 1

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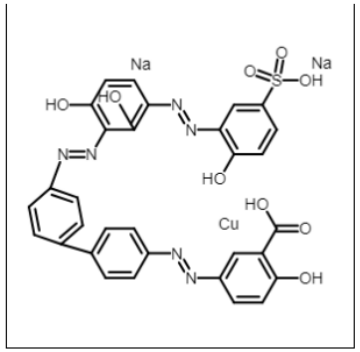
Is the compound a precursor or TP?: Transformation product

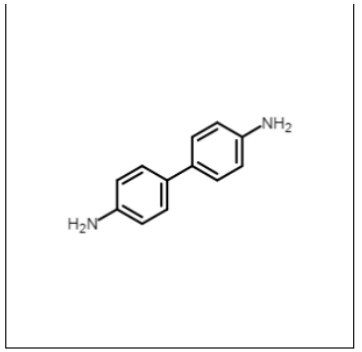
Comment

Input_compound	source_ID	cids	LeadMine_CID	Input_SMILES	LeadMine_SMILES
C.I. Direct Brown 95	5082	135585372	7111	C1=CC(=CC=C1C2=CC=C(C=C2)N=NC3=C(C=CC(=C3[O-])N=NC4=C(C=CC(=C4)S(=O)(=O)[O-])[O-])O)N=NC5=CC(=C(C=C5)O)C(=O)[O-].[Na+].[Na+].[Cu+2]	C1=CC(=CC=C1C2=CC=C(C=C2)

Input compound structure



Potential parent or TP structure



Text in HSDB:

Benzidine
derived azo dyes may be degraded metabolically in the gut or liver in man to free benzidine or monoacetylbenzidine. /Benzidine derived azo dyes/

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Using ShinyTPs

~/PhD/ShinyTPs - Shiny

http://127.0.0.1:6255 | Open in Browser | Publish

ShinyTPs

Menu | About | PubChem Transformations | Transformations by compound | Transfomration reaction curration | Unidentified compound names

Select a input compound: C.I. Direct Brown 95

Select a transforamtion product CID: 7111

Select an entry: 1

Transformation type

Enzyme

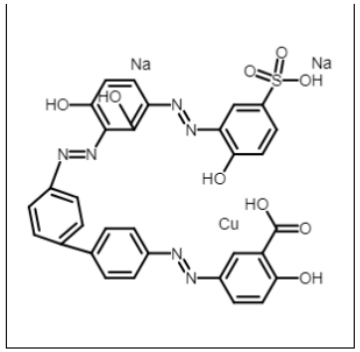
Biosystem

Is the compound a precursor or TP?: Transformation product

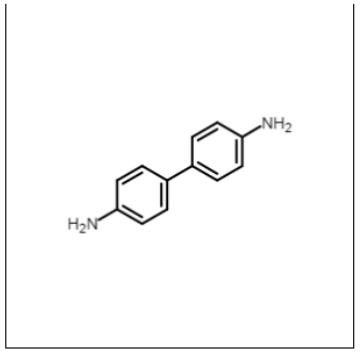
Comment

Input_compound	source_ID	cids	LeadMine_CID	Input_SMILES	LeadMine_SMILES
C.I. Direct Brown 95	5082	135585372	7111	C1=CC(=CC=C1C2=CC=C(C=C2)N=NC3=C(C=CC(=C3[O-])N=NC4=C(C=CC(=C4)S(=O)(=O)[O-])[O-])O)N=NC5=CC(=C(C=C5)O)C(=O)[O-].[Na+].[Na+].[Cu+2]	C1=CC(=CC=C1C2=CC=C(C=C2)

Input compound structure



Potential parent or TP structure



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Using ShinyTPs

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1

Please add the transformation type if specified in the text

Please add the enzyme if specified in the text

Please add the biosystem if specified in the text

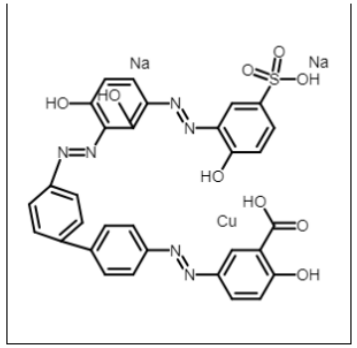
Human

Is the compound a precursor or TP?

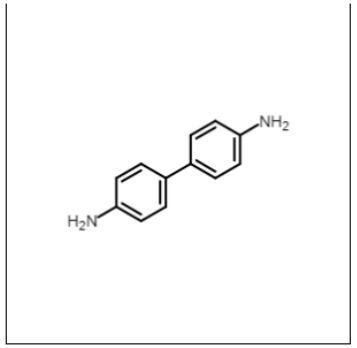
Transformation product

Comment

Input compound structure



Potential parent or TP structure



Text in HSDB:

Benzidine
derived azo dyes may be degraded metabolically in the gut or liver in man to free benzidine or monoacetylbenzidine. /Benzidine derived azo dyes/

Selected Reactions

Save

Show 10 entries Search:

	Predecessor_CID	Predecessor_Name	Successor_CID	Successor_Name	Transformation	Biosystem	Enzyme	source_ID	Source	Source_Descript
1	135585372	C.I. Direct Brown 95	7111	Benzidine	Metabolism	Human	NA	5082	HSDB	HSDB is a toxicc the toxicology o chemicals. See https://pubcher

Showing 1 to 1 of 1 entries Previous 1 Next

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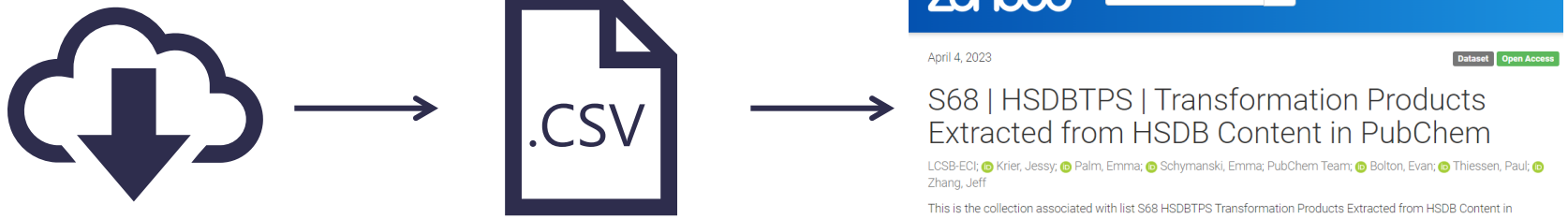
What to do next

Download Saved reactions

What to do next



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Saved reactions

Zenodo: Transformations from HSDB

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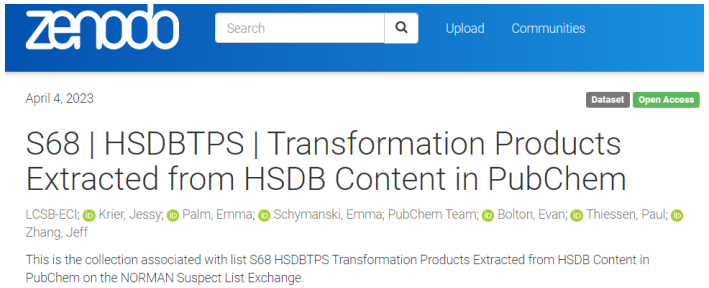
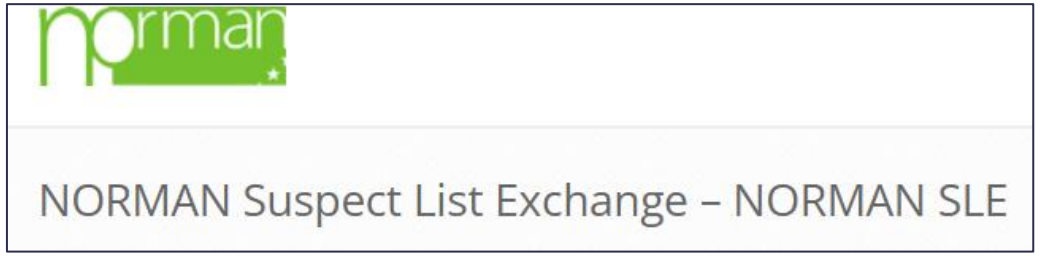
What to do next

Download

Saved reactions



Zenodo: Transformations from HSDB



NORMAN S68 list

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Curated reactions

6.2 Transformations

4 items View More Details

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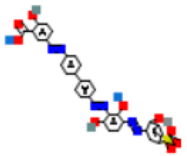
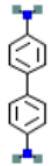
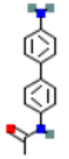
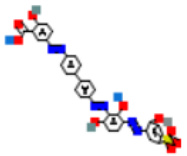
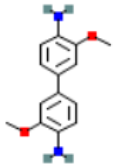
SORT BY Please Choose One

Predecessor	Predecessor Name	Successor	Successor Name	Transformation	Enzyme	Evidence DOI
	C.I. Direct Brown 95		Benzidine	Metabolism		10.5281/zenodo.382
	C.I. Direct Brown 95		Monoacetylbenzidine	Metabolism		10.5281/zenodo.382
	C.I. Direct Brown 95		Diacetylbenzidine	Metabolism		10.5281/zenodo.382
	C.I. Direct Brown 95		ortho-Dianisidine	Metabolism		10.5281/zenodo.382

PubChem Transformations

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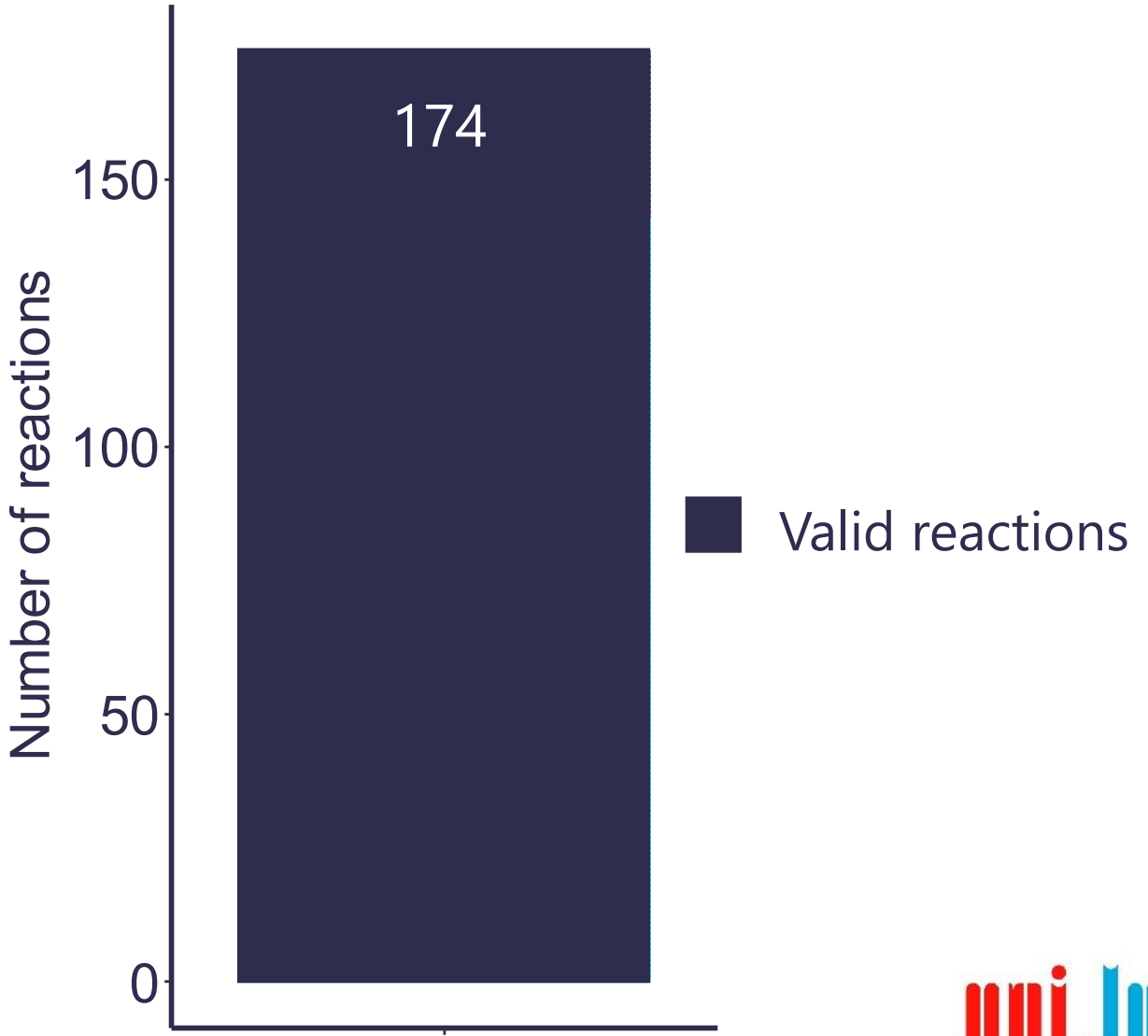
Curated reactions

Tested on compounds from 5 datasets:

- 28 compounds from NORMAN-SLE
- 8 compounds from the PubChem PFAS Tree
- 33 compounds on the ChemSec PBT SIN-list
- 8 compounds from internal PMT list
- 16 compounds in the CompTox azo-dyes dataset



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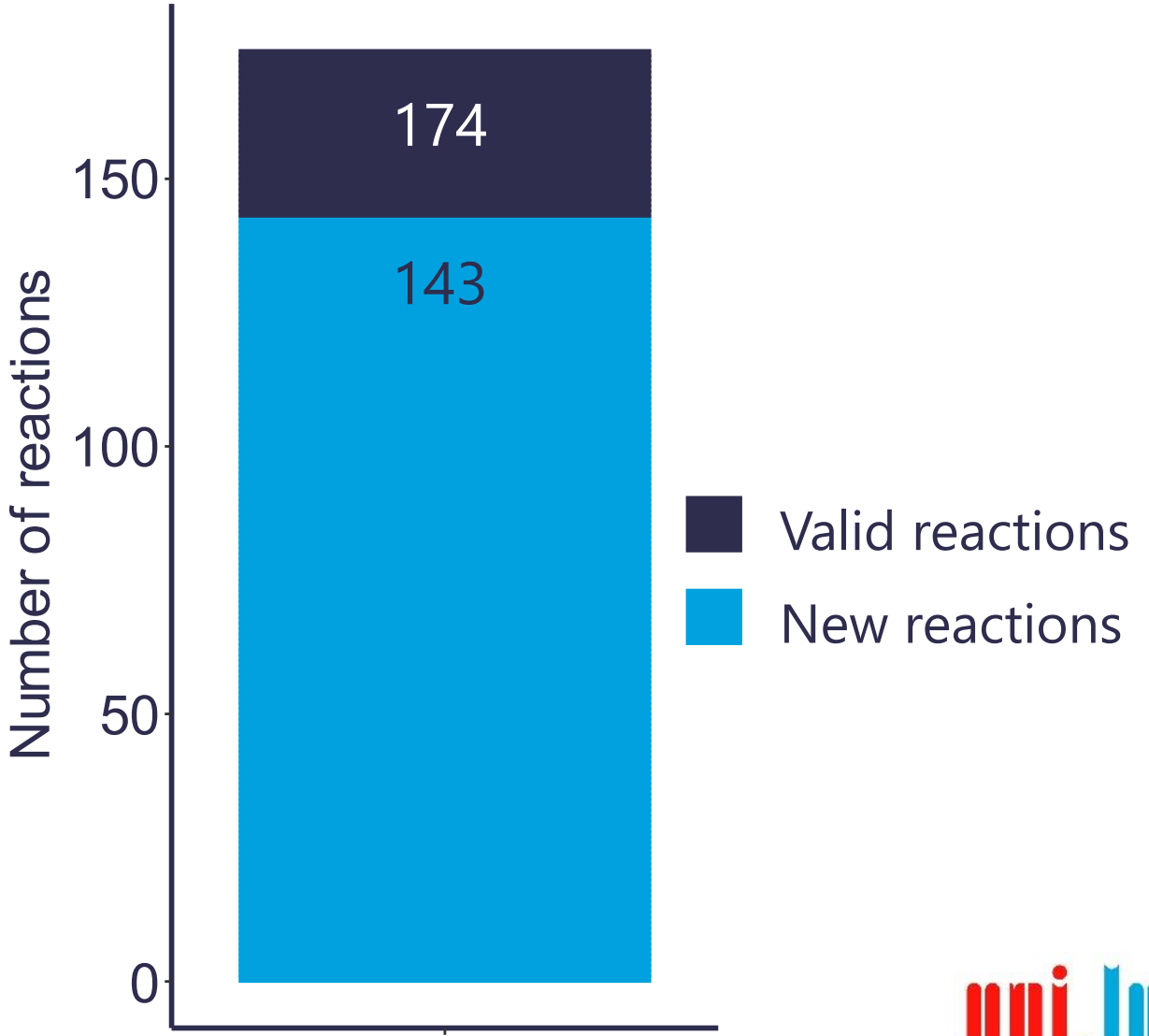
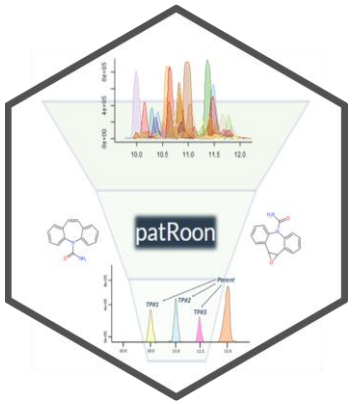
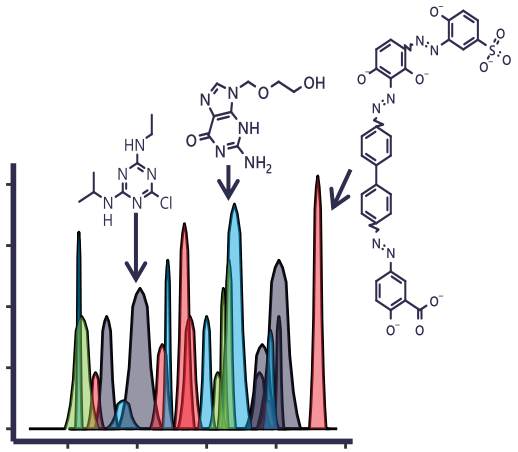


Incorporation into MS workflows in patRoon





Parents suspect screening

Helmus et al., J Cheminform, 2021, DOI: [10.1186/s13321-020-00477-w](https://doi.org/10.1186/s13321-020-00477-w)

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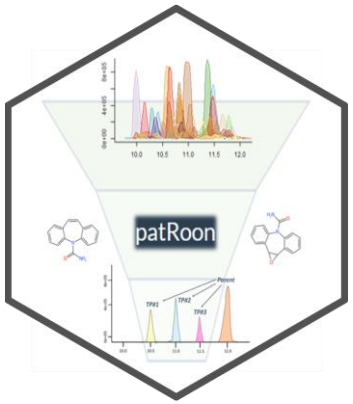
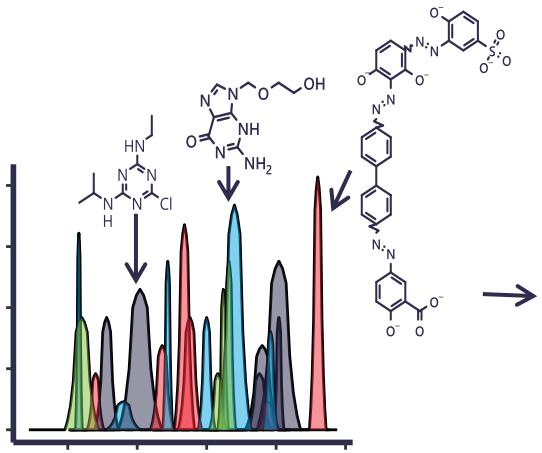
Incorporation into MS workflows in patRoon

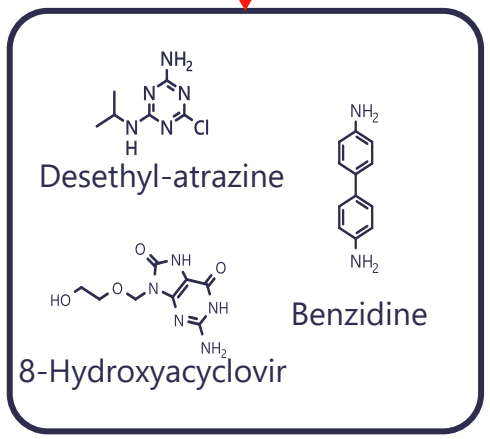




Parents suspect screening

ShinyTPs

PubChem Transformations



TP library

Helmus et al., J Cheminform, 2021, DOI: [10.1186/s13321-020-00477-w](https://doi.org/10.1186/s13321-020-00477-w)

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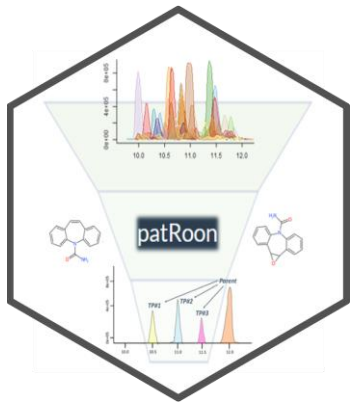
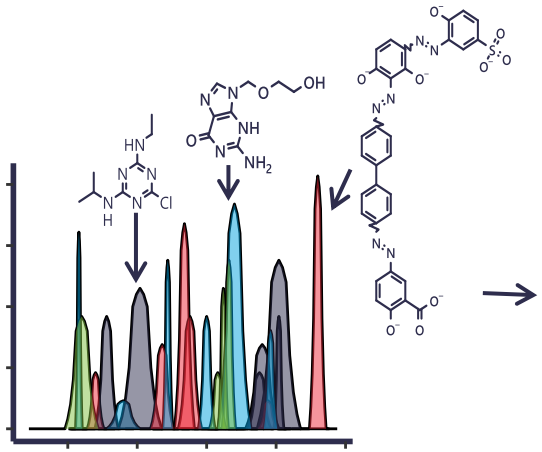
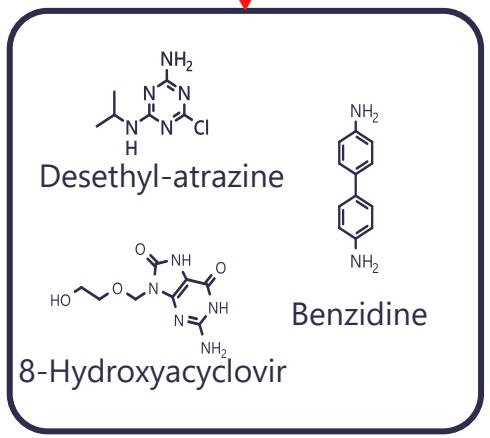
Incorporation into MS workflows in patRoon

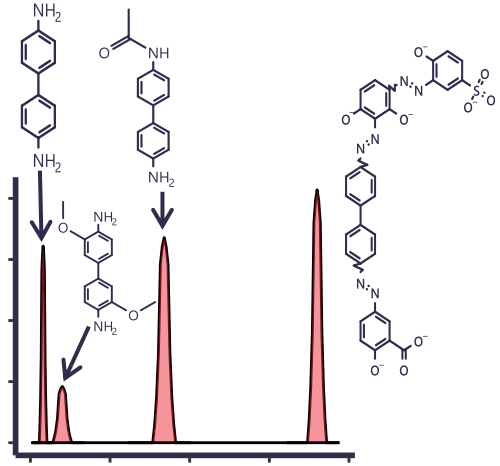




Parents suspect screening



TP library



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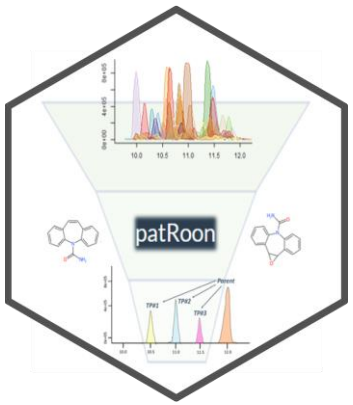
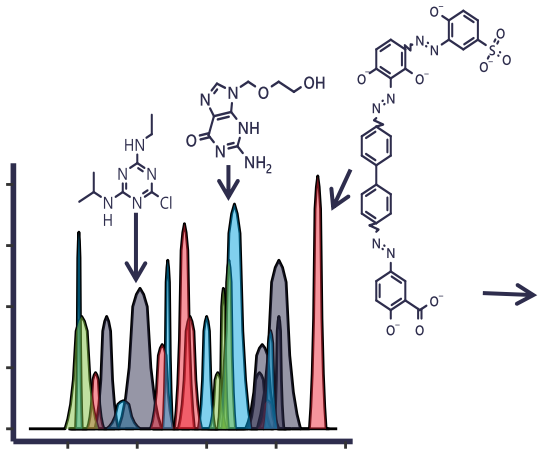
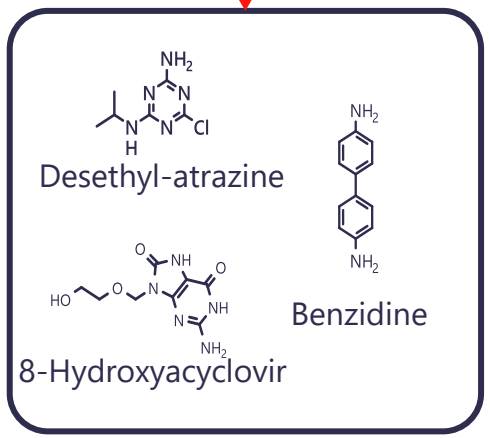




Parents suspect screening



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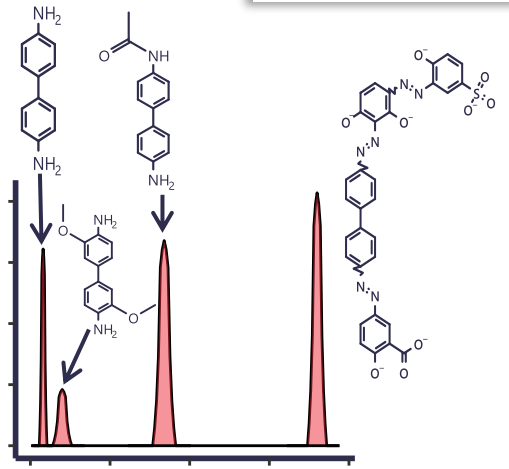
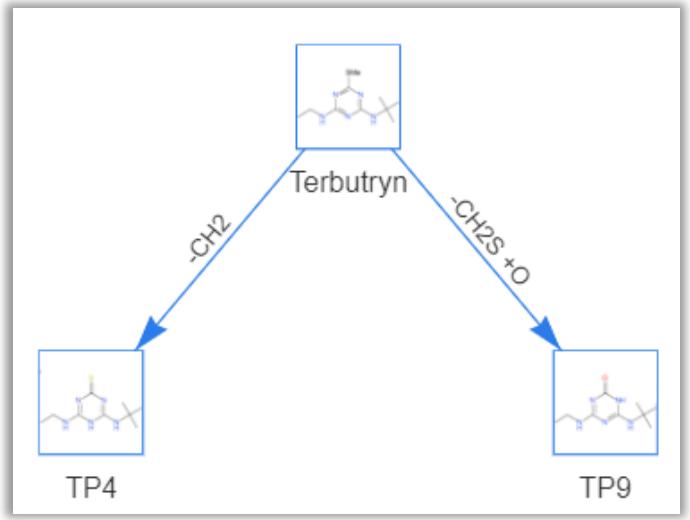


TP suspect screening



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Acknowledgements

Luxembourg National Research Fund

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emma.palm@uni.lu

ShinyTPs

Find and use ShinyTPs

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Compound selection data sources

28 compounds from NORMAN-SLE

NORMAN is a network of stakeholders working towards enhancing exchange of information about emerging substances. The compounds were randomly selected from the subset of S0 that had information in the Metabolism and Metabolites section with HSDB as the data source. List S0 is a compilation of all NORMAN suspect lists.

8 compounds from the PubChem PFAS Tree

The PubChem PFAS Tree contains the PFAS and other fluorinated compounds in PubChem. All compounds from the "Molecule contains PFAS parts larger than CF2/CF3" section that also had information in the Metabolism and Metabolites section with HSDB as the data source were selected

33 compounds on the ChemSec PBT SIN-list

The ChemSec SIN list contains hazardous chemicals used in a variety of products. All compounds meeting the persistent, bioacumulative and toxic were selected if they also had information in the Metabolism and Metabolites section.

Compound selection data sources

8 compounds from internal PMT list

The internal PMT list comes from the ZeroPM project and contained 38 compounds at the time of use. For the development and testing of ShinyTPs all compounds with information in the Metabolism and metabolites section with HSDB as the data source were selected.

16 compounds in the CompTox azo-dyes dataset

This list contains 4103 azo-dyes assembled from public sources. For the development and testing of ShinyTPs all compounds with information in the Metabolism and metabolites section with HSDB as the data source were selected.

Links:

https://www.norman-network.com/nds/SLE/
https://pubchem.ncbi.nlm.nih.gov/classification/#hid=120
https://chemsec.org/business-tool/sin-list/
https://zeropm.eu/
https://comptox.epa.gov/dashboard/chemical-lists/AZODYES