

Estimation of toxicity via T.E.S.T. (v5.1) and WebTEST

#249



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OBJECTIVES

- Redesign of the interface
- Improved structure searching
- Improved calculation speed
- Incorporation of Chemical Transformation Simulator (CTS)
- Mac OS version of T.E.S.T.
- Web interface for running T.E.S.T. models (WebTEST)
- WebTEST models can be accessed via API calls

APPROACH

- Downloadable T.E.S.T. Java application was redesigned to be more user friendly and run calculations faster
- T.E.S.T. was converted into a web-service based application (WebTEST)
- EPA's CTS web-service was incorporated into the single chemical mode of T.E.S.T. to estimate properties of breakdown products

IMPACT

- T.E.S.T. has been made more accessible by redesigning the application and providing a web-based version.
- T.E.S.T. can now estimate the toxicity of environmental breakdown products via CTS

For more information: martin.todd@epa.gov;
<https://www.epa.gov/chemical-research/toxicity-estimation-software-tool-test>;
<https://comptox.epa.gov/dashboard/predictions/index>

The screenshot displays the T.E.S.T. software interface. At the top, the chemical structure of Cyclopentadiene dimer is shown. Below it, the word "RESULTS" is prominently displayed. A table provides a comparison of experimental values with consensus, hierarchical clustering, single model, group contribution, and nearest neighbor predictions for various properties. On the right, a sidebar allows users to select properties to predict, with checkboxes for toxicological and physical properties.

Property	Experimental Value	Consensus	Hierarchical clustering	Single model	Group contribution	Nearest neighbor
96 hour fathead minnow LC50	3,407 -Log10(mol/L) 51,796 mg/L	4,198 -Log10(mol/L) 8,383 mg/L	3,781 -Log10(mol/L) 21,877 mg/L	4,482 -Log10(mol/L) 4,358 mg/L	4,759 -Log10(mol/L) 2,301 mg/L	3,769 -Log10(mol/L) 22,506 mg/L
48 hour D. magna LC50	4,100 -Log10(mol/L) 10,501 mg/L	4,087 -Log10(mol/L) 10,831 mg/L	4,032 -Log10(mol/L) 12,294 mg/L	3,980 -Log10(mol/L) 13,838 mg/L	4,248 -Log10(mol/L) 7,468 mg/L	
48 hour T. pyriformis IGC50		3,588 -Log10(mol/L) 14,818 mg/L	3,534 -Log10(mol/L) 10,703 mg/L		4,363 -Log10(mol/L) 5,735 mg/L	
Oral rat LD50	2,573 -Log10(mol/kg) 353,425 mg/kg	1,580 -Log10(mol/kg) 3476,044 mg/kg	1,608 -Log10(mol/kg) 3259,919 mg/kg			1,552 -Log10(mol/kg) 3706,498 mg/kg
Bioconcentration factor	2,412 Log10 258,232	2,683 Log10 482,204	2,349 Log10 223,464	2,740 Log10 549,449	3,200 Log10 1583,486	2,444 Log10 278,083

Estimation of toxicity via T.E.S.T. (v5.1) and WebTEST

T.E.S.T 5.1. Single Chemical Mode

T.E.S.T. (Toxicity Estimation Software Tool)

File Help

Enter a CAS, SMILES, Name, InChi, InChiKey, or DTXSID and click Search

Search

Molecule ID:

Name:

Search included database of 871K curated substances

Calculation Options

Endpoint: Daphnia magna LC50 (48 hr) ?

Method: Consensus ?

☐ Relax fragment constraint ?

☐ Run CTS Hydrolysis ?

Ability to run CTS

Select output folder:

C:\Users\TMARTI02\OneDrive - Environmental Protection Agency (EPA)\Profile\Documents\MyToxicity3

Browse...

☒ Create detailed reports ?

Draw Chemical

Edit View Atom Bond Tools Drawing Help

Chemical structure: 1-chloronaphthalene

Switch to Batch Mode Calculate

Estimation of toxicity via T.E.S.T. (v5.1) and WebTEST

T.E.S.T 5.1. Batch Mode

T.E.S.T. (Toxicity Estimation Software Tool)

File Help

Search the database by CAS, SMILES, Name, InChI, InChIKey, or DTXSID (one per line)

Automatic

Draw chemical

Delete selected

Clear table

Search

Calculation Options

Endpoint: Daphnia magna LC50 (48 hr)

Method: Consensus

☐ Relax fragment constraint

Select output folder:

C:\Users\TMARTI02\OneDrive - Environmental Protection Agency (EPA)\Profile\Documents\MyToxicity3

☐ Create reports

Batch list of chemicals (double click a row to edit a chemical)

#	ID	Name	Formula	Error
1	50-48-6	5H-Dibenzo(a,d)cycloheptene-delt...	C20H23N	
2	54-11-5	Pyridine, 3-(1-methyl-2-pyrrolidinyl)...	C10H14N2	
3	56-23-5	Methane, tetrachloro-	CCl4	
4	57-92-1	D-Streptamine, O-2-deoxy-2-(meth...	C21H39N7O12	
5	58-08-2	1H-Purine-2,6-dione, 3,7-dihydro...	C8H10N4O2	
6	58-55-9	1H-Purine-2,6-dione, 3,7-dihydro...	C7H8N4O2	
7	58-89-9	Cyclohexane, 1,2,3,4,5,6-hexachlo...	C6H6Cl6	
8	62-53-3	Benzenamine	C6H7N	
9	67-56-1	Methanol	CH4O	
10	67-68-5	Sulfinylbis-methane (9CI)	C2H6OS	
11	68-12-2	Formamide, N,N-dimethyl-	C3H7NO	
12	71-43-2	Benzene, pure	C6H6	
13	72-43-5	Benzene, 1,1'-(2,2,2-trichloroethyl...	C16H15Cl3O2	
14	75-25-2	Methane, tribromo-	CHBr3	
15	75-35-4	1,1-Dichloroethene (9CI)	C2H2Cl2	
16	76-44-8	4,7-Methano-1H-indene, 1,4,5,6,7...	C10H5Cl7	
17	78-48-8	Phosphorothioic acid, S,S,S-trib...	C12H27OP3	
18	79-06-1	2-Propenamide	C3H5NO	
19	79-92-5	(1)-2,2-Dimethyl-3-methylenecyclo...	C10H16	
20	79-94-7	Phenol, 4,4'-isopropylidenebis(2,6...	C15H12Br4O2	
21	87-86-5			
22	88-73-3			
23	89-61-2			
24	90-12-0			
25	90-13-1			
26	90-43-7			
27	91-20-3			
28	91-22-5			
29	91-58-7			
30	91-94-1			
31	95-36-3			
32	95-51-2			
33	95-57-8			
34	95-76-1			
35	96-45-7			
36	99-85-0			
37	99-86-5			
38	101-55-3			
39	103-69-5			
40	104-76-7			
41	104-94-9			
42	105-53-3			
43	106-47-8			
44	106-48-9			
45	107-92-6			
46	108-18-9			
47	108-39-4			

Prediction results: Daphnia magna LC50 (48 hr)

Results		Individual methods													
Index	ID	Query	SmilesRan	Error	Exp_Value: -Log10(mol/L)	Pred_Value: -Log10(mol/L)	Exp_Value: mg/L	Pred_Value: mg/L	Exp_Value: mg/L	Pred_Value: mg/L	Exp_Value: mg/L	Pred_Value: mg/L	Exp_Value: mg/L	Pred_Value: mg/L	Exp_Value: mg/L
1	50-48-6	50-48-6	C=1C=CC2=C(C1)C(=CC...		5.55	5.16	0.78	1.93							
2	54-11-5	54-11-5	N=1C=CC=C(C1)C2N(C)C...		4.73	3.81	3.00	25.01							
3	56-23-5	56-23-5	ClC(Cl)(Cl)Cl		3.64	3.98	34.99	16.00							
4	57-92-1	57-92-1	O=CC1(O)C(OC(OC2C(O)...		3.08	1.56	487.17	15921.66							
5	58-08-2	58-08-2	O=C1C2=C(N=CN2C)N(C)C...		3.03	3.03	182.09	181.67							
6	58-55-9	58-55-9	O=C1C=2N=CNC2N(C=O...		2.57	2.86	482.76	247.61							
7	58-89-9	58-89-9	ClC1C(Cl)C(Cl)C(Cl)C(Cl)...		5.39	4.36	1.19	12.72							
8	62-53-3	62-53-3	NC=1C=CC=CC1		5.37	4.50	0.40	2.97							
9	67-56-1	67-56-1	OC		0.99	2.02	3287.21	304.06							
10	67-68-5	67-68-5	O=S(C)C		0.49	1.61	24999.37	1924.62							
11	68-12-2	68-12-2	O=CN(C)C		0.70	2.32	14453.63	352.23							
12	71-43-2	71-43-2	C=1C=CC=CC1		2.48	3.47	258.68	26.26							
13	72-43-5	72-43-5	ClC(Cl)(Cl)C(C1=CC=C(O...		7.09	6.14	2.83E-02	0.25							
14	75-25-2	75-25-2	BrC(Br)Br		3.74	4.44	45.99	9.25							
15	75-35-4	75-35-4	ClC(Cl)=C		3.28	3.85	50.87	13.57							
16	76-44-8	76-44-8	ClC1=C(C)C2(C)C3C(C)...		6.78	6.42	6.24E-02	0.14							
17	78-48-8	78-48-8	O=P(SCCCC)SCCCC)SC...		7.68	6.99	6.63E-03	3.20E-02							
18	79-06-1	79-06-1	O=C(N)C=C		2.65	3.61	159.52	17.30							
19	79-92-5	79-92-5	C=C1C2CCC(C2)C1(C)C		3.79	4.41	22.00	5.33							
20	79-94-7	79-94-7	BrC=1C=C(C=C(Br)C1O)C...		4.84	7.68	7.90	1.14E-02							
21	87-86-5	87-86-5	ClC=1C(Cl)=C(C)C(O)C...		5.56	6.08	0.73	0.22							
22	88-73-3	88-73-3	O=[N+](O-)]C=1C=CC=CC...		3.64	4.20	36.09	9.92							
23	89-61-2	89-61-2	O=[N+](O-)]C=1C=CC(Cl)=C...		4.25	4.61	10.77	4.71							
24	90-12-0	90-12-0	C=1C=CC2=C(C1)C=CC=...		5.00	4.53	1.42	4.20							
25	90-13-1	90-13-1	ClC1=CC=CC=2C=CC=C...		5.01	4.79	1.59	2.64							
26	90-43-7	90-43-7	OC=1C=CC=CC1C=2C=C...		5.38	5.04	0.71	1.57							
27	91-20-3	91-20-3	C=1C=CC=2C=CC=CC2C1		4.15	4.24	9.14	7.42							
28	91-22-5	91-22-5	N=1C=CC=C2C=CC=CC12		3.53	4.01	38.12	12.76							
29	91-58-7	91-58-7	ClC=1C=CC=2C=CC=CC...		5.50	5.10	0.51	1.30							
30	91-94-1	91-94-1	ClC=1C=C(C=CC1N)C2=...		5.38	5.37	1.05	1.08							
31	95-36-3	95-36-3	C=1C=C(C(C=CC1C)O)C		4.53	4.29	3.55	6.18							
32	95-51-2	95-51-2	ClC=1C=CC=CC1N		5.19	4.92	0.82	1.52							

Save to Excel (.xlsx) Save to text (.csv)

Batch results
displayed in real
time

Estimation of toxicity via T.E.S.T. (v5.1) and WebTEST

CTS Integration: estimate properties of breakdown products

T.E.S.T. (Toxicity Estimation Software Tool)

File Help

Enter a CAS, SMILES, Name, InChi, InChiKey, or DTXSID and click Search

Molecule ID: 115-86-6

Name: Triphenyl phosphate

Draw Chemical

Edit View Atom Bond Tools Drawing Help

Calculation Options

Endpoint: Fathead minnow LC50 (96 hr)

Method: Consensus

☐ Relax fragment constraint

☒ Run CTS

Hydrolysis

Hydrolysis

Abiotic Reduction

Human Metabolism

Select output folder:

C:\Users\TMARTI02\OneDrive - Environmental Protection Agency (EPA)\Profile\Documents\MyToxicity3

Browse...

☐ Create detailed reports

Prediction results including environmental transformation products: Fathead minnow LC50 (96 hr)

Index	ID	Query	SmilesRan	Error	Exp_Value: -Log10(mol/L)	Pred_Value: -Log10(mol/L)	Exp_Value: mg/L	Pred_Value: mg/L
1	115-86-6	triphenyl phosphate	O=P(OC=1C=CC=CC1)(O...		5.54	5.93	0.93	0.39
2	838-85-7	Product of 115-86-6, Accu...	O=P(O)(OC=1C=CC=CC1)...		N/A	5.65	N/A	0.56
3	108-95-2	Product of 115-86-6, Accu...	OC=1C=CC=CC1		3.50	3.39	30.11	38.69

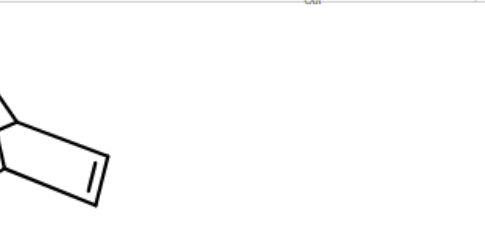
Switch to Batch Mode Calculate

Estimation of toxicity via T.E.S.T. (v5.1) and WebTEST

WebTEST Interface

<https://comptox.epa.gov/dashboard/predictions/index>

Cyclopentadiene dimer



United States Environmental Protection Agency

Chemistry Dashboard

Predictions

Property	Experimental Value	Consensus	Hierarchical clustering	Single model	Group contribution	Nearest neighbor
96 hour fathead minnow LC50	4.320 -Log10(mol/L) 6.135 mg/L	4.221 -Log10(mol/L) 7.710 mg/L	4.197 -Log10(mol/L) 8.148 mg/L	4.012 -Log10(mol/L) 12.482 mg/L	4.242 -Log10(mol/L) 7.347 mg/L	4.433 -Log10(mol/L) 4.730 mg/L
48 hour D. magna LC50	4.147 -Log10(mol/L) 9.137 mg/L	4.237 -Log10(mol/L) 7.422 mg/L	4.137 -Log10(mol/L) 9.355 mg/L	4.130 -Log10(mol/L) 9.503 mg/L	4.264 -Log10(mol/L) 6.972 mg/L	4.418 -Log10(mol/L) 4.896 mg/L
48 hour T. pyriformis IGC50	2.880 -Log10(mol/L) 168.974 mg/L	3.411 -Log10(mol/L) 49.758 mg/L	3.092 -Log10(mol/L) 103.622 mg/L		3.574 -Log10(mol/L) 34.197 mg/L	3.567 -Log10(mol/L) 34.766 mg/L
Oral rat LD50	2.418 -Log10(mol/kg) 489.576 mg/kg	2.114 -Log10(mol/kg) 985.677 mg/kg	2.146 -Log10(mol/kg) 916.183 mg/kg			2.082 -Log10(mol/kg) 1060.442 mg/kg
Bioaccumulation factor	2.360 Log10 229.086	2.351 Log10 224.335	2.368 Log10	2.511 Log10	2.011 Log10 102.507	2.514 Log10 326.333
Developmental toxicity		false				false
Ames mutagenicity	false					false
Estrogen Receptor RBA		-5.225 Log10 6.65×10^{-6}	-6.438 Log10 3.64×10^{-7}	-6.438 Log10 3.64×10^{-7}		-2.800 Log10 0.000

100%

Layout Clean Up Aromatize Dearomatize Calculate Check Structure Calculated Values Recognize Molecule 3D Viewer

Settings Help About

Chemical structure of Cyclopentadiene dimer

United States Environmental Protection Agency

Chemistry Dashboard

Predictions

Property	Experimental Value	Consensus	Hierarchical clustering	Single model	Group contribution	Nearest neighbor
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Layout Clean Up Aromatize Dearomatize Calculate Check Structure Calculated Values Recognize Molecule 3D Viewer

Settings Help About

Chemical structure of Cyclopentadiene dimer

United States Environmental Protection Agency

Chemistry Dashboard

Predictions

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Developmental toxicity		false				false
Ames mutagenicity	false					

Estimation of toxicity via T.E.S.T. (v5.1) and WebTEST

WebTEST “GET” API Call

URL/endpointAbbreviation?smiles=desiredSmiles&method=methodAbbreviation

where URL = <https://comptox.epa.gov/dashboard/web-test/>

Method	Abbreviation
Hierarchical clustering	hc
Single model	sm
Nearest neighbor	nn
Group contribution	gc
Consensus	consensus (default)

Endpoint	Abbreviation
Fathead minnow LC50 (96 hr)	LC50
Daphnia magna LC50 (48 hr)	LC50DM
T. pyriformis IGC50 (48 hr)	IGC50
Oral rat LD50	LD50
Bioaccumulation factor	BCF
Developmental Toxicity	DevTox
Mutagenicity	Mutagenicity
Normal boiling point	BP
...	...

JSON	Raw Data	Headers
Save	Copy	
uuid:	"55547f4f-f966-48e8-b831-a0d217998064"	
predictionTime:	1520539090089	
software:	"T.E.S.T (Toxicity Estimation Software Tool)"	
softwareVersion:	"5.01"	
condition:	"25°C"	
endpoint:	"Water solubility at 25°C"	
method:	"Hierarchical clustering"	
▼ predictions:		
▼ 0:		
id:	"C_1520539090089"	
smiles:	"OCC"	
expValMolarLog:	"-1.337"	
expValMass:	"1001180.703"	
predValMolarLog:	"-1.338"	
predValMass:	"1002625.241"	
molarLogUnits:	"-Log10(mol/L)"	
massUnits:	"mg/L"	

Summary

- T.E.S.T. can now search EPA's DSSTOX database
- Calculations are performed faster
- Properties of environmental breakdown products can now be estimated using CTS
- Calculations can now be run on the web using WebTEST using a graphical interface and API calls

Future work

- Map all data sets to DSSTOX identifiers
- Add additional data and endpoints/properties
- Add models to predict properties of PFAS
- Replace legacy QSAR methods with python web-service based methods (e.g. SVM, RF, DNN)
- Make single chemical output display in the software rather than web browser
- Batch mode of WebTEST

References

U.S. EPA (2020). "[User's Guide for T.E.S.T. \(version 5.1\) \(Toxicity Estimation Software Tool\): A Program to Estimate Toxicity from Molecular Structure.](#)"