

NASKAH TUTORIAL

PREDIKSI TOKSISITAS SENYAWA MENGUNAKAN PROTOX

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WEBSITE PROTOX

<https://tox.charite.de/protox3/>

DATA YANG HARUS DISIAPKAN

- Pubchem-Name senyawa atau
- Canonical Smiles senyawa atau
- File senyawa dalam format .pdb atau .mol

Note: File senyawa dalam format .pdb dan .mol dapat diketahui Canonical Smiles-nya melalui website Online SMILES Translator and Structure File Generator (<https://cactus.nci.nih.gov/translate/>)

1. Buka website ProTox
2. Pilih TOX PREDICTION

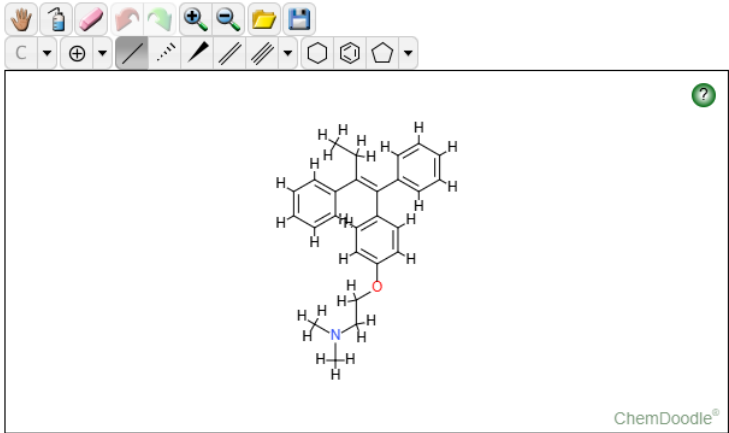


3. Masukkan data senyawa berupa Pubchem-Name/Canonical Smiles/Menggambar senyawa pada ChemDoodle

Pubchem-Name: search e.g. [Tamoxifen](#) [Tolcapone](#) [Vorinostat](#) [Troglitazone](#) [Aspirin](#)

Canonical Smiles: smiles e.g. [CCC\(=C\(C1=CC=CC=C1\)C2=CC=C\(C=C2\)OCCN\(C\)C\)C3=CC=CC=C3](#)

Selected molecule : Tamoxifen



ChemDoodle®

To load a molecule click . The deletes clicked atoms and deletes everything on the canvas.

4. Pilih organ toxicity, toxicity end points atau parameter lain yang diinginkan untuk diprediksi → Start Tox-Prediction

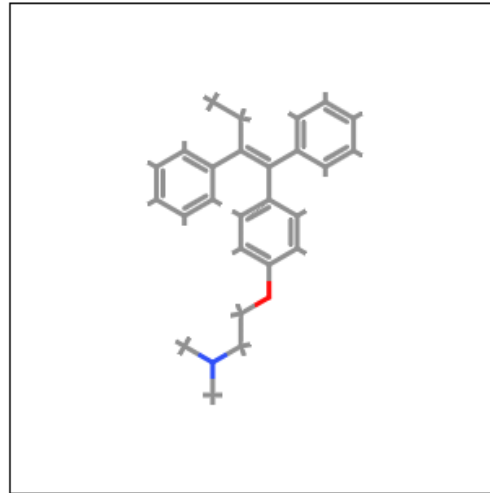
Acute Toxicity and binding to 16 toxicity targets is always computed, further models can take ~10s time each

Organ Toxicity ☒ Hepatotoxicity ☒ Neurotoxicity ☒ Nephrotoxicity ☒ Respiratory toxicity ☒ Cardiotoxicity	Molecular Initiating Events ☐ Thyroid hormone receptor alpha (THR α) ☐ Thyroid hormone receptor beta (THR β) ☐ Transthyretin (TTR) ☐ Ryanodine receptor (RYP) ☐ GABA receptor (GABAR) ☐ Glutamate N-methyl-D-aspartate receptor (NMDAR) ☐ α -amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPA) ☐ Kainate receptor (KAR) ☐ Acetylcholinesterase (AChE) ☐ Constitutive androstane receptor (CAR) ☐ Pregnane X receptor (PXR) ☐ NADH-quinone oxidoreductase (NADHox) ☐ Voltage gated sodium channel (VGSC) ☐ Na ⁺ /I ⁻ symporter (NIS)
Toxicity end points ☒ Carcinogenicity ☒ Immunotoxicity ☒ Mutagenicity ☒ Cytotoxicity ☒ BBB-barrier ☐ Ecotoxicity ☒ Clinical toxicity ☒ Nutritional toxicity	
Tox21 Nuclear receptor signalling pathways ☐ Aryl hydrocarbon Receptor (AhR) ☐ Androgen Receptor (AR) ☐ Androgen Receptor Ligand Binding Domain (AR-LBD) ☐ Aromatase ☐ Estrogen Receptor Alpha (ER) ☐ Estrogen Receptor Ligand Binding Domain (ER-LBD) ☐ Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	
Tox21 Stress response pathways ☐ Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE) ☐ Heat shock factor response element (HSE) ☐ Mitochondrial Membrane Potential (MMP) ☐ Phosphoprotein (Tumor Suppressor) p53 ☐ ATPase family AAA domain containing protein 5 (ATAD5)	Metabolism ☐ Cytochrome CYP1A2 ☐ Cytochrome CYP2C19 ☐ Cytochrome CYP2C9 ☐ Cytochrome CYP2D6 ☐ Cytochrome CYP3A4 ☐ Cytochrome CYP2E1

5. Print Toxicity Report dan file Excel, CSV atau PDF hasil prediksi toksisitas

HASIL PREDIKSI TOKSISITAS

Oral toxicity prediction results for input compound



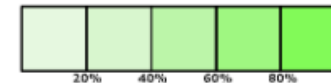
Predicted LD50: 1190mg/kg

Predicted Toxicity Class: 4



Average similarity: 100%

Prediction accuracy: 100%



[Print Toxicity Report](#)

Name	Tamoxifen
Molweight	371.52
Number of hydrogen bond acceptors	2
Number of hydrogen bond donors	0
Number of atoms	28
Number of bonds	30
Number of rotatable bonds	8
Molecular refractivity	119.72
Topological Polar Surface Area	12.47
octanol/water partition coefficient(logP)	6

HASIL PREDIKSI TOKSISITAS

Toxicity Model Report				
Copy Excel CSV PDF				
Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	<u>Hepatotoxicity</u>	dili	Active	0.69
Organ toxicity	<u>Neurotoxicity</u>	neuro	Active	0.87
Organ toxicity	<u>Nephrotoxicity</u>	nephro	Inactive	0.90
Organ toxicity	<u>Respiratory toxicity</u>	respi	Active	0.98
Organ toxicity	<u>Cardiotoxicity</u>	cardio	Inactive	0.77
Toxicity end points	<u>Carcinogenicity</u>	carcino	Inactive	0.62
Toxicity end points	<u>Immunotoxicity</u>	immuno	Active	0.96
Toxicity end points	<u>Mutagenicity</u>	mutagen	Inactive	0.97
Toxicity end points	<u>Cytotoxicity</u>	cyto	Inactive	0.93
Toxicity end points	<u>BBB-barrier</u>	bbb	Inactive	1.0
Toxicity end points	<u>Clinical toxicity</u>	clinical	Inactive	0.56
Toxicity end points	<u>Nutritional toxicity</u>	nutri	Inactive	0.74

Merah/Active → Toksik

Hijau/Inactive → Tidak toksik

KLASIFIKASI DOSIS TOKSIK DAN KELAS TOKSISITAS

Toxic doses and toxicity classes

Toxic doses are often given as LD50 values in mg/kg body weight. The LD50 is the median lethal dose meaning the dose at which 50% of test subjects die upon exposure to a compound.

Toxicity classes are defined according to the globally harmonized system of classification of labelling of chemicals ([GHS](#)). LD50 values are given in [mg/kg]:

- Class I: fatal if swallowed ($LD50 \leq 5$)
- Class II: fatal if swallowed ($5 < LD50 \leq 50$)
- Class III: toxic if swallowed ($50 < LD50 \leq 300$)
- Class IV: harmful if swallowed ($300 < LD50 \leq 2000$)
- Class V: may be harmful if swallowed ($2000 < LD50 \leq 5000$)
- Class VI: non-toxic ($LD50 > 5000$)

**THANK
YOU**