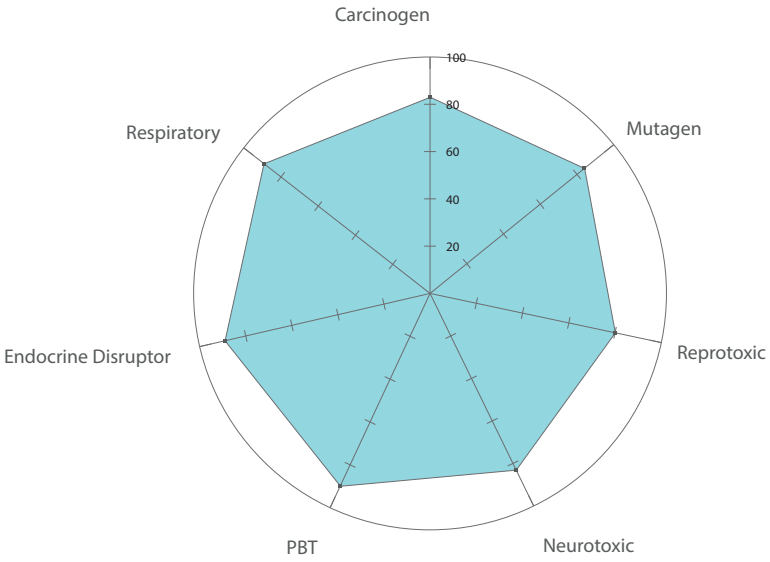
IN SILICO COMPOUND TOXICITY PROFILE (CTP) FROM CHEMICAL STRUCTURE



› Predicts seven toxicity endpoints – i.e. carcinogen, mutagen, reprotoxic, neurotoxic, PBT, ED, respiratory – from a selection of chemical descriptors

› Saves money and time by limiting the number of compounds to be assessed with *in vitro/in vivo* assays

› Provides early toxicity alerts for prioritizing the safest compounds .

HOW DOES IT WORK?

› Input requirements: Chemical structure in sdf format or others

› Descriptors are generated from the input structure.

› The study chemical is then associated with a numerical value ranging from 0 to 100% which is used to classify it as toxic or non-toxic according to each of the seven QSAR statistical models.

ADVANTAGES

› Less compounds to be synthesized and guided *in vitro* assays leading to reduced cost and gain of time

› Early management of safety during R&D, securing the process and increasing the chance of being compliant with the continually evolving reglulatory requirements

› Taking into account concerns towards less animal testing and environmental impacts, may improve value and visibility of your company brand

OUTCOME FOR COMPOUND DEVELOPMENT

Early toxicity alerts

Prioritize safest compounds

Substitute toxic compounds

SAFETY BY DESIGN® APPROACH

Optimize and secure your compound development process by assessing the safety at an early stage

CUSTOMIZED SERVICE

Our service is tailored on your real needs to generate toxicty alerts on your proprietary chemicals using a range of models or specific models of interest to you.

GUIDE TOWARDS RIGHT DECISIONS

We guide you towards decisions to prioritize compounds with a better safety profile or to find suitable substitutes.

HARMONIC PHARMA

SAFETY BY DESIGN

DATASETS FOR TOXICITY ENDPOINT

Toxicity endpoints have been set up with diverse validated sources including *in vitro* and/or *in vivo* data.
Data have been carefully curated and duplicates have been removed.

› **Carcinogen:** 11137 molecules

› **Mutagen:** 3878 molecules

› **Reprotoxic:** 11428 molecules

› **Neurotoxic:** 3100 molecules

› **PBT:** 2364 molecules

› **Endocrine Disruptors (ED):** 3844 molecules

› **Respiratory Sensitizer:** 3171 molecules

A dataset of 1953 molecules with a LD50>5000 mg/kg in rat is used as safe compounds to validate the predictive strength of the models.

MODEL ASSESSMENT

Models are quantitative-structure activity relationships (QSAR) that calculate the toxicity endpoints using a selection of chemical descriptors.

› Robustness of the models is assessed with large and unbiaised training datasets through leave-one-out and 10-fold cross-validation.

› Performance is assessed using recognized statistical methods as illustrated in the table below.

STATISTICS FOR PREDICTIVE QSAR MODELS

QSAR model	AUC	Sensitivity	Specificity
Carcinogen	82%	77%	83%
Mutagen	84%	84%	84%
Reprotoxic	78%	79%	80%
Neurotoxic	84%	92%	83%
PBT	91%	95%	90%
Endocrine Disruptor	86%	85%	89%
Respiratory	84%	90%	89%

DOMAIN OF APPLICABILITY

Prior to be processed, each study molecule is checked with regard to the domain of applicability of our models.

TECHNICAL SUPPORT

We provide you with a personalized B2B relationship all along the data analysis and working meetings.

COMPLEMENTARY APPROACHES

We offer additional methods deriving from spherical harmonic based representations to decipher the mechanism of action of your compound.

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For more information on any of our services, please visit our website
www.harmonicpharma.com

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