	QMRF identifier (JRC Inventory):**Q17-33-0032**
	QMRF Title:**Polar narcosis QSAR for fathead minnow acute toxicity**
	Printing Date:**Apr 16, 2018**

1.QSAR identifier

1.1.QSAR identifier (title):

Polar narcosis QSAR for fathead minnow acute toxicity

1.2.Other related models:

1.3.Software coding the model:

2.General information

2.1.Date of QMRF:

7 September 2009

2.2.QMRF author(s) and contact details:

[1]Fania Bajot Liverpool John Moores University

[2]Mark Cronin Liverpool John Moores University + 44 151 231 2402 m.t.cronin@ljmu.ac.uk

http://www.staff.livjm.ac.uk/phamcron/qsar/qsar1.htm

2.3.Date of QMRF update(s):

2.4.QMRF update(s):

2.5.Model developer(s) and contact details:

[1]Fania Bajot Liverpool John Moores University

[2]Mark Cronin Liverpool John Moores University + 44 151 231 2402 m.t.cronin@ljmu.ac.uk

http://www.staff.livjm.ac.uk/phamcron/qsar/qsar1.htm

2.6.Date of model development and/or publication:

7 September 2009

2.7.Reference(s) to main scientific papers and/or software package:

2.8.Availability of information about the model:

The model is non-proprietary. Information on the algorithm and training set is publicly available.

2.9.Availability of another QMRF for exactly the same model:

none

3.Defining the endpoint - OECD Principle 1

3.1.Species:

Fathead minnow (Pimephales promelas)

3.2.Endpoint:

3.Ecotoxic effects 3.3.Acute toxicity to fish (lethality)

3.3.Comment on endpoint:

96 hours

3.4.Endpoint units:

Moles per litre

3.5.Dependent variable:

Fathead minnow LC50 values (moles per litre) were logarithmically transformed (to base 10) and multipled by minus 1

3.6.Experimental protocol:

Toxicity data were extracted from the US EPA ECOTOX database (http://cfpub.epa.gov/ecotox/) and were compiled by Raevsky (2009).

3.7.Endpoint data quality and variability:

Data extracted from the US EPA ECOTOX database, therefore likely to be of variable quality

4.Defining the algorithm - OECD Principle 2

4.1.Type of model:

QSAR

4.2.Explicit algorithm:

QSAR

Linear regression analysis

log 1/LC50= 0.694 log P - 3.73

4.3.Descriptors in the model:

log P dimensionless logarithm of octanol-water partition coefficient

4.4.Descriptor selection:

One descriptor (log P) chosen empirically from a knowledge of mechanism of action

4.5.Algorithm and descriptor generation:

log P was calculated from SMILES string

4.6.Software name and version for descriptor generation:

KOWWIN v1.67

KOWWIN is part of EPISuite software

Available for download from http://www.epa.gov/oppt/exposure/pubs/episuite.htm

http://www.epa.gov/oppt/exposure/pubs/episuite.htm

4.7.Chemicals/Descriptors ratio:

66 chemicals / 1 descriptor

5.Defining the applicability domain - OECD Principle 3

5.1.Description of the applicability domain of the model:

Applicability domain covers a log P range from 0.48 to 6.09. The acute toxicity values (negative logarithm of molar value) ranged from -3.84 to 0.58.

The compounds selected have been identified as polar narcotics to fish. i.e. they are non-reactive and cause lethality by accumulation at cellular membranes. They are characterised by being simple organic compounds including phenol derivatives and aniline derivatives.

5.2.Method used to assess the applicability domain:

5.3.Software name and version for applicability domain assessment:

5.4.Limits of applicability:

Polar narcosis mechanism of acute fish toxicity.

6.Internal validation - OECD Principle 4

6.1.Availability of the training set:

Yes

6.2.Available information for the training set:

CAS RN: Yes

Chemical Name: Yes

Smiles: Yes

Formula: No

INChI: No

MOL file: No

6.3.Data for each descriptor variable for the training set:

All

6.4.Data for the dependent variable for the training set:

All

6.5.Other information about the training set:

43 simple organic compounds including phenol derivatives and anilines derivatives

6.6.Pre-processing of data before modelling:

None

6.7.Statistics for goodness-of-fit:

r^2adjusted for degrees of freedom = 0.713

standard error = 0.480

Fishers statistic = 105

6.8.Robustness - Statistics obtained by leave-one-out cross-validation:

leave-one-out cross validated r^2= 0.691

6.9.Robustness - Statistics obtained by leave-many-out cross-validation:

6.10.Robustness - Statistics obtained by Y-scrambling:

6.11.Robustness - Statistics obtained by bootstrap:

6.12.Robustness - Statistics obtained by other methods:

7.External validation - OECD Principle 4

7.1.Availability of the external validation set:

No

7.2.Available information for the external validation set:

CAS RN: No

Chemical Name: No

Smiles: No

Formula: No

INChI: No

MOL file: No

7.3.Data for each descriptor variable for the external validation set:

No

7.4.Data for the dependent variable for the external validation set:

No

7.5.Other information about the external validation set:

7.6.Experimental design of test set:

7.7.Predictivity - Statistics obtained by external validation:

7.8.Predictivity - Assessment of the external validation set:

7.9.Comments on the external validation of the model:

8.Providing a mechanistic interpretation - OECD Principle 5

8.1.Mechanistic basis of the model:

All compounds are considered to act by polar narcosis. This is well established for non-reactive compounds. Acute lethality is brought about by accumulation in cellular membranes causing their disruption and ultimately death of the organism. The ability of the compound to accumulate in a cellular membrane is thought to be related to its intrinsic hydrophobicity. Hydrophobicity of these compounds is modelled by log P.

8.2.A priori or a posteriori mechanistic interpretation:

As stated in Section 8.1, hydrophobicity is related to log P and is known to the controlling factor in the acute lethal toxicity of polar narcotic compounds. Compounds in this data set were selected a priori on the basis that they acted as polar narcotics.

8.3.Other information about the mechanistic interpretation:

9.Miscellaneous information

9.1.Comments:

This model is related to a large number of models for polar narcosis for acute fish toxicity.

9.2.Bibliography:

[1]Raevsky OA, Grigor'ev VY, Dearden JC & Weber EE (2009). Classification and Quantification of the Toxicity of Chemicals to Guppy, Fathead Minnow, and Rainbow Trout. Part2. Polar Narcosis Mode of Action . QSAR & Combinatorial Science 28, 163-174.

[2]US EPA ECOTOX database http://cfpub.epa.gov/ecotox/

9.3.Supporting information:

10.Summary (JRC QSAR Model Database)

10.1.QMRF number:

Q17-33-0032

10.2.Publication date:

2017-09-21

10.3.Keywords:

fathead minnow;Pimephales promelas;acute fish toxicity;polar narcosis;

10.4.Comments:

former Q19-39-8-318