**INTRODUCTION & OBJECTIVES**

Toxics and tranquilizers (BTAs) are potentially hazardous chemicals that adversely affect humans and other non-target species, and are on the list of substances of very high concern (SVHC) in the European regulation of chemicals REACH. BTAs are synthetic molecules used in various industrial processes (to obtain pharmaceuticals and agricultural products), and have a wide application as anti-corrosives, cleaning agents for textiles, flame retardants, photographic emulsions, etc. Furthermore, they are abundantly used as components of liquid cooling agents for aircraft and airport runways. Because of their wide use they have been found distributed throughout the environment, mainly in water compartments. The amount of experimental data available for these substances is insufficient for a conservative characterization of their environmental and toxicological profile and they have been included among the four classes of chemicals studied in the European FP7 Project CASTADER (Case studies on the Development and Application of In Situ Techniques for Environmental Hazard and Risk Assessment) [1].

**OBJECTIVES:**

- Development of QSAR models, by different modeling approaches (MLR, OLS and PLS), for the three key organisms for the aquatic ecosystem (Alga, Daphnia and Fish), in order to define the potential aquatic toxicological profile of BTAs.

- Development of Daphnia-Fish Interspecies Quantitative Correlation. 

**MATERIALS & METHODS**

**UI**

**METHODS**

**ENDPOINTS**

- Algae (Pseudokirchneriella subcapitata): EC50 96h; Daphnia (Daphnia magna): EC50 48h; Fish ( Oncorhynchus mykiss): LC50 96h; rat: LD50.

**STRUCTURES**

- Molecular structures were drawn and minimized by the semi-empirical method AM1 in HYPERCHEM software, and converted into SMDs for the OpenBabel software [2].

**TOOLS OF VALIDATION**

- Internal stability verified by R², Q², RMSECV, RMSEP and RIRMSSE.

**DESCRIPTIONS**

- Dragon 5.5, Dragon 6, CASTADER online platform [6].

**ALGORITHM**

- Multiple linear regression (MLR) performed by Partial Least Squares (PLS).

**SYSTEMS**

- Leverage (Distance to model in the X space)

**REFERENCES**

[1] CASTADER FP7 PROJECT - www.castader.eu


[4] (www.castader.eu)/database/

**RESULTS**

- Further enlargement of the dataset with 50 additional azo-aromatic compounds.

- The chemical classified as outlier is removed and a new validation is made. The RMSEP is increasing with more than a factor 2 after the outlier removal.

**DISCUSSION**

- Different robust and externally predictive QSAR models have been developed to predict the aquatic toxicity of BTAs in Algae, Daphnia and Fish.

- Interspecies Quantitative Correlation – Linear regression model has been developed to predict Fish acute toxicity from Daphnia toxicity data. This model has been externally validated and has comparable performances as the one for Fish.

- A profile of the aquatic toxicity has been defined for 35 BTAs by PCA. PCI separates chemicals globally more toxic, in the analyzed aquatic scenario, from less hazardous BTAs (Trend of Aquatic Toxicity).

- Work in progress to create QSAR classification and regression models to predict the cumulative aquatic toxicity of BTAs on the basis of their chemical structures. 

- Results obtained from the QSAR modeling of mammalian toxicity highlight the influence of input data quality on QSAR performances, and the importance of external validation to avoid overestimation of predictivity.

**CONCLUSIONS**

- Development of QSAR models for the aquatic toxicity of BTAs in Algae, Daphnia and Fish. 

- Interspecies Quantitative Correlation – Linear regression model has been developed to predict Fish acute toxicity from Daphnia toxicity data. This model has been externally validated and has comparable performances as the one for Fish. 

- A profile of the aquatic toxicity has been defined for 35 BTAs by PCA. PCI separates chemicals globally more toxic, in the analyzed aquatic scenario, from less hazardous BTAs (Trend of Aquatic Toxicity). 

- Work in progress to create QSAR classification and regression models to predict the cumulative aquatic toxicity of BTAs on the basis of their chemical structures. 

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