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New tools to predict toxicity of fire retardants

Researchers have developed new tools to screen previously untested fire-retardant chemicals for potential toxicity. The tools – known as Quantitative Structure-Activity Relationship (QSAR) models – could allow regulatory decisions to be made in the absence of experimental data, saving time and money by prioritising risk assessments for the most hazardous substances.

Under EU REACH regulations[1], all chemicals manufactured or imported into Europe in quantities over 1 tonne must be registered with detailed information on the potential hazards to human and/or environmental health. However, REACH is still in its early stages (implemented in 2007) and only 4,500 chemicals out of an estimated 30,000 have been registered so far. Since policy decisions restricting the use of chemicals are necessary now, scientists have developed tools to help make swifter decisions where specific experimental data is lacking.

One way that scientists can predict the toxicity of a particular chemical without known toxicological information, is by applying QSAR models developed on experimental data of known substances, recognising the structural features responsible for the studied activity.. This is because the structural aspects and function of chemicals are related.

Scientists under the EU project[2] have developed and evaluated a range of QSAR models for brominated flame retardants (BFR), which are commonly incorporated into plastics, wood and textiles to increase fire resistance. Experimental evidence has found that some BFRs have health effects as endocrine disruptors, which disturb the hormonal system, potentially affecting metabolism, growth and development.

The scientists evaluated existing information on BFRs with known chemical structures and toxicities. The analysis was carried out on six 'biological end points' of endocrine disruption, mainly quantifying estrogen, progesterone and androgen receptor binding. These can include activating a normal hormonal response at the wrong time or to an excessive extent ('agonistic') or preventing hormone activation altogether ('antagonistic').

They identified in total, for the six endpoints, 13 simple structural characteristics in the BFRs – known as molecular descriptors – and created QSAR models relating different combinations of the descriptors to the toxicity classes of the chemicals, ranging from Class 1 (inactive) to Class 3 (high potential for hormonal disruption). The best-performing models, externally validated on separate sets of BFRs with known activity, were used to predict the toxicity of 243 unknown BFRs by using the structural characteristics found in the previously developed models. The results revealed that about half of the previously untested BFRs in the study were predicted as potential endocrine disruptors (with varying activity depending on the test). Also two chemicals proposed in the EU regulations as alternatives to decabromo diphenyl ether, which is the primary component of the highly marketed deca-BDE mixture, were screened as potentially active.

This study has allowed a better understanding of the structural elements that lead to particular toxic effects. Such structures can alert scientists to high endocrine disruption potential in unknown BFRs and help develop safer alternatives.

As more and more scientific data become available, a greater number of chemicals will be used to develop the QSAR models, and the quality of predictions of toxicity for unknown chemicals will continue to improve, say the researchers.

1. Registration, Evaluation, Authorisation and restriction of Chemicals (REACH). See: http://ec.europa.eu/environment/chemicals/reach/reach_intro.htm
2. CAse studies on the Development and Application of in-Silico Techniques for Environmental hazard and Risk assessment (CADASTER) is supported by the European Commission under the Seventh Framework Programme. See: www.cadaster.eu

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Contact: ester.papa@uninsubria.it
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