Introduction and Aims

- Read-across is increasingly being seen as a solution in toxicity prediction.
- Read-across follows from the formation of groups, or categories, of similar compounds.
- Grouping compounds, relevant to the prediction of human organ level toxicity, is the use of reactive fragments associated with known mechanisms of toxicity e.g. reactive hepatotoxicity.
- The aim of this study was to illustrate how categories can be formed and linked to Adverse Outcome Pathways (AOPs). This method is also used to prepare training sets for (Q)SAR work.

Chemotypes

- The chemotype is the molecular fragment or sub-structure associated with a Molecular Initiating Event (MIE).
- Chemotypes can be a combination of a structural fragment and physico-chemical properties (such as logP).
- For liver toxicity, reactive hepatotoxicity is a MIE.
- The chemotypes for specific endpoints, e.g., hepatotoxicity, are also coded as SMARTS and/or CSRML. Some chemotypes can be used as chemical Mode of Action (MoA) classifiers.

Adverse Outcome Pathways

- AOPs record information relating to the perturbation of biochemical pathways which may result in an adverse effect.
- AOPs provide a means of organising toxicological information.
- The Molecular Initiating Event of the AOP can be defined in terms of identifiable chemistry to provide the “domain” of the AOP.

Conclusions

- A strategy is presented to allow molecular initiating events (from AOPs) to guide category formation for cosmetic ingredients.
- The workflow will be available in KNIME as a computational tool to make in silico assessments of chronic toxicity. The COSMOS database (or any other database) can be searched via the KNIME workflow and toxicological data can be retrieved.

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