Development of the TOXIN Knowledge Graph for Assisting Animal-free Risk Assessment of Cosmetic Ingredients

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1 Purpose

Currently, no validated animal-free replacement methods exist to assess repeated dose toxicity. This poses serious problems for developing new chemical compounds, particularly cosmetics, where animal use has been fully banned in the EU since the implementation of Regulation (EC) N°1223/2009 [1]. Nevertheless, Integrated Approaches to Testing and Assessment (IATA) have been introduced by the Organisation for Economic Co-operation and Development (OECD) to support chemical safety assessment. IATAs rely on an integrated analysis of existing information combined with generating new information using non-testing (e.g., grouping and read-across) and alternative testing methods (e.g., in vitro and in silico). Here, we developed the TOXIN Knowledge Graph (KG) [2] to gather and maintain existing safety data of annexed cosmetic ingredients to contribute to non-animal systemic toxicity assessments.

2 Materials and Methods

To create the TOXIN KG, a dataset of 93 scientific opinions dealing with 88 different cosmetic ingredients, published between 2009 and 2019 by the Scientific Committee on Consumer Safety (SCCS), was selected. The data was first captured in Microsoft Office Excel for user-friendliness. Next, the data files were converted into CSV format for ease of data processing and subsequently transformed into RDF graphs that are machine readable using a standardized mapping language called R2RML. The primary use of TOXIN KG is to look for organ-specific toxicological information. Here, a search tool with specific filters focused on liver effects has been developed. Furthermore, the tool allows retrieving Hazard Evaluation Support System (HESS) in silico prediction directly from the OECD QSAR toolbox, generates SMILES, and grades studies semi-automatically using the ToxRtool for the Klimisch score. To provide a systemic representation of toxicological concepts and relationships, the ToXic Process Ontology (TXPO) has been imported and enriched with the Ontology of Genes and Genomes and biological pathways repositories, e.g., Reactome. Hence, the remaining SCCS opinions before 2009 and after 2019 can be included in the KG semi-automatically using ontology-based data annotation.

3 Outcome

Based on the search filters, 52 cosmetic ingredients showed at least one liver-related toxicity parameter. From those compounds, 16 also bared structural alerts for hepatotoxicity predicted by the OECD QSAR toolbox. Based on this outcome, four ingredients (Basic Red 51, Hydroxypropyl p-phenylenediamine and its dihydrochloride salt (A165), Triclosan, and HC Yellow n° 13) were selected for targeted in vitro testing using human liver-relevant cell systems, which is possible due to the implementation of enriched TXPO into TOXIN KG allowing to link an observed effect in the existing (in vivo) data to a toxicological pathway and genes involved [3]. This information, together with the in silico data and the additionally generated in vitro data is instrumental to set up IATA case studies.

References

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