(Quantitative) structure-activity relationship models for genotoxicity

Commonly used acronym: *(Q)SAR models for genotoxicity*

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Contact person

Birgit Mertens

Organisation

Name of the organisation Sciensano

Department Scientific Direction Chemical and Physical Health Risks

Country Belgium

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research, Regulatory use - Routine production, Translational - Applied Research
Type of method	In silico

DESCRIPTION

Method keywords

VEGA Hub

Derek Nexus

Sarah Nexus

bacterial mutagenicity

chromosome damage

prediction models

in vitro micronucleus

ames test

Scientific area keywords

in silico models

DNA damage

genotoxicity

Toxicology

Method description

In silico tools are computer-assisted methodologies with a high-throughput that allow to predict the toxic potential of compounds without experimental testing. Consequently, *in silico* tools are time-, cost- and animal-saving in nature. The most commonly used methods are (quantitative) structure-activity relationship ((Q)SAR) models. These methodologies are based on the hypothesis that similar structures are expected to display similar biological (or toxicological) properties and mechanisms of action. Especially for (bacterial) mutagenicity, a wide variety of (Q)SAR models with good reliability exist. The bacterial reverse gene mutation test (often referred to as 'Ames test') has been the golden standard for testing mutagenicity for decades and consequently, a large collection of data is available to build robust prediction models. For the other toxicological endpoints including chromosome damage, (Q)SAR models are often still in a less advanced state although important progress has been made over the last years. (Q)SAR models are particularly of interest for priority setting or when no or limited amounts of the compound are available. Within our lab, we have the most experience with the genotoxicity models present in the open source VEGA Hub and with the commercial software Derek and Sarah Nexus.

Lab equipment

Computer software:

- Commercial software: Derek Nexus, Sarah Nexus

- Open source software: VEGA Hub (https://www.vegahub.eu/)

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

(Q)SAR models are time-, cost- and animal-saving in nature.

Moreover, the (Q)SAR models in the VEGA Hub are freely available.

Challenges

The reliability of the (Q)SAR models will depend on the quality of the data that have been used to build the model. For bacterial mutagenicity, large datasets are available, and consequently, a large number of relatively robust (Q)SAR models have been developed. Less data are available for other genotoxic endpoints such as *in vitro* and *in vivo* chromosome damage resulting in general in models with lower reliability.

Modifications

By extending/improving the underlying datasets and/or the underlying mathematical tools, new and/or updated (Q)SAR models for genotoxicity are constantly being developed.

Future & Other applications

Currently, we have the most experience with the application of (Q)SAR models for genotoxicity. However, we are also exploring their use for other toxicological endpoints such as carcinogenicity and endocrine activity.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

1. Baderna D, Van Overmeire I, Lavado GJ, Gadaleta D, Mertens B. In Silico Methods for Chromosome Damage. Methods Mol Biol. 2022;2425:185-200. doi: 10.1007/978-1-0716-1960-5_8. PMID: 35188633.

2. Barhdadi S, Mertens B, Van Bossuyt M, Van De Maele J, Anthonissen R, Canfyn M, Courselle P, Rogiers V, Deconinck E, Vanhaecke T. Identification of flavouring substances of genotoxic concern present in e-cigarette refills. Food Chem Toxicol. 2021 Jan;147:111864. doi: 10.1016/j.fct.2020.111864. Epub 2020 Nov 18. PMID: 33217530.

3. Van Bossuyt M, Raitano G, Honma M, Van Hoeck E, Vanhaecke T, Rogiers V, Mertens B, Benfenati E. New QSAR models to predict chromosome damaging potential based on the in vivo micronucleus test. Toxicol Lett. 2020 Sep 1;329:80-84. doi: 10.1016/j.toxlet.2020.04.016. Epub 2020 Apr 29. PMID: 32360788.

4. Van Bossuyt M, Van Hoeck E, Vanhaecke T, Rogiers V, Mertens B. Prioritizing substances of genotoxic concern for in-depth safety evaluation using non-animal approaches: The example of food contact materials. ALTEX. 2019;36(2):215-230. doi: 10.14573/altex.1810011. Epub 2018 Nov 28. PMID: 30488084.

5. Van Bossuyt M, Van Hoeck E, Raitano G, Vanhaecke T, Benfenati E, Mertens B, Rogiers V. Performance of In Silico Models for Mutagenicity Prediction of Food Contact Materials. Toxicol Sci. 2018 Jun 1;163(2):632-638. doi: 10.1093/toxsci/kfy057. PMID: 29579255.

6. Van Bossuyt M, Van Hoeck E, Vanhaecke T, Rogiers V, Mertens B. Safeguarding human health using in silico tools? Arch Toxicol. 2017 Jul;91(7):2705-2706. doi: 10.1007/s00204-017-1931-z. Epub 2017 Feb 8. PMID: 28180947.

7. Ates G, Raitano G, Heymans A, Van Bossuyt M, Vanparys P, Mertens B, Chesne C, Roncaglioni A, Milushev D, Benfenati E, Rogiers V, Doktorova TY. In silico tools and transcriptomics analyses in the mutagenicity assessment of cosmetic ingredients: a proof-of-principle on how to add weight to the evidence. Mutagenesis. 2016 Jul;31(4):453-61. doi: 10.1093/mutage/gew008. Epub 2016 Mar 15. PMID: 26980085.

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