An evaluation of selected (Q)SARs/expert systems for the Prediction of Skin Sensitization Potential

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Abstract

Predictive testing to characterize substances for their skin sensitization potential has historically been based on animal models such as the Local Lymph Node Assay (LLNA) and the Guinea Pig Maximization Test (GPMT). In recent years, EU regulations have gathered available data for skin sensitization and assess its accuracy. The views expressed are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.

Aims

- Gather available data for skin sensitization and assess its accuracy
- Determine the performance metrics for three expert systems
- Assess the performance of the models

Selected Expert Systems

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<tr>
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<th>Accuracy</th>
<th>Sensitivity</th>
<th>Specificity</th>
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</thead>
<tbody>
<tr>
<td>Derek Nexus</td>
<td>71%</td>
<td>65%</td>
<td>55%</td>
</tr>
<tr>
<td>VEGA</td>
<td>44%</td>
<td>56%</td>
<td>80%</td>
</tr>
<tr>
<td>TIMES-SS</td>
<td>67%</td>
<td>63%</td>
<td>55%</td>
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</tbody>
</table>

Global performance of the expert systems

The LLNA dataset generated using the OECD eChemPortal has a registered structure in DSSTox. The VEGA developers in their own evaluations had noted that all of their expert systems have different approaches of characterizing their applicability domains and how this impacts the prediction derived. If VEGA has a prediction rated as good and the substance is predicted to be a non-sensitizer, it is also certain to be a non-sensitizer. Most substances fall outside of the domain of TIMES-55, however those that lie within its domain do have a balanced accuracy that is comparable to the animal tests.

Conclusions

- • The balanced accuracies of the GPMT and LLNA data when compared to one another ranged from 70% to 85%.
- • Derek Nexus and TIMES-55 were most successful at predicting skin sensitizers from a global performance perspective.
- • Substances that lie within the TIMES-55 domain gave predictions that had the same balanced accuracy as the animal data.

References

Derek Nexus (http://www.lhasalimited.org/products/derek-nexus.htm)
TIMES-SS: https://comptox.epa.gov/dashboard
VEGA: https://oasis-lmc.org/products/software/times.aspx
http://www.caesar-project.eu/

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