Characterizing the Disposition and Effects of Dimethylformamide in Humans Using in Silico Modeling

EmmaKate Raisley, Tierney Johnson, Dr. Brad Reisfeld
Department of Chemical and Biological Engineering
Colorado State University, Fort Collins, CO, USA
Background

- Target compound: Dimethylformamide
- Pharmacokinetic and Physiologically Based Modeling
- Utilize PKSim software
- Calibrate with company data

Figure 1. DMF metabolism in vivo.
Methods/Experimental Setup

Figure 2. Basic PBPK model strategy
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3828005/

Figure 3. Specific metabolite strategy for DMF

Figure 4. Rat data from Scailteur et al.
Results

**Model Inputs**

<table>
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<tr>
<th>Name</th>
<th>Top Container</th>
<th>Organ</th>
<th>Molecule</th>
<th>Value</th>
<th>Value Origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound type 0</td>
<td></td>
<td></td>
<td>Dimethyl Formamide</td>
<td>73.09 g/mol</td>
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<td>Is small molecule</td>
<td></td>
<td></td>
<td>Dimethyl Formamide</td>
<td>6.70</td>
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<tr>
<td>Molecular weight</td>
<td></td>
<td></td>
<td>Dimethyl Formamide</td>
<td>1.46 Log Units</td>
<td>Unknown</td>
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<tr>
<td>pH value 0</td>
<td></td>
<td></td>
<td>Dimethyl Formamide</td>
<td>95.00 %</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

**Model Outputs**

Figure 5. Basic inputs necessary to run the model.

Figure 6. Output of the DMF model.
### Discussion/Next Steps

- Further parameterize the PKSim model to increase its accuracy.
- Compare the outputs against the biomonitoring data received from a corporate partner.
- Further calibrate the model with the corporate partner data.
- Utilize the PK Sim model to improve predictions of exposure versus adverse effects.
- Develop a pharmacodynamic model to pair with the pharmacokinetic model.

### Conclusions

- The current model is showing the concentration over time of DMF in the urine that would be expected.
- The final outputs are consistent with DMF concentrations over a similar exposure plan (Scailteur et al.)
- We now plan to target our research to include more all main DMF metabolites rather than just HMMF and then extrapolate this model to humans.
- Our current approach of *in silico* modeling seems to be a promising method for accurate predictions of DMF concentrations.
What benefits did you get from your SURE experience?

• Had the opportunity to work in a collaborative team with people from different majors, levels of experience and backgrounds.

• Learned how to use and became comfortable with a completely new software program with the help of my teammates and mentor.

• Had the opportunity to dive deep into a single project for the length of a semester and begin to understand the goal at hand comprehensively rather than just a small part of it.

• Applied knowledge I learned from different classes to real life problems and helped to bring more meaning to the topics and techniques being taught.

References & Acknowledgements


Thank you to the Suzanne and Walter Scott Foundation, Tointon Family Foundation, The Filsinger Family, Caterpillar Inc., and Contributors to the Dean’s Innovation fund for making the SURE program possible.
Thank you