Enabling PBPK model development through the application of freely available techniques for the creation of a chemically-annotated collection of literature

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The creation of Physiologically Based Pharmacokinetic (PBPK) models for a new chemical requires the selection of an appropriate model structure and the collection of a large amount of data for parameterization. Commonly, a large proportion of the needed information is collected from previously published PBPK models for compounds analogous to the chemical of interest. A key difficulty in quickly developing new models is therefore the identification of appropriate chemical analogs within PBPK model literature. To reduce the burden on researchers of finding the appropriate literature to inform new modeling efforts, we sought to collect a comprehensive listing of chemicals contained in the corpus of PBPK articles and embed them into a chemically searchable database for facile analog identification. To cull the list of chemicals from PBPK literature, we investigated the use of three easily accessible methods: collecting chemicals via MeSH controlled vocabulary processing abstracts using OSCAR4 text-mining software, and annotating abstracts using chemicalize.org. In total, just over 300 unique compounds spanning a variety of chemical classes were identified as having completed PBPK models from over 1700 articles. Additional annotations of PBPK model details including species, lifestage, number of compartments, gender, and exposure routes were tabulated. These data were then imbedded into the Toxicokinetic Knowledge Base (TKKB), an internal website for chemically querying available toxicokinetic information. Several case studies were completed documenting the usefulness of TKKB in collecting relevant PBPK model structures and parameters for target chemicals.