

in Table 1 and briefly discussed below.

Table 1. Summary information regarding the evaluated literature.

Title of the study	Physicochemical Parameter Prediction Tools	Multimedia Mass Balance Models	Study Aim	References
Comparison of Two Screening Level Risk Assessment Approaches for Six Disinfectants and Pharmaceuticals	EPIWIN	EUSES	To determine risk of pharmaceuticals and disinfectants	(Van Wezel & Jager, 2002) ⁶
Expanding the Applicability of Multimedia Fate Models to Polar Organic Chemicals	sp-LFERs, pp-LFERs	Modified Level III Model	To show that implementation of pp-LFERs can reduce errors and uncertainty in multimedia fate modeling	(Breivik & Wania, 2003) ⁸
Evaluating the Environmental Fate of Pharmaceuticals Using a Level III Model Based on Poly-parameter Linear Free Energy Relationships	EPIWIN	Modified Level III Model	To widen applicability of MM models for polar chemicals (i.e. pharmaceuticals) by integrating pp-LFERs	(Zukowska, Breivik, & Wania, 2006) ¹⁰
Including Degradation Products of Persistent Organic Pollutants in a Global Multi-Media Box Model	CATABOL, EPIWIN	ChiMoChem	To consider effects of degradation products on persistence, spatial range, and Arctic contaminant potential	(Schenker, Scheringer, & Hungerbühler, 2007) ²²
Development and Exploration of an Organic Contaminant Fate Model Using Poly-Parameter Linear Free Energy Relationships	pp-LFERs	CoZMo-POP2	Single parameter LFERs based CoZMo-POP2 was improved by changing sp-LFER to pp-LFER by testing on polar chemicals	(Brown & Wania, 2009) ¹¹
On the Replacement of Empirical Parameters in Multimedia Mass Balance Models with QSPR Data	EPI Suite, L-QSPR, PCA-QSPR, QSPR	OECD Tool	Experimental based inputs of MM models were changed with QSPR derived inputs to reduce time and cost	(Puzyn, 2011) ⁹
A New Metric for Long-Range Transport Potential of Chemicals	QSPR, LFER models	FATE	To evaluate the LRTP of chlorinated and brominated congeners of benzenes, furanes, diphenyl ethers, dibenzo-p-dioxins, biphenyls and naphthalenes by using QSPR-FATE model	(Kawai et al., 2014) ¹⁷
Estimation of Physicochemical Properties of 52 Non-PBDE Brominated Flame Retardants and Evaluation of Their Overall Persistence and Long-range Transport Potential	EPI Suite, SPARC	OECD Tool	To evaluate the relationship between the properties on the molecular weight and chemical structure	(Kuramochi, Takigami, Scheringer, & Sakai, 2014) ¹⁸
A Modeling Assessment of the Physicochemical Properties and Environmental Fate of Emerging and Novel Per- and Polyfluoroalkyl Substances	COSMOtherm, SPARC, EPI Suite	OECD Tool	Reevaluation of novel alternatives for long-chain perfluoroalkyl acids and their precursors	(Gomis, Wang, Scheringer, & Cousins, 2015) ¹⁹
Novel Flame Retardants: Estimating the Physical-Chemical Properties and Environmental Fate of 94 Halogenated and Organophosphate PBDE Replacements	EPI Suite, SPARC, Aboak	OECD Tool	Testing persistence and long range transport potential of novel flame retardants replacing PBDEs	(Zhang et al., 2016) ²⁰
Estimation of Physicochemical Properties of 2-ethylhexyl-4-methoxycinnamate (EHMC) Degradation Products and Their Toxicological Evaluations	EPI Suite	OECD Tool	To determine physicochemical properties and fate of 2-ethylhexyl-4-methoxycinnamate (EHMC) and its transformation products	(Gackowska, Studziński, Kudlek, Dudziak, & Gaca, 2018) ²¹
Organophosphate Ester Transport, fate, and Emissions in Toronto, Canada, Estimated Using an Updated Multimedia Urban Model	EPI Suite, CATALOGIC	Multimedia Urban Model (MUM)	To predict aggregate emissions of selected organophosphate ester to urban air and their fate in the urban area	(Rodgers, Truong, Jantunen, Helm, & Diamond, 2018) ²³
Can Poly-Parameter Linear-Free Energy Relationships (pp-LFERs) Improve Modelling Bioaccumulation in Fish?	sp-LFERs, pp-LFERs	One-compartment model, multi-compartment model	To understand the effect of applying pp-LFERs on the bioconcentration prediction in various types of fish model	(Zhao, Jonas, & Sweetman, 2018) ²⁴

Integrated utilization of property estimation models with MM require modeling only of chemicals that are within the applicability domain (AD)⁸. AD is a hypothetical space that is bordered by structural similarity and range of endpoint. Predictions are credible only if chemicals are located in applicability domain⁹. Furthermore, many chemicals have complicated partitioning tendency. Extending AD could be achieved by adding experimental partitioning coefficients, multiple sp-LFER equations, or pp-LFERs integration to multimedia fate models. The last option can allow for assessing several types of chemicals with polar functional groups⁸. For example, Zukowska et al.¹⁰ investigated three pharmaceuticals by implementing a pp-LFER based MM model. After the model was parameterized with respect to a real drainage basin, chemical based input requirement was satisfied by EPI Suite and the literature¹⁰. In addition to being able to model relatively polar chemicals, additional phases could also be considered without additional input requirement⁸ by coupling MM models with property estimation tools. Also, the pp-LFER based models can supply mechanistic perspectives for several interactions and polar or nonpolar chemicals¹⁰.

However, finding credible descriptors, effects of environmental conditions on pp-LFERs and inadequacies in empirical data necessary for generation of pp-LFERs were stated as challenges for combining pp-LFERs with MM models. In spite of these, Breivik et. al. (2003) envisioned that "chemical risk assessment tools of the future may ultimately require no other chemical input parameter than molecular structure"⁸. The results of pp-LFER based and sp-LFER based MM models were not significantly different as compared to model parametrization. Therefore, Brown et al. (2009) recommended that selection of sp-LFER or pp-LFER depended on the availability of input parameters. They evaluated that this was increasingly becoming possible owing to increasing available data¹¹. Typically, hydrophobic persistent organic pollutants (POPs) were modeled by MM models⁶. Drugs that are similar to POPs can be evaluated by MM models that were originally generated for POPs⁴. Polar and/or ionized drugs can be relatively single media pollutants, so single medium based fate models such as water quality models may be enough¹⁰. However, the metabolism of pharmaceuticals by the human body and uncertainty due to loss mechanisms should be regarded when applying single medium based models²³. Furthermore, equivalent aqueous based fate models can be preferred in place of fugacity based ones to determine fate of ionized compounds⁴.

Schenker et al. (2007) investigated fate of original chemicals and their transformation products using a QSPR-MM scheme to estimate joint persistence, spatial range and Arctic contamination potential. This allowed detecting environmentally-benign parent compounds that might have hazardous degradation products or vice versa¹². Uncertainties in property estimation could be high and more credible predictions for half-lives, K_{oc} and K_H were necessitated. Unless half-lives of structurally similar compounds or isomers are differentiated, the effects of transformation products could not be understood¹³.

Hydrophobic and non-ionized chemicals can be assessed successfully by QSPR integrated MM models. In case of polar and ionized compounds, requirement of some improvements was highlighted by Jagiello and coworkers⁴. In addition to an increasing volume of pharmaceuticals, existence of different functional groups complicates their fate determination. QSPR models can frequently predict physicochemical properties, pharmacokinetics, and bioconcentration factors for POPs and chemicals with persistent, bioaccumulative and toxic (PBT) characteristics. QSPR implementation for drugs could be restricted by AD and lack of validation. Therefore, local models for each specific chemical class were suggested¹⁵. In addition to uncertainties in MM models, physicochemical properties are generally obtained for neutral species. Hence, the credibility of QSPR-MM modeling could be lower in case of ionized chemicals assessment. Available MM models should then incorporate pH as a parameter and pKa of chemicals. Despite some difficulties, QSPR-MM modeling was evaluated as reasonable as long as a stronger association between modelers and experimentalists can be maintained⁴. Inaccurate data in physicochemical properties for environmental fate models can be reduced by correlations. For example, the smallest deviation from experimental partitioning coefficients or temperature dependences of physicochemical properties could be considered by applying mathematical relationships¹⁴.

Di Guardo and coworkers¹⁵ compiled improvements in MM models and highlighted that AD of MM models were extended for polar and ionizable organic chemicals. Also, these models were implemented for nanoparticles, and microplastics¹⁵. Furthermore, biological substances (i.e. proteins, bacteria, prions, etc.) might be modeled by MM models⁵. Also, model parameters have been updated. Additional environmental media, and processes have been integrated into MM models. Sensitivity and uncertainty analysis were utilized with MM models. Additionally, MM models were assessed as satisfactory for highly dynamic cases with high accuracy. In spite of these improvements, methodology development in partition coefficients for polar and ionizable chemicals, and more realistic environmental media might be introduced to environmental fate models¹⁵.

By computational design, physical and chemical properties of chemicals and so their possible fate could be estimated. Further studies might be beneficial for better estimation of properties such as soil partitioning, and for all physicochemical properties of polar and ionizable chemicals. The more predictive success such property estimation tools have, the better chance we have of preventing negative environmental impacts of synthetic organic chemicals. Currently, screening is performed for organic chemicals in food additives, food packaging, pharmaceutical, and personal products, to some degree. Integrating computational methods to improve a holistic screening methodology for different types of organic chemicals could constitute a significant step towards application of pollution-prevention strategies in the chemical sector.

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