How can we simplify the use of dermal absorption data in the non-dietary risk assessment of pesticides?

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INTRODUCTION

Dermal absorption values are used to translate external exposure doses into systemic exposures for the non-dietary risk assessment of pesticides. Dermal absorption estimates are mostly derived from the results of in vitro dermal penetration studies.

While the Environmental Protection Agency of the United States of America (US EPA) derives a common dermal absorption factor for active substances covering all related products, the European Food Safety Authority (EFSA) requests estimates based on individual concentrations covering the intended use rates of specific products. The latter poses challenges because it disconnects the exposure dose from the applied dose in absorption studies, which may not be suitable in scenarios where concentration is not relevant. The current approach binds resources because the assessment is complicated and time consuming. The approach also results in very conservative absorption estimates, as it compounds the conservatism already built into the assay design, which then often triggers further studies that also need to be incorporated into exposure assessments and evaluations.

METHODOLOGY

We analysed the EFSA dermal absorption database (EFSA DA DB), 30 human in vitro studies from CropLife Europe (CLE) companies, where $\geq$3 in-use dilution concentrations were tested, and 15 dermal absorption triple pack datasets. Instead of considering tested concentrations, the relationship of applied dose and absolute absorption is investigated on a decadic logarithmic scale.

Linear models were fitted to the data and their slopes investigated.

RESULTS

Our analysis shows that, for all investigated datasets, the absolute dermal absorption is directly dependent on the absolute dose applied, when considered on a decadic logarithmic scale. The slopes of the linear models are between 0 and 1, with many slopes being compatible with 1 when using 95 % confidence intervals. This relationship is concordant with the toxicological axiom that risk, if characterised by internal exposure surrogate data, is driven by exposure dose.

DISCUSSION

Our analysis shows that, based on an absolute amount, the relative absorption is approximately constant. Hence, a single average dermal absorption value can be derived by a simple calculation algorithm, when studies with multiple tested concentrations are available. Here, a linear model can be fitted to the data assuming a slope of 1.

This approach greatly simplifies risk assessment and frees up resources enabling us to explore exposure refinements. The approach may also serve to harmonise global dermal absorption estimation.