Retrospective Analysis of Dermal Absorption Triple Pack Data

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Highlights

- Dermal absorption can be estimated using the **"triple pack,"** which combines in vivo rat, in vitro rat, and in vitro human data to calculate an estimated **human dermal absorption factor (DAF)**.
- We conducted a **retrospective evaluation** of **agrochemical formulations** to compare the DAF derived from each individual method and the triple pack.
- **These comparisons support potentially using in vitro data alone for DAF derivation for human health risk assessment of pesticides**.

Conclusions

- The human in vitro assay provided a similar or higher estimate of dermal absorption than the triple pack.
- However, rat in vitro studies would still have utility if human in vitro data were not available.
- In vitro data provided estimates of dermal absorption that were at least as protective as in vivo rat data, and thus could also be considered adequate for use in establishing dermal absorption factors.

DAF Calculations and Comparisons

- Dermal absorption affects the potential for a chemical to be toxic when absorbed through the skin. A higher DAF means the chemical is more readily absorbed.
- The "triple pack" combines results from in vivo rat, in vitro rat, and in vitro human studies to calculate an estimated human DAF as described by the following equation:

$$\textit{triple pack DAF} = \textit{rat in vivo} \times (\textit{human in vitro} \div \textit{rat in vitro})$$

Comparison of Absorbance Ratio Calculations

1. $\frac{\textit{rat in vitro}}{\textit{rat in vivo}}$
2. $\frac{\textit{human in vitro}}{\textit{rat in vitro}}$
3. $\frac{\textit{human in vitro}}{\textit{rat in vivo}}$
4. $\frac{\textit{human in vitro}}{\textit{triple pack DAF}} = \frac{\cancel{\textit{human in vitro}}}{\textit{rat in vivo} \times \frac{\cancel{\textit{human in vitro}}}{\textit{rat in vitro}}} = \frac{\textit{rat in vitro}}{\textit{rat in vivo}}$

Impact of Assay Variability

Example of absorbance ratio calculations:
Rat in vitro assay data for a pesticide formulation

R in Vitro

potential Abs (TS 3-20)	36.7
SD	2.07
TS 1 and 2	1.41
SD	0.545

R in Vitro

potential Abs (TS 3-20)	28
SD	4.332
TS 1 and 2	0.6
SD	0.2

Rat in Vitro

	Pot Abs (TS 3-20)	TS 1 and 2	Pot Abs (TS 1-20)
Max (+1SD)	38.77	1.955	40.725
Mean	36.7	1.41	38.11
Max (-1SD)	34.63	0.865	35.495

Rat in Vitro

	Pot Abs (TS 3-20)	TS 1 and 2	Pot Abs (TS 1-20)
Max (+1SD)	32.332	0.8	33.132
Mean	28	0.6	28.6
Max (-1SD)	23.668	0.4	24.068

Max Ratio (TS 3-20)	Max Ratio (TS 1-20)
1.638	1.692

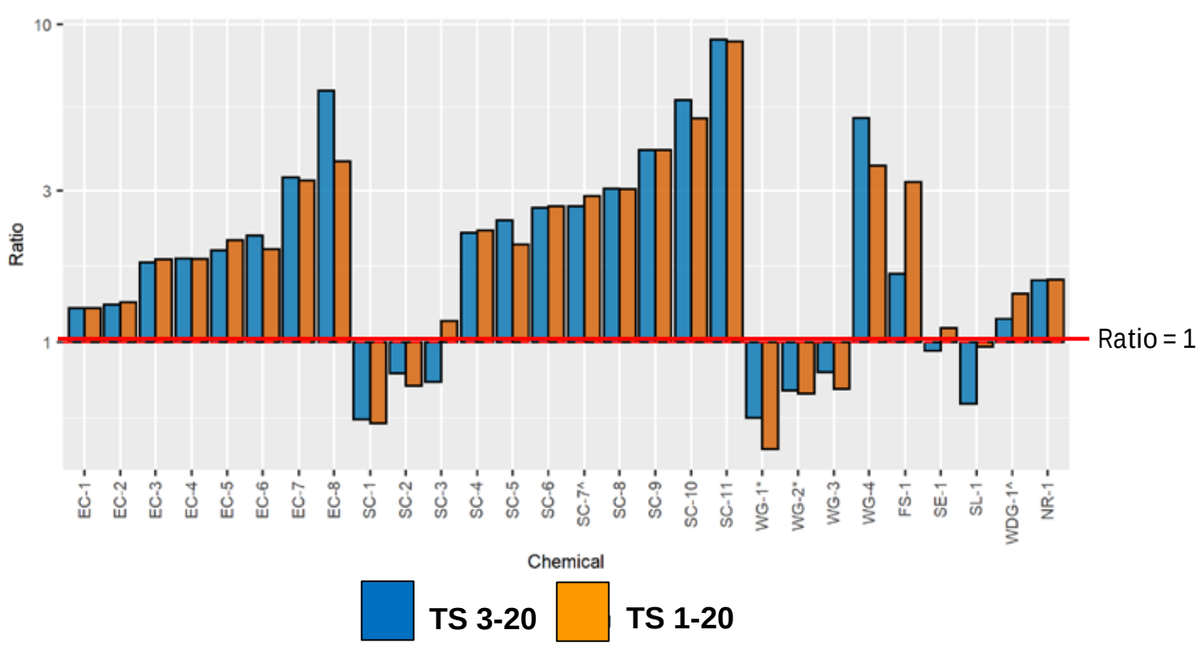
TS3-20 Ratio	TS 1-20 Ratio
1.311	1.333

Min Ratio (TS 3-20)	Min Ratio (TS 1-20)
1.071	1.071

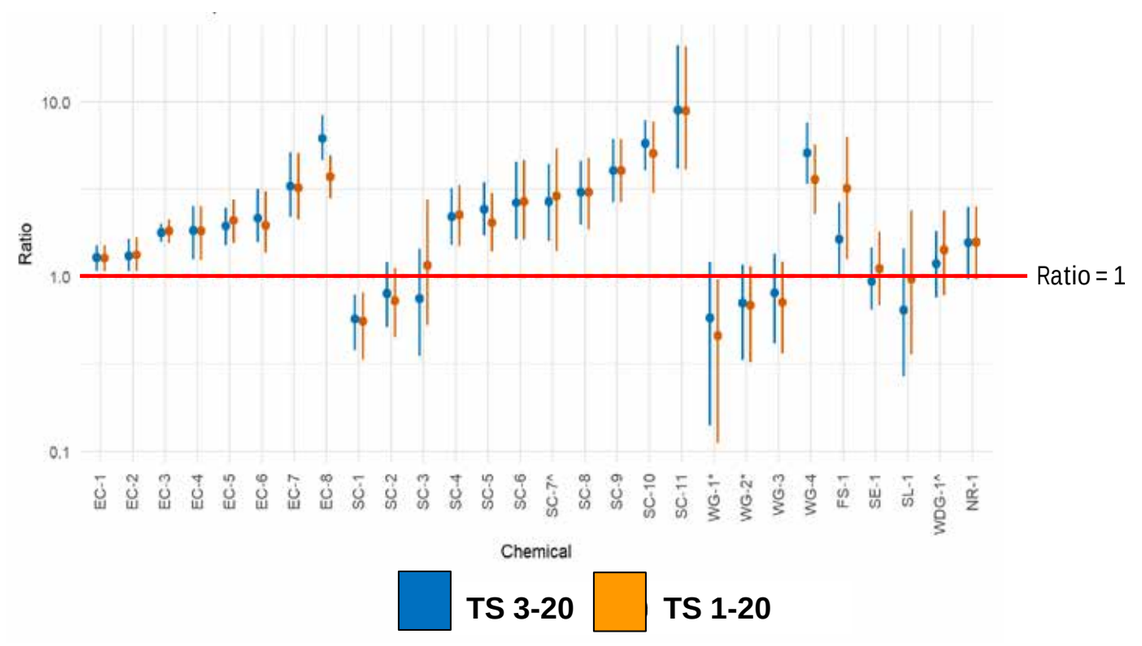
TS = tape strips; Pot Abs = potential absorption

- Maximum (Max) and minimum (Min) ratios were calculated to establish the range of possible outcomes for a particular type of test (here, rat in vitro) for a particular formulation.
- Max ratio = ratio of the sum of the mean and standard deviation (SD) of replicate measurements (in the numerator) and the difference of the mean and SD (in the denominator).
- Min ratio = ratio of the difference of the mean and SD (in the numerator) and the sum of the mean and SD of replicate measurements (in the denominator).
- We considered variability when comparing various absorbance ratios (graph below right).

Human In Vitro vs Triple Pack DAF (also Rat In Vitro vs Rat In Vivo)



Mean absorbance ratios



Range of possible ratios using Max and Min ratios

- Of the formulations examined, 26% (8/30) had human in vitro values that were less than the triple pack DAFs.
- However, all eight of these values were within 0.5-fold of one another based on mean values.
- When variability was considered, the in vitro human value was at least as protective as the triple pack DAF for most (29/30) formulations.
- Including all tape strips in the calculation had little impact.

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A summary of NICEATM and ICCVAM activities at the Eleventh World Congress is available on the National Toxicology Program website at **https://ntp.niehs.nih.gov/go/wc11**.