

## 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.

## 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:

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

### Comparison of Absorbance Ratio Calculations

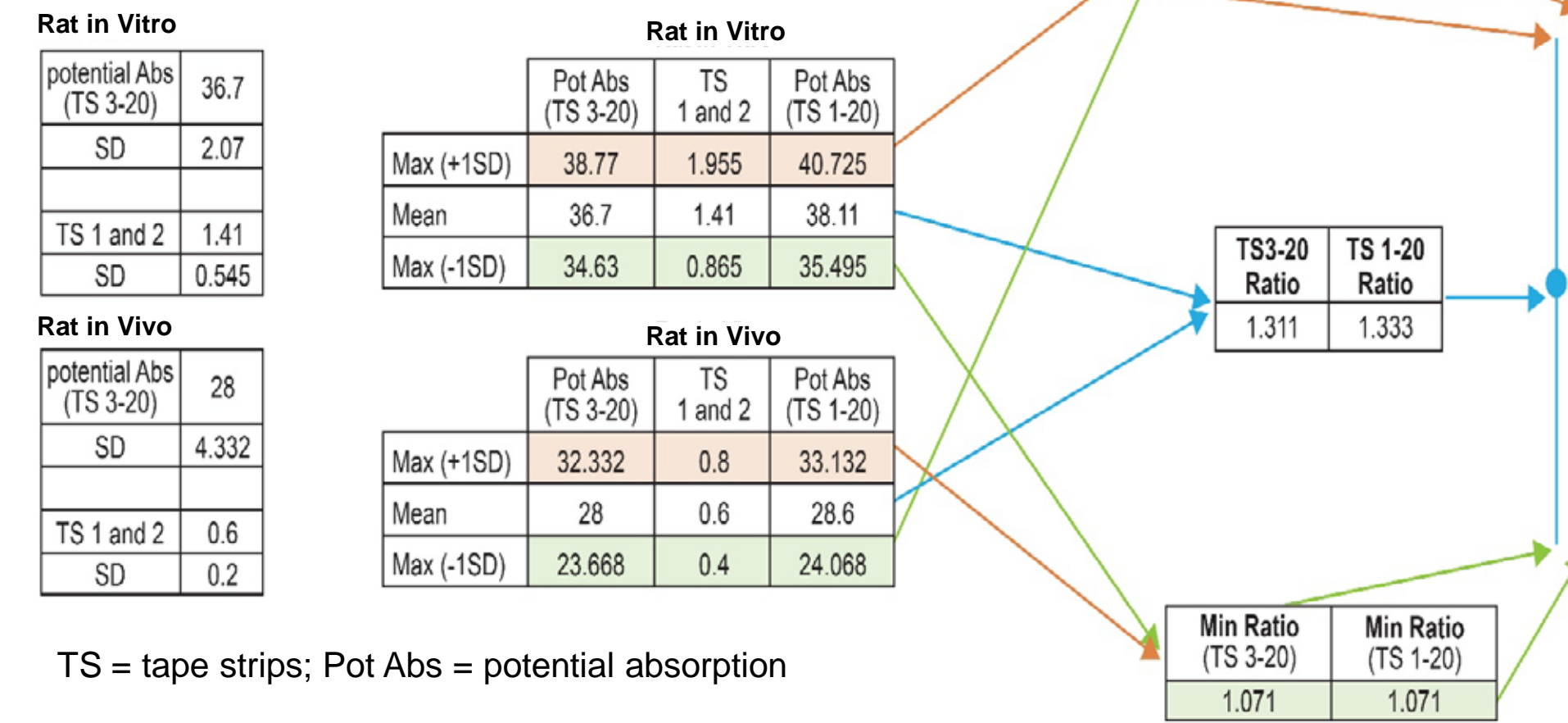
1.  $\frac{\text{rat in vitro}}{\text{rat in vivo}}$
2.  $\frac{\text{human in vitro}}{\text{rat in vitro}}$
3.  $\frac{\text{human in vitro}}{\text{rat in vivo}}$
4.  $\frac{\text{human in vitro}}{\text{triple pack DAF}} = \frac{\text{human in vitro}}{\text{rat in vivo} \times \text{human in vitro}}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

## Formulation Types in This Analysis

Formulation type	Number of formulations
Emulsifiable concentrate (EC)	8
Flowable concentrate for seed treatment (FS)	1
Oil dispersion (OD)	2
Suspension concentrate (SC)	11
Soluble liquid (SL)	1
Water dispersible granules (WDG)	1
Suspo-emulsion (SE)	1
Wettable granules (WG)	1
Not reported (NR)	4
<b>Total</b>	<b>30</b>

## Impact of Assay Variability

### Example of Absorbance Ratio Calculations: Rat in vitro assay data for a pesticide formulation



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 (graphs at right).

## Conclusions

- Absorption through in vitro human skin was found to be similar to or less than that observed in rat skin (in vitro and in vivo) for all formulations.
- The human in vitro assay provided a similar or higher estimate of dermal absorption than the triple pack
- For human health risk assessment, in vitro assays using human skin would be preferable. Such tests would be directly relevant to the species of interest (humans) and avoid any overestimation of dermal absorption using rat models.
- However, rat in vitro studies would still have utility if human in vitro data were not available.
- In vitro rat data provide estimates of dermal absorption that are at least as protective as in vivo rat data, and thus could also be considered adequate for use in establishing dermal absorption factors.

## More Information

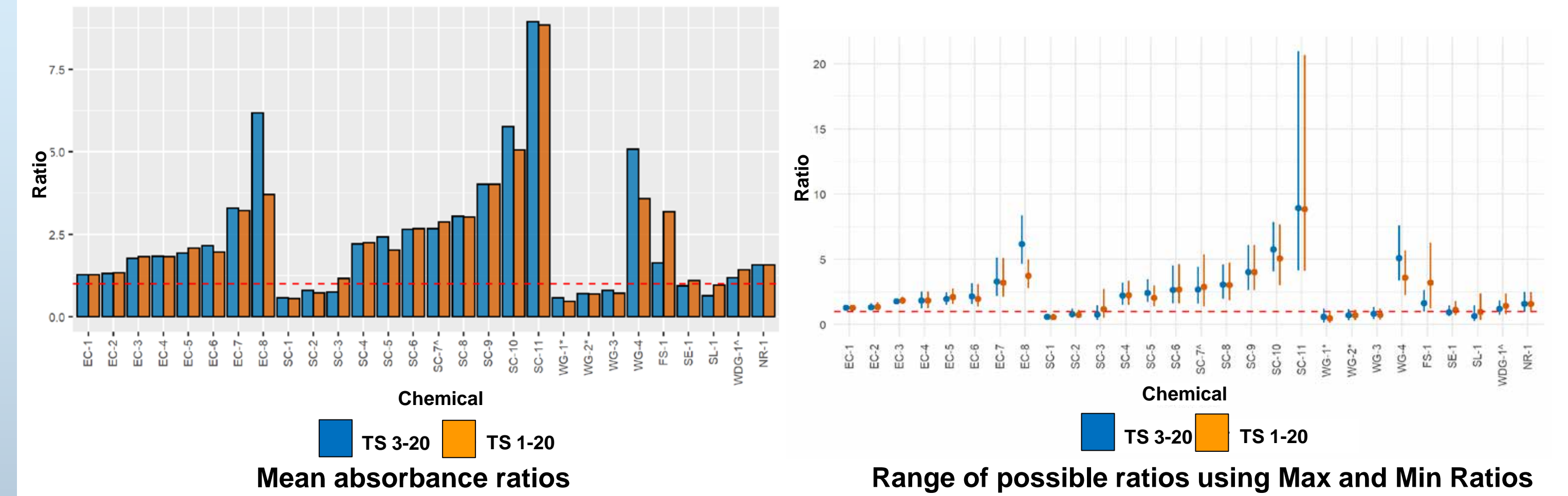
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## Human In Vitro vs Triple Pack DAF (also Rat In Vitro vs Rat In Vivo)

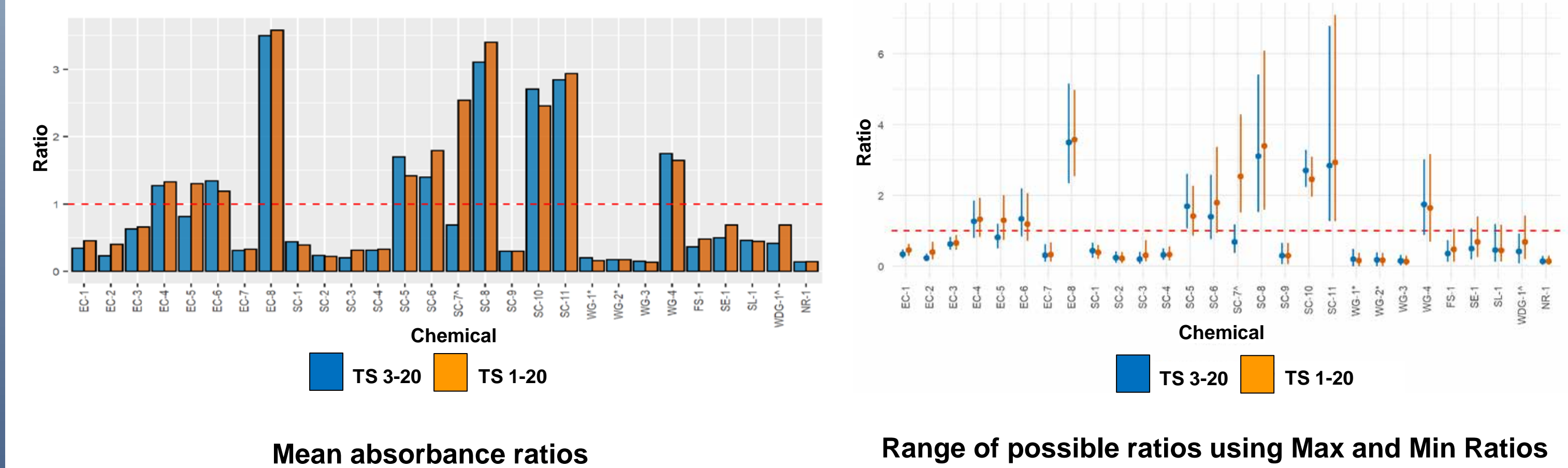
### Low dose group – time-matched comparison at 24 hr



- 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.

## Human In Vitro vs Rat In Vivo

### Low dose group – time-matched comparison at 24 hr



- The ratio of in vitro human:in vivo rat absorption was  $\leq 1$  for two-thirds of the formulations evaluated.
- For the remaining one-third of the formulations, ratios ranged from 1.27 to 3.50, meaning that the in vitro human absorbance value would actually be more protective than the in vivo rat value.
- Similar results were observed in the human in vitro: rat in vitro comparison (data not shown).
- Including all tape strips in the calculation had little impact.