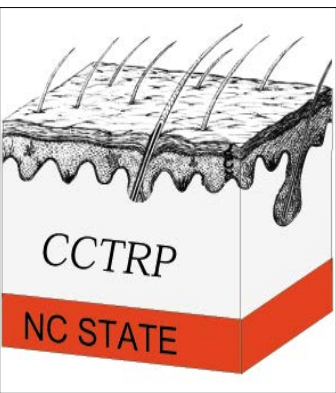


***In Vivo* Skin Absorption of ortho-Phenylphenol in Metalworking Fluid Formulations**

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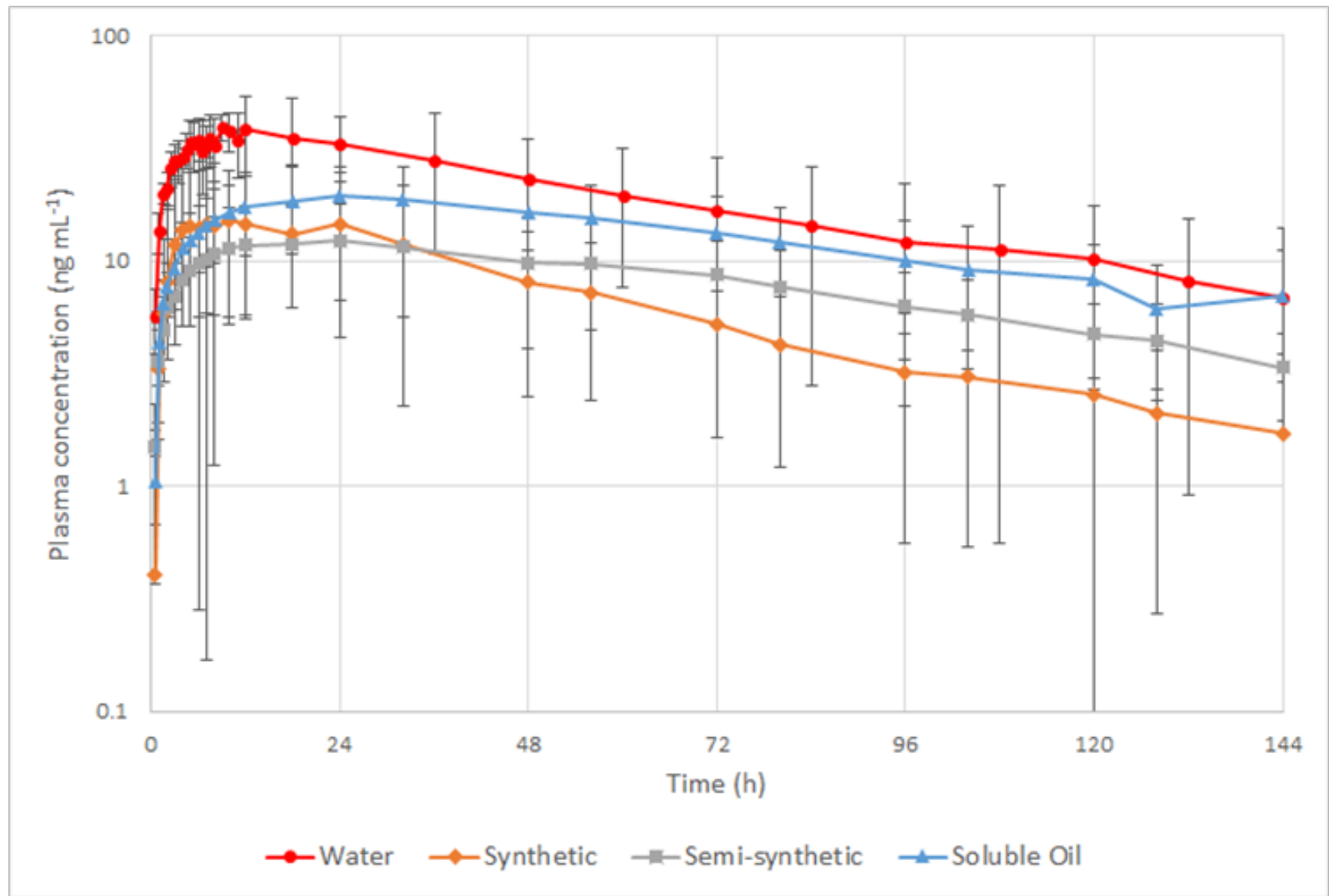


Introduction

- Millions of workers have an occupational exposure to metalworking fluids (MWF).
- **Study Objective:** Investigate the effect of different metalworking fluid formulation on the in vivo skin absorption of performance additives.
- The additive chosen to study was the biocide, ortho-phenylphenol (OPP).
- Pigs were topically dosed with ^{14}C -labelled OPP in one of 4 formulations:
 - 100% water
 - 95% water and 5% synthetic MWF
 - 95% water and 5% semi-synthetic MWF
 - 95% water and 5% soluble oil MWF



Plasma Profile of ^{14}C -OPP



Pharmacokinetic Parameters

Parameter	Water	Synthetic	Semi-synthetic	Soluble oil
Dose (μg)	1230 ± 0	760 ± 303	1324 ± 2	1317 ± 1
Body weight (kg)	19.7 ± 2.4	18.1 ± 1.9	29.6 ± 1.3	24.1 ± 0.7
T_{max} (h)	16.3 ± 12.1	11.0 ± 8.1	17.4 ± 10.4	24.0 ± 5.7
C_{max} (ng mL^{-1})	44.7 ± 8.9	17.6 ± 13.8	13.1 ± 5.9	19.9 ± 6.9
Cl/F ($\text{mL h}^{-1} \text{kg}^{-1}$)	18.0 ± 12.7	36.8 ± 26.1	28.8 ± 12.3	21.4 ± 7.8
Vd/F (L kg^{-1})	1.50 ± 0.65	2.24 ± 1.08	2.57 ± 1.34	2.20 ± 0.54
$T_{1/2}$ (h)	56.5 ± 14.3	39.9 ± 21.8	60.9 ± 13.9	70.5 ± 12.6
MRT (h)	51.9 ± 7.9	46.0 ± 8.9	58.9 ± 2.3	60.3 ± 2.2
AUC_{0-144} (h ng mL^{-1})	2815 ± 1466	983 ± 668	1211 ± 542	1816 ± 771

¹⁴C-OPP % Dose

	Water	Synthetic	Semi-synthetic	Soluble oil
Dosing device	33.7 ± 7.6	37.8 ± 19.5	45.0 ± 10.7	45.9 ± 6.8
Dose remaining on skin	0.24 ± 0.16	0.12 ± 0.05	0.12 ± 0.04	0.19 ± 0.19
Dose area	0.19 ± 0.02	0.07 ± 0.03	0.06 ± 0.03	0.06 ± 0.03
Tissues	12.9 ± 1.1	6.3 ± 2.3	5.4 ± 0.3	6.3 ± 0.9
Urine	28.89 ± 8.5	29.2 ± 12.6	19.3 ± 6.6	22.1 ± 8.0
Feces	0.18 ± 0.08	0.40 ± 0.64	0.13 ± 0.08	0.26 ± 0.04
Total absorbed	43.6 ± 8.2	38.4 ± 10.6	25.8 ± 7.0	29.9 ± 9.2
Total recovery	78.0 ± 12.1	77.1 ± 30.1	71.8 ± 11.3	77.2 ± 6.1

Conclusions

- OPP was predominantly eliminated via the kidneys
- The results of this study closely follow our previous *in vitro* work.
- Total %dose absorbed follows the trend:
water > synthetic > semi-synthetic = soluble oil
- OPP ($\log P = 3.09$) is more likely to remain in lipophilic formulations on the skin surface.
- OPP is more likely to diffuse across the skin membrane in hydrophilic formulations

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