Assessment of human toxicokinetics and metabolism of propylene glycol ethylether (PGEE)

H. Paschoud[1,2], M. Borgatta[1,2], S. Werner[2,3,4], L. Suter-Dick[2,3], R. Deepthi Puligilla[2,4], J. Huwyler[2,4] and N.B. Hopf[1,2]

[1] Center for Primary Care and Public Health (Unisanté), Route de la Corniche 2, 1066 Epalinges, University of Lausanne, Switzerland. helene.paschoud@unisante.ch ; nancy.hopf@unisante.ch ; myriam.borgatta@unisante.ch

[2] Swiss Center for Applied Human Toxicology (SCAHT), Basel, Switzerland.

[3] School of Life Sciences, University of Applied Sciences and Arts Northwestern Switzerland, Muttenz, Switzerland. laura.suterdick@fhnw.ch ; sophie.werner@fhnw.ch

[4] Division of Pharmaceutical Technology, Department of Pharmaceutical Sciences, University of Basel, Basel, Switzerland. ramya.puligilla@unibas.ch ; joerg.huwyler@unibas.ch

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STATE OF THE ART

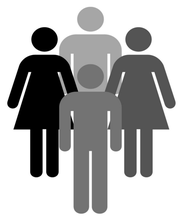
Propylene glycol ethers are **organic solvents** present in **cleaning and paint products**.

Introduced to replace ethylene glycol ethers, known to have reprotoxic and neurotoxic effects...
... but the **toxicity** of propylene glycol ethers is still **unknown** and **rarely assessed for neurotoxicity**.

Propylene glycol ethylether (**PGEE**, CAS no. 1569-02-4) was present in **1,333 products** found on the Swiss market in 2021.

No data exists for human PGEE toxicokinetics and on possible toxic adverse effects.

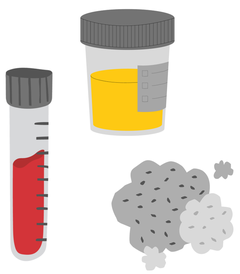
METHOD



Four volunteers were exposed to PGEE in an exposure chamber under controlled conditions during four hours.

Four different exposure conditions were used: 25, 30 or 35 ppm at rest, and 35 ppm with physical exercice.

A research nurse collected blood samples.
Each volunteer collected urine samples themselves.
A research assistant collected exhaled air samples.



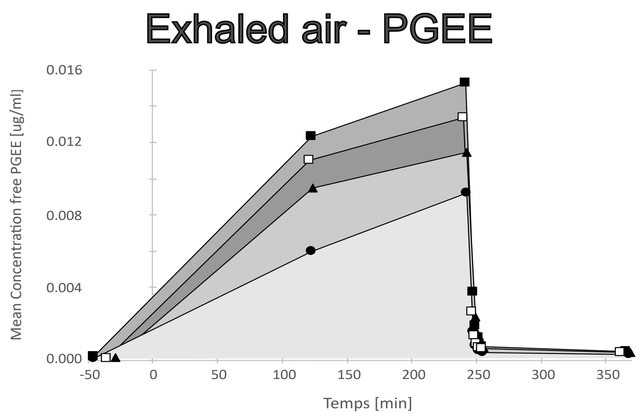
Metabolism of the β-PGEE isomer to 2EPA was evaluated using human S9 liver fractions in vitro (cell lysate containing free enzymes).

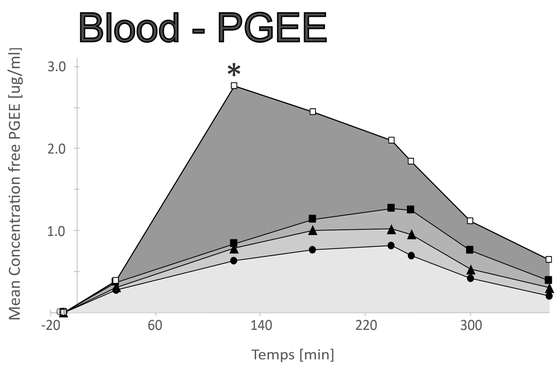
Zebrafish larvae were used to evaluate the blood-brain barrier (BBB) integrity following exposures to PGEE IC50.

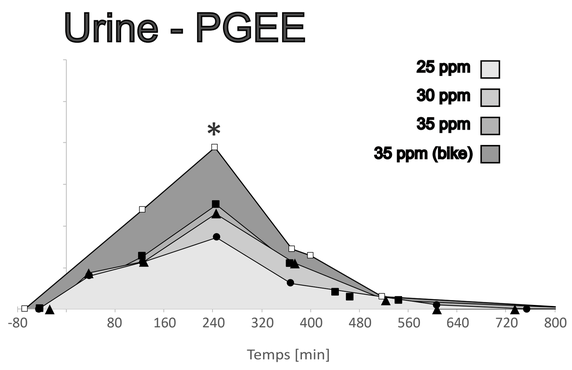
Zebrafish larvae figure is taken from Biorender.

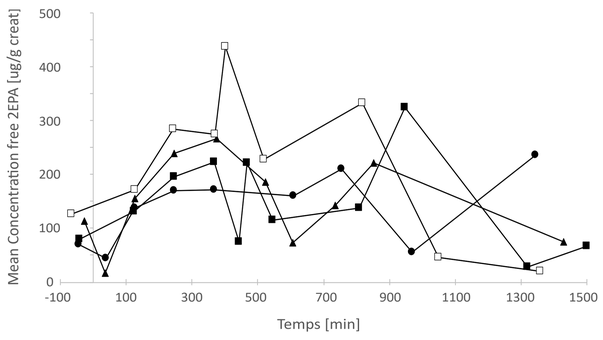
RESULTS

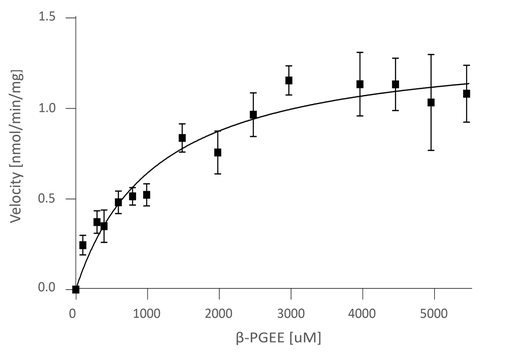
Significant changes (*) in absorption and elimination rate were observed **following physical exercice** in urine and blood.



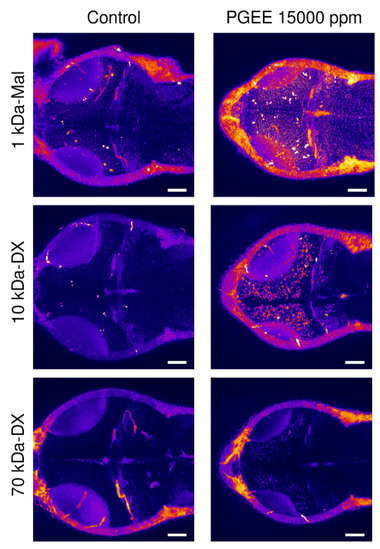








Michaelis-Menten-Kinetic : Km = 1133 uM
Vmax = 1.37 nmol/min/mg



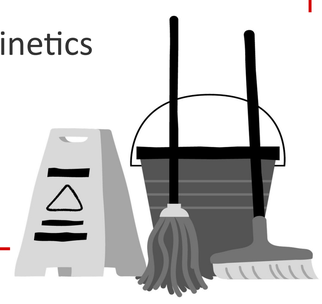
A **significant increase** in extracellular permeability from blood vessels into the surrounding brain parenchyma (1-10 kDa) was observed **following PGEE exposure** in zebrafish larvae.

CONCLUSIONS

The maximal concentrations (Cmax) in blood, urine and exhaled air were reached at the end of exposure for all conditions at rest. The internal dose increased with increasing air concentrations and effort. The PGEE elimination was fast, around 10 hours in urine and 2 minutes in exhaled air.

In vitro liver enzymes can metabolize β-PGEE to 2EPA with low to moderate clearance, while the volunteer results did not show a clear 2EPA kinetics as expected. Other possible metabolites should be explored (e.g., 3EPA).

Significant effects on zebrafish larvae BBB integrity were observed when larvae were exposed to PGEE at IC50. As PGEE exposure affects the BBB, the possible neurotoxic effects of PGEE should be investigated.



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