Impact of evaporation on skin uptake of volatile chemicals

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Background

- Many chemicals known to be absorbed through skin are highly volatile
- Evaporation may significantly decrease the amount available for absorption following e.g. an accidental spill on the skin
- Yet, surprisingly few studies address evaporation in relation to dermal absorption

Aim

- Investigate impact of evaporation on dermal absorption of chemicals
- Discuss evaporation in relation to skin notation

Absorption rate

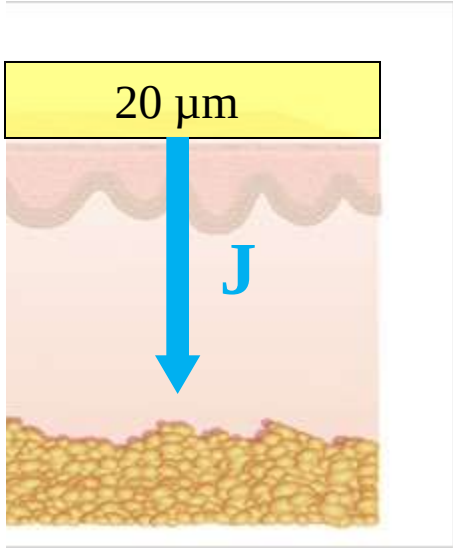
Assume 20 µm chemical is evenly distributed on the skin surface

Steady-state dermal absorption rate calculated by Fick's first law of diffusion:

$$J = K_p \cdot C \quad (g\,cm^{-2}h^{-1})$$

K_p *skin permeability coefficient (cm/h)*

C *concentration* (g/cm^3)



C equal to density since only pure chemical considere

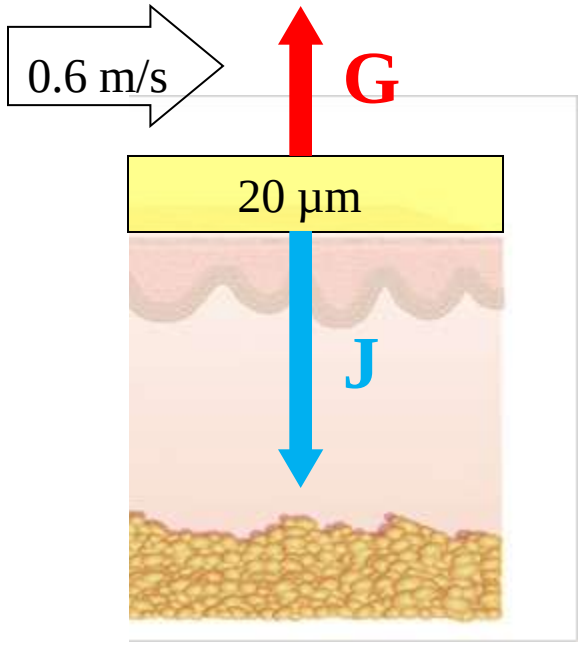
J or K_p taken from Johanson & Rauma 2008

Evaporation rate

Evaporation rate of chemical calculated according to McCready & Saghir 2007:

$$G = \frac{M \cdot p_{vap} \cdot k_g}{10^4 \cdot R \cdot T} \quad (g\,cm^{-2}h^{-1})$$

M	*molar mass (g/mol)*
p_{vap}	*vapour pressure (Pa)*
R	*universal gas constant (J/mol/K)*
T	*temperature (set to 303K=30ºC)*
k_g	*mass transfer coefficient in air (m/h)*



k_g calculated by Sparks method (Lyman et al. 1990),
depends mainly on molecular volume and weight, and air speed

Absorbed fraction

$$F = \frac{J}{G + J} \qquad (unitless)$$

J *dermal absorption rate (g cm^{-2} h^{-1})*

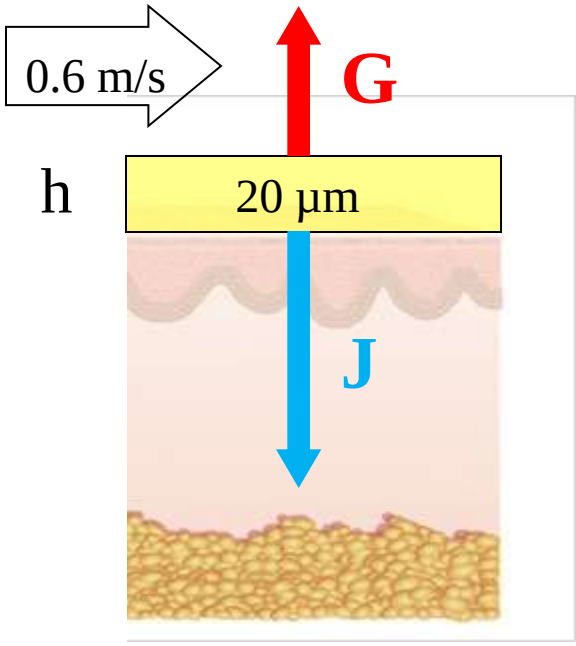
G *evaporation rate (g cm^{-2} h^{-1})*

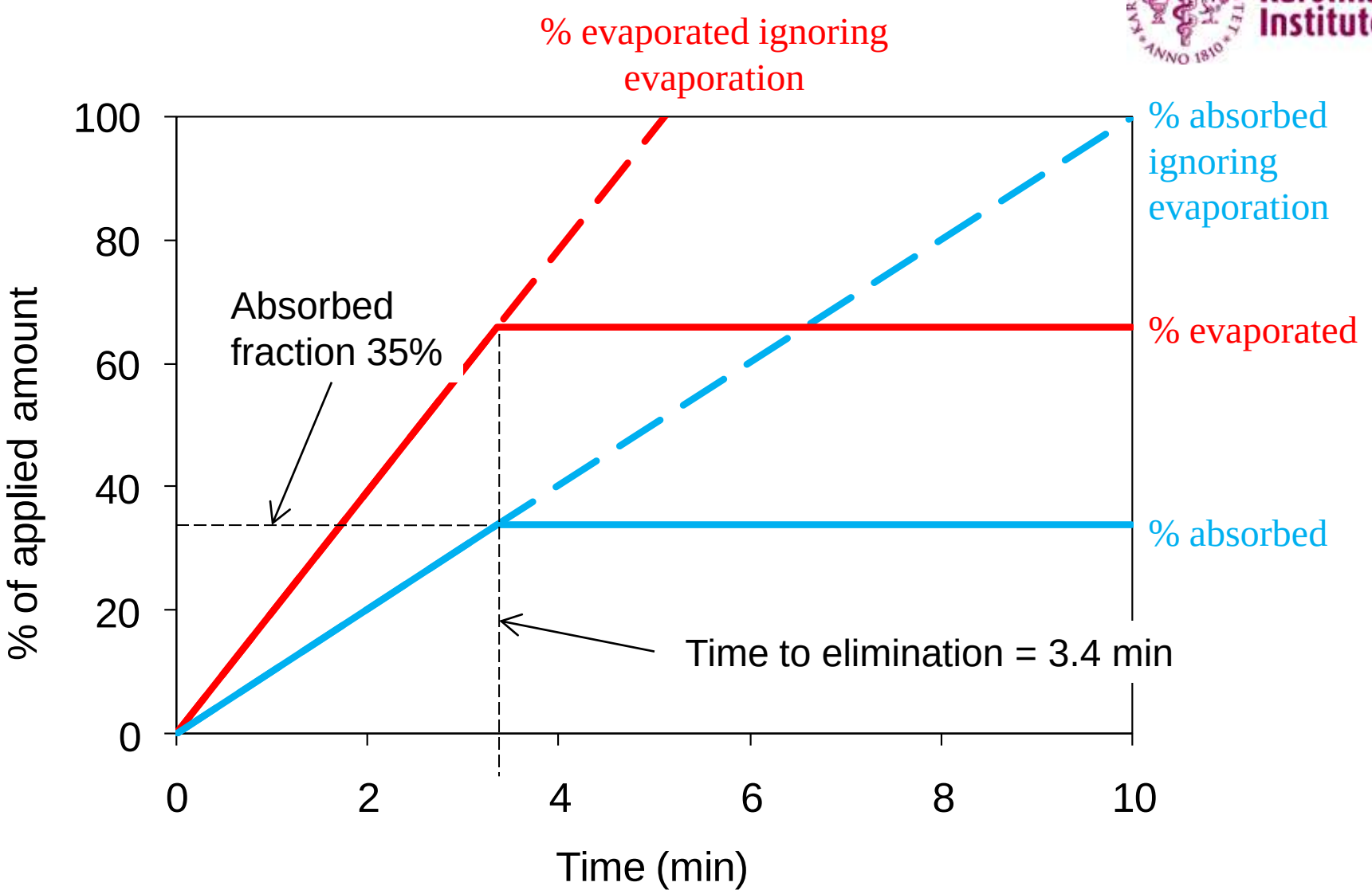
Time to elimination

$$T_{el} = \frac{C \cdot h}{G + J} \qquad (h)$$

C *concentration (g/cm^3)*

h *initial film thickness of chemical, arbitrarily set to 0.002 cm (20 µm)*





Example: Evaporation and absorption of N,N-dimethyl-acetamide

Results

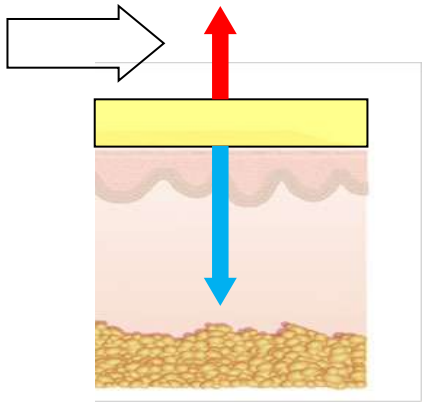
Out of 73 chemicals with a skin notation on Swedish OEL list…

…57 with less than 50% absorbed (F<0.5)

Vinyl chloride

…evaporation rate varies from 10^{2} to 10^{-5} on a relative scale (10 000 000-fold)

Hydroquinone



Pentachlorophenol

…absorbed fraction varies from 0.997 to 10^{-5} (100 000-fold)

Tetrahydrofuran

…time to elimination varies from 0.2 seconds to 4 days (1 000 000-fold)

Evaporation in relation to skin notation

SCOEL Key Document on criteria for skin notation
(European Commission 1999)
Contribution to body burden

- Skin notation if dermal absorption may contribute significantly to body burden
- Meaning of significant established on case-by-case basis
- May in general be of the order of 10% or more of the respiratory uptake during exposure at the OEL (8-h TWA)
- Note: no statement on extent of exposure

Evaporation in relation to skin notation

SCOEL Key Document on criteria for skin notation

Volatility

- Direct skin contact with highly volatile liquids (low b.p.) not likely to result in appreciable skin uptake
- Solids and liquids with low b.p. / low vapor pressure may give rise to skin exposure both by direct contact and impingement of aerosols
- Skin of forearms and hands comes in contact with a lot more air than what is inhaled

Evaporation in relation to skin notation

The ECETOC criteria (ECETOC 1993)**:**

Skin notation when exposure of both hands and lower arms (2000 cm^2) for 1 h is expected to contribute more than 10% to the systemic dose, compared to the amount absorbed via inhalation exposure at the OEL during a full 8-h work day (10 m^3 air, 50% absorbed)

1. Calculate dermal dose $= abs rate \cdot skin\ area \cdot duration = J \cdot 2000 \cdot 1$

2. Calculate inhaled dose $= air\ level \cdot abs\ fraction \cdot air\ volume = OEL \cdot 50\% \cdot 10$

3. Calculate ratio $= \frac{dermal\ dose}{inhaled\ dose}$

4. Take decision $Ratio > 0.1 \Rightarrow Skin\ notation$

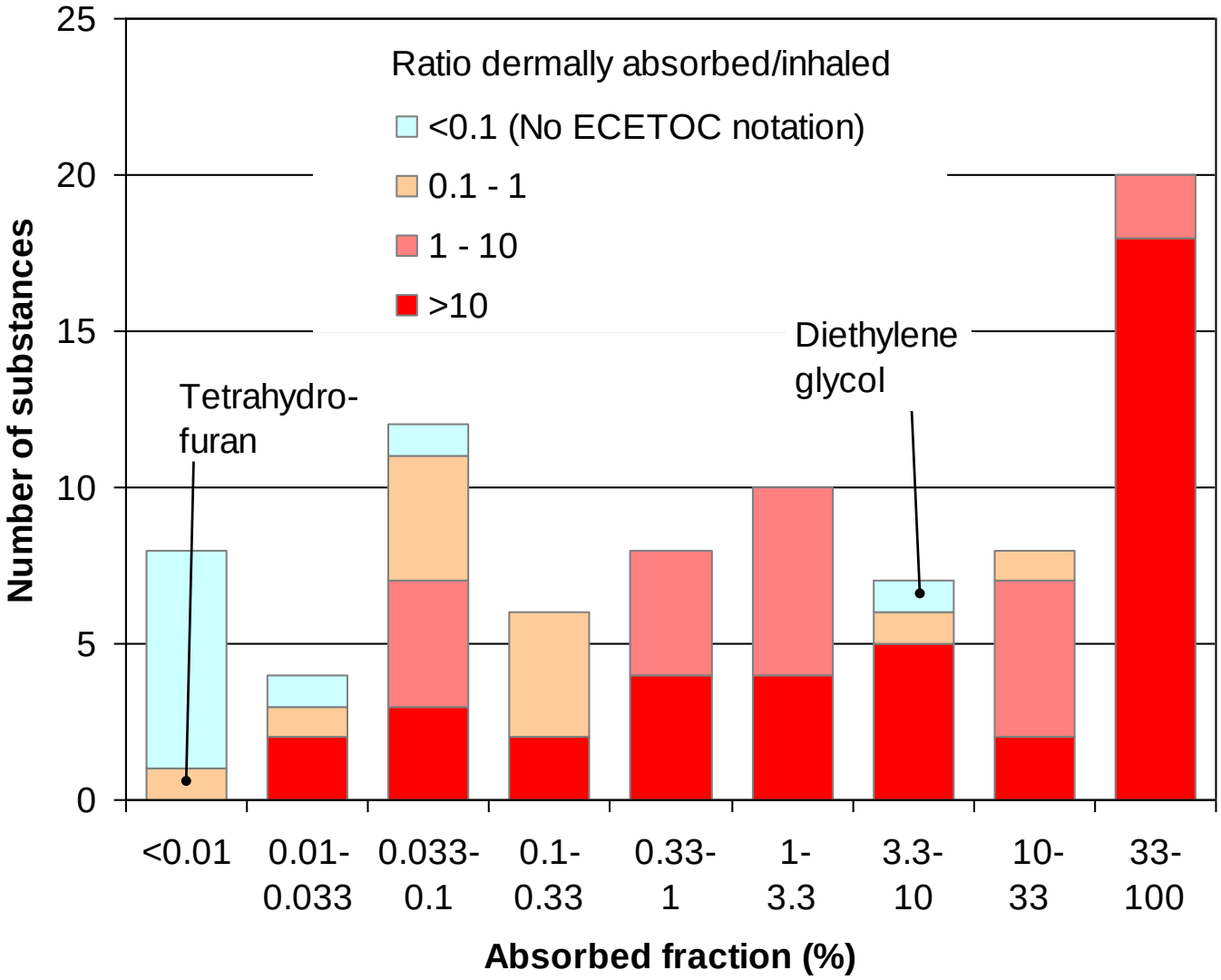
- Infinite dose assumed
- Loss by evaporation not considered

SCOEL criteria

- 10% of systemic dose
- No assumption on exposed area
- No assumption on duration
- Evaporation considered qualitatively

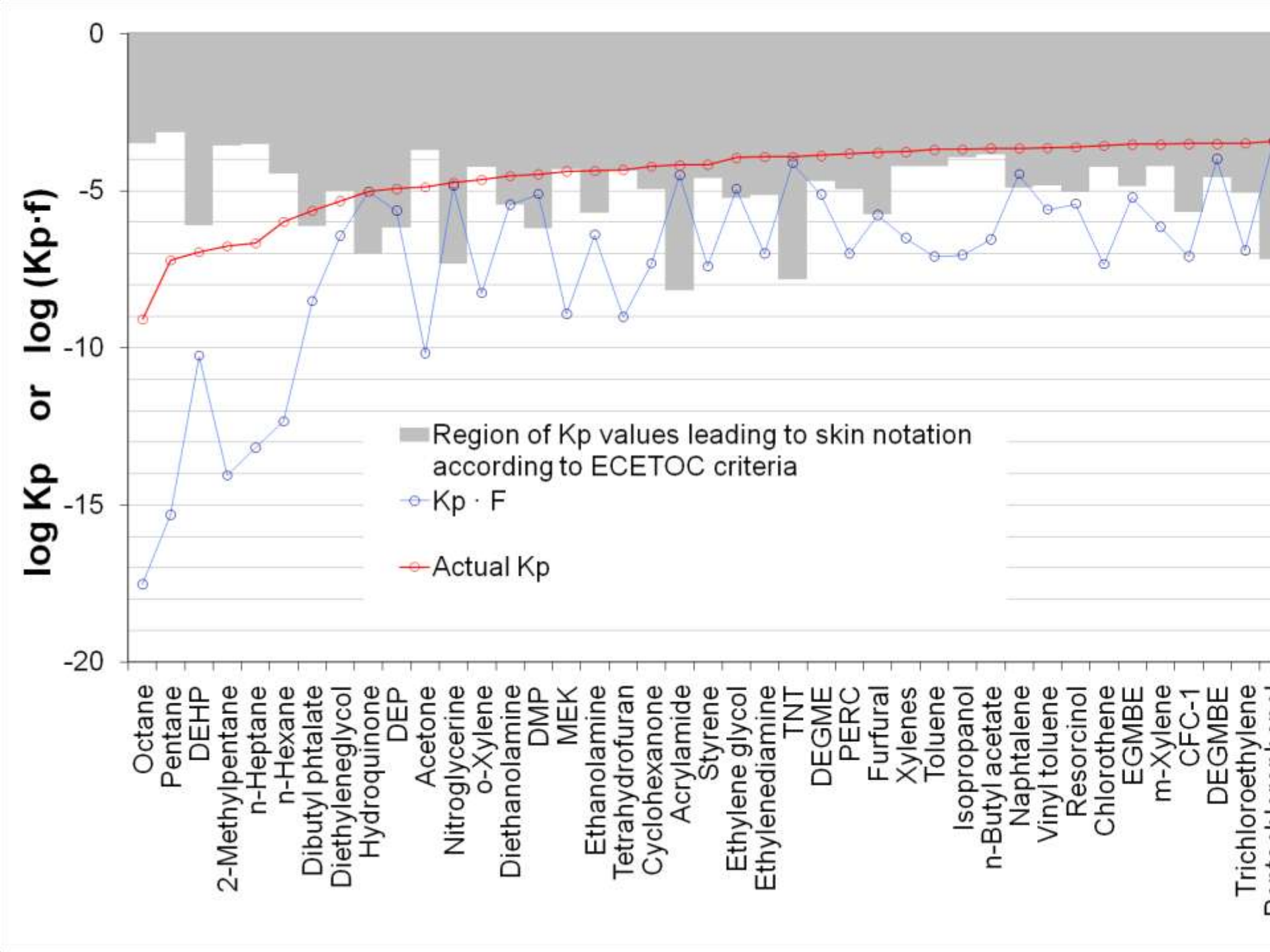
ECETOC criteria

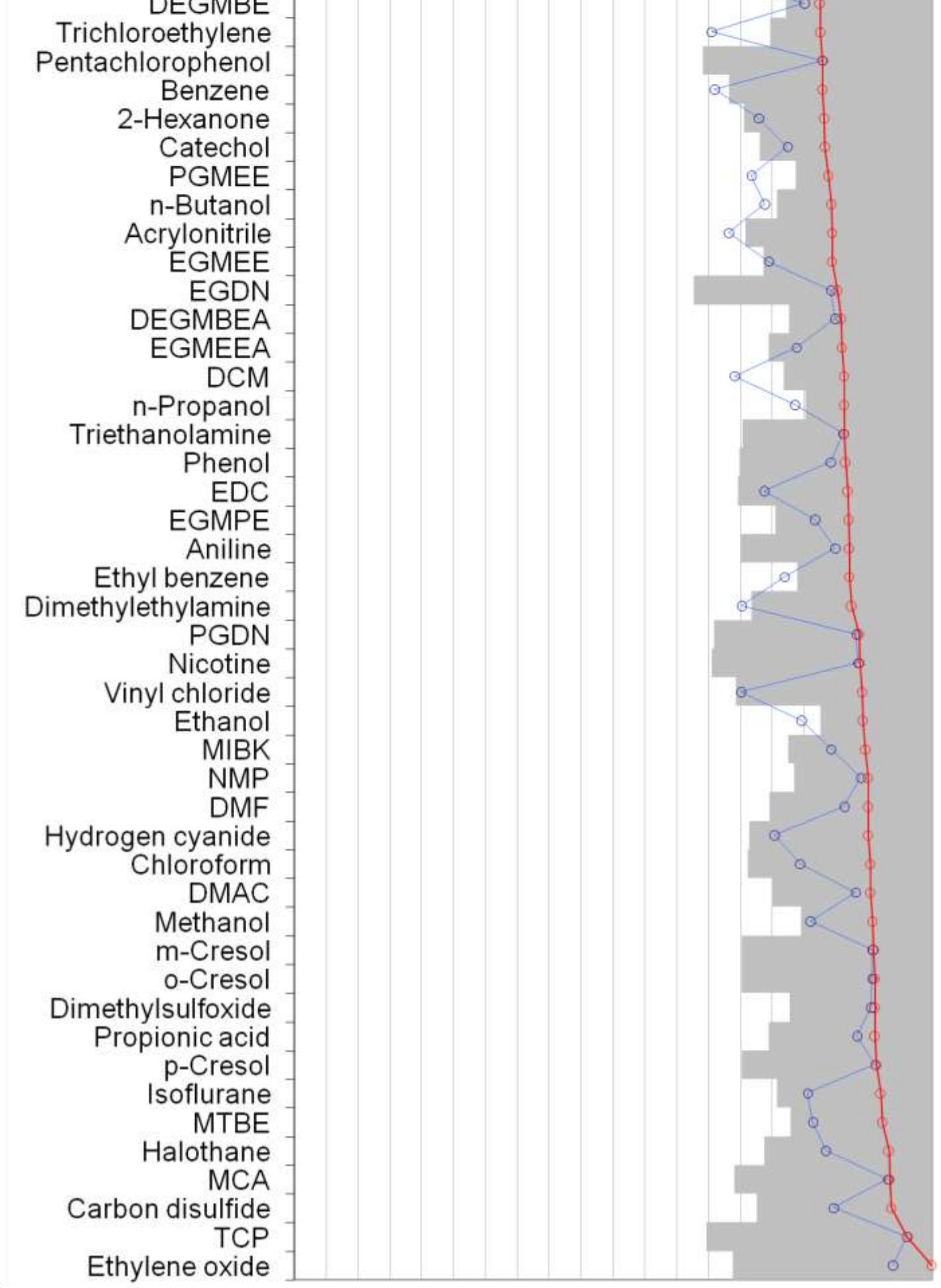
- 10% of systemic dose
- 2000 cm2
- 1 h
- Evaporation not considered



Absorbed fraction in relation to the ECETOC criteria for skin notation

Most chemicals have an absorbed fraction below 33%


log Kp or log (Kp·f)
0
-5
-10
-15
-20
Region of Kp values leading to skin notation according to ECETOC criteria
Kp · F
Actual Kp
Octane
Pentane
DEHP
2-Methylpentane
n-Heptane
n-Hexane
Dibutyl phtalate
Diethyleneglycol
Hydroquinone
DEP
Acetone
Nitroglycerine
o-Xylene
Diethanolamine
DMP
MEK
Ethanolamine
Tetrahydrofuran
Cyclohexanone
Acrylamide
Styrene
Ethylene glycol
Ethylenediamine
TNT
DEGME
PERC
Furfural
Xylenes
Toluene
Isopropanol
n-Butyl acetate
Naphtalene
Vinyl toluene
Resorcinol
Chlorothene
EGMBE
m-Xylene
CFC-1
DEGMBE
Trichloroethylene


DEGMBE
Trichloroethylene
Pentachlorophenol
Benzene
2-Hexanone
Catechol
PGMEE
n-Butanol
Acrylonitrile
EGMEE
EGDN
DEGMBEA
EGMEEA
DCM
n-Propanol
Triethanolamine
Phenol
EDC
EGMPE
Aniline
Ethyl benzene
Dimethylethylamine
PGDN
Nicotine
Vinyl chloride
Ethanol
MIBK
NMP
DMF
Hydrogen cyanide
Chloroform
DMAC
Methanol
m-Cresol
o-Cresol
Dimethylsulfoxide
Propionic acid
p-Cresol
Isoflurane
MTBE
Halothane
MCA
Carbon disulfide
TCP
Ethylene oxide

Conclusions

Evaporation varies widely between chemicals

- Ranges from practically negligible to completely dominating source of elimination from skin surface

Huge variability in exposure duration (time to elimination)

- Skin notations: assumption of uniform exposure duration (e.g. 1h in the ECETOC criterion) and infinite dose misleading

References

- ECETOC. Strategy for assigning a skin notation. ECETOC, Bruxelles, Document No. 31, 1993 (revised).

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- Lyman WL, Reehl WF, Rosenblatt DH. Handbook of chemical property estimation methods: Environmental. Behavior of Organic Compounds, American Chemical Society, Washington, DC, Chapter 17, 1990, pp 13-14.

- McCready DI, Saghir SA. Consideration of skin evaporation in a dermal exposure assessment. International Conference on Occupational & Environmental Exposures of Skin to Chemicals, 2007.

Acknowledgement

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