

*Improvement of skin penetration
prediction for volatile compounds
used in cosmetics*

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Cosmetics

Wide range of applications...

Hair dye, Hygiene,
Skin care, Sun Care,
Hair Care, Make up,
...

... with a wide range of formulations...

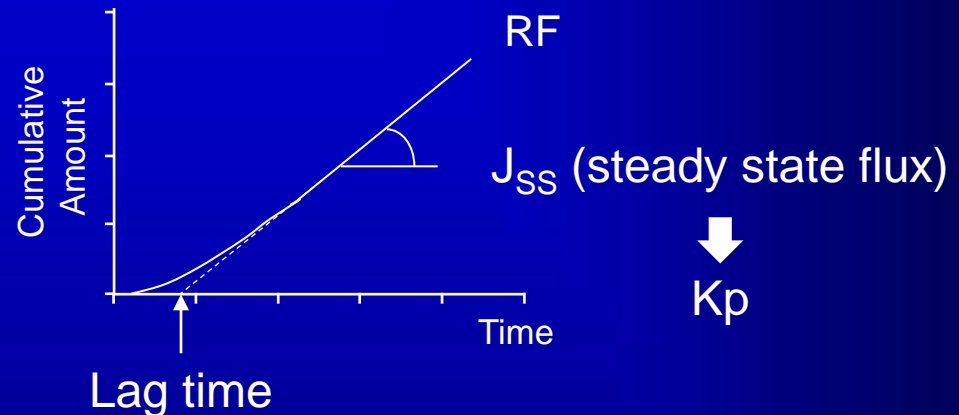
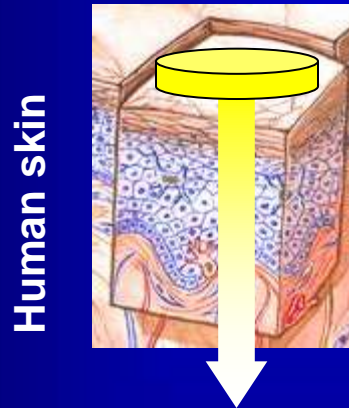
Emulsion,
Cream,
Gel,
...

... with a wide range of raw materials.

Polymer, Fragrance,
Extract, Organic
Inorganic,
...



Modelling skin penetration



For infinite dose in water $\log K_p = -2.71 - 0.0061 MW + 0.71 \log P$

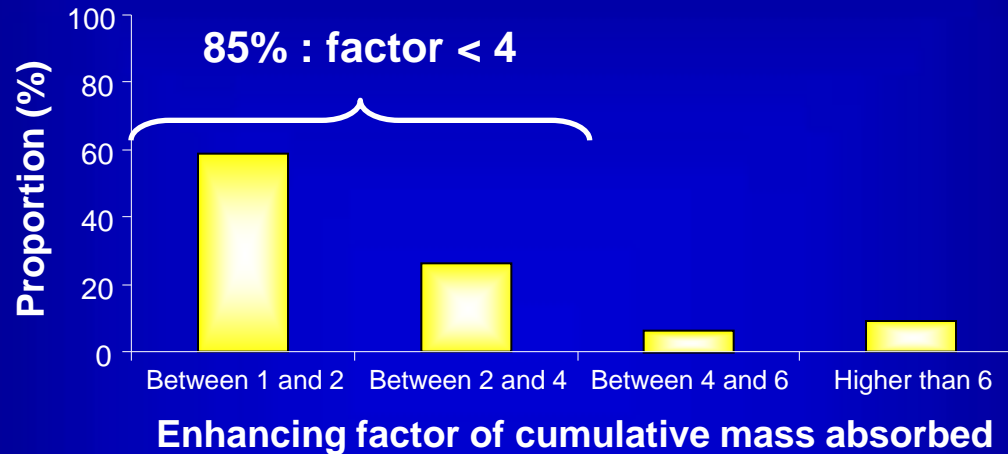
Potts R. O. and Guy R. H. Pharm. Res. 1992, 9, 663-669

A prediction model should consider :

- type of vehicle
- conditions of use
- physico-chemical properties

Grégoire S. and al. *British Journal of Dermatology* 2009, 160, 80-91.

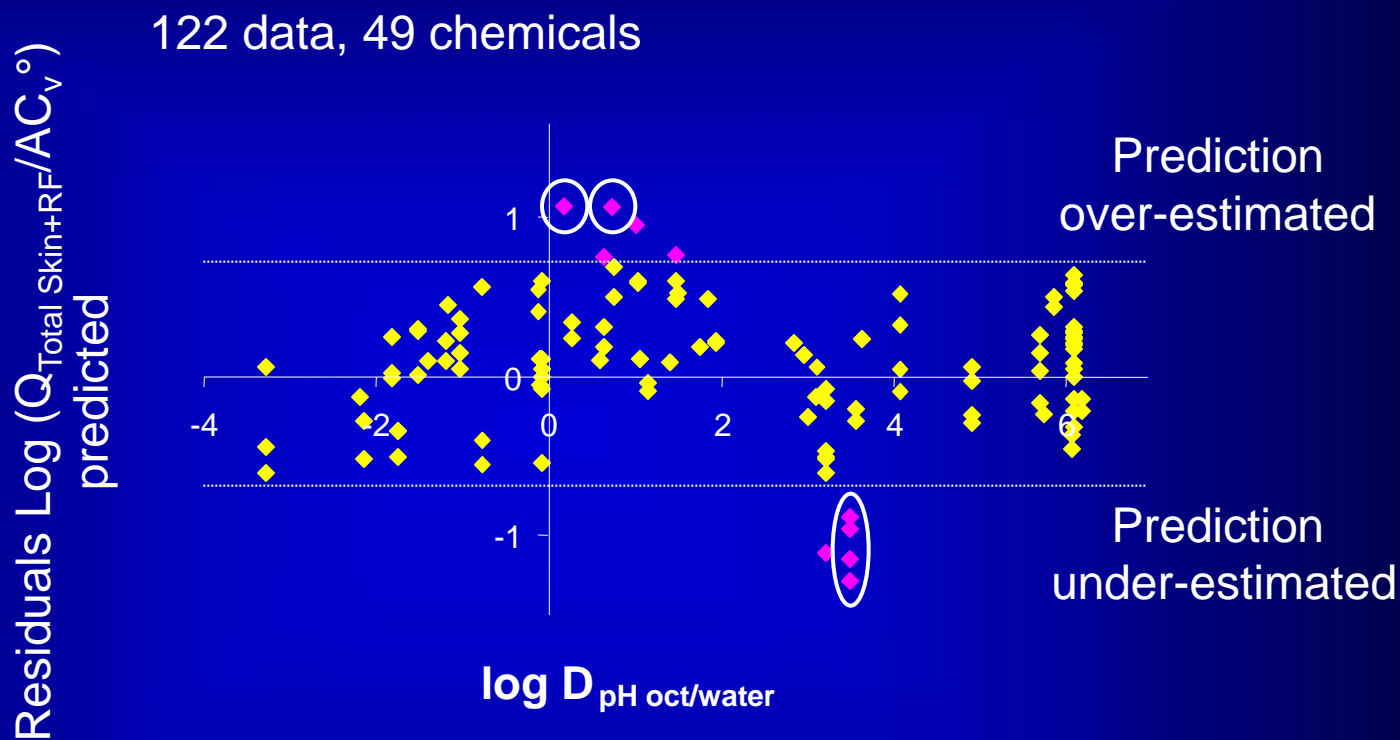
34 chemicals evaluated with two or more formulations



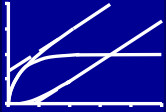
- ↪ Negligible vehicle effect regarding the expected precision of the model
- ↪ Modelling of vehicle as a biphasic entity of oil and water
- ↪ Partition of the aqueous chemical fraction phase with the stratum corneum

$$\frac{Q_{\text{total skin+RF}}}{AC_v^\circ} = \left(\frac{Q_{\text{total skin+RF}}}{AC_v^\circ} \right)_{\text{Cleek \& Bunge}} \frac{f_w}{f_w + (1 - f_w) 10^{a \log D_{\text{pH oct/water}}}}$$

Results



122 Individual Data		49 Chemicals	
Well predicted	Wrong predicted	Well predicted	Wrong predicted
91,8 %	8,2 %	93,9 %	6,1 %



Ingredients with high chemical volatility :

Solvent, Fragrance, Essential oils ...

Extend the applicability domain of the model to volatile chemicals

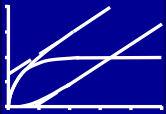
Mohlin P. and al. 11th PPP, 2008_

“Evaporation may significantly decrease the amount available for absorption...”

Kasting, G.B.; Miller, M.A. J. Pharm. Sc. 2005, 95, 268-280

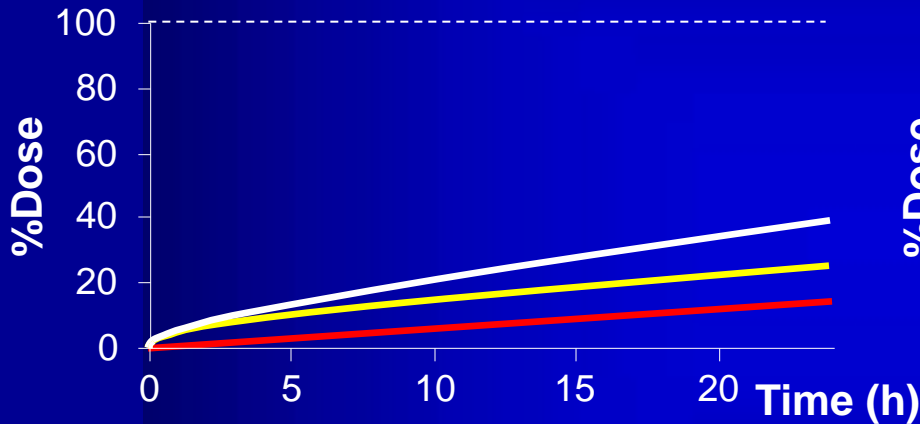
Skin diffusion model including evaporation.

Theoretical cases



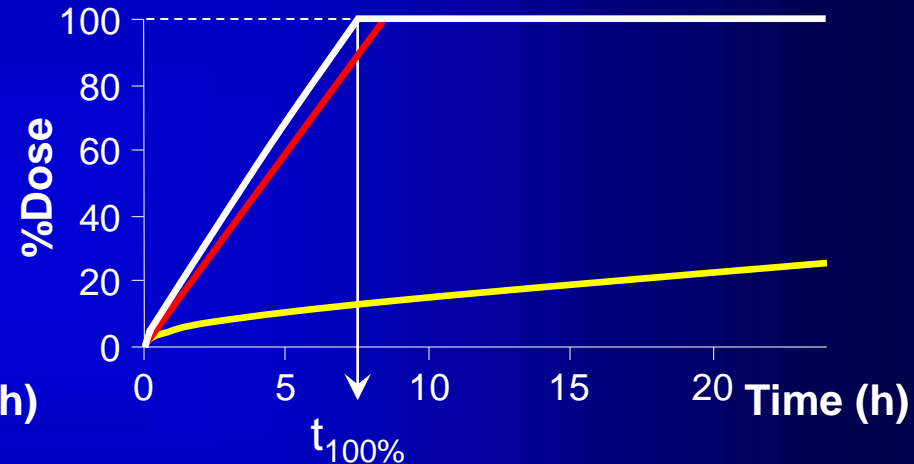
- Total Skin + RF
- Evaporated
- Total

Low volatility



➔ No impact on skin uptake

High volatility



➔ Limitation of skin uptake

Search for time $t_{100\%}$: $\%Dose_{\text{Total Skin+RF}} + \%Dose_{\text{evaporated}} = 100\%$

➔ Used $t_{100\%}$ as exposure time to predict $\%Dose_{\text{Total Skin+RF}}$

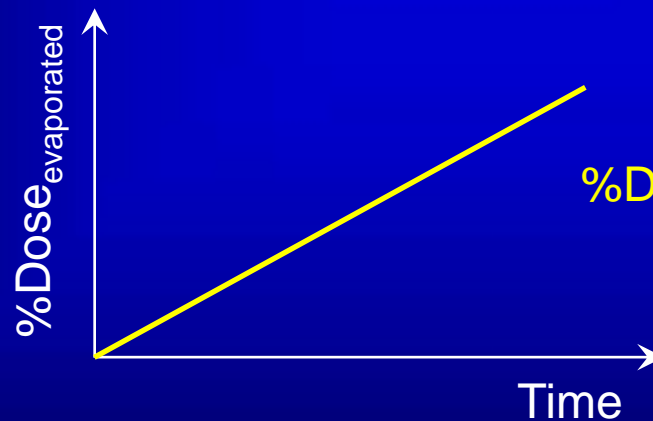
Evaporation rate k_{evap}

$$k_{\text{evap}} = \frac{k_g P_{\text{VP}} \text{MW}}{7.610^5 RT}$$

with P_{vp} : vapor pressure
 MW : molecular weight
 k_g : mass transfer coefficient in air

$$k_g = \frac{6320u^{0,78}}{\text{MW}^{1/3}}$$

u : wind velocity adjacent to skin

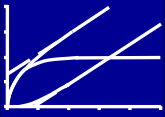


$$\% \text{Dose}_{\text{evaporated}} = f(\text{MW}, P_{\text{vp}}, t, \mathbf{u})$$

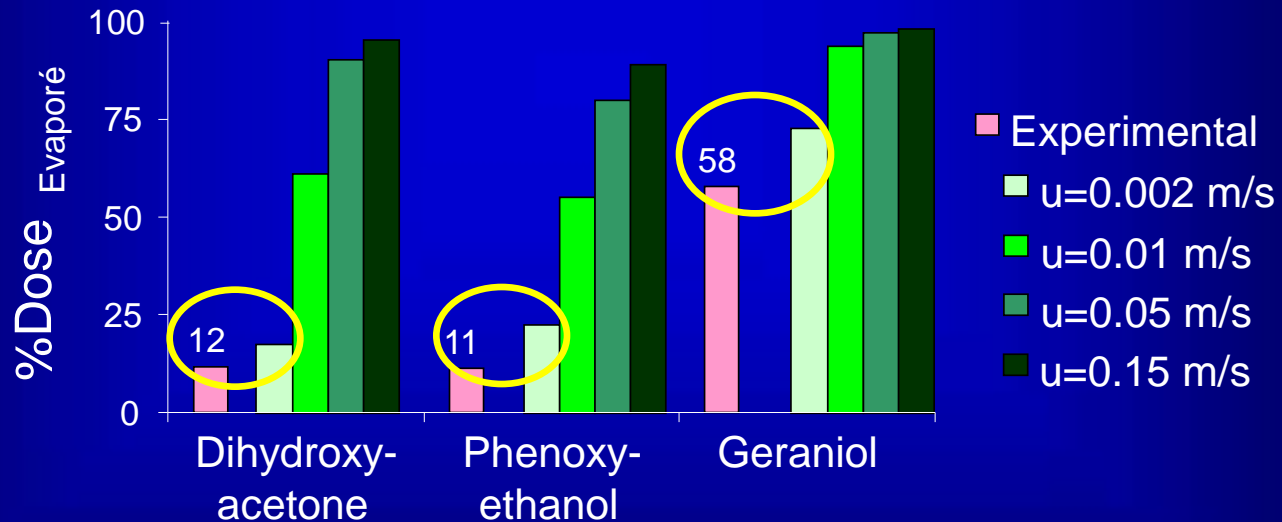
Wind velocity defined as a variable in the model

Wind velocity

3 to 7 mg.cm⁻² of emulsion O/W applied on ex-vivo human skin for 24 h



	MW (g.mol ⁻¹)	P _{vp} (torr)
Geraniol	154	3.0 10 ⁻²
Dihydroxyacetone	90	2.1 10 ⁻²
Phenoxyethanol	138	7.0 10 ⁻³



Lowest wind velocity : Best fit with experimental data

Application to Terpenes



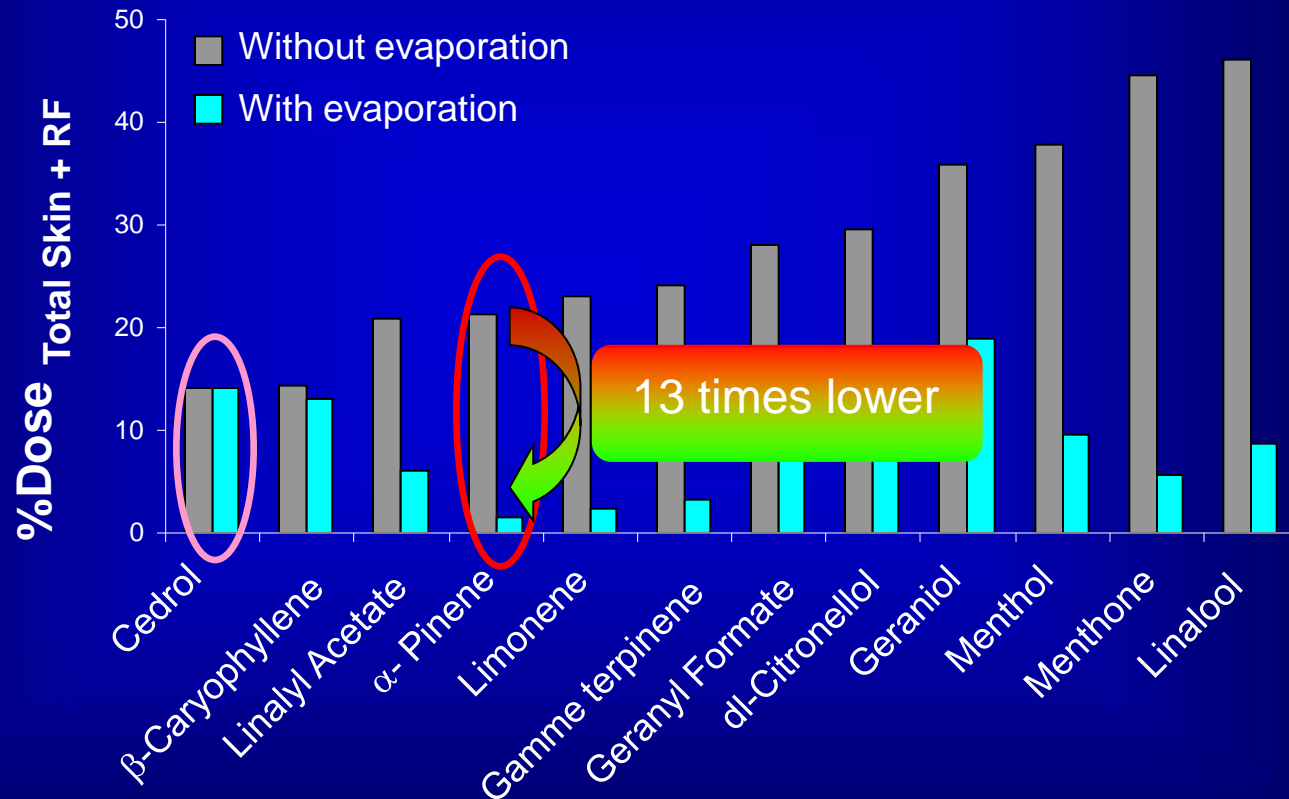
12 Terpenes : Ingredients of fragrance, essential oils

	MW (g.mol ⁻¹)	log P	Vapor pressure (mm Hg)
α- Pinène	136	4,83	4,8E+00
Limonene	136	4,57	2,0E+00
Gamme terpinene	136	4,50	1,1E+00
Menthone	154	3,05	3,7E-01
Linalool	154	2,97	1,6E-01
Linalyl Acetate	196	3,93	1,1E-01
Menthol	156	3,40	1,1E-01
Geranyl Formate	182	3,47	6,8E-02
dl-Citronellol	156	3,91	4,4E-02
β-Caryophyllene	204	6,45	3,1E-02
Geraniol	154	3,56	3,0E-02
Cedrol	222	4,53	1,2E-04

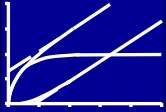
Application to Terpenes



2 mg/cm² of formulation containing Terpene at 1% applied for 16 hours



Conclusions



- ✓ Development of prediction model with high performance (>93% - 49 chemicals)
- ✓ Adjustment of the wind velocity parameter in the prediction model
- ✓ Extension of the applicability domain to volatile chemicals

The prediction model considers :

- type of vehicle
- conditions of use
- physico-chemical properties

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