



# RECENT ADVANCES ON TOPICAL, TRANSDERMAL AND NAIL DRUG DELIVERY

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**SAMPLING THE STRATUM CORNEUM TO  
QUANTIFY DRUG UPTAKE FROM TOPICAL  
PRODUCTS**

# **ACKNOWLEDGE/DISCLAIMER**

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# BIOEQUIVALENCE OF TOPICAL PRODUCTS

❖ Clinical trials required for:

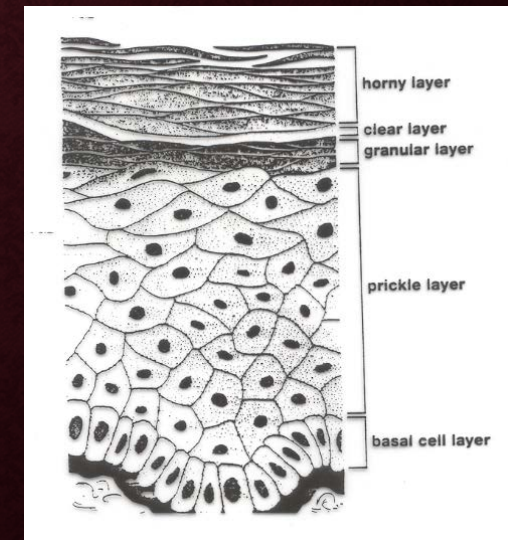
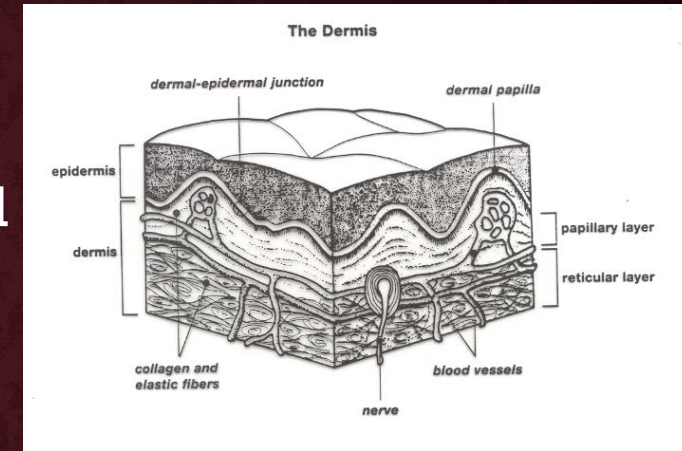
- a. approval of generic products
  - b. replacement of approved product following compositional changes.
- ✓ exception: corticosteroids (vasoconstrictor assay)

☹ Relatively insensitive, time-consuming and costly.

? Can topical BE be assessed through use of appropriate *in vitro* and/or *in vivo* surrogate tests.

❖ All surrogate tests have limitations but that they do not all have the same limitations:

- the results of one test complement those of another.



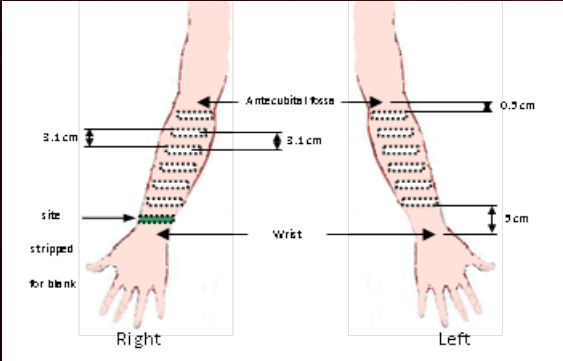


Tape stripping study  
Diclofenac Sodium  
Solaraze gel (3%), Voltaren gel (1%) and  
Pennsaid solution (2%).

Optimizing metrics for the assessment of BE  
between topical products  
N'Dri-Stempfer et al., Pharm. Res. 25 (2008)

1. Ethics approval by RIHSC and REACH
2. Target: 14 healthy adults for interim analysis.  
Current N=12
3. (2 uptake + 2 clearance) skin sites /formulation).

4. SC depth sampled determined by TEWL & 30 tapes /site maximum.



6 hours uptake

Formulations removed from ALL sites



Uptake sites tape-stripped

Clearance sites protected

17 hours clearance

Clearance sites tape-stripped

Tapes cut & weighed

Tape stripping



Tapes weighed

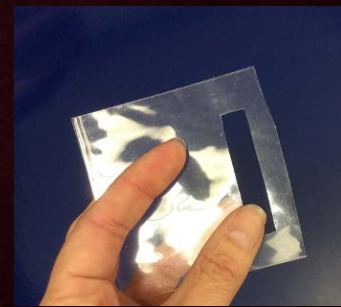
Tapes grouped & extracted

HPLC UV



Formulation removal:  
 1. dry cellulose tissue paper +  
 2. two IP 70%. wipes  
 Each wipe passed three times.

Formulation applied (mg)	Solaraze 3%	Voltaren 1%	Pennsaid 2%
Uptake	155.9 ± 8.3	82.5 ± 5.6	79.6 ± 6.7
Clearance	159.3 ± 16.8	85.0 ± 47	81.4 ± 4.8
Target formulation	165	82.5	82.5
Drug applied per site (mg)	4.95	0.825	1.65

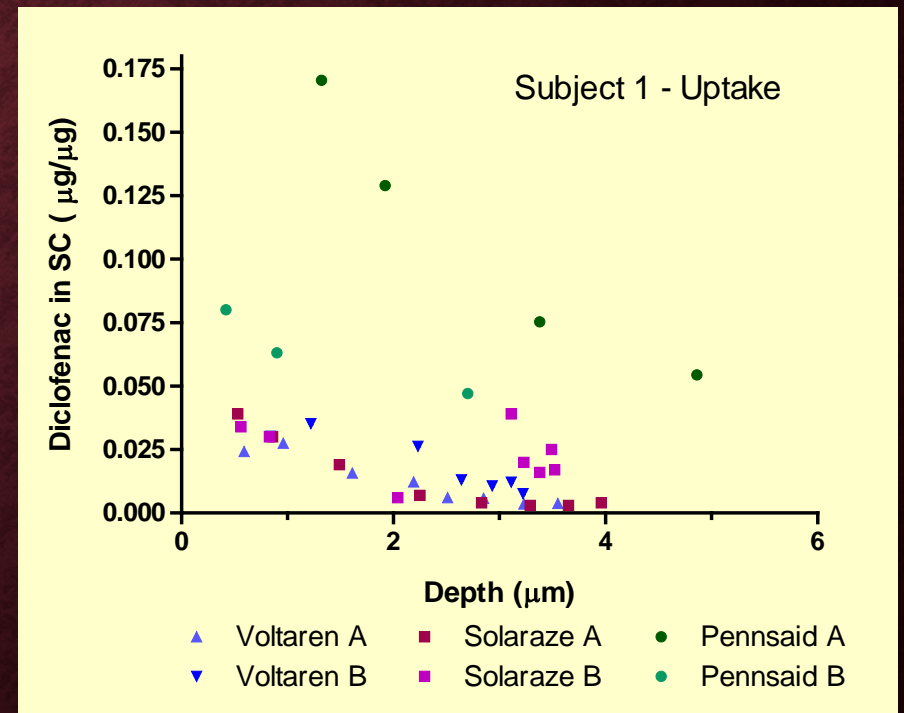




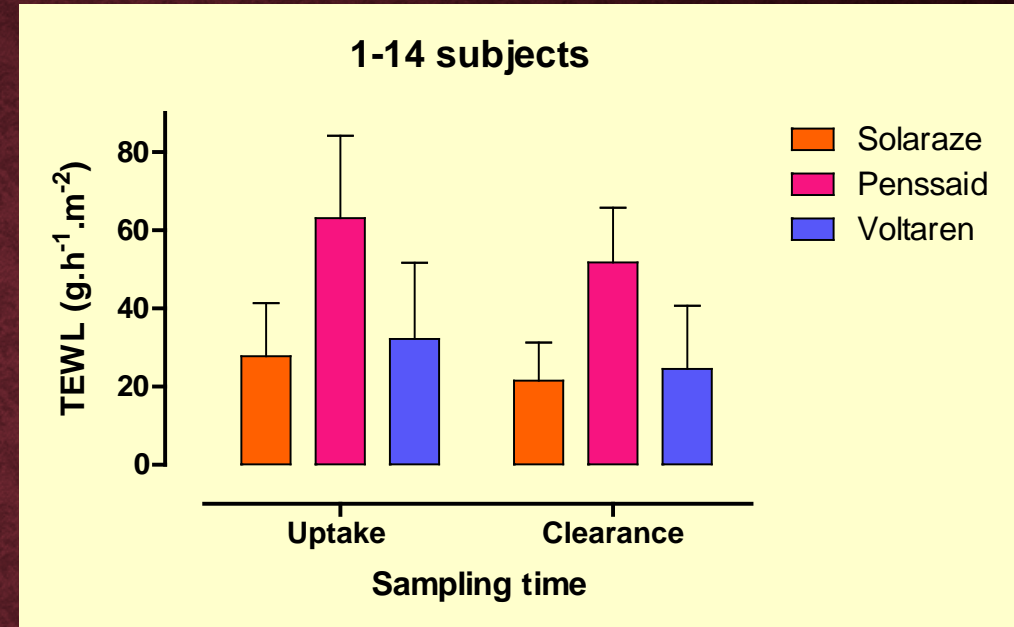
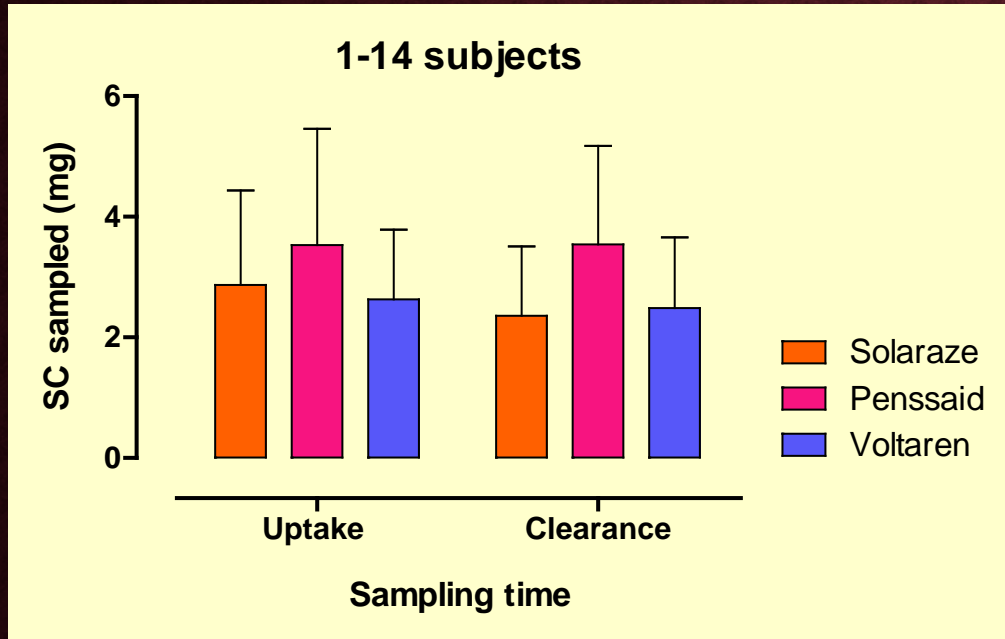
SC removed (mg)	Solaraze	Voltaren	Pennsaid
Uptake	$2.87 \pm 1.57$	$2.63 \pm 1.15$	$3.53 \pm 1.93$
Clearance	$2.36 \pm 1.15$	$2.48 \pm 1.17$	$3.54 \pm 1.64$

SC depth ( $\mu\text{m}$ )	Solaraze	Voltaren	Pennsaid
Uptake	$5.74 \pm 3.13$	$5.74 \pm 3.13$	$7.06 \pm 3.85$
Clearance	$4.71 \pm 2.31$	$4.97 \pm 2.35$	$7.09 \pm 3.27$

Final TEWL ( $\text{g}\cdot\text{h}^{-1}\cdot\text{m}^{-2}$ )	Solaraze	Voltaren	Pennsaid
Uptake	$32.2 \pm 19.5$	$30.7 \pm 20.5$	$63.1 \pm 21.1$
Clearance	$24.5 \pm 16.8$	$24.2 \pm 17.4$	$51.8 \pm 14.0$

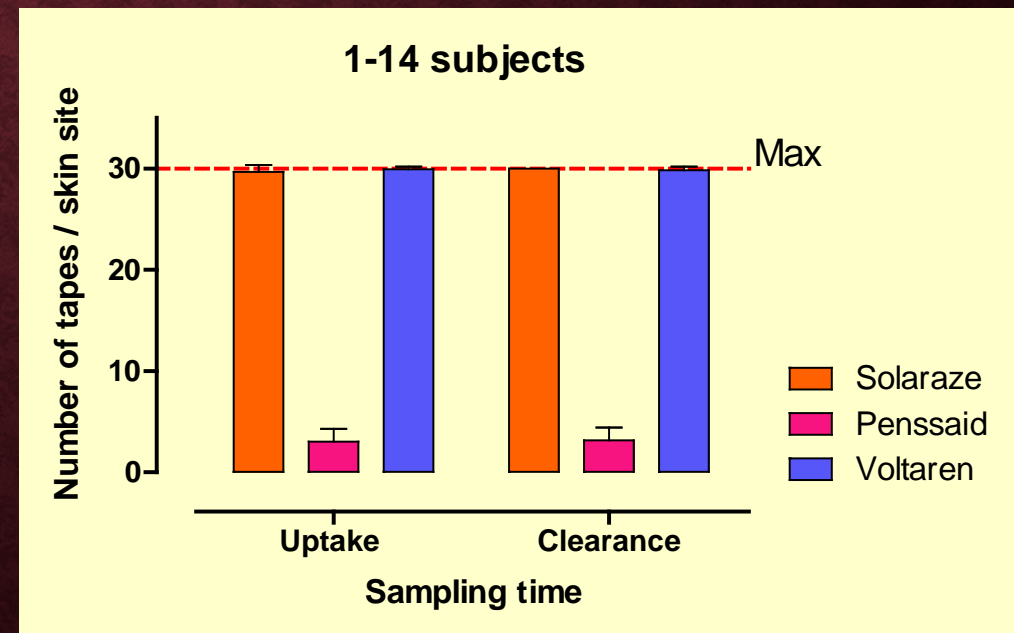




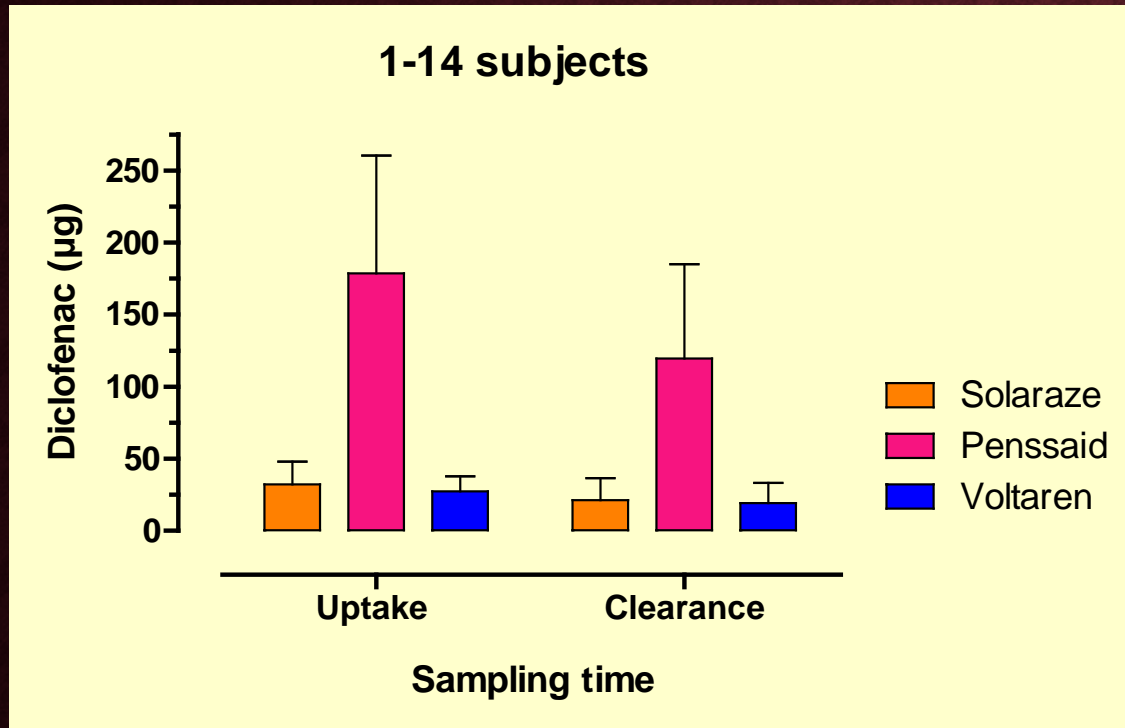


### Two-way ANOVA:

- Formulation: n.s
- Uptake/Clearance: n.s.
- Interaction: n.s.
- Pairing effective:  $p < 0.005$



# DICLOFENAC RECOVERY

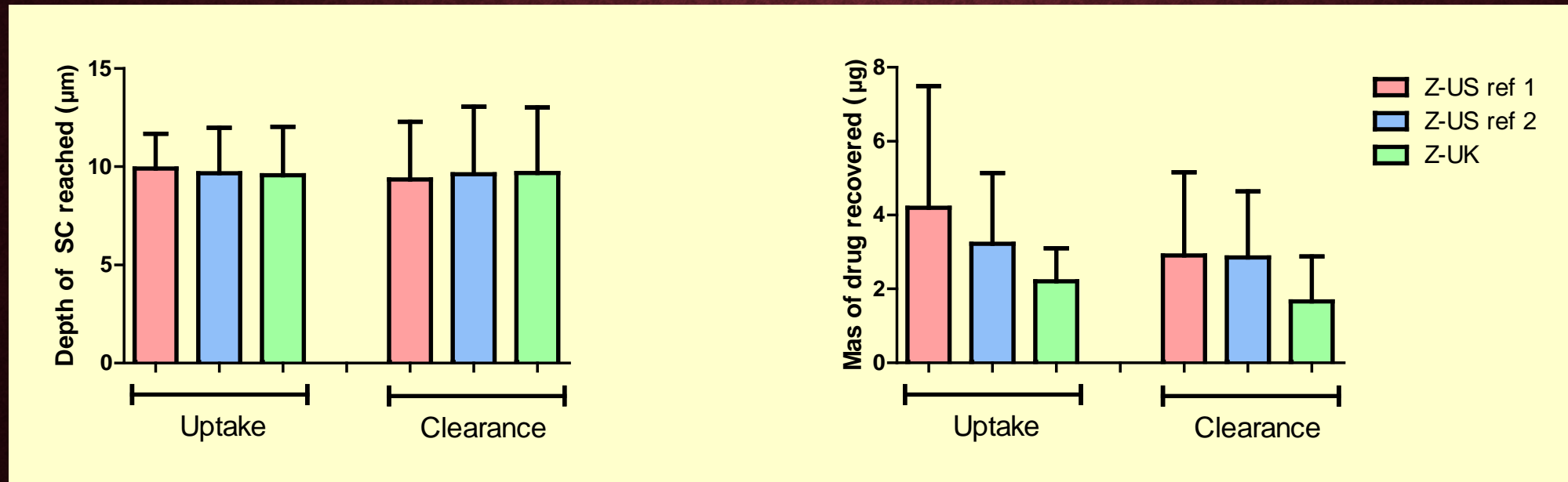


## Two-way ANOVA:

- Formulation: (  $p < 0.0001$  )
  - Pennsaid  $\neq$  Solaraze (  $p < 0.001$ ; uptake and clearance )
  - Pennsaid  $\neq$  Voltaren (  $p < 0.001$ ; uptake and clearance )
  - Voltaren = Solaraze
- Uptake/Clearance:  $p < 0.0001$
- Pairing effective:  $p < 0.0001$
- Interaction:  $p < 0.0004$

Diclofenac	Solaraze 3%	Voltaren 1%	Pennsaid 2%
Applied per site (mg)	4.95	0.825	1.65
Uptake recovery (µg)	32.19 ± 15.9	27.50 ± 10.2	178.5 ± 81.9
Clearance recovery (µg)	21.3 ± 15.2	19.2 ± 15.2	119.5 ± 65.5
% recovery (uptake)	0.65 ± 0.32	3.33 ± 1.24	10.81 ± 4.94
Clearance / Uptake	0.67 ± 0.43	0.75 ± 0.67	0.71 ± 0.31

# ACICLOVIR (ON-GOING)



## Branch A:

Zovirax Cream (USA) [reference]

Zovirax Cream (USA) [test]

Zovirax Cream (UK) [test].

# CONCLUSIONS

- DPK (tape-stripping) approach differentiated formulations of diclofenac expected to provide different drug absorption and topical bioavailability.
- Uptake and clearance data led to similar conclusions.
- Pennsaid sites:
  - Higher (~ double) TEWL
  - Required less (16-22) tapes than other formulation sites (29-30)
  - Greater amount (~1.3 fold) and deeper (~1.3 fold) SC removed
  - Higher (~ 5-6 fold) diclofenac recovery from tapes.
- Local side effects (redness, skin irritation) consistent with tape-stripping and the formulation's composition.
- Methodological issues (formulation application and removal, tape-stripping procedure, TEWL measurements, tapes grouping and extracting) need careful consideration when DPK is used to establish BE of topical products.

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Scientific Lead for Topical & Transdermal Drug Products

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# Thanks for your attention!