Assessing topical drug clearance from the skin using Raman spectroscopy

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PURPOSE

For topical dermatological products with target sites of action in the viable epidermal and/or upper dermal compartment of the skin, it has been challenging to quantify the **local concentration profiles** because drug clearance from the viable cutaneous tissue is not well-characterised.

Without such knowledge, it is difficult – if not impossible – to predict *a priori* whether therapeutically relevant concentrations of the drug can be achieved in the skin 'compartment' and the duration over which such therapeutically relevant concentrations can be maintained.

OBJECTIVE

To test the hypothesis that spectroscopic (specifically, **Raman**) imaging may offer a **non-invasive, accurate, sensitive and reproducible** method to determine the **rate at which a topically administered drug is cleared from the skin**.

METHODS

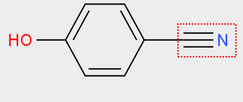
RAMAN SPECTROSCOPY

- Renishaw inVia Raman microscope working in reflection mode.
- Sample illuminated with a pre-calibrated 785 nm (150 mW) laser.
- *Ex vivo* abdominal pig skin on an aluminum support.

Molecule of interest

Cyanophenol (CP) has strong -C≡N Raman signal (2230 cm^{-1}) in a frequency range where skin is spectroscopically 'transparent'.

Cyanophenol

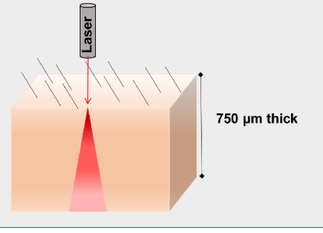


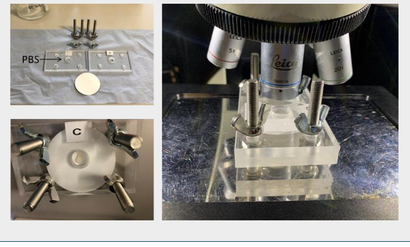
Cyanophenol formulations

1. Saturated solution (**170 mg mL^{-1}**) of CP in **50:50 v/v propylene glycol (PG)-water**;
2. 25% saturated solution (**42.5 mg mL^{-1}**) of CP in **50:50 v/v PG-water;**
3. Saturated solution (**17 mg mL^{-1}**) of CP in **10:90 v/v PG-water**.

The CP formulations (300 µL) were applied to the skin surface for **6 hours** under occlusion (Parafilm)**;** the skin surface was then cleaned. The tissue was cut into smaller pieces and mounted in a simple sample holder (unoccluded) that permitted tissue hydration to be maintained while sequential, 'top-down' Raman measurements (n = 6) were recorded of CP clearance from the skin over the next 6 hours.

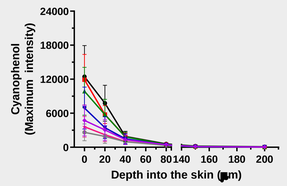
"Top-down" experiments



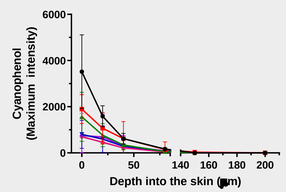


RESULTS

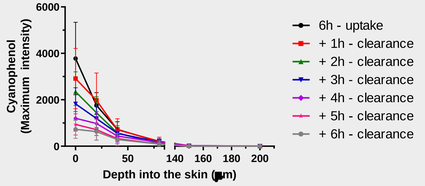
Saturated CP (170 mg mL^{-1}) in 50:50 v/v PG-water



Saturated CP (17 mg mL^{-1}) in 10:90 v/v PG-water

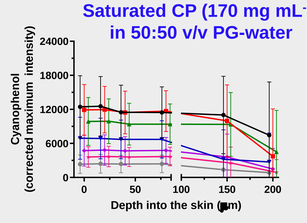


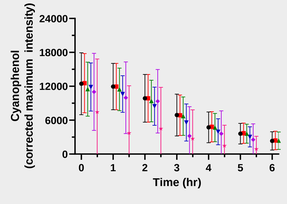
25% saturated CP (42.5 mg mL^{-1}) in 50:50 v/v PG-water



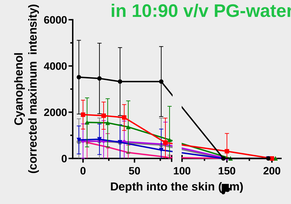
Correction for the signal attenuation: The CP signals measured in the "top-down" experiments were corrected using the Amide I intensity (from keratin) at 1650 cm^{-1}

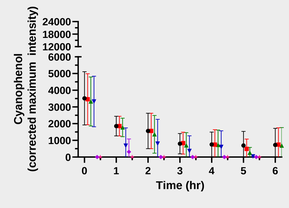
Saturated CP (170 mg mL^{-1}) in 50:50 v/v PG-water



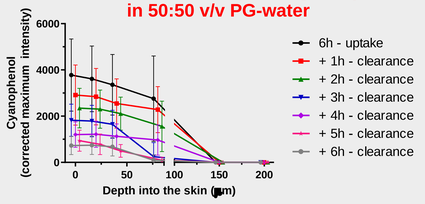


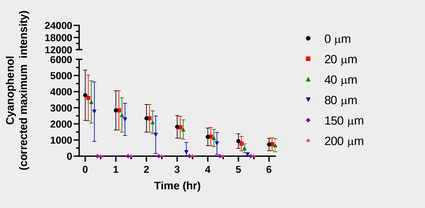
Saturated CP (17 mg mL^{-1}) in 10:90 v/v PG-water





25% saturated CP (42.5 mg mL^{-1}) in 50:50 v/v PG-water





CONCLUSIONS

- It was possible to monitor the clearance of CP from the skin over 6 hours.
- Particularly noteworthy from the results, however, is the very proportional relationship between Raman signal and the degree of saturation of CP in the applied formulations (i.e., 1 versus 0.25) and the ability of the noninvasive technique to distinguish the performance of the clearly different products applied to the skin.
- Overall, Raman spectroscopy can track drug clearance from the skin from different formulations and differentiate (in a semi-quantitative manner) between formulations.
- CP signal attenuation with depth causes the signal-to-noise ratio to become so small that detection is no longer possible (see long clearance times for 25% saturated CP).

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The views expressed in this poster do not reflect the official policies of the U.S. Food & Drug Administration or the U.S. Department of Health & Human Services; nor does any mention of trade names, commercial practices, or organization imply endorsement by the U.S. Government.

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