

SUPPORTING INFORMATION

Monitoring Drug Crystallization in Percutaneous Penetration Using Localized Nanothermal Analysis and Photothermal Microspectroscopy

Choon Fu Goh,^{*,†,‡} Jonathan G. Moffat,[§] Duncan Q. M. Craig,[†] Jonathan Hadgraft,[†] and Majella E. Lane[†]

[†]Department of Pharmaceutics, UCL School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX, United Kingdom

[‡]Discipline of Pharmaceutical Technology, School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia

[§]Asylum Research, Oxford Instruments Company, Halifax Road, HP12 3SE High Wycombe, United Kingdom

* Corresponding author:

Choon Fu Goh

Discipline of Pharmaceutical Technology, School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia

Phone: +604-6532074. Fax: +604-6570017. Email: gohchoonfu@hotmail.com / choonfugoh@usm.my

Figure S1 and S2 show the proposed mechanisms of the creation of the green domain and double transitions in TTM measurements.

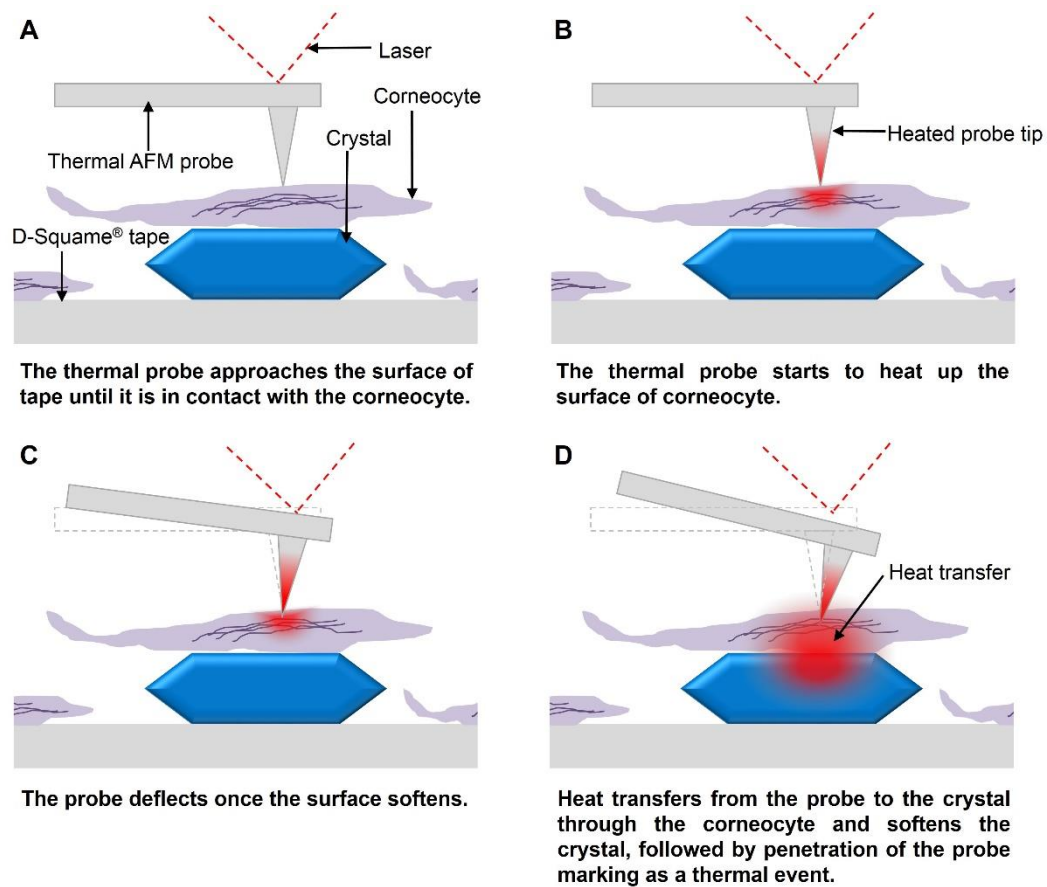
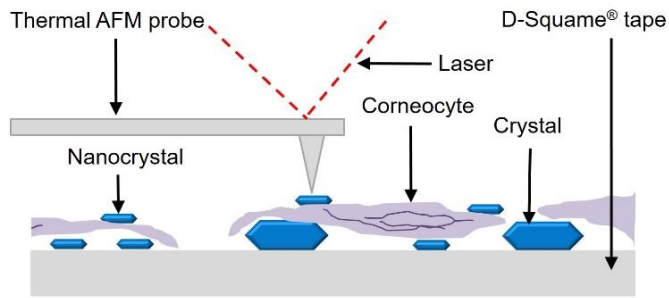
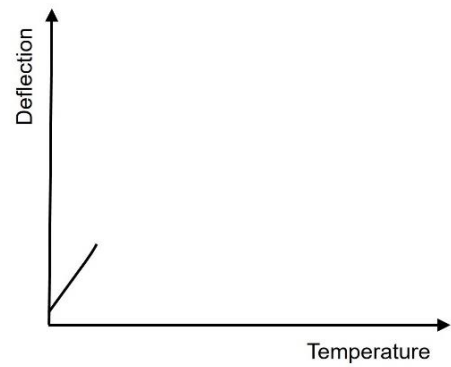
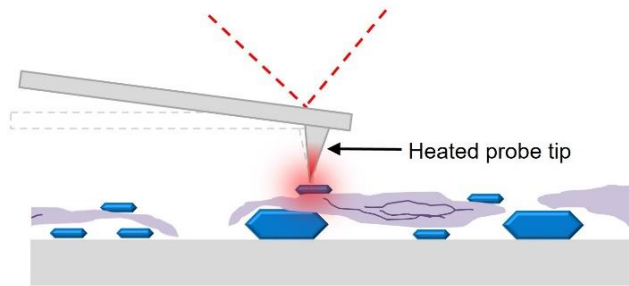


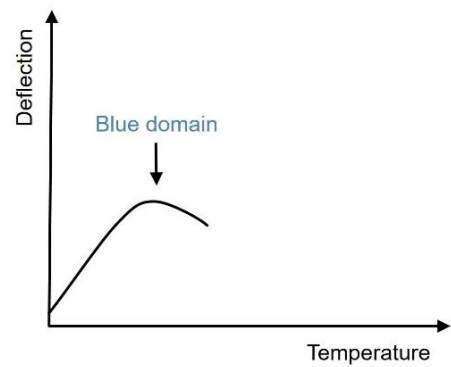
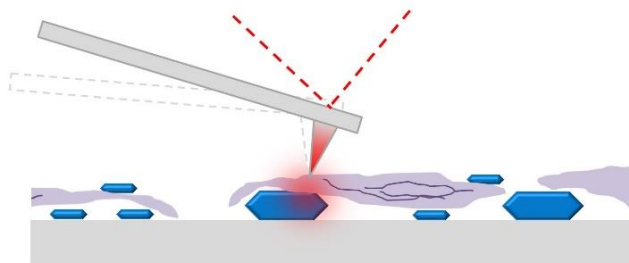
Figure S1 The proposed mechanism of the creation of the green domain in the TTM image scanning over a tape with PSC and crystals

A

The thermal probe engages with the surface of the tape and is in contact with the nanocrystals on the corneocytes.

**B**

The probe deflects once the nanocrystals melt and generates a transition (blue domain).

**C**

Before reaching the retraction limit, the probe continues to deflect and heats the corneocytes beneath the melted nanocrystals, resulting in the formation of a second transition (green domain).

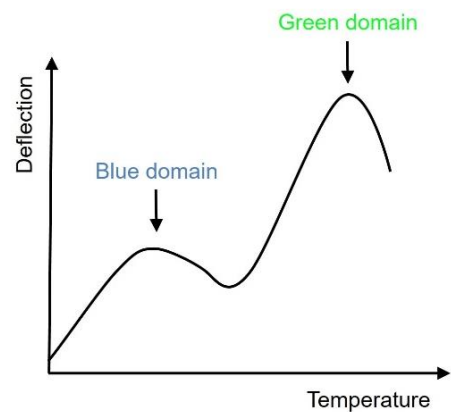


Figure S2 Schematic diagrams of the formation of double transitions in the TTM image

Figure S3 and S4 show the PTMS measurements for untreated PSC, PSC treated with PG and IBU crystals.

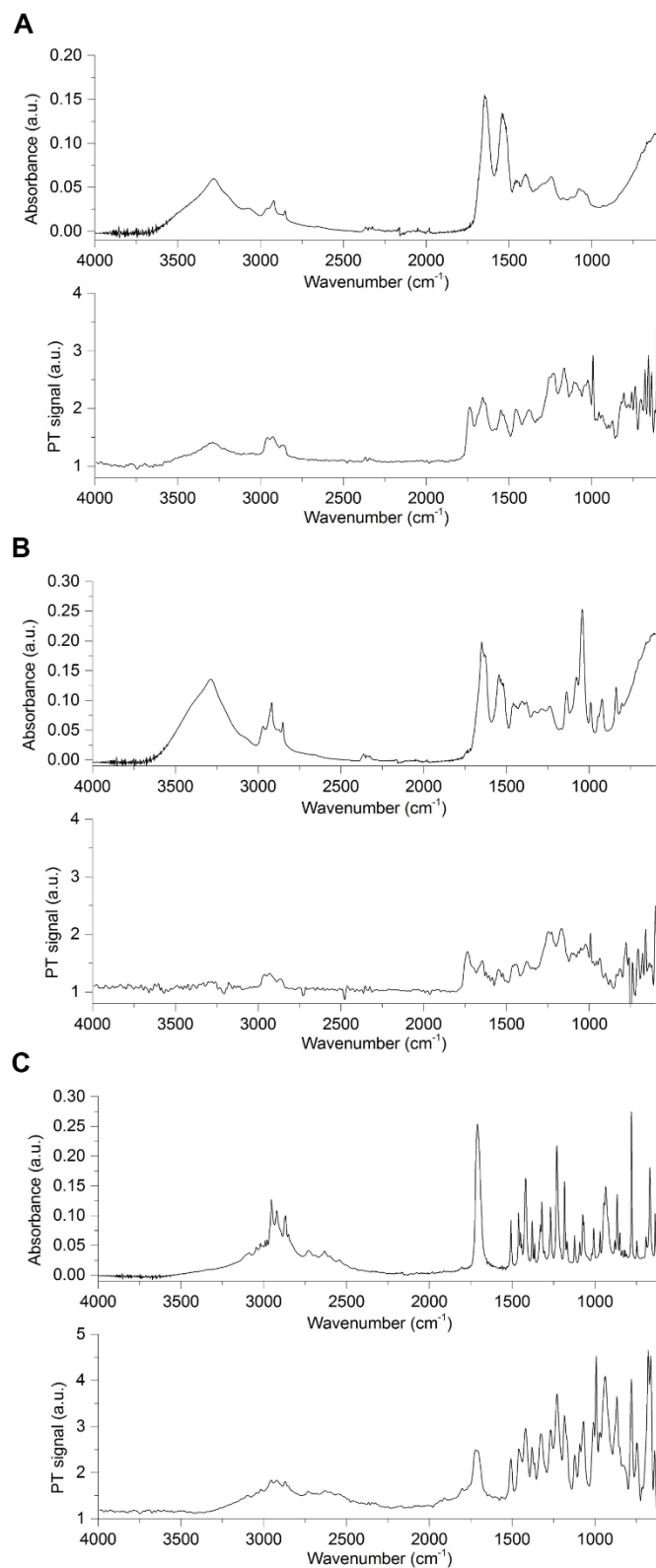


Figure S3 ATR-FTIR spectra (upper panel) and photothermal FTIR (lower panel) spectra for (A) untreated PSC, (B) PSC treated with PG and (C) IBU crystals

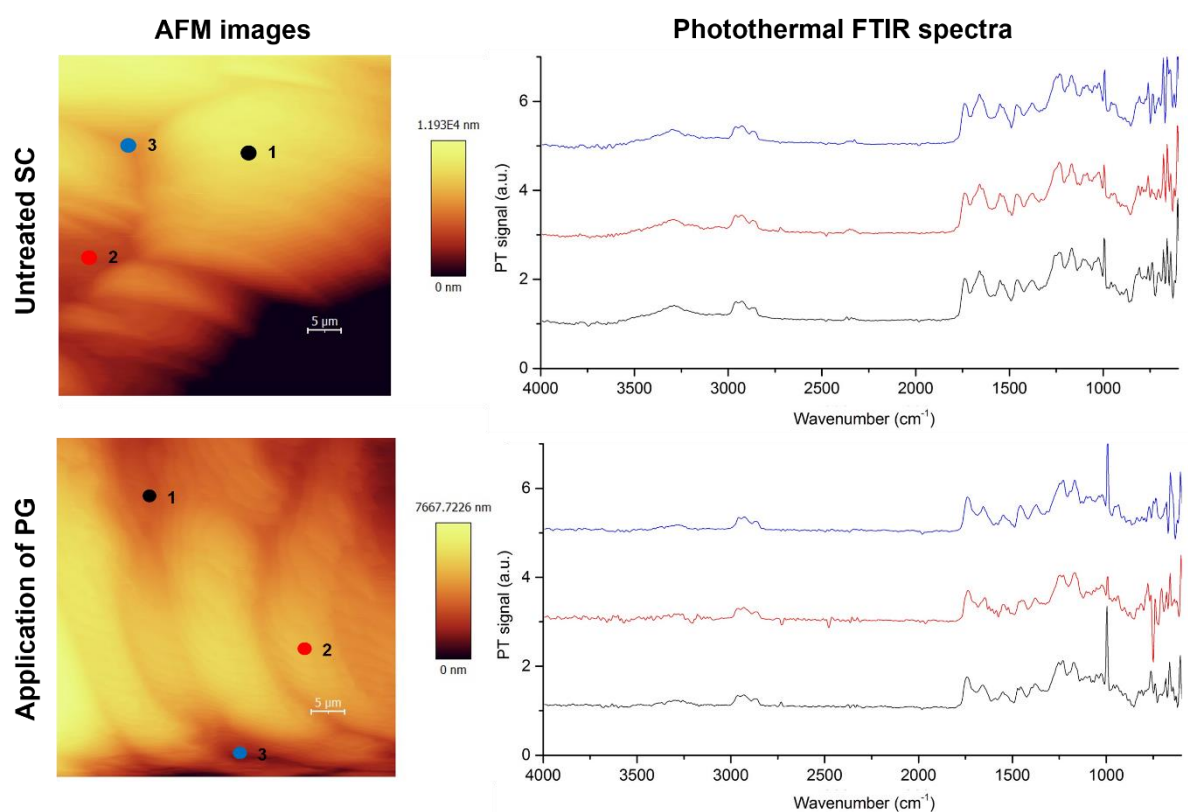


Figure S4 AFM images and corresponding photothermal FTIR spectra of PSC (with and without application of PG) on the first tape strip