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The role of the excipient povidone in an advanced gel formulation specially designed for the treatment of dry skin conditions

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Introduction

Emollient Doublebase Dayleve™ Gel (DELP) comprising a high level of oils and the humectant glycerol, plus the film-forming agent povidone (PVP), is commonly prescribed in the UK for the treatment of dry skin conditions, such as eczema and psoriasis, when substantial and long-lasting emolliency is needed.

The aim of this study was to investigate the role of PVP in this formulation by comparing the evaporative retention and microstructure of DELP with and without PVP. An alternative emollient cream, Diprobase Cream™ (DIPC), was included as a comparator.

Materials & Methods

Gravimetric investigation

- Dynamic Vapour Sorption (DVS) was used to measure mass changes (evaporative loss) of the formulations over 3h at three relative humidities (RH) of 50%, 30% and 10% and a fixed temperature of 32°C ± 0.5°C.
- Three replicates comprising standardised amounts were used for each formulation.
- Data were collected and analysed using DVS software (v 3.01 Surface Measurements Systems). Statistical analysis was performed using t-Test to compare the means.

Microstructural investigation

- The microstructural properties of the formulations were observed using cryo-Scanning Electron Microscopy (SEM), using a FEI Quanta 200 F microscope, operated under routine SEM conditions (ultra-high vacuum; Field Emission), and augmented with a PP3000T cryo preparation chamber by Quorum Technologies.
- The formulations were mounted on a brass specimen holder and plunge frozen in liquid nitrogen slush. The frozen specimen was fractured inside the cryo preparation chamber with a remotely controlled blade, followed by partial sublimation to remove all the water from the samples (8 and 10 min at -95°C and -100°C) and surface sputtering with platinum (5-10 mA for 30 seconds).

Acknowledgment

- Cryo-SEM sample preparation and imaging were performed by Mr David McCarthy, Experimental Officer at the Electron Microscopy Unit, School of Pharmacy, UCL, UK.

Results and Discussion

Significant differences ($p<0.05$) in weight loss over time were observed between the DELP gels with and without PVP (Figure 1). At all three RHs, the PVP-containing gel lost less weight compared with the identical gel without PVP. This weight loss is most likely formulation water, and the differences cannot be accounted for by the slightly higher water content of DELP without PVP. This indicates that the PVP helps to bind water into the structural matrix. In addition, both gels lost significantly less weight compared with the DIPC emollient cream.

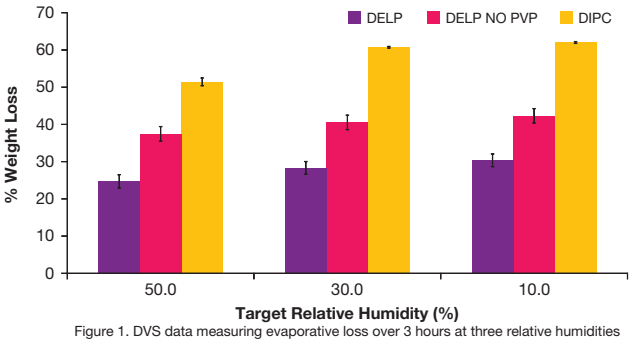

Figure 1. DVS data measuring evaporative loss over 3 hours at three relative humidities

The cryo-SEM images suggested microstructural differences between DELP gel with and without PVP (Figure 2). Carbopol gels have been reported to form "honeycombed" polymeric structures when observed under cryo-SEM[1], which is evident here. The spherical structures are most likely oil droplets dispersed within the gel structure and stabilised by the polymer network. With the PVP, the polymeric network appears to be tighter and the oil droplets are smaller. The tighter polymer network observed in the PVP-containing formulation may explain the reduced weight loss in Figure 1 – owing to evaporating formulation water having to diffuse through a more resistant/tighter microstructural matrix.

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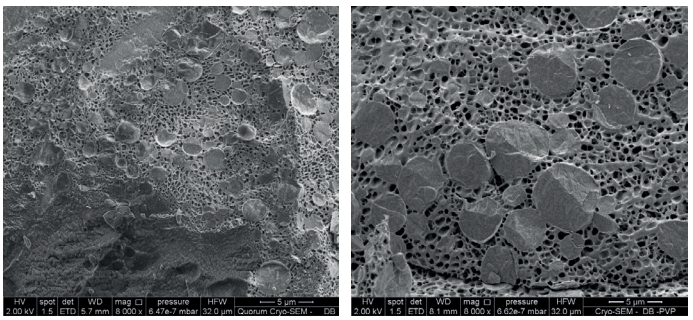

DELP gel | DELP gel with no PVP

Figure 2. Cryo-SEM images of DELP and DELP with no PVP

The cryo-SEM images obtained for the DIPC cream formulation show a relatively dense network of 'lamellar' microstructures (Figure 3). In contrast to DELP formulations, the oily phase in this oil in water cream is not clearly distinguished.

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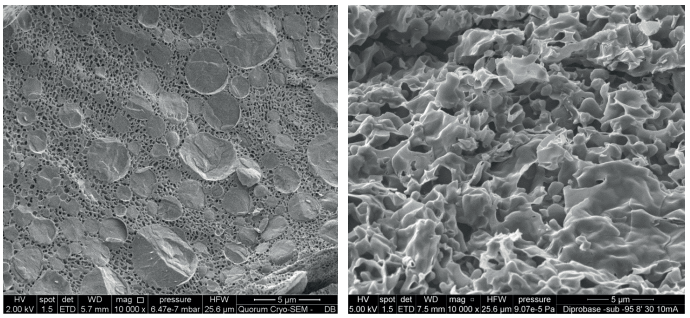

DELP gel | DIPC cream

Figure 3. Cryo-SEM images of DELP and DIPC

In a previous clinical study comparing DELP (with PVP) and DIPC applied twice daily, DELP achieved significantly longer-lasting and better cumulative skin hydration and was generally preferred by subjects[2]. The observed structural differences between these two products, and the propensity for DELP gel to hold onto formulation water, may be contributing factors to the superior *in vivo* performance of DELP gel.

Conclusion

The results of this study show that PVP significantly improves the water holding capacity of DELP, possibly by changing the gel's microstructure. This may help explain DELP's substantial, and long lasting, emolliency observed *in vivo.*

[1]Kim J.Y., Song J.Y., Lee, E.J. and Park S.K. (2003). "Rheological properties and microstructures of carbopol gel network system" *Colloid & Polymer Science* **281**(7): 614-623
[2]Gallagher J., Rosher P., Walker J. and Hart V.A. (2012). "An *in vivo* comparison of two commercially available topical emollients in the UK, DELP gel and DIPC cream " presented at the 70th Annual Meeting of the American Academy of Dermatology, San Diego, USA. Doublebase Dayleve and Diprobase are Trade Marks

Please turn over for poster summary.

The role of the excipient povidone in Doublebase Dayleve Gel – an enhanced gel formulation

Doublebase Dayleve Gel contains a high level of emollient oils and the humectant glycerol, plus the film-forming agent povidone (PVP). It is commonly prescribed in the UK for the treatment of dry skin conditions when long lasting protection is needed and the convenience of as little as twice daily application.

This study aimed to investigate the role of PVP in this formulation by comparing the evaporative retention and microstructure of Doublebase Dayleve Gel with and without PVP, with a comparator emollient cream.

The study summarised overleaf shows that PVP significantly improves the water holding capacity of Doublebase Dayleve Gel, which supports the substantial and long lasting emolliency observed *in vivo*.

Summary of Poster Overleaf:

- Dynamic Vapour Sorption (DVS) was used to measure mass changes (evaporative loss) of the formulations over 3h at three relative humidities (RH) of 50%, 30% and 10% and at a fixed temperature 32°C ± 0.5°C.
- Doublebase Dayleve Gel (with PVP) lost significantly ($p<0.05$) less weight compared with the identical gel without PVP at all three RHs. Both gels lost significantly less weight compared with the comparator emollient cream. This weight loss is most likely formulation water.
- Microstructural properties of the formulations were observed using cryo-Scanning Electron Microscopy (SEM). Under SEM the gel matrix can be seen as a "honeycombed" polymeric structure with evenly dispersed small oil droplets. The addition of PVP in the formulation appears to enhance the carbomer gel matrix to give a 'tighter' structure with smaller oil droplets.
- In contrast, the structure of the emollient cream is very different with no clearly distinguished oily phase.

Conclusion:

"The results of this study show that PVP significantly improves the water holding capacity of DELP, possibly by changing the gel's microstructure. This may help explain DELP's substantial, and long lasting, emolliency observed *in vivo*."