Emollient product design: objective measurements of formulation structure, texture and performance, and subjective assessments of user acceptability

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Abstract

Background. The choice of prescribed emollients is usually based on cost and patient preference. Differences in formulations can affect user acceptability.

Aim. To compare the physical performance, user acceptability and various product design features of two emollient gels that are prescribed in the UK and alleged to be therapeutically interchangeable because their formulations are described as having the same contents of oily ingredients.

Results. We found that there are in fact significant measurable differences between the structure and performance of the two formulations, which materially affect their user acceptability. These differences are attributed to the use of different types of gelling agents and other ingredients of differing grades/quality and concentrations, and probably due to the formulations being made by different manufacturing processes. We also identified other product design features that are important to user appeal, including the type of container in which the formulations are presented, the type of dispensing devices provided, and the nature and form of the supplied user instructions.

Conclusion. Patients and prescribers should be aware that there can be important differences in performance and user appeal between emollients, even between products that, superficially, may appear to be very similar. These important performance aspects should be characterized for new emollient introductions to encourage better informed product selection.
formulations in their normal states and after contact with salt. We also explored the perceived importance of various other differences between the designs of these two products that potentially might affect their user appeal and therapeutic usefulness.

**Methods**

**Sample preparation**

Salt-treated samples were prepared by sprinkling 2.0 ± 0.1 g of NaCl onto 20 ± 0.4 g of each formulation, and gently mixing by folding the formulation onto itself 10 times, using a spatula. The samples were then left to stand for 30 min. Untreated control samples for each emulsified gel were folded in the same manner without adding salt.

**Microscopy**

Approximately 20 mg of treated and control samples of each formulation were mixed with Nile Red fluorescent dye. The samples were then placed on microscope slides and pressed with coverslips for 5 s. After 1 h, the samples were viewed under a laser microscope (Eclipse 90i; Nikon Instruments Inc., Amsterdam, the Netherlands) at × 60 magnification.

**Firmness/stiffness and stickiness by texture analysis**

Aliquots (50 g) of treated and control samples of DBG and ZDG were weighed into a beaker and subjected to compression using a 35-mm diameter cylindrical probe (TA-HDplus; Stable Microsystems, Godalming, Surry) to measure firmness/stiffness and stickiness. The probe compressed the sample by 15 mm distance after an initial trigger force of 0.5 N at a rate of 0.5 mm/s. When the 15 mm target distance was reached, the probe returned to the starting position at 10 mm/s and recorded the force required to separate the probe from the sample. This force is an indicator of stickiness. Samples were analysed in triplicate.

**Spreadability by texture analysis**

Aliquots (1.1 ± 0.1 g) of treated and control samples were compressed between two glass plates using predetermined forces of 1, 5, 20, 40 and 50 N. At each force, the area of spread was recorded and calculated. Different samples were used for the measurements of spreadability at each force applied.

**Product satisfaction questionnaire**

With full ethics approval (University of Greenwich ethics committee), 67 adult participants completed a structured questionnaire asking whether they preferred either product or liked them both equally, in respect to various product design features addressing: (i) the physical appearance/look of the formulations, (ii) the suitability and performance of the containers and dispensing devices, (iii) the accompanying written instructions and medical advice, and (iv) the handling characteristics of the two gel formulations.

**Statistical analysis**

A binomial test was carried out to identify statistical differences between any preferences between the products. This test was carried out separately for each design feature, with a null hypothesis of equal preference for the two emollients. The tests were performed using the PROBBNML() function from an SAS data step, so they are exact binomial probabilities. The P values were all very much smaller than the cut-off of 0.05.

**Results**

**Gross characteristics of gels**

On visual inspection, there were noticeable differences between the surface characteristics and consistencies of the two emulsified gels. DBG has a smooth and homogeneous structure, whereas ZDG is lumpy and

![Figure 1](image_url)
heterogeneous. Figure 1a–d shows the appearance of the two gel structures before and after coming into contact with salt. The DBG structure (Fig. 1a) largely broke down into a liquid (Fig. 1c) after contact with salt, whereas the ZDG structure (Fig. 1b) did not break down, and in fact appeared to curdle and become firmer (Fig. 1d).

**Microscopic characteristics of gels**

Microscopic examination also revealed differences between the two emulsion gels, both in their normal states (Fig. 2a,e) and following salt exposure. For DBG, the structural matrix stabilizing the oil droplets broke down completely (Fig. 2b–d), releasing the oil from the emulsion. For ZDG, however, microscopic examination suggests that the emulsion structure did not break down to the same extent and manner as DBG (Fig. 2f–h).

**Firmness/stiffness and stickiness using texture analysis**

Considerable differences were observed between the two untreated formulations in terms of firmness and stickiness. ZDG appeared to have a significantly firmer (Fig. 3a) and stickier polymeric structure than that of DBG (Fig. 3b). Upon treatment with salts, the polymeric structure of DBG readily broke down, resulting in extensive loss of firmness, whereas under the same conditions the firmness of ZDG scarcely changed.

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**Figure 2** (a–h) Laser microscopy images of different areas of Doublebase gel (DBG) and Zerodouble gel (ZDG) samples before and after salt treatment obtained at × 60 magnification.

**Figure 3** (a) Firmness/stiffness and (b) stickiness indicators of Doublebase gel (DBG) and Zerodouble gel (ZDG) before and after exposure to salt. ZDG* and DBG* indicate salt-treated samples.
Both gels appeared to lose their stickiness once exposed to salt. Notable differences were observed between the two gels in terms of spreadability (Fig. 4). DBG spread more easily than ZDG, and even more so after exposure to salt. Interestingly, no such effect was observed for ZDG, as there was no substantial difference between ZDG samples before and after salt treatment.

**Product satisfaction questionnaire**

Of the 67 participants who were screened and completed the study, 26 were men and 41 were women. Most participants (77.6%) were in the 18–30 age group. The product satisfaction questionnaire results are presented in Table 1. The results showed that >88% of subjects reported that the look of the DBG formulation was smoother/more uniform, appeared to be of a better quality and looked more appealing to use, while 89.6% said they would prefer the DBG formulation for long-term use and >79% of subjects felt that the DBG pump presentation looked more convenient, more hygienic, easier to use and more suitable for medicinal products of this sort than the squeeze-bottle presentation used by ZDG. When asked which user instructions encouraged the most patient benefit from using the product and contained the most helpful advice on how to look after dry skin, over 68% of subjects favoured the information leaflet supplied with DBG rather than the ‘peel and read’ label supplied with ZDG. In addition, 74.6% reported that they preferred the handling characteristics of theDBG formulation. All the binomial tests were highly statistically significant ($P < 0.001$).

**Discussion**

Emollients are available in various formulation types, including emulsified creams, ointments, lotions and gels. They perform a crucial role in the treatment and management of dry skin conditions such as eczema and psoriasis.

The sensory profile of leave-on emollients has to be cosmetically acceptable in order to encourage patients to use them properly, and emulsified gel formulations...
of the formulation with salts on the skin. Ideally, this occurs when spreading it over the skin and by the interaction of the skin, resulting in skin barrier damage,18 whereas other ingredients can have beneficial effects.

As explained above, the observed differences in performance may be partly attributed to the differing gelling agents used, as different grades of carbomer behave differently (Table 2). The differences are also likely to be influenced by the product formulation, if they contain other ingredients of differing grades/quality and concentrations. They are almost certainly made by different manufacturing processes, and it is known that even the order in which ingredients are added can influence product performance. Other researchers have observed that for topically applied dosage forms, small changes in the formulation or manufacturing process can significantly affect both quality and efficacy.13–16 Performance differences have also been attributed to other factors such as occlusivity, pH, viscosity, droplet size, partition coefficients and the ionic nature of ingredients. Bearing in mind that emollients are designed to produce an oily, partially occlusive film over the surface of the skin and fill the interstices between the desquamating corneocytes abundant in dry skin conditions, their occlusivity is bound to be influenced by the viscosity, molecular weight and spreading characteristics of the formulation.17 Changes in viscosity, for example, can alter occlusivity and skin retention of the dosage form and even percutaneous absorption.15 Another important consideration is the effect of the formulation on skin pH. Some formulation excipients can increase the pH of the skin, resulting in skin barrier damage,18 whereas other ingredients can have beneficial effects by decreasing skin pH19 and promoting the skin’s acid mantle. For example, the skin’s innate antimicrobial properties are optimal at acidic pH, as Staphylococcus and other pathogenic bacteria favour neutral pH and are inhibited in an acidic environment.20 Additionally, in an acidic environment, normal desquamation of the stratum corneum is a controlled process regulated by the enzymes kallikreins 5 and 7.21 However, at higher pH, desquamation of skin cells can run out of control, damaging the stratum corneum barrier.20

For topically applied licensed medicines, there is universal acceptance that two ostensibly similar formulations cannot be assumed to be therapeutically equivalent. Indeed, this important principle explains why regulatory authorities require generic manufacturers to demonstrate that their products are indeed bioequivalent to the innovator formulation. This is very important for topically applied dosage forms, as differing physicochemical characteristics are known to

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**Table 2 Composition of Doublebase and Zerodouble gels.**

| Function         | DBG               | ZDG               |
|------------------|-------------------|-------------------|
| Emollients       | Isopropyl myristate 15%; liquid paraffin 15% | Isopropyl myristate 15%; liquid paraffin 15% |
| Preservative     | Phenoxyethanol    | Phenoxyethanol    |
| Humectant        | Glycerol          | Glycerin          |
| Emulsifier       | Carbomer          | Acrylates         |
| Emulsifier/SWA   | Sorbitan laurate  | Sorbitan laurate  |
| pH modifier      | Triethanolamine   | Triethanolamine   |
| Water base       | Purified water    | Purified water    |

DBG, Doublebase gel; SWA, surface-wetting agent; ZDG, Zerodouble gel.

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render ostensibly similar formulations therapeutically nonequivalent. The performance differences reported here confirm this important principle. In stark contrast, however, for self-certified Class I medical devices, there is no independent regulatory assessment of their quality, safety or effectiveness, and the important matter of therapeutic equivalence can be completely ignored. This is something that regulatory authorities, healthcare professionals, prescribers and patients should take into consideration, because important performance differences do exist, even between formulations that, superficially, may seem to be very similar.

In addition to these important formulation differences, other product design features were found to significantly influence the user appeal and acceptability of DBG and ZDG. The DBG pump pack presentation was significantly more popular than the ZDG squeeze bottle, in terms of convenience, hygiene and ease of use. Although not tested in our study, leachates from certain types of plastic containers are also known to affect the biocompatibility of topical dosage forms, especially for patients with sensitive skin. It is also notable that two-thirds of users felt that the more comprehensive style of patient instruction leaflet supplied with DBG was likely to encourage the most patient benefit.

Conclusion

By combining both objective instrumental measurements and users’ subjective assessments of product performance and acceptability, we have demonstrated important differences between two prescribed emollient gels that are alleged to have the same oil content and apparently comparable lists of ingredients. It is therefore important to recognize that emollients from different manufacturers are not the same as one another, and for prescribing purposes should not be grouped into a ‘class’ and regarded as being interchangeable. When choosing between gel emollients, patients and prescribers should be aware that there can be important performance differences, even between products that, superficially, may appear to be very similar. The performance of new emollient introductions should be properly characterized in order to inform product selection.

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