

A COMPARATIVE PHYSICOCHEMICAL AND COSMETIC EVALUATION OF GENERIC TOPICAL CORTICOSTEROID PRODUCTS

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ABSTRACT: Comparison and evaluation of physicochemical properties of the six betamethasone-17-valerate creams available locally were studied. Tests that were conducted include stiffness/hardness, grittiness, colour, odour, homogeneity (phase separation), pH, weight of loss, tackiness (stickiness) and microscopic examination. A point grading system was used to assess and compare the products. Results revealed that Betnovate™ and Camnovate™ to be the most superior followed by Beavate™, Setrosone™, Betasone™ and Uniflex™ (*JUMMEC 2002; 2:114-117*)

Introduction

Topical corticosteroids available locally comprises largely of locally manufactured and imported generic preparations. Physicochemical and cosmetic properties of these products do contribute to patient compliance, wherein the greater the level of patient acceptability of the product, the more likely the patient will be using it and hence comply to the prescribed therapy (1). With a number of the marketed products being locally manufactured, betamethasone-17 valerate cream is selected for this study. Literature search has not shown any work that has been done to compare physicochemical and cosmetic properties of any generic topical corticosteroids that are marketed in Malaysia.

This study assesses and compares the physicochemical properties of betamethasone-17-valerate creams available locally.

Methodology

The six products tested were Betnovate™, Betasone™, Camnovate™, Setrosone™, Uniflex™ (see Table 1 for details of manufacturer, distributor and packing). Apart from Betnovate™, the original product which is imported, the remaining products are locally manufactured in Malaysia. Samples of the six products of betamethasone-17-valerate cream, each containing 0.1% w/w of the steroid, were obtained from either the manufacturer or importer. The respective samples were labeled as products A, B, C, D, E and F. The samples were stored at room temperature except during the evaluation of homogeneity (phase separation).

A parallel, in vitro evaluation of the cosmetic and physicochemical properties of the six betamethasone-17-valerate creams were undertaken. The evaluation was conducted using well established methods such as pH determination, phase separation, weight loss and mi-

croscopic examination to evaluate the shape and homogeneity of the globules. Subjective determination was also used to assess the odour, and stiffness or spreadability of the samples (1).

Below is a brief description of the methodology apply for the evaluation of the physicochemical and cosmetic properties of the samples obtained:

- Determination of pH was conducted using an electrode attached to a pH meter.
- Phase separation study was conducted in a water bath where the test material was immersed in a water bath at 37 °C and at 55 °C for 120 minutes. Signs of bleeding or phase separation were examined at regular intervals and the time when any

Table 1. Details of the products tested

| Product name | Manufacturer | Distributor | Packing |
|----------------------|---------------------------------|---|-----------------------------|
| Beavate™ | Upha Corporation (M) Sdn.Bhd | Upha Corporation (M) Sdn.Bhd | 15g 500g |
| Betasone Asia Pharm™ | Asia Pharm. Products Sdn.Bhd | Antah Pharma | 500g |
| Betnovate™ | Glaxo Wellcome | Glaxo Wellcome Malaysia (WM) & Zuellig (EM) | 5gx12's 15gx12's 100g |
| Camnovate™ | Camden/Mico Sdn.Bhd | Antah Pharma | 450g |
| Setrosone™ | Strand Pharm. (M) Sdn.Bhd | Strand Pharm (M) Sdn.Bhd | 450g |
| Uniflex™ | Xepa-Soul Pattinson (M) Sdn.Bhd | Xepa-Soul Pattinson (M) Sdn.Bhd | 450g |

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- physical change (bleeding or liquefaction) was observed was noted.
- (c) Weight loss determination was conducted over a period of sixty days storage at room temperature whereby the test material was weighed at specific recorded and assessed using a grading system.
- (d) Microscopic evaluation was conducted using a scanning electron microscope and photographs were taken to assess the shape and homogeneity of the globules of the products tested.
- (e) The stickiness of the test material was assessed by applying a portion of cream to a microscope slide and covering it with a cover glass. The time taken for the cover glass to slide down the slide was recorded and rated using grading system.
- (f) The colour of the test material was assessed objectively by comparing all the test materials against a white paper and rating the colour.
- (g) The test material was sniffed at to assess the odour.

- (h) The test material was examined for visible signs of grittiness and also by touch.

Each one of these properties was compared using a four point grading system where the most acceptable product is given a score of one and the least acceptable product is given score of four. A summation of these scores were then carried out and the product with the least total score is considered superior to the rest of the other products.

Result

The individual and total assessment scores of the evaluation of the six betamethasone-17-valerate creams are presented in Table-2.

Betasone and Beavate were of an optimal consistency whereas Betnovate tend to be slightly runny. The rest of the products namely Uniflex, Camnovate and Setrosone were slightly stiff. A stiff product might be difficult to spread upon application to the skin and this can be hindrance to patient compliance (2,3).

Table 2. Assessment scores for the six topical corticosteroid

| Physicochemical/ cosmetic property | Betnovate™ | Uniflex™ | Betasone™ | Beavate™ | Camnovate™ | Setrosone™ |
|--|------------|----------|-----------|----------|------------|------------|
| Stiffness/ hardness ^a | 2 | 2 | 1 | 1 | 2 | 2 |
| Grittiness ^b | 1 | 1 | 1 | 1 | 1 | 1 |
| Colour ^c | 1 | 1 | 1 | 1 | 1 | 1 |
| Odour ^d | 2 | 3 | 1 | 1 | 1 | 2 |
| Homogeneity (phase separation) ^e | 1 | 1 | 4 | 2 | 1 | 1 |
| PH ^f | 1 | 2 | 4 | 2 | 2 | 2 |
| Weight of loss ^g | 1 | 1 | 1 | 1 | 1 | 3 |
| Tackiness (stickiness) ^h | 2 | 4 | 1 | 2 | 2 | 2 |
| Microscopic examination ⁱ | 1 | 4 | 3 | 4 | 1 | 2 |
| Overall score | 12 | 19 | 17 | 15 | 12 | 16 |

Comments

^a 1-optimal consistency; 2-slightly stiff/runny; 3-moderately stiff/runny; 4-very stiff/runny.

^b 1-least gritty (excellent); 2-slightly gritty; 3-moderately gritty; 4-most gritty (poor).

^c 1-white/off white (excellent); 2-good; 3-fair; 4-poor.

^d 1-odourless/pleasant; 2-mild odour; 3-unpleasant odour; 4-very strong unpleasant odour.

^e 1-Phase separation (bleeding) after exposure to 55°C for up to 120 minutes: 1-excellent (no separation in 80 to 120 minutes); 2-good (separation between 50 and 80 minutes); 3-fair (separation between 20 and 50 minutes); 4-poor (separation between 5 and 20 minutes).

^f 1-excellent (pH 4.4 to 5.5) 2-good (pH 4.0 to 4.5 and 5.5 to 6.0); 3-fair (pH 3.5 to 4.0 and 6.0 to 6.5); 4-poor (pH below 3.5 and above 6.5).

^g Weight loss after 60 days storage at 25°C: 1-excellent (0 to 1 % weight loss); 2-good (1 to 2 % weight loss); 3-fair (2 to 5 % weight loss); 4-poor (more than 5 % weight loss).

^h 1-excellent (15 to 25 seconds); 2-good (10 to 15 seconds and 25 to 30 seconds); 3-fair (5 to 10 seconds and 30 to 35 seconds); 4-poor (above 35 seconds and below 5 seconds).

All the samples were not gritty and therefore score one point each. With regards to colour, Betasone was off-white while the remaining products were white. White or off white is generally considered to be the desirable colour for a cream.(3,4)

Beavate and Betasone were found to be odourless, whereas Camnovate gave a pleasant scent, therefore obtaining score of one point each. Betnovate had a very faint antiseptic —like odour and Setrosone, a waxy-like odour, with Uniflex exuding an unpleasant odour. The latter odour may adversely affected compliance and was therefore considered not desirable.(3,4)

In the homogeneity (phase separation) study, Betnovate, Uniflex, camnovate and Setrosone remained homogenous up to 120 minutes immersion in a water bath at 37 °C and at 55 °C. However, Betnovate and Camnovate were observed to be in a liquid state. Beavate started to liquefy at 10 to 20 minutes following which, at 50 to 80 minutes, the product started to separate into 2 layers namely the oily layer floating at the top and aqueous layer at the bottom. Betasone bled at 10 to 20 minutes and as 120 minutes time point

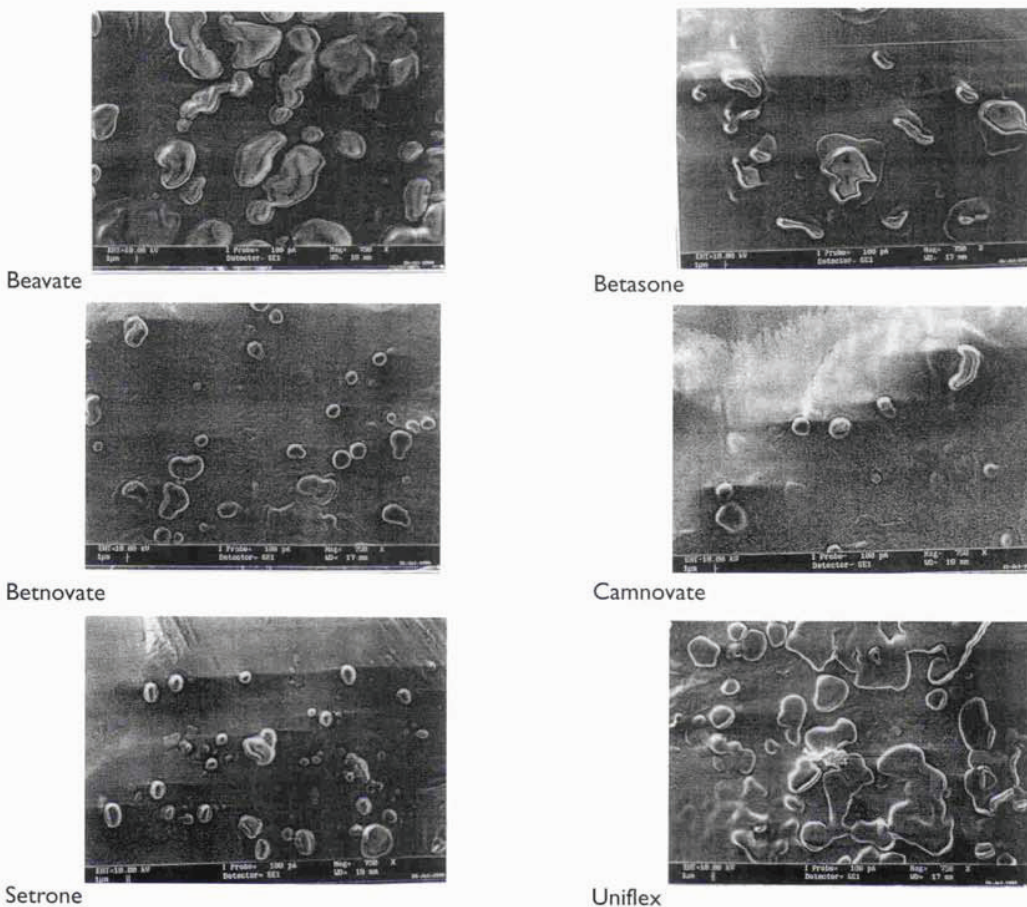
was approached, the product looked streaky but did not separate into two layers like Beavate.

The pH of the six products varied from 3.02 to 5.90. A significant reduction in the pH of Camnovate and Setrosone were recorded after 40 days of storage. All the products had weight loss of less than 1% after sixty days storage with the exception of Setrosone which recorded a weight loss of 2.2%.

Due to the high degree of tackiness of the product tested, a one-cent coin had to be glued to the outer surface of the cover glass to detach from the slide. The results from the tackiness assessment showed that Uniflex took the longest average time (56.10 ± 6.47 seconds) to detach from the microscope slide. This indicated that Uniflex was the most tacky preparations of the six. On the other hand, Betnovate and Beavate recorded the shortest time for detachment of the cover glass (13.63 ± 2.25 seconds). The remaining products recorded times ranging from 15.90 ± 6.47 to 22.40 ± 8.21 seconds) to detach from the microscope slide.

The scanning electron microscope examination revealed that the Betnovate, Camnovate and Setrosone samples

Figure 1. Scanning Microscopy pictures of six topical corticosteroid



possessed fairly circular shaped globules. Betnovate and Camnovate appeared more homogenous in relation to globule size. Betasone, Beavate, and Uniflex, on the other hand, showed irregularly shaped globules, over a wide size range and generally much larger globule sizes compared to, Betnovate, Camnovate and Setrosone. The globules seen in Beavate and Uniflex were very closely positioned to each other. Thus, electron microscopic examination indicated that Betnovate and Camnovate creams appeared to be relatively more stable compared to others, in relation to the globule size and distribution (2,3,4,5) with Setrosone placed third.

Conclusion

Based on the data collected, Betnovate and Camnovate received the best overall scores and therefore could be considered to be superior, compared to the remaining product with regards to the physicochemical and cosmetic properties evaluated. Beavate could be deduced to be superior to Betasone and Setrosone but inferior to Betnovate and Camnovate. Setrosone received

lower total scores than Betasone and therefore could be considered superior to Betasone. Uniflex was found to be inferior compared to the rest of the products.

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