

THE EFFECT OF TOPICAL APPLICATION ON THE HOMOGENEITY OF A FINELY POWDERED DRUG SUSPENDED IN AN OINTMENT BASE

E.A. Hill, N.A. Orr, School of Pharmacy, Sunderland Polytechnic, Green Terrace, Sunderland. SR1 3SD

Topical therapy should, in principle, allow highly active drugs to be applied on, or in close proximity to, the selected target site in the skin with minimal risk of toxic systemic involvement. Highly uniform dispersions of drug both in the preparation and on the skin are essential to achieve consistent coverage of affected areas with optimum drug levels. The problem is particularly acute when potent drugs are present at low concentrations (Hersey & Cook 1973).

The distribution of hydrocortisone particles suspended in hydrocortisone ointment B.P. 1% has been investigated (Orr et al 1980a) and the content uniformity assessed (Orr et al 1980b). Positively skewed distributions in content uniformity were found in some of the ointments studied and were attributed to the presence of agglomerates of hydrocortisone particles remaining undispersed in the formulation after mixing. Manual application of an ointment having a positively skewed drug distribution may influence the final distribution of drug on the skin if further mixing occurs. Investigations of this effect were made using hydrocortisone ointment spread on excised porcine skin.

Approximately 0.5g of hydrocortisone ointment B.P. 1% was spread with a circular rubbing motion over 9cm² of excised porcine skin until completely covered. The ointment was known to have a skewed drug content (coefficient of skewness $\sqrt{b_1} = 3.56$) attributed to the presence of agglomerates of hydrocortisone of up to 500 μm diameter. The skin was then subdivided into sections of 1cm². Each section was weighed and the ointment removed and assayed quantitatively for the presence of hydrocortisone using high performance liquid chromatography. The ointment free skin sections were recovered and reweighed. The weight of ointment was determined and the concentration of hydrocortisone over each 1cm² section was calculated (Table 1); the drug content distribution of the ointment was found to be significantly positively skewed ($\sqrt{b_1} = 1.82$, P normal distribution < 0.01)

Table 1: The range, mean and coefficient of variation of the percentage content of hydrocortisone spread over 1cm² of porcine skin.

	Min. Value	Max. Value	Mean	Coefficient of variation
Conc ⁿ Distribution	0.83%	1.45%	1.05%	7.8%

The physical application of the ointment to a skin surface apparently does not produce an homogenous distribution of drug. This result might be considered surprising since considerable shear forces must have been imposed to obtain an ointment film averaging approximately 65 μm in thickness presumably breaking down any agglomerates present greater than 65 μm in diameter. It is probable that agglomerates of drug may have been trapped in ridges present on the skin surface avoiding the shearing action of rubbing during application. Diseased skin may present an extremely irregular surface of plaques or fissures which may prevent a suitable even distribution of ointment over the affected area by this method of application. Consequently inhomogenous distributions of drug or possibly intact agglomerates may remain on the skin surface, adversely influencing the therapeutic efficiency of the product.

Hersey, J.A. Cook, P.C. (1973) *J. Pharm. Pharmac.* 25 Suppl. 121P
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