Hydrocortisone 17-Butyrate: A New Topical Corticosteroid
Preliminary Report

R.N. Brogden, R.M. Pinder, Phyllis R. Sawyer, T.M. Speight and
G.S. Avery

Australasian Drug Information Services, Auckland

Table of Contents

Summary . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . . .. 249
1. Experimental Studies in Animals .................................. 250
2. Human Pharmacology ........................................ 250
   2.1 Vasoconstrictor Activity ................................ 250
   2.2 Skin Penetration .................................... 250
   2.3 Effect on Adrenal Function .............................. 251
   2.4 Effect on Skin Thickness ................................ 252
   2.5 Pharmacokinetics .................................. 252
3. Therapeutic Trials ...................................... 253
   3.1 Psoriasis ......................................... 253
   3.2 Eczema .......................................... 254
   3.3 Facial Conditions .................................... 254
   3.4 Various Inflammatory Dermatoses .......................... 254
4. Side-Effects .................................. . ....... 255
5. Contra-Indications ........... . ................. . ........ 255
6. Precautions .......................................... 255
7. Administration ........................................ 256

Summary

Hydrocortisone 17-butyrate is a new non-fluorinated topical corticosteroid for use in psoriasis, eczema and other inflammatory dermatoses. In double-blind paired comparisons with other topical corticosteroids, the efficacy of hydrocortisone 17-butyrate 0.1% has generally been indistinguishable from that of triamcinolone acetonide 0.1%, fluocinolone acetonide 0.025% or betamethasone 17-valerate 0.1% in patients with eczema or psoriasis.

When applied to the face of patients with atrophy superimposed on rosacea and perioral dermatitis resulting from prolonged use of fluorinated topical corticosteroids, hydrocortisone 17-butyrate 0.1% did not prevent the beneficial effect of systemic tetracycline nor

1 'Locoid' (Gist-Brocades).
the disappearance of telangiectasis, and tended to be more effective than hydrocortisone 1%. This result suggests that hydrocortisone 17-butyrate may be suitable for long-term use on facial lesions, although the occurrence of moderate rebound eruption in about 10% of patients indicates the need for caution.

The findings suggest that hydrocortisone 17-butyrate may be less liable to cause skin atrophy and adrenal suppression than some other potent topical corticosteroids, but trials to date have been too short to allow definite conclusions regarding possible long-term effects and have not involved infants or children.

1. Experimental Studies in Animals

In rats, hydrocortisone 17-butyrate inhibited granuloma formation around cotton pellets containing 4.5mg of the drug inserted beneath the skin. Granuloma formation around an unmedicated cotton pellet on the other side of the body was not inhibited, suggesting that 4.5mg of hydrocortisone 17-butyrate had little systemic effect when placed beneath the skin, although thymus and adrenal weight are reduced at this dose (lowest dose causing involution of thymus 1.5mg, lowest dose causing reduction of adrenal weight 4.5mg). On the other hand, triamcinolone acetonide exerted a systemic effect at a dose (1.5mg) required to inhibit granuloma formation (unpublished data).

Hydrocortisone 17-butyrate exerts a greater systemic effect than an equal dose of hydrocortisone 21-acetate, but this compound has only about one-thirtieth the vasoconstrictor activity of hydrocortisone 17-butyrate (section 1.2). Hydrocortisone 13.5mg per pellet did not entirely prevent granuloma formation around the medicated pellet.

2. Human Pharmacology

2.1 Vasoconstrictor Activity

The blanching effect of alcoholic solutions of various topical corticosteroids when applied to the intact normal skin under occlusive dressings is a reasonably accurate indicator of their therapeutic anti-inflammatory activity.

Vasoconstriction is evident when 0.03mg/ml of hydrocortisone 17-butyrate is applied to normal skin under an occlusive dressing, but a concentration of 0.1mg/ml of hydrocortisone 21-acetate is required to produce vasoconstriction (Engel et al., 1974). The degree of blanching produced by 0.03mg/ml hydrocortisone 17-butyrate is greater than that produced by the 0.1mg/ml of hydrocortisone (Engel et al., 1974).

2.2 Skin Penetration

In experiments employing epidermal sheets mounted in a diffusion chamber, Ponec and Polano (1972) found that penetration of hydrocortisone 17-butyrate through the epidermis was influenced by the nature of the base and the concentration of the drug, but not by serum binding or by refreshment of the receptor fluid. Penetration of hydrocortisone 17-butyrate from an oil-in-water cream was greater at a concentration of 0.05% than at 0.01%. In another study in vitro, Ponec-Waelsch and Polano (1974) found that the addition of an emulsifier to 'plastibase' or of 40% propylene glycol to an oil-in-water cream (which caused the complete dissolution of 0.1% hydrocortisone 17-butyrate in the aqueous phase of the cream) greatly enhanced penetration of the corticosteroid. Penetration by hydrocortisone 17-butyrate was greater when in an alcoholic lotion than in a cream base (Ponec and Polano,