TRANSFORMATION OF BETAMETHASONE 17-VALERATE BY SKIN MICROFLORA

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Clinical observation has shown that in patients undergoing topical steroid therapy their condition may become tolerant to the therapeutic effect of these drugs. One possible explanation of this apparent tachyphylaxis is the conversion of the steroid to a less active form by skin microflora. In this communication we report the transformation of betamethasone 17-valerate by skin organisms isolated from two patients receiving prolonged treatment with this steroid.

Bacteria, obtained from both normal and steroid treated diseased skin, were incubated with betamethasone 17-valerate (100 µg/ml) in minimal medium (Davis and Mingioli 1950) supplemented with 0.2% w/v peptone and 0.2% w/v glucose (pH 7.2). Staphylococci and micrococci isolated from dermatologically healthy skin were unable to degrade betamethasone 17-valerate. Strains of S. aureus and S. xylosus isolated from psoriatic lesions and S. aureus obtained from eczematous skin all transformed this ester to betamethasone. The presence of betamethasone in chloroform extracts of the whole culture was detected by thin layer chromatography (Brookes et al 1981) and confirmed by normal phase high pressure liquid chromatography (LiChrosorb Si60 column; 0.2% v/v acetic acid, 8% v/v ethanol, 30% v/v dichloromethane in n-hexane, mobile phase). Control experiments showed evidence of isomerisation to betamethasone 21-valerate but no spontaneous hydrolysis of betamethasone 17-valerate to betamethasone in the absence of these organisms (Table 1).

Table 1 Transformation of betamethasone 17-valerate by skin micro-organisms.

	Standards			Extracts	
	Betamethasone 17-valerate	Betamethasone 21-valerate	Betamethasone	Culture	Control
TLC(Rf values)	0.48	0.62	0.26	0.48 0.26	0.48 0.63
HPLC(retention times in min)	1.75	1.45	3.50	1.75 3.50	1.75 1.45

The isomerisation of betamethasone 17-valerate to betamethasone 21-valerate is pH dependent, occurring readily at a neutral or alkaline pH but not under acid conditions. Experiments were repeated at pH 5.7 where isomerisation is negligible but the bacteria were still able to grow. The results showed no hydrolysis of betamethasone 17-valerate to betamethasone with any organism indicating that natural isomerisation to the 21-valerate ester is a necessary prerequisite for microbial hydrolysis. In confirmation, bacteria incubated with betamethasone 21-valerate yielded this ester and betamethasone whereas cell free controls gave only betamethasone 21-valerate.

Thus betamethasone 17-valerate can be transformed to betamethasone by the skin flora of patients treated with this steroid. The relative percutaneous absorption efficiencies of these two steroids have been judged by a skin blanching test to be 450:1 (Florence and Attwood 1981). Similar transformations did not occur with a range of other steroid esters tested.

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Davis, B D, Mingioli, E S (1950) J. Bact. 60: 17
Florence, A T, Attwood, D (1981) Physicochemical Principles of Pharmacy, London, MacMillan p359

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