DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 15(11), 1881-1888 (1989)

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IN VITRO RELEASE OF BETAMETHASONE -17- VALEREATE FROM VARIOUS DERMATOLOGICAL BASES.

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ABSTRACT

Betamethasone -17- Valereate release characteristics, from several commercial dermatological bases, were evaluated before and after dilution with several excipients.

It was found that betamethasone releases faster from creams than from ointments. In addition the release of the corticosteroid is affected by the composition of the diluting excipient.

INTRODUCTION

Drug release studies from semisolid bases such as gels, ointments, creams, lotions etc., are used today for the quality control of the final products and also in the developement and in-vitro evaluation of new dermatological vehicles [1].

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Betamethasone 17-valereate, is used in the form of cream or ointment in the therapy of certain dermatological diseases. In extended skin disorders commercial betamethasone topical bases are used after dilution with several excipients [2].

The reason for this dilution is to avoid a possible systemic action of the drug, following extensive transdermal absorption. For the clinical dermatologist however, the question remains as to how and to what extent, the release pattern of the corticosteroid could be modified, after the dilution of the cream or ointment with a certain excipient.

The purpose of this study is to evaluate the in-vitro release patterns of betamethasone-17-valereate from topical bases, before and after their dilution.

The results of this work may become useful to the clinical dermatologist in evaluating the differences between the release patterns of betamethasone from the topical bases tested and their efficacy in therapy.

MATERIALS

The topical bases of betamethasone 17-valereate used were: Four commercial products of betamethasone, namely products A, B, C, and D. Products A and B were creams, while C and D were ointments. Additionaly product A was used after mixing (1/1) with Filovit (Filoderm), Nutraderm (Alcon Laboratories) and Cold cream [3].

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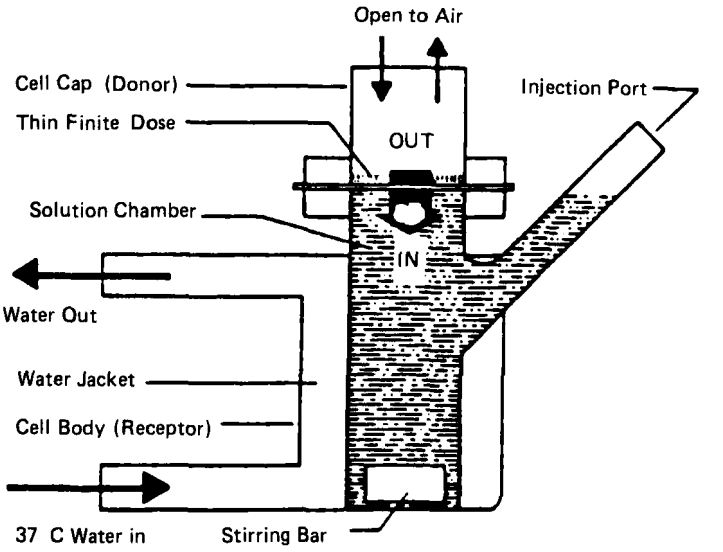

FIGURE 1
Franz's diffusion cell

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Instruments

a. Franz's Diffusion cell [4] [Fig.1].

b. HPLC consisting of a solvent delivery system (Waters model 590), a Universal injector (Waters model U6K), a column (μBondapak C18 RP, Waters), a Spectrophotometer (Lambda- Max Model 481 Waters) and a recorder (BBC SE120).

In-Vitro study

The In-Vitro study of betamethasone-17-valereate from the previously described topical bases was carried out with Franz's diffusion cell. In the upper compartment (donor compartment) of the system were placed 4.0 gr of the base, while the lower compartment (acceptor compartment) contained 15.0 ml of buffer solution pH=5 [5]. The cell was preheated to 37 ± 0.5° C and this

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TABLE 1.

% Release of Betamethasone 17-Valereate from Dermatological Bases. (Numbers in parenthesis indicate Standard Deviation.)

TIME (min)	PRODUCT A cream	PRODUCT B cream	PRODUCT C + Nutraderm	
30	0.95 (.21)	1.15 (.03)	0.92 (.17)	
60	1.55 (.45)	2.22 (.34)	1.32 (.07)	
90	2.14 (.23)	2.97 (.26)	1.63 (.06)	
120	2.88 (.38)	3.43 (.31)	2.20 (.12)	
150	3.83 (.47)	3.76 (.25)	2.77 (.6)	
180	4.95 (.32)	4.00 (.33)	3.30 (.13)	
TIME (min)	PRODUCT A + Filovit	PRODUCT B + cold cream	PRODUCT C ointment	PRODUCT D ointment
30	1.23 (.07)	2.37 (.16)	0.33 (.08)	0.58 (.08)
60	1.88 (.17)	3.58 (.17)	0.52 (.10)	1.18 (.09)
90	2.37 (.16)	3.82 (.15)	0.64 (.05)	1.43 (.01)
120	2.81 (.11)	4.30 (.05)	0.64 (.06)	1.61 (.15)
150	3.15 (.10)	5.03 (.17)	0.76 (.08)	2.15 (.05)
180	3.82 (.17)	5.75 (.16)	0.76 (.10)	2.26 (.07)

temperature maintained during the whole experiment. The two compartments were separated with an artificial cellulose membrane [6].

At fixed time intervals (0, 30, 60, 90, 120, 150, 180 min) 100µl aliquots of the buffer solution was drawn off and analyzed with the following HPLC method: Mobile phase: Acetonitrile/Water (70/30), flow rate: 2.5ml/min, Pressure: 1300psi, max: 254nm. All experiments were performed in triplicate.

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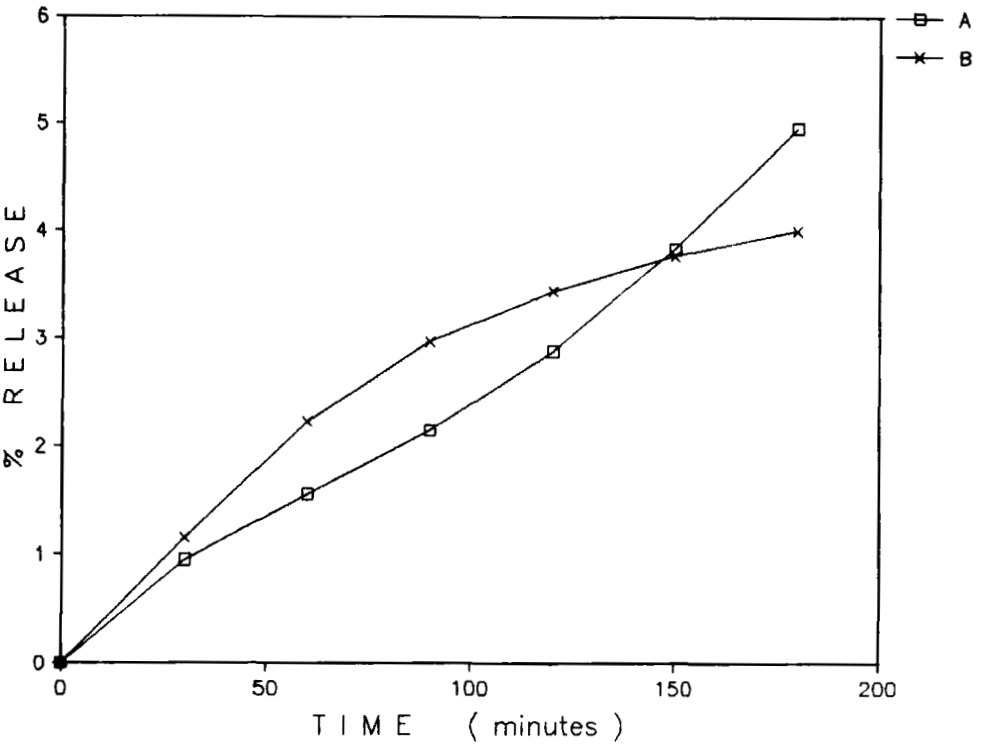

FIGURE 2.
% Release of betamethasone 17-valereate from commercial creams. (Product A, B).

RESULTS AND DISCUSSION

Table 1 shows the results from the release study of betamethasone 17-valereate, from dermatological formulations tested.

As indicated in Figure 2 the release pattern of the corticosteroid, from commercial creams A and B appeared with no substantial difference, while the release rate of the drug from the commercial ointments C and D showed a significant difference [Fig 3].

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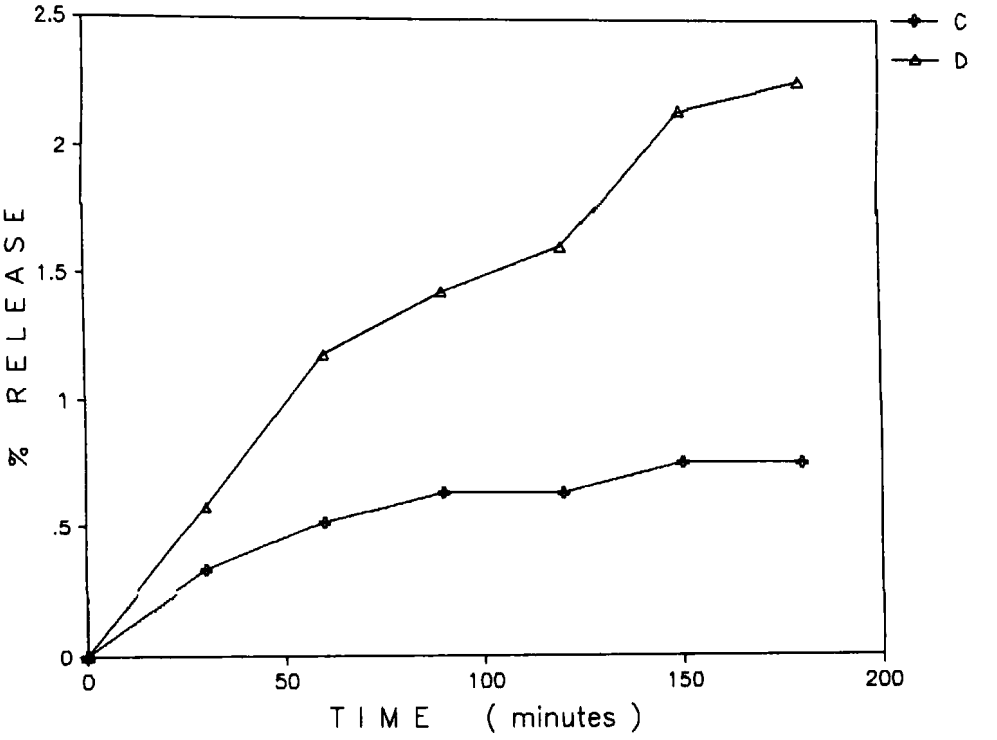

FIGURE 3.
% Release of betamethasone 17-valereate from commercial ointments. (Product C, D).

From the comparison of betamethasone release rates from creams and ointments, it can be concluded that the previous release the drug faster than the latter. This finding is attributed mainly to the lipophilic character of the drug due to which betamethasone tends to stay longer in the more lipophilic bases, which in this study are the ointment products C and D.

Furthermore, the effect of diluting excipients on the release rate of drug from cream A was studied. The diluents used were the creams Filovit, Nutraderm

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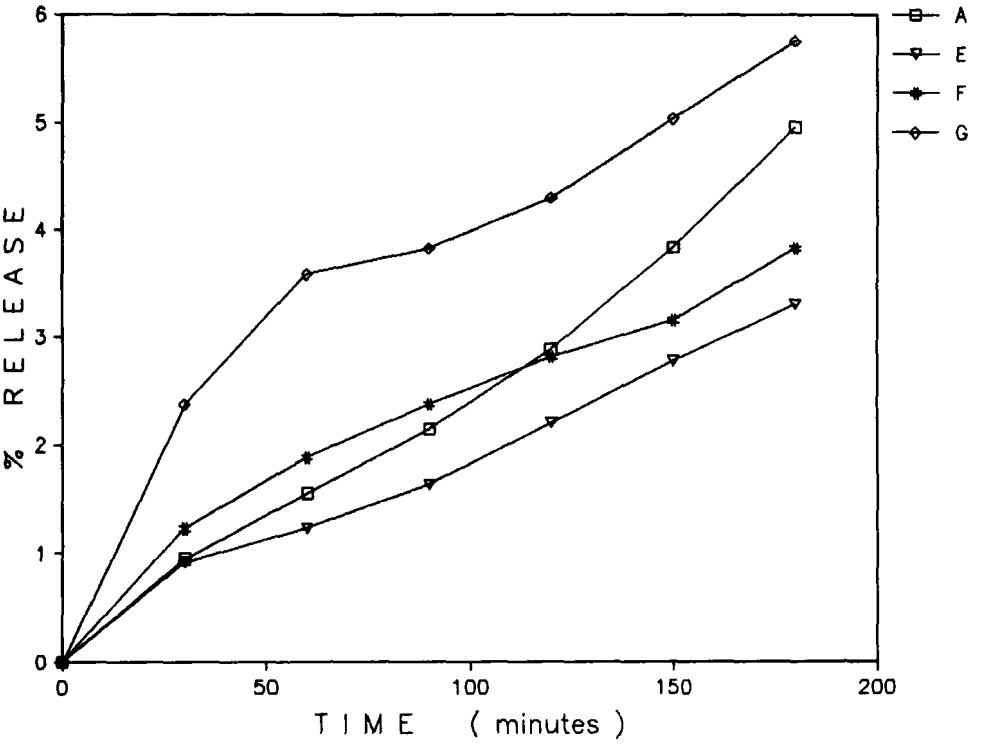

FIGURE 4.
% Release of betamethasone 17-valereate from commercial product A and after its dilution. (A: Product A, E: Product A + Cold cream, F: Product A + Filovit G: Product A + Nutraderm .

(emulsions o/w) and the Cold cream (emulsion w/o). Each of the above diluents was mixed with commercial cream A in a 1 to 1 ratio.

From the results outlined in Figure 4 and Table 1 it can be concluded that the release rate of betamethasone from cream A before and after dilution with Filovit and Nutraderm showed no marked differences, while dilution of cream A with cold cream increases the release rate of betamethasone.[Fig.4] This can be attributed to an

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observed reversion of phases of the cream A after its dilution with cold cream. Because of this reverse, the active ingredient is now located in the external phase of the final product (w/o), while in the cream A (o/w) it was in the internal phace. The presence of betamethasone in the external phase facilitated its diffusion to the acceptor compartment, since in this case the drug motecules are in direct contact with cellulose membrane. This phenomenon promotes the rate of release of the drug and therefore the therapeutic efficacy of the product.

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