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The effects of surface preparation on the penetration of hydrocortisone through canine skin

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Abstract

This study investigated the effects of common skin surface preparations on the penetration kinetics of hydrocortisone through canine skin. Thoracic skin from five dogs was clipped of hair, divided between five treatment groups and prepared as follows: shaved (S); tape-stripped with adhesive bandage (TS); cleaned with aqueous chlorhexidine (Aq-C); cleaned with alcoholic chlorhexidine (Al-C); or allocated to the control group and had no further preparation performed (C). The skin samples were mounted in Franz-type diffusion cells and transdermal hydrocortisone penetration was measured over 30 h. The pseudo-steady-state flux (J_{SS}) of hydrocortisone through S, Al-C, Aq-C and TS skin was, respectively, 2.3 ($P = 0.021$), 2.2 ($P = 0.037$), 2.0 ($P = 0.070$) and 1.5 ($P = 0.351$) times greater than through the control skin, but there were no significant differences in the lag times (t_{lag}) for hydrocortisone penetration between the groups. The study has shown that some skin surface preparations can significantly increase the subsequent penetration of hydrocortisone through canine skin in vitro.

Keywords: Transdermal penetration; Hydrocortisone; Skin; Canine; Skin preparation

Introduction

Pharmaceuticals formulated for topical application are popular in veterinary medicine for a number of reasons, including the ease and non-invasiveness of dermal application. However, the relatively hairy skin of many animals may act as a physical barrier to a topical formulation, reducing the contact between the drug and the skin. To overcome this factor, some form of surface preparation often precedes the topical application of a drug to the skin of veterinary patients. For example, hair overlying the site of the intended dermal application may be removed with electric clippers or by shaving. Additionally, the skin may be cleaned of surface debris with an antiseptic solution, such as aqueous or alcoholic chlorhexidine.

A problem concerning skin preparations is, however, the potential to alter the outermost layer of the epidermis, the stratum corneum, which is known to be the major barrier to the transdermal penetration of most drugs (Barry, 2001; Madison, 2003). Fortunately, the permeability of this layer can be reliably estimated with in vitro penetration studies using excised skin (Franz, 1975). In vivo and in vitro studies have shown that alteration of the stratum corneum by skin disease (Schaefer et al., 1977; Bronaugh et al., 1986) or experimentally induced physical or chemical injury can result in increased skin permeability to water (Berenson and Burch, 1951; Monteiro-Riviere et al., 2001) and a number of drugs (Scott and Dugard, 1986; Moon et al., 1990; Pelletier et al., 1990; Wilhelm et al., 1991; Higo et al., 1992; Mills and Cross, 2006a) in many species, including humans, rats, mice, guinea-pigs, pigs and horses. The consequences of enhanced skin permeability include potentially higher than intended systemic drug concentrations

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and the occurrence of adverse effects in the patient, as illustrated in Fig. 1.

The effects of some skin preparations, such as shaving (Pelletier et al., 1990; Mills and Cross, 2006a), tape stripping (Feldmann and Maibach, 1965; Scott and Dugard, 1986; Moon et al., 1990; Higo et al., 1992; Mills and Cross, 2006a) and cleaning (Moon et al., 1990; Pelletier et al., 1990; Wilhelm et al., 1991; Mills and Cross, 2006a), on transdermal drug penetration in humans and some animals have already been investigated. However, the anatomical differences in skin between species, particularly in the thickness and composition of the stratum corneum layer (Monteiro-Riviere, 1991), results in variable transdermal drug penetration kinetics in normal skin (Hunziker et al., 1978; Reifenrath et al., 1984). This study was performed to investigate the effects of common veterinary skin surface preparations on the in vitro penetration of hydrocortisone, a frequently used topical anti-inflammatory, through canine skin.

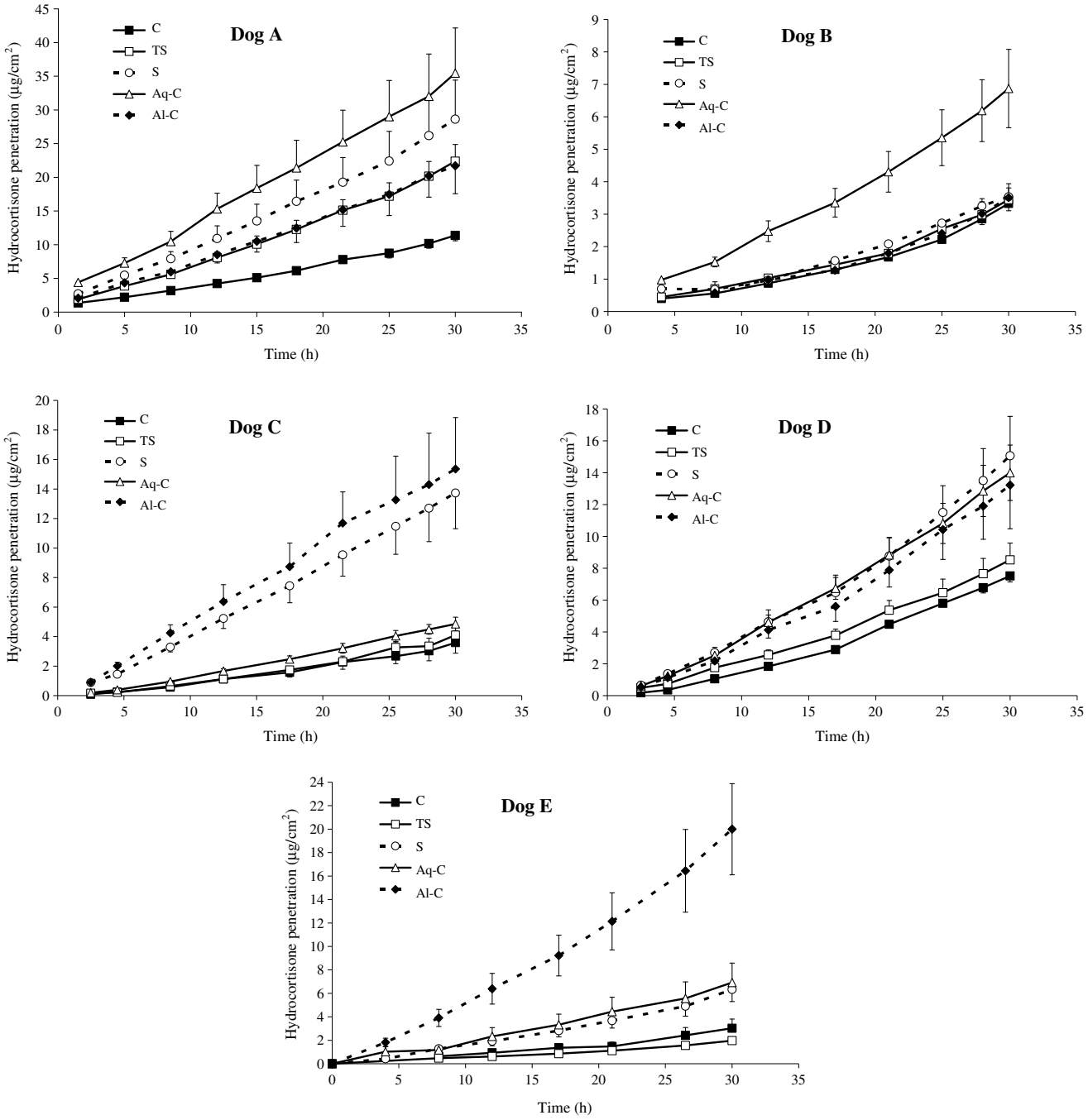

Fig. 1. Permeation profiles of hydrocortisone through the skin of five dogs (A–E) following skin surface preparations. Control (C); tape-stripped (TS); shaved (S); cleaned with 0.5% w/v aqueous chlorhexidine solution (Aq-C) or cleaned with 0.5% w/v alcoholic chlorhexidine solution (Al-C). The cumulative amount of hydrocortisone entering the receptor solution per square centimetre of skin is marked on the *Y*-axis. Each data point represents the averaged value from a number of skin replicates (4–6). The vertical error bars represent one standard error of the mean.