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The effects of pH and polarity of electrode on the remaining propranolol within human skin

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The transport of ionic and polar solutes across human skin is not favoured by passive diffusion, but it can be promoted by iontophoresis. Iontophoresis is a process of enhancing and controlling the penetration of ionic drugs through the skin by application of a voltage drop across the skin membrane. The ionic drug is introduced in a reservoir containing an electrode (Liu et al. 1988).

There is no document to show whether any drug remains in the skin during iontophoresis. In the present study the effects of pH and polarity of the electrode on the amount of propranolol remained within the human skin have been investigated. In vitro studies were carried out by sandwiching human epidermis between two glass chambers (50 mM HEPES buffer and 20 mM isotonic HEPES in donor and receptor chambers, respectively. The donor chamber (stratum corneum side) contained buffer (pH 6.3 or 9) and the receptor chamber (dermal side) contained buffer (pH 7.4). [^{3}H] propranolol HCl was spiked into donor phase (1μCi/ml) and iontophoretic current (direct current) passed for 15, 30, 45, 60, 90 and 120 min. After 120 min the amount of propranolol was determined within the skin and in donor and receptor phases (n=3). The iontophoretic current used was 0.38 mA/cm^2. Table 1 shows the effects of pH and the polarity of the electrode on the percentage of propranolol remained within the skin and that of the drug passed across the skin. An increase in pH of donor phase resulted in an increase in the percentage of propranolol disappeared from the donor phase. Because the percentage of unionized propranolol at pH 9 is more than that at pH 6 (pKa of propranolol is 9.5). The similar trend is observed for the percentages of propranolol remained within the human skin. But different results were produced for percentages of propranolol observed at receptor phase.

Table 1. Effect of pH and polarity of electrode in the donor phase on the amount of propranolol remained within the skin, in receptor and donor phases .

polarity of electrode	pH	remained[a] (%)	passed[b] (%)	donor phase[c] (%)
Anode	6.3	4	13	83.0
	9.0	21	5	74.0
Cathode	6.3	23	0.2	76.8
	9.0	54	0.3	55.7
Passive	6.3	15	0.4	84.6
	9.0	48	0.1	51.9

[a] remained within the skin; [b]detected in receptor phase; [c] detected in donor phase

The present study showed that the amount of the drug disappeared in the donor phase was not equal to the amount of drug detected at the receptor phase and some drug was kept within the skin. According to Table 1 when the cathodic electrode is placed in the donor phase the percentage of propranolol remained within the skin is more than when the donor phase is anodic.This finding suggests for positively charged drugs such as propranolol HCl that when they are intended for systemic use (higher percentages of passed drugs are desirable) the donor phase should be anode. Whereas, for local preparations which should work in the skin (the higher percentage of the remained drug is desirable) the cathode electrode should be placed in the donor phase.

Liu, J.C., Sun, Y., Siddique, O., Chien, Y.W., Shi, W.M., Li, J. (1988) Int. J. Pharm., 44, 197-204.