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Clinical evaluation of passive and iontophoretic amethocaine formulations by AC impedance spectroscopy

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Gel formulations (Ametop™) based on the amethocaine phase-change system (McCafferty & Woolfson 1988) provide rapid, deep and long-lasting cutaneous local anaesthesia. Ideally, a forty minute application of Ametop™ provides up to six hours anaesthesia (Woolfson et al 1990). Recently, Woolfson and co-workers (1998) formulated a novel, moisture-activated amethocaine bioadhesive patch device. The clinical profile of this dosage form has not yet been established. The aim of this study is to assess the clinical performance of the amethocaine patch and compare it with both passive-diffusion and iontophoretic amethocaine gel systems.

Gels and patches for passive diffusion were formulated as described previously (McCafferty & Woolfson 1988; Woolfson et al 1998). Iontophoretic preparations were formulated to contain 1% amethocaine hydrochloride in a hydrophilic matrix. Local Ethical committee approval was obtained for all clinical experiments. Volunteer pain score studies were randomised and double-blinded in design. Gels (under occlusion) and patches (pre-wetted for 15 seconds) were applied to the ventral forearm of volunteers (n = 30). Passive formulations were left on the forearm for 40 minutes. Iontophoresis was carried out at 1mA for 10 minutes. Pain was assessed on a four point scale by volunteers (Cooper et al 1987). A.c. impedance spectroscopy was carried out as described previously (McAdams et al 1995). Changes in skin resistance (R_p) and capacitance (K) were determined both during and after application of gels and patches for a total duration of two hours.

Pain scores recorded (Fig. 1) indicate that passive-diffusion amethocaine gel and patch formulations exhibit similar clinical profiles, providing at least four hours of effective anaesthesia. Iontophoretic delivery provided only 8-10 minutes effective anaesthesia. Changes in R_p for passive diffusion (Fig. 2) indicate that depressions in R_p relative to placebo become apparent after approximately twenty minutes. These changes are maintained beyond the point at which the formulation is removed from the skin. In the case of iontophoretic delivery, R_p rapidly returns to the placebo level once iontophoresis ceases. Similar changes were observed in K. The duration of depression of R_p from the placebo level correlates closely with the pain scores. This suggests that passive-diffusion gel and patch formulations exhibit similar clinical profiles, whereas iontophoresis provides a completely different clinical response. Therefore, a.c. impedance spectroscopy may be of use in predicting the absorption of topically applied drugs.

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McAdams et al (1995) 9th Int. Conf. Elect. Bioimp., Heidelberg, 344-347
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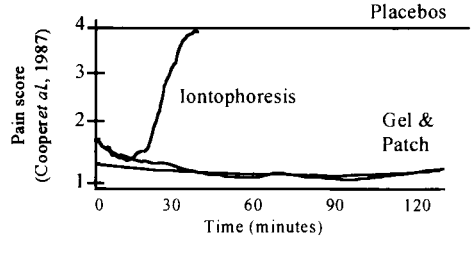

Figure 1. Typical pain scores for passive-diffusion gels and patches, iontophoretic gels, and placebos.

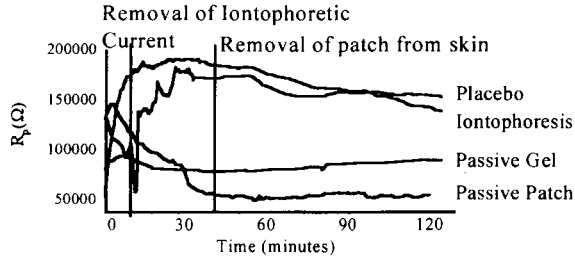

Figure 2. Typical impedance plots of R_p against time for passive-diffusion gels and patches, iontophoretic gels, and placebos.