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The role of glycosaminoglycans on the skin partitioning of ibuprofen

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Hyaluronan, incorporated as an excipient in formulations, has been found to modify the cutaneous biodisposition of topically applied diclofenac (Brown et al, 1995). For any drug to be absorbed topically, it must first partition from the vehicle into the skin. Most reported vehicle-skin partition studies are carried out by immersing a prescribed area of skin directly into the aqueous-based vehicle, allowing both sides of the skin to be exposed to solution (Pandit et al, 1989; Maitani et al, 1991). The aims of this study were to develop an improved *in vitro* method for determining the partition of drug into skin and to utilise the method to compare the effect of glycosaminoglycans (GAGs), such as hyaluronan (HA) with chondroitin sulphate (CT), heparin (HP) and a cellulose-based polysaccharide, sodium carboxymethylcellulose (SCMC), on the partitioning of ibuprofen into skin.

Ibuprofen (0.02 mg ml^{-1}) dissolved in an aqueous polymer solution was equilibrated with full thickness skin (1.30 cm in diameter) for 48 h, at 32 °C. The skin was mounted in a polypropylene partition cell, specifically designed for this study, which allowed only the stratum corneum surface to be exposed to the polymer solution. Partition studies were undertaken by placing cell in a shaking-bath. The ibuprofen concentration partitioning into the skin was determined using HPLC. Analysis was performed isocratically using a LDC Analytical CM 4000 and a Spherisorb C18 column. The mobile phase consisted of 73%v/v phosphate buffer (45 mM, pH 7) and 27%v/v acetonitrile: tetrahydrofuran (7:3 v/v). The flow rate was 1.1 mL/min, injection volume 100 μL and λ_{max} 273 nm.

Figure 1 shows the amount of ibuprofen partitioning into skin from 1% polymer solutions in deionised water, compared to the control (deionised water alone). It was found that the amount of ibuprofen partitioning into skin after 48 h from 1% formulations of HA, CT, and HP was significantly ($p<0.05$) greater than the control. In contrast, the partition of ibuprofen into skin from 1% SCMC was not significantly different from control. These results imply that GAGs may promote the partitioning of drug into skin and support the hypothesis that HA might enhance the topical localisation of drugs. The mechanisms by which the GAGs are promoting partition has not been determined and future studies should further investigate the partitioning of the polymers into the skin.

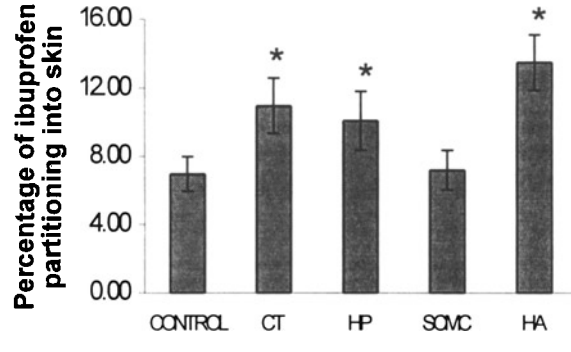

Figure 1. The percentage of available ibuprofen partitioning into skin from control and 1% polymer solutions (mean ± sd, n=4). * indicates significant difference from control ($p<0.05$).

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Pandit, N.K. et al (1989) Int. J. Pharm. 50:7-13.