An investigation into electroporation to increase drug permeation into the eye

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Drug delivery to the eye, especially to treat intraocular diseases, is a formidable challenge since the eye is exquisitely impervious to foreign substances. For many diseases affecting the inner eye, intravitreal injection is the main route of drug delivery. To avoid the inherent disadvantages of intravitreal injection, we investigated electroporation – the application of brief pulses of large voltage – as a means of enhancing the permeation of topically applied drugs into the eye. Electroporation to the eye is currently being researched for gene delivery (Oshima et al, 1998).

In vitro experiments were conducted using a specially designed diffusion cell and fresh cattle eyeballs. The latter were placed in the diffusion cells, with the cornea facing upwards and the back of the eye ball being bathed in a liquid medium. A flanged cylinder was placed on the cornea and a donor lidocaine solution was added. Pulses of high voltage were applied via a cathode to the donor solution which was then left in place for 1h. The anode was present underneath the eye ball. Four different electric protocols (where pulse number, voltage, duration and interval were varied) were used. The control experiments were conducted in the same way, except that no voltage was applied. At the end of the experiment, the eyeball was dissected and lidocaine levels in the different eye tissues was measured (shown in Table 1).

It can be seen that electrical application had a significant effect on drug permeation into the sclera (T test, $P<0.05$), but not into the cornea or the lens and the vitreous humor. The absence of drug

in the deeper tissues and the lack of drug permeation enhancement into the cornea could be due to the relatively mild electrical protocols that were used to avoid damage to the eye.

To conclude, we have shown the potential of electroporation to increase drug permeation into the eye. In future, stronger electrical protocols will be investigated to determine effects on drug permeation into the inner eye tissues, bearing in mind the potential for eye irritation.

1. Oshima Y, Sakamoto T, Yamanaka I, Nishi T, Ishibashi T, Inomata H (1998), Gene Therapy, 5: 1347-1354.

Drug levels in eye tissues.

Eye tissues	Drug concentration (mcg/g, mcg/ml) mean and (SD) are shown, n=5				
	Control	Protocol 1	Protocol 2	Protocol 3	Protocol 4
Cornea	4179 (517)	5135 * (158)	3945 (386)	4390 (677)	4908 (255)
Aqueous humour	1139 (537)	1637 (446)	1504 (453)	1657 (302)	1349 (202)
Sclera	149 (54)	227 * (46)	261 * (23)	299 * (99)	263 * (49)
Lens	ND	ND	ND	ND	ND
Vitreous humour	ND	ND	ND	ND	ND

ND – not detected; * - significantly different to control (Students t test, $P < 0.05$)