EFFECT OF IONTOPHORESIS ON TRANS-SCLERAL PERMEATION OF CYTOCHROME C

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PURPOSE: New therapies for posterior segment diseases involve the use of macromolecules, currently administered by repeated intravitreal injection. Iontophoretic trans-scleral delivery could be a promising non-invasive alternative. The aim of this work was to investigate the effect of iontophoresis on trans-scleral delivery of cytochrome c, a positively charged peptide (12.4 kDa) chosen as model compound.

METHODS: Permeation experiments, both passive and current-assisted, were performed in Franz-type diffusion cells using porcine sclera as a barrier. The receptor compartment, filled with degassed HEPES solution (25 mM, pH 7.4), was thermostated at 37 °C. Anodal iontophoresis was applied for two hours (permeation followed up to 5 hours) using Ag/AgCl electrodes and salt bridges. The effect of current density (1.5, 3 and 6 mA/cm^2), donor solution composition and cytochrome c concentration (5, 10, 40 and 70 mg/ml) were tested. Experiments were also performed using a neutral permeant (FD-150, 1 mg/ml), alone or in combination with cytochrome c (5 or 70 mg/ml), to assess the effect of cytochrome c on electroosmotic flow.

RESULTS: Iontophoresis enhanced cytochrome c transport across the sclera proportionally with the raise of current density. When 6 mA/cm^2 were applied, the amount permeated after 2 hours increased 30 times compared to passive diffusion. Neither ionic strength of the vehicle nor the presence of neutral polymers in the donor solution affected permeation. On the contrary negatively charged polymers prevented it. Permeant concentration in the donor solution affected the extent of transport, but the enhancement was not strictly proportional to the raise of concentration. This could be due to the hindering effect (concentration dependent) of cytochrome c on electroosmotic flow, as confirmed by experiments performed with FD-150.

CONCLUSIONS: These results indicate that anodal iontophoresis could be an effective strategy to promote cytochrome c trans-scleral permeation.