In Vitro Optimization of Amikacin Reverse Iontophoresis

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**AIM OF THE WORK**

Amikacin (AK) is an aminoglycosidic antibiotic active against most of gram-negative bacteria. Systemic aminoglycosides can produce hearing loss and balance difficulties and toxicity towards renal function. Therefore a careful monitoring of plasmatic aminoglycosides concentrations is required.

We intended to optimize AK reverse iontophoresis extraction across the skin. Objectives of the work were to examine the effect of the composition of the extracting buffer, replacing saline solution with citrate buffer, on AK extraction. Acetaminophen (AM), a polar non-ionized molecule, was used as marker, to quantify electroosmotic contribution to overall AK extraction.

**METHODOLOGY**

**Reverse Iontophoresis:**

- Anodal iontophoresis: HEPES 25 mM; NaCl 133 mM
  - pH 4.0
  - pH 8.0

- Cathodal iontophoresis: HEPES 25 mM; NaCl 133 mM; pH 7.4
  - AK bisulphate 200 µM; AM 1 mM

**AK HPLC analysis:**

Samples derivatized with 1-fluoro-2,4-dinitrobenzene (FDNB) to be UV-Vis detectable:
- 100 µl of the sample mixed with 300 µl of methanol, 40 µl of NaOH 0.05 and 50 µl of methanolic solution of FDNB (180 mg/ml).
- Mixture heated at 90°C for 10 min.
- Column: 10 µm µBondapack® (300X4.6 mm) thermostated at 45°C
- Mobile phase: acetonitrile: water 47:53 (v/v)+ 0.1% acetic acid
- Flow: 1 ml/min
- Spectrophotometric detection: 365 nm

**RESULTS**

**AK cathodal extraction at different pH (average ± sd)**

- pH 4.0: AK extraction was independent of pH and always in the anode-to-cathode direction, in agreement with the positive charge of the drug.
- pH 8.0: The presence of AK in the bathing solution did not modify AM extraction at pH 4.0. AM extraction was reduced in presence of AK at pH 8.0. AK can alter permselectivity of the skin, reducing electroosmotic flow.

**AM cathodal extraction with different buffers (average ± sd)**

- NaCl 133 mM: AK extracted (nMol/cm²) 19.86±4.27, AM extracted (nMol/cm²) 8.79±1.52
- Citrate buffer 25 mM: AK extracted 19.55±0.62, AM extracted 20.64±3.25
- Citrate buffer 50 mM: AK extracted 12.73±3.09, AM extracted 14.68±2.01

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**AK cathodal extraction with different buffers**

- HEPES 25 mM; NaCl 133 mM; pH 7.4
- Trisodium citrate 25 mM or 50 mM pH 8

**REFERENCES**