Therapeutic Drug Monitoring of Gabapentin by Reverse Iontophoresis

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Purpose
Gabapentin possesses complex pharmacokinetic properties and narrow therapeutic index which necessitates dose individualization and constant therapeutic drug monitoring. Current methods for the drug monitoring are considered to be invasive and possess low patient compliance. This study investigates the feasibility of reverse iontophoresis as an alternative non invasive method for clinical and therapeutic monitoring of gabapentin.

Methods
In vitro reverse iontophoresis extraction of gabapentin was carried out across full thickness Sprague-dawley rat skin using Franz diffusion cell. Anodal iontophoresis (0.5 mA/cm²) was applied using a custom made DC power source for a period of 3 h. Different concentrations of gabapentin (0.5-20 µg/mL) in phosphate buffered saline (pH 7.4) was placed in the donor compartment (5 mL) and the same buffer was used in receiver (1 mL). Samples were drawn at every 30 min intervals and analyzed. Similarly, control experiments were run in parallel with iontophoresis at 0 mA/cm². In vivo studies were carried out by placing both chambers at 1 cm distance on the abdominal skin of rats and a current density of 0.5 mA/cm² was applied for 2 h. Gabapentin fluxes extracted by reverse iontophoresis and concentrations in the blood were measured.

Results
In vitro data suggest that application of reverse iontophoresis (anodal) can extract detectable amount of gabapentin from the subdermal compartment. The iontophoretically extracted gabapentin flux exhibited a good linear correlation (r²=0.89) with the subdermal concentration studied, which includes clinically relevant level (1-10 µg/mL). Gabapentin is highly charged at physiological pH, and exist as a zwitterion (pKₐ1=3.7 and pKₐ2=10.7). Amount of gabapentin extracted is the contribution of electromigration and electroosmosis (anode to cathode direction). In vivo data indicate that the concentration of gabapentin extracted in the cathode was proportional to the blood plasma levels, with a lag time of 30 min, and suggesting a good correlation between iontophoretically extracted fluxes and blood plasma levels.

Conclusion
The results observed confirm the feasibility of reverse iontophoresis for monitoring gabapentin at clinically relevant levels and appears to offer an alternative approach to the existing invasive monitoring methods such as venipuncture.

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