Continuous versus Discontinuous Application Modes of Iontophoresis on the Trans-ungual Delivery of Itraconazole
A. S. Kushwaha, M. R. Jacob, S. N. Murthy
University of Mississippi

**Purpose**
Itraconazole is one of the most potent drugs used for the treatment of onychomycosis. The main objective of this project was to compare continuous versus discontinuous mode of iontophoresis application on the trans-ungual delivery of itraconazole.

**Methods**
Itraconazole hydrochloride salt was synthesized and purified. The salt was characterized by Mass spectroscopy and Differential Scanning Calorimetry (DSC). Antifungal activity of the itraconazole base and salt was evaluated using Clinical and laboratory Standards institute (CLSI) assay method. *In vitro* transport of itraconazole was studied using porcine hoof membrane in Franz diffusion cells. Constant DC current (0.5mA/cm²) was applied for 3 days at 8 h/day in case of discontinuous mode and in the continuous mode, the same current strength was applied for 24 h. Samples were collected at definite time points. The itraconazole retained in the hoof membrane was extracted by dissolving hoof membrane in 1M NaOH solution and samples were analyzed by HPLC.

**Results**
The Mass spectra and DSC confirmed the formation of hydrochloride salt. Antifungal activity of itraconazole salt was not significantly different from that of itraconazole base. The amount of drug permeated across the hoof membrane in case of continuous mode was 0.91 ± 0.105 µg/cm² whereas in case of discontinuous mode, it was 4.34 ± 0.22 µg/cm² which was ~ 5 folds more than the continuous mode. However, the amount of drug retained in the nail plate did not differ significantly between the two approaches (4.95 ± 1.52 µg/mg Vs 4.8 ± 1.2 µg/mg in case of discontinuous and continuous modes respectively).

**Conclusion**
Itraconazole hydrochloride is as potent as its base as an antifungal agent. The Salt form is relatively more soluble and amenable to iontophoresis. Despite the electrical dose being same, the discontinuous mode resulted in significantly higher permeation of drug than the continuous mode.