Pharmacokinetics of ulifloxacin, the active metabolite of prulifloxacin, into human muscle.

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Objective. Prulifloxacin is a broad-spectrum oral fluoroquinolone antibacterial agent. After absorption, prulifloxacin is metabolized by esterases to active metabolite ulifloxacin. The drug has a long elimination half-life, allowing once-daily administration. The aim of this study was to evaluate the penetration and the pharmacokinetics of ulifloxacin in human muscle of patients undergoing major and minor orthopaedic surgery (hand surgery and nailing for hip fracture) after prulifloxacin administered orally in a single 600 mg dose. **Methods**. Fifteen Patients (5 groups of 3 patients) received a single oral dose of prulifloxacin 600 mg at 2, 4, 6, 8 or 12 hours preoperatively; in addition three patients were used as control group. During surgery, samples of muscle were collected at the same time and ulifloxacin concentrations were determined in muscle tissue by a previously described high-performance liquid chromatography method with UV detection (Pellegrino et al., 2008). The pharmacokinetic parameters ($t_{1/2}$, AUC, C_{max}, T_{max},) of ulifloxacin were computed using a standard non-compartmental methods. **Results.** The mean maximum plasma concentration (C_{max}) in human muscle was 2.47± 0.203 µg/ml with a peak time (T_{max}) of 2.0 ± 0.27 hours and a mean half-life of the elimination phase ($t_{1/2}$) of 13.3± 0.36 hours. The mean areas under the curve from time 0 to inf ($AUC_{0\text{-}inf}$) for muscle was 49.1 ±4.23 µg/g x h. The muscle/plasma AUC ratio was 6.72 (the mean ulifloxacin AUC of human plasma after 600 mg oral dose was obtained from published data of Picollo et al., 2003). **Conclusions.** The results of this study shown the ability of prulifloxacin to penetrate in human muscle with concentration values higher than MICs for pathogens frequently involved in muscle bacterial infections and the value of muscle/plasma AUC ratio provide evidence of high concentration in peripheral target tissues such as muscle. The relatively long terminal half-life of prulifloxacin observed in our study, let suppose that a once-daily applications will show sufficient clinical efficacy and patients compliance.

Pellegrino et al. (2008). *J Pharm Biomed Anal.* 47(3):567-74.
Picollo et al. (2003). *Arzneimittelforschung.* 53(3):201-5.