

# Effect of Tinidazole on Norfloxacin Disposition

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## Abstract

Co-administration of norfloxacin (NFX) and tinidazole (TNZ) has been used for the treatment of gastrointestinal and urinary tract infections. Concomitant oral administration of NFX with TNZ may affect NFX absorption and consequently its blood concentration and pharmacological effect. The present study was undertaken to investigate the effect of TNZ at the usual clinical dosage on the pharmacokinetics of NFX in healthy volunteers. This study was conducted as an open-label, randomized, two-way crossover experimental design. After an overnight fast, subjects were randomized to receive a single oral dose of NFX 400 mg alone and the fixed-dose combination (FDC) of NFX /TNZ 400 mg/600mg on two different occasions separated by 1 week washout period between treatments. Blood samples were collected up to 24 h postdose, and plasma was analyzed for NFX concentrations by using HPLC. The pharmacokinetic properties of NFX after FDC administration were compared with NFX administered alone. Twelve healthy subjects were enrolled (6 in each part), and all subjects completed the study. None of the participants showed any sign of adverse drug reactions during or after the completion of the study. The 90% confidence interval (CI) between NFX alone and when co-administered with TNZ indicated the presence of an interaction between NFX and TNZ, which would significantly increase the systemic rate and exposure of NFX absorption. The co-administration of TNZ with NFX increased the AUC and Cmax of NFX significantly compared with administration of NFX alone. The AUC and Cmax of NFX alone were 6.0" g.hr/mL (2.3-9.8) and 0.87" g/mL (0.4-1.6), respectively whereas the corresponding AUC and Cmax values after administration of FDC were 7.1" g.hr/mL (4.0-10.6) and 0.97" g/mL (0.4-1.7), respectively. The respective geometric mean ratios of NFX for AUC and Cmax with TNZ were 1.197 [90% CI, 0.941-1.522] and 1.087 (90% CI, 0.807 -1.463) compared with NFX alone. Both Tmax and Ka of NFX showed a significant decrease after administration of the combination compared to administration of NFX alone. The peak plasma concentration reached

at 1.3 h (0.6-2.4) and 1.9 h (0.4-4.4) after oral administration of FDC and NFX alone, respectively. Both NFX and TNZ were well tolerated. The interaction of TNZ with fluoroquinolones should be investigated to determine whether this interaction is limited to NFX or if other fluoroquinolones have the same pharmacokinetic interactions. Further studies are necessary to determine the role of P-gp and other transporters on NFX disposition and pharmacokinetics. Additionally, the influence of TNZ on the physiological activity of GIT should be investigated.

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