Effect of Tinidazole on Norfloxacin Disposition

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Abstract

Background: 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.
Objective: The present study was undertaken to investigate the effect of TNZ at the usual clinical
dosage on the pharmacokinetics of NFX in healthy volunteers. Methods: 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 hours 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. Results: 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 C compared with administration of NFX alone. The AUC and C
max
max
 of NFX significantly
 of NFX alone were 6.0 µg.hr/mL
(2.3-9.8) and 0.87 µg/mL (0.4-1.6), respectively whereas, the corresponding AUC

and C
administration of FDC were 7.1 µg.hr/mL (4.0-10.6) and 0.97 µg/mL (0.4-1.7), respectively. The
respective geometric mean ratios of NFX for AUC and C
max
1.522] and 1.087 (90% CI, 0.807 -1.463) compared with NFX alone. Both T
max
values after
with TNZ were 1.197 [90% CI, 0.941-
max
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 1.9h (0.4-4.4) after oral
administration of FDC and NFX alone, respectively.
Conclusions: Both NFX and TNZ were well tolerated. The interaction of TNZ with fluroquinolones
should be investigated to determine whether this interaction is limited to NFX or if other
fluroquinolones have the same pharmacokinetic interactions. Further studies are necessary to determine

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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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