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## Microbiological Transformation of Enrofloxacin by the Fungus *Mucor ramannianus*

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Fluoroquinolones are synthetic antimicrobial agents that are active against a broad spectrum of pathogenic gram-negative bacteria as well as some gram-positive bacteria and mycoplasmas (11). Several fluoroquinolones are used in clinical medicine. The metabolism of enrofloxacin by *Mucor ramannianus* was investigated as a model for the biotransformation of veterinary fluoroquinolones by zygomycetous fungi. Cultures grown at 28˚C in 500 ml flasks containing 100 ml of a sucrose-peptone broth on a rotary shaker at 200 rpm. After 2 days the culture was dosed with enrofloxacin in concentration 100 mg/L. After 21 more days the mycelia was separated by filtration. The culture fluid was extracted with methylene chloride in a separatory funnel and solvent was evaporated in *vacuo*. The products were analysed by HPLC. 22% of the original enrofloxacin remained. Three metabolites were purified by high-performance liquid chromatography and initially characterized by the UV/visible absorption spectra. They were identified by ESI/MS/MS and ESI/LC/MS mass and nuclear magnetic resonance spectrums as 1-cyclopropyl-7-(4-ethyl-4-oxopiperazinyl)-6-fluoro-4-oxohydroquinoline-3-carboxylic acid (enrofloxacin *N*-oxide, 62% of the peak area at 280 nm, $[MH]^+$ = *m/z* 376), 7-(4-acetylpiperazinyl)-1-cyclopropyl-6-fluoro-4-oxohydroquinoline-3-carboxylic acid (*N*-acetylciprofloxacin, 8.0%, $[MH]^+$ = *m/z* 374), and 1-cyclopropyl-7-{[2-(ethylamino)ethyl]amino}-6-fluoro-4-oxohydroquinoline-3-carboxylic acid, 3.5%, $[MH]^+$ = *m/z* 334. We observed the transformation of enrofloxacin by *M. ramannianus*, including *N*-oxidation, *N*-dealkylation, *N*-acetylation, and breakdown of the piperazine ring. About formation of *N*-acetylciprofloxacin we propose that enrofloxacin is first converted to ciprofloxacin by *N*-dealkylation and then the resulting ciprofloxacin is *N*-acetylated to give *N*-acetylciprofloxacin.