

**Summary:**

Bacteria such as staphylococci may survive phagocytosis and later cause recurrence of the infection (8) (9). Baytril accumulates in white blood cells at up to 100 times the corresponding plasma concentrations, killing intraphagocytic bacteria reliably (10).

Beyond that, phagocytes accumulating at the site of infection in large amounts may act as “drug delivery devices” to the infected focus (15).

Many antimicrobials, which are able to cross cell membranes of phagocytes, have some interaction with their host cells (7). Under clinical conditions, fluoroquinolones such as Baytril do not negatively affect cell viability, phagocytosis or chemotaxis of phagocytic cells.

In contrast, these drugs have been shown to have a synergistic effect with the major killing mechanisms used by phagocytes (7).

Intracellular killing mechanisms are not successful in destroying all organisms phagocytized by white blood cells (8), (9). Phagocytes provide an environment in which intracellular pathogens may be sheltered from antimicrobial drugs. Surviving organisms such as staphylococci might reinfect the host or cause persistent infections despite antimicrobial therapy. Thus, the ability of a drug to reach therapeutic concentrations within the phagocytes is likely to influence the therapeutic outcome of the disease.

Enrofloxacin and its main metabolite ciprofloxacin have been shown to concentrate in phagocytic cells. In experimental studies on canine alveolar macrophages, Boeckh et al. found concentrations of up to 100 times the corresponding plasma values. As intraphagocytic drug concentrations by far exceeded the corresponding plasma levels, it was concluded that intracellular accumulation is an active process (10).

Many antimicrobials, which are able to cross cell membranes of phagocytes, have some interaction with their host cells (7). For fluoroquinolones like Baytril, it was successfully demonstrated under in vitro conditions that there are no detrimental effects on viability, phagocytosis, or chemotaxis of neutrophils, mononuclear cells and peritoneal macrophages.

In contrast, these drugs have been shown to exhibit a synergistic effect with the major killing mechanisms used by phagocytic cells, namely oxidative damage of the pathogens due to superoxide production (respiratory burst) (7). Fluoroquinolones additionally have been demonstrated to synergistically utilize oxygen-dependent killing mechanisms used by phagocytes to enhance their intracellular killing ability (7). These effects of fluoroquinolones on polymorph nuclear cells and macrophages as important parts of the immune system result in more effective phagocytosis and killing of pathogens at the site of infection.

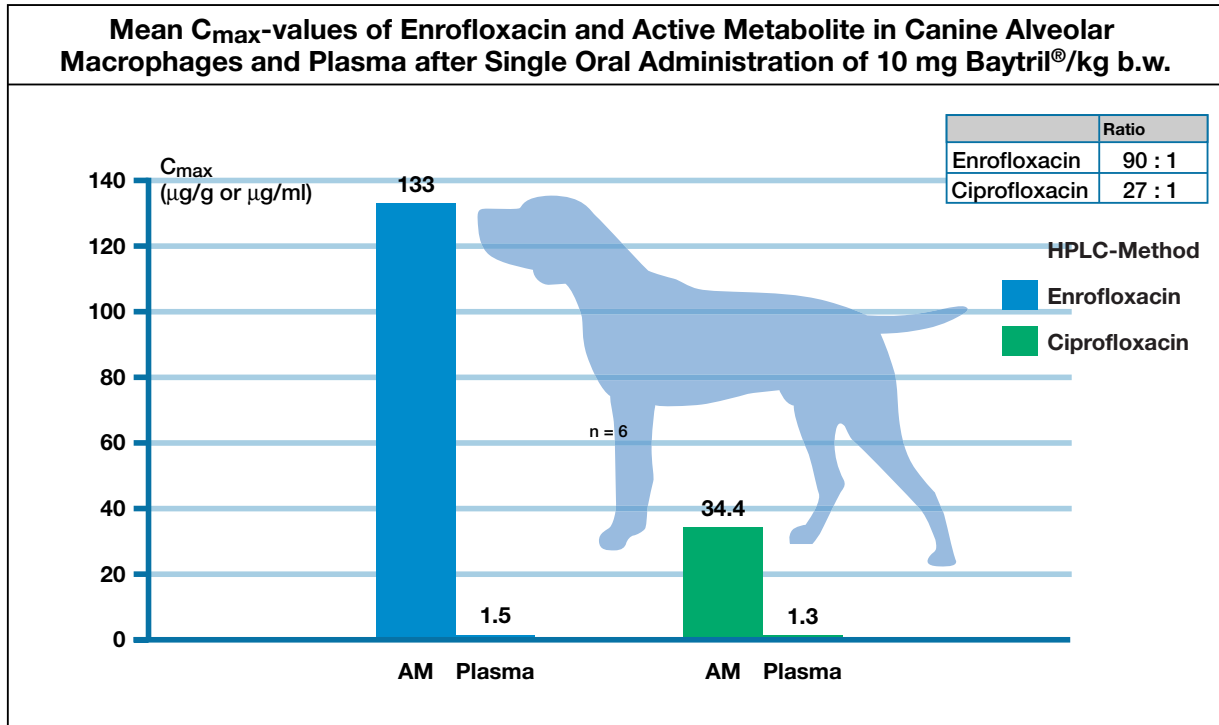
On chemotactic stimulation, mobile phagocytes accumulate at the site of infection in large numbers. Cells loaded with high concentrations of active drug seem to be a reasonable vehicle for delivering fluoroquinolones directly to the infected tissues (7). In a drug-free environment these drugs rapidly efflux from the phagocytes and act directly against pathogens. Phagocytes, therefore, were proposed to act as the “drug delivery device” for fluoroquinolones to the site of infection (15).

<b>Intracellular Disposition Characteristics of Antimicrobials in Phagocytic Cells</b>				
<b>Drug Class</b>	<b>Intracellular Diffusion</b>	<b>Distribution to Lysosomes</b>	<b>Distribution to Cytosol</b>	<b>Activity</b>
<b>Fluoroquinolones</b>	<b>Excellent</b>	<b>No</b>	<b>Yes</b>	<b>High</b>
<b>β-Lactams</b>	<b>Poor</b>	<b>No</b>	<b>No</b>	<b>Variable</b>
<b>Aminoglycosides</b>	<b>Poor</b>	<b>Yes</b>	<b>No</b>	<b>Variable</b>
<b>Chloramphenicol</b>	<b>Excellent</b>	<b>No</b>	<b>Yes</b>	<b>High</b>
<b>Macrolides</b>	<b>Excellent</b>	<b>Yes</b>	<b>Yes</b>	<b>Variable</b>
<b>Lincosamides</b>	<b>Excellent</b>	<b>Yes</b>	<b>Yes</b>	<b>Low</b>

Aucoin 1996. (7)

<b>Effect on Phagocytes</b>				
<b>Drug Class</b>	<b>Chemotaxis</b>	<b>Oxidative Burst</b>	<b>Phagocytosis</b>	<b>Killing</b>
<b>Fluoroquinolones</b>	<b>No effect</b>	<b>Enhanced</b>	<b>Enhanced</b>	<b>Enhanced</b>
<b>β-Lactams</b>	<b>Variable</b>	<b>No effect</b>	<b>Enhanced</b>	<b>Variable</b>
<b>Aminoglycosides</b>	<b>No effect</b>	<b>No effect</b>	<b>Decreased</b>	<b>Decreased</b>
<b>Macrolides</b>	<b>No effect</b>	<b>No effect</b>	<b>Enhanced</b>	<b>None</b>

Aucoin 1996. (7)



Boeckh et al. (1999) (modified) (10)

References

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