GRANULAR CTC PREMIXES ARE *NOT* CREATED EQUAL

AUREOMYCIN®
VS GENERICS

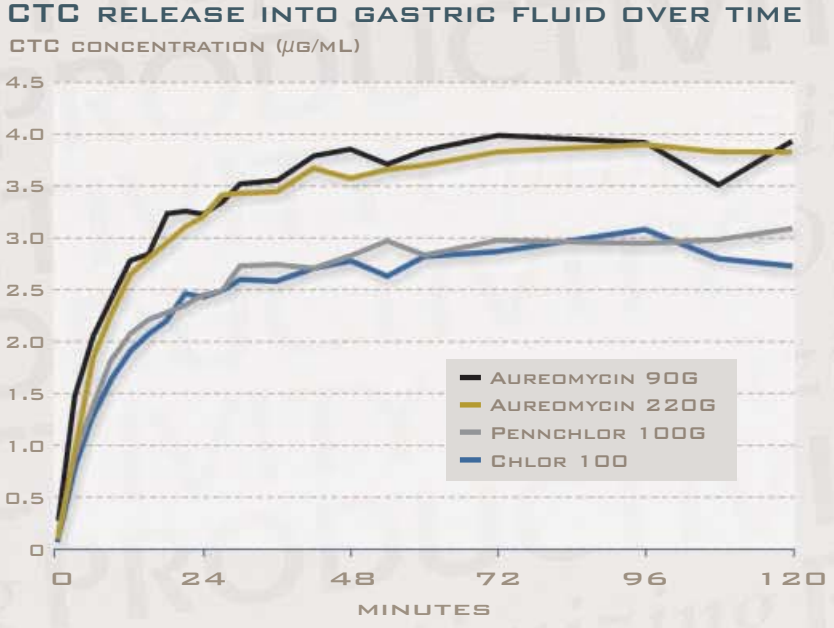
- *More drug released into gastric fluids*
- *More uniform blood/lung levels*
- *More time with therapeutic drug concentrations*
- *Better palatability*
- *Better therapeutic predictability*

A major factor affecting the ultimate quality of a chlortetracycline (CTC) granular premix is the release of drug from the granule into gastrointestinal fluids of the pig. Drug extraction is critical for the success of a treatment program, determining how much antibiotic will become available to reach the site of infection.

Two recent studies compared the ability of Aureomycin® and generic granular CTC premixes to release drug into simulated gastric fluids, and compared the plasma accumulation of CTC in pigs.[1]

AUREOMYCIN VS GENERICS: RELEASE FROM THE PREMIX

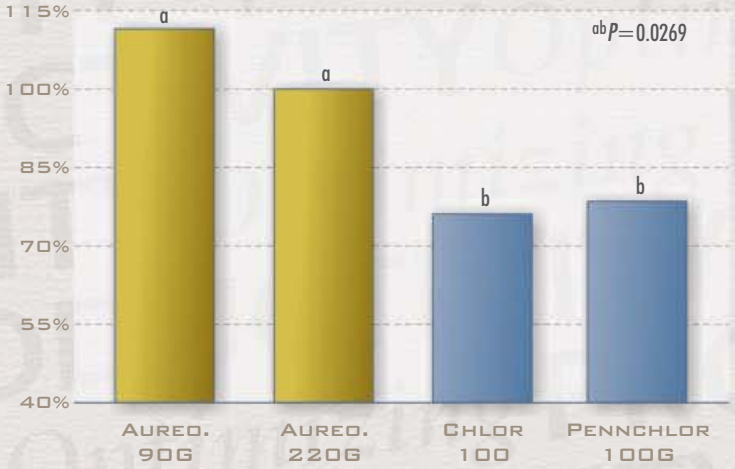
- 4 brands of granular CTC premix available in North America were tested: Aureomycin® 90G (US), Aureomycin® 220G (Canada; equivalent to Aureomycin 100G in the US), Chlor 100, and Pennchlor® 100G.
- An *in vitro* dissolution study measured the release of CTC from medicated feeds after immersion in simulated gastric fluid (pH 1.6 at 40°C for 2 h), and interactions of dissolved CTC with feed components.
- The average concentration of dissolved CTC released into the simulated gastric fluids was measured as a function of time.
- The rates of increase in drug concentration were significantly greater ($P<0.03$) for Aureomycin-medicated feeds than for rations containing Chlor 100 or Pennchlor 100G.



Aureomycin vs Generics: release from the premix (cont.)

- CTC release from medicated feed was significantly (P=0.027) impacted by the brand of premix.
- Feeds made with Aureomycin released, on average, 37% more CTC than feeds containing Chlor 100 or Pennchlor 100G.

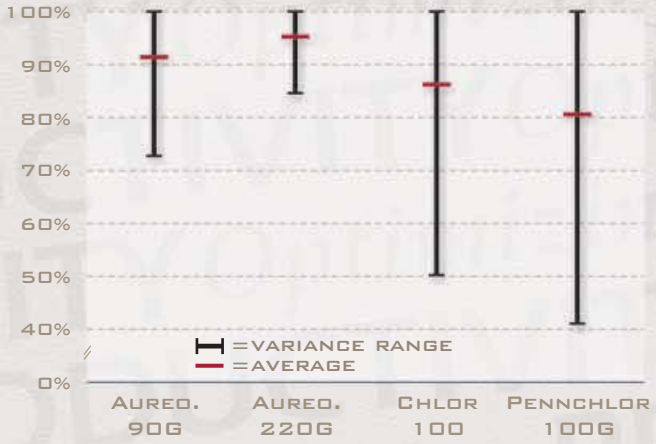
Relative % CTC release in simulated gastric fluid, using Aureomycin 220G as the reference brand



Aureomycin vs Generics: blood levels in pigs

- An *in vivo* steady-state accumulation study involved 16 pigs fed rations fortified with 550 ppm CTC, offered at 12-h intervals (2% body weight). Blood samples were collected over time following the 1st, 7th (at steady state), and 9th consecutive medicated meal.
- A plasma concentration of 0.5 μg/mL for 100% of the dosing interval was deemed the target criterion for clinical efficacy.[2-5] Plasma CTC accumulation is indicative of lung accumulation because the drug readily equilibrates between plasma and lung tissue (lung CTC concentrations could be up to 3-times higher than plasma levels[6]).
- An odds ratio analysis by Dr. John Deen, University of Minnesota, showed that pigs fed Aureomycin 90G were 9% more likely than Pennchlor 100G to achieve therapeutic blood and lung levels; pigs fed Aureomycin 220G were 13% more likely than Chlor 100 to achieve therapeutic blood and lung levels.
- Aureomycin 220G provided the most uniform CTC plasma exposure above the target concentration (0.5 μg/mL), with Aureomycin 90G statistically similar (P=0.20).

Percent of time that CTC plasma > 0.5 μg/mL



- Significantly greater variances (less uniformity) in plasma exposure to CTC were found with Chlor 100 (P=0.02) and Pennchlor 100G (P=0.04).
- Pigs in the Chlor 100 and Pennchlor 100G treatment groups experienced as much as 14 hours/day of steady-state exposure to *sub-therapeutic CTC levels.*
- A deterrent effect on initial feed consumption was observed in some pigs fed the generic products, further compromising drug availability.

Aureomycin® 90 Granular

Available in the US in a premix containing 90 g/lb chlortetracycline.

Aureomycin® 220 Granular

Available in Canada in a premix containing 220 g/kg chlortetracycline.
(equivalent to Aureomycin 100G marketed in the US)

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1. del Castillo, Wolff. *AASV Proc* 2006; 143-148.
2. Cunha, Mattoes. *Antimicrobial Pharmacodynamics in Theory and Clinical Practice*, 2002.
3. Wolff. *AASV Proc* 2003; 34:181-184.
4. Nielsen, Gyrd-Hansen. *J Vet Pharm Ther* 1996; 19:305-311.
5. del Castillo, et al. *AASP Proc* 2000; 89-93.
6. Asanuma et al. *J Animal Drugs* 1986; 6(9):1-14.

TAKE TIME OBSERVE LABEL DIRECTIONS

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