

Thesis Title                      Pharmacokinetic Study of Intramammary  
Ampicillin and Cloxacillin in Dairy Cows  
and Detection of Their Residues in Milk

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### ABSTRACT

To study pharmacokinetics and detect drug residues in milk, concentrations of intramammary ampicillin and cloxacillin in serum and milk of lactating cows were determined after intramammary administration of Ampiclox<sup>R</sup>. The first experiment was performed in healthy lactating cows receiving one syringe of Ampiclox<sup>R</sup> containing 75 mg ampicillin and 200 mg cloxacillin. Blood samples were drawn at 0, 0.50, 1, 2, 4, 6, 8 and 10 h after intramammary administration. Drug concentrations in serum were analysed by a high pressure liquid chromatography (HPLC) technique. The results in this experiment showed that the concentrations of ampicillin and cloxacillin in bovine serum were below the detection limits of HPLC method (ampicillin  $0.5 < \mu\text{g/ml}$ ; cloxacillin  $< 0.1 \mu\text{g/ml}$ ). In experiment 2, the concentrations of ampicillin and cloxacillin in milk of 10 healthy lactating cows were detected after single dose of Ampiclox<sup>R</sup> was administered intramammarily to each animal. Milk samples were collected at 0, 1, 3, 6, 12, 18, 24, 30, 36, 48, 60 and 72 h after dosage. The

concentrations of ampicillin and cloxacillin in milk from uninfused quarter udders were also below the detection limits, whereas 0.87–96.20  $\mu\text{g/ml}$  ampicillin and 0.20–504.01  $\mu\text{g/ml}$  cloxacillin were found in milk from directly infused quarters within 12 hours and 24 hours after dosage for ampicillin and cloxacillin, respectively. The mean value of elimination half-life of ampicillin was  $1.86 \pm 0.27$  hours and of cloxacillin was  $2.31 \pm 0.27$  hours. Finally, in the third experiment, 10 mastitis cows were treated with single dose of Ampiclox<sup>R</sup> 3 times every 12 hours as recommended dose for effective mastitis treatment. Milk samples were collected from treated and untreated quarter udder separately at 0, 1, 3, 6, 9, 12, 18, 24, 30, 36, 42, 48, 60, 72, 84 and 96 h after first dose treatment. Ampicillin and cloxacillin concentrations in milk from untreated quarter udders were found below the detection limits but 0.76–128.04  $\mu\text{g/ml}$  ampicillin and 0.77–562.20  $\mu\text{g/ml}$  cloxacillin were detected in milk from treated quarter udders during 36 hours and 42 hours after first dose treatment for ampicillin and cloxacillin, respectively. The comparison of ampicillin concentrations in milk from healthy cows and mastitis cows showed significant difference at 1, 3 and 6 h after dosage ( $P < 0.05$ ). No significant difference of milk cloxacillin concentrations in two groups of animals was observed ( $P < 0.05$ ).

The results in this present study indicated that Ampiclox<sup>R</sup> had poor penetration. Drugs did not absorb and distribute to blood circulation and other uninfused quarters in detectable amounts. With single dose infusion, the depletion rate of Ampiclox<sup>R</sup> in milk was 24 hours. With multiple dose therapy (3 infusions), the depletion rate of Ampiclox<sup>R</sup> was 42 hours. Mastitis conditions affected ampicillin concentrations in milk.