INFLUENCE OF FEED TYPE ON THE PHARMACOKINETICS OF CEPHALOTHIN ADMINISTERED TO LACTATING GOATS

INFLUENCIA DEL TIPO DE ALIMENTACIÓN SOBRE LA FARMACOCINÉTICA DE CEFALOTINA ADMINISTRADA A CABRAS EN LACTACIÓN

Rule, R.1*, R. Lacchini2, A. García Román3, A. Antonini2 and P. de Buschiazzo4

1Commission of Scientific Research of the Province of Buenos Aires. Argentina.
2Department of Introduction to Animal Production. Faculty of Agricultural and Forestry Science. La Plata University. Argentina.
3Faculty of Veterinary. University of Cordoba. Spain.
4University Center of Pharmacology. School of Medicine. National University of La Plata. Argentina.

*Correspondence should be sent to: Dr. R. Rule. Calle 63 Nro. 216. (1900). La Plata. Argentina. Tel.Fax. 54-221-421-6932. E-mail: robertorule@yahoo.com.ar

ADDITIONAL KEYWORDS
Plane of nutrition.

SUMMARY

The general aim of this study was to determine the influence of the nutritional condition on the pharmacokinetic profile of cephalothin administered to lactating goats exposed to restricted and normal diets.

Twenty-two healthy Creole pregnant goats, during the 4th and 5th month of pregnancy, with a body weight ranging from 25 to 50 kg, were used. They were randomized into 3 groups: experiment 1 (E1) (n=8), experiment 2 (E2) (n=8) and experiment 3 (E3) (n=6). Animals of E1, E2 and E3 grazed in a restricted way based on effected nutritional recomendations by INRA for goats. E2 animals were fed with the addition of an excess of calories in their diets. E3 group received grass plus an addition of an equilibrated supplement.

The lactating goats (E1, E2 and E3) received at 45 pospartum a single dose of cephalothin by i.v. route (20 mg/kg b. w.). Blood and milk samples were obtained at selected times. The cephalothin concentrations in plasma and milk were determined by high-performance liquid chromatography assay. The presence of antibiotic residues in milk was detected by means of a biological method (Delvotest® SP, Gist-Brocades). The pharmacokinetic profile of cephalothin administered to lactating goats fitted a two-compartmental model. The plasma terminal half-life (t½), area under the curve (AUC) and volume of distribution at steady state (Vss) was significantly higher in E3 (t½= 0.6 ± 0.3 h; AUC= 13.0 ± 1.4 µg/ml/h; Vss= 817.8 ± 219.9 ml/kg) Vs E1 (t½= 0.2 ± 0.1 h; AUC= 9.6 ± 2.0 µg/ml/h; Vss= 571.5 ± 103.5 ml/kg) and E2 (t½= 0.3 ± 0.1 h; AUC= 9.5 ± 1.4 µg/ml/h; Vss= 625.6 ± 128.4 ml/kg). The area under the curve (AUC) and penetration (P) in milk of cephalothin were significantly higher in E3 (AUC= 12.5 ± 7.0 µg/ml/h; P= 83.2 ± 27.6%) than in E1 (AUC= 0.2 ± 0.1 µg/ml/h; P= 2.3 ± 2.2%) and E2 (AUC= 3.7 ± 4.6 µg/ml/h; P= 26.6 ± 38.1%).

In conclusion, the pharmacokinetic profile in plasma and milk of cephalothin administered to lactating goats were determined...
lactating goats was in fact altered by the protein-restricted diets with which the animals were fed.

RESUMEN

El objetivo del trabajo es determinar la influencia de las condiciones nutricionales sobre el comportamiento farmacocinético de cefalotina administrada parenteralmente en cabras lecheras en producción, al ser alimentadas con raciones restringidas y equilibradas.

Se utilizaron 22 cabras Criollas, sanas, preñadas dentro del 4º y 5º mes de gestación y con pesos corporales entre 25 y 50 kg. Los animales fueron agrupados en forma aleatoria en tres experiencias (experiencia 1 (E1) (n= 8), experiencia 2 (E2) (n= 8) y experiencia 3 (E3) (n= 6). Los tres grupos se sometieron a un pastoreo restringido sobre la base de las recomendaciones nutricionales efectuadas por el INRA para caprinos. Los animales del grupo E2 recibieron una suplementación tendente a desequilibrar en exceso la energía de la ración. En tanto que, los del E3 recibieron un suplemento equilibrado.

La administración de cefalotina por vía intravenosa (i.v.) (20 mg/kg de peso) se realizó a los 45 días posparto. Las muestras sanguíneas y lácteas fueron recogidas a tiempos controlados. La cuantificación de cefalotina en plasma y leche fue realizada mediante técnicas de cromatografía líquida de alta resolución. La determinación de los residuos de cefalotina en leche fue realizada mediante un método biológico. Los parámetros farmacocinéticos fueron calculados utilizando modelos compartimentales y no compartimentales y comparados estadísticamente. Resultados: El tiempo medio de la fase de disposición lenta \( (t_{1/2\cdot \lambda z}) \), área bajo la curva (AUC) y volumen de distribución en estado estacionario \( (V_{ss}) \) fueron significativamente más elevados en la E3 (\( t_{1/2\cdot \lambda z}= 0,6 \pm 0,3 \text{ h}; \ AUC= 13,0 \pm 1,4 \text{ µg/ml/h}; V_{ss}= 817,8 \pm 219,9 \text{ ml/kg} \)) versus E1 (\( t_{1/2\cdot \lambda z}= 0,2 \pm 0,1 \text{ h}; \ AUC= 9,6 \pm 2,0 \text{ µg/ml/h}; V_{ss}= 571,5 \pm 103,5 \text{ ml/kg} \)) y E2 (\( t_{1/2\cdot \lambda z}= 0,3 \pm 0,1 \text{ h}; \ AUC= 9,5 \pm 1,4 \text{ µg/ml/h}; V_{ss}= 625,6 \pm 128,4 \text{ ml/kg} \)). El área bajo la curva y el pasaje a leche (P) de cefalotina fueron significativamente más elevados en la E3 (\( \text{AUC}= 12,5 \pm 7,0 \text{ µg/ml/h; P}= 83,2 \pm 27,0\% \)) que en la E1 (\( \text{AUC}= 0,2 \pm 0,1 \text{ µg/ml/h; P}= 2,3 \pm 2,2\% \)) y E2 (\( \text{AUC}= 3,7 \pm 4,6 \text{ µg/ml/h; P}= 26,6 \pm 38,1\% \)).

En conclusión, los parámetros farmacocinéticos en plasma y leche de cefalotina administrada a cabras, en lactación, alimentadas con dietas restringidas en proteínas fueron diferentes a los valores obtenidos en animales con dietas equilibradas.

INTRODUCTION

Cephalosporins are antibiotics chemically related to the penicillins. Both have in common a beta-lactamic ring as part of their structure. These antibiotics interfere with the normal synthesis of the bacterial cell wall and are effective against the majority of the gram-positive Cocci and some gram-negative Bacilli such as *Escherichia coli*, *Proteus mirabilis* and *Klebsiella pneumoniae* (Booth and McDonald, 1987).

Cephalothin is a first-generation cephalosporin that is poorly absorbed in the digestive tract and thus has to be administered parenterally to obtain a systemic effect. This antibiotic is distributed mainly in the extracellular fluid and excreted by the kidneys and it is hard to find in cerebrospinal fluid (Booth and McDonald, 1987, Caprile, 1988).

The goat flocks in the Province of Buenos Aires (Argentina) are managed under fluctuant conditions, as regards the quality and quantity of food provided throughout the year. The forages fed are abundant and generally rich in...
nitrogen during spring and summer, decreasing in availability and nitrogen content towards fall and winter. That variability on the quality and quantity of food offered leads to metabolic alterations that become apparent during pre and post kidding. To overcome these problems, supplementation with an energy source such as corn is used with a certain degree of effectiveness.

As the diet can modify the action of the antibiotics administered (Oukessou and Toutain, 1992), it is of interest to know the pharmacokinetics of the antibacterial compounds administered to animals which are fed different diets and are under different nutritional status.

The aim of this study is to determine the influence of nutrition on the pharmacokinetics of cephalothin administered to lactating goats, fed restricted and balanced rations to create different nutritional conditions.

MATERIALS AND METHODS

Animals. Twenty-two healthy pregnant Creole goats were used. Goats were pregnant of singles or twins and were on the 4th and 5th month of gestation, with a body weight ranging from 25 to 50 kg. Animals were distributed at random in three experimental groups: experiment 1 (E1) (n=8), experiment 2 (E2) (n=8) and experiment 3 (E3) (n=6).

Experiment 1. The animals grazed native grasslands. The main species in the pasture were *Trifolium repens* and *Lolium perenne*. The dry matter (DM) contents were determined by drying them in a microwave (Bruno et al., 1995) until no changes in weight were observed. The dry matter values ranged between 20 and 27 percent. According to the nutritional requirements of dairy goats proposed by INRA (INRA, 1990) in the software Programa Violeta, E.T.S.I.A. (1988), the animals were restricted in one third of their daily forage intake to create a deficit in dry matter, energy and protein intake. The forage intake was estimated once per week by the difference in weights in the goats between the beginning and the end of the grazing time, considering the dry matter content of the pasture.

Experiment 2. The animals received the same amount of forage as in E1 plus a supplementation of corn grain so as to create an unbalanced diet with excess of energy.

Experiment 3. The goats in this experiment received a forage-based diet plus a supplementation of hay, soybeans, corn, wheat middlings, CaCO₃ and NaCl to meet the INRA (INRA, 1990) requirements.

All the animals (E1, E2, E3) were weighted once per week, before and after grazing. The animals were provided water *ad libitum* during the night and the rest of the day that remained off the pasture. The day of weighin, water was provided (*ad libitum*) after being weighted.

Chemical composition of the diets. The estimated composition of the diets fed during the goats’ gestation and lactation periods in E1, E2 and E3 are shown in table I.

Dose and route of cephalothin administration. The lactating goats (E1, E2 and E3) received at 45 pospartum a single dose of cephalothin

Archivos de zootecnia vol. 56, núm. 216, p. 809.
RULE, LACCHINI, GARCÍA ROMÁN, ANTONINI AND BUSCHIAZZO

Sampling. After the i.v. administration of cephalothin, blood samples were collected (5 ml each one) from the left jugular vein at 5, 10, 15 and 30 minutes and at 1, 2, 3, 4, 6, 8, 12, 24, 48 and 72 hours post-administration of the antibiotic. Milk samples were collected (approximately 0.5 ml each one) starting at 15 minutes and following the blood sampling strategy.

Processing and preservation of samples. Blood samples were centrifuged at 1500 x g for 5 min to separate the plasma. Milk and plasma samples were stored at –18°C until the antibiotic concentrations were quantified.

Quantification of the antibiotic. The cephalothin concentrations in plasma and milk were determined by high-performance liquid chromatography assay. Briefly, the samples were allowed to thaw and then mixed in 250-µl aliquots with 100 µl of 0.02 M H₃PO₄/KH₂PO₄ buffer (pH 2.6), 20 µl of 30% (v/v) perchloric acid and 250 µl of methanol. The specimens were then centrifuged at 1000 g for 5 min and the supernatants recovered. Finally, 20 µl of each supernatant was injected into a Lichrosphere cc125/4, RP 18, 100-5 column (Merck, USA) with a 13% (v/v) acetonitrile solution in 0.02 M H₃PO₄/KH₂PO₄ buffer as the mobile phase of a high-performance liquid chromatography system (Thermo Separation, USA), equipped with an UV absorbance detector at 254 nm wavelength to analyse cephalothin.

Table I. Estimated chemical composition of the diets fed during the goats’ gestation and lactation periods in experiments 1 (E1), 2 (E2) and 3 (E3). (Composición química estimada de las dietas consumidas por la cabras durante los periodos de gestación y lactación en los experimentos 1 (E1), 2 (E2) y 3 (E3)).

<table>
<thead>
<tr>
<th>Feed (units)</th>
<th>Animals in gestation periods</th>
<th>Animals in lactation period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E1</td>
<td>E2</td>
</tr>
<tr>
<td>Dry matter (g)</td>
<td>400</td>
<td>650</td>
</tr>
<tr>
<td>Metabolizable energy (percent)</td>
<td>912</td>
<td>1755</td>
</tr>
<tr>
<td>Crude protein (g)</td>
<td>59</td>
<td>84</td>
</tr>
<tr>
<td>Crude fiber (g)</td>
<td>118</td>
<td>125</td>
</tr>
<tr>
<td>DM avg (percent)</td>
<td>66</td>
<td>72</td>
</tr>
<tr>
<td>DM min (percent)</td>
<td>66</td>
<td>122</td>
</tr>
<tr>
<td>ME avg (percent)</td>
<td>42</td>
<td>80</td>
</tr>
<tr>
<td>ME min (percent)</td>
<td>43</td>
<td>62</td>
</tr>
<tr>
<td>P avg (percent)</td>
<td>66</td>
<td>94</td>
</tr>
</tbody>
</table>

(DM avg)= Percentages of coverage of the average requirements of dry matter. (DM min)= Percentages of coverage of the minimum requirements of dry matter. (ME avg) Percentages of coverage of the average requirements of metabolizable energy. (ME min) Percentages of coverage of the minimum requirements of metabolizable energy. (P avg) Percentages of coverage of the average requirements of crude protein. (P min) Percentages of coverage of the minimum requirements of crude protein.
concentrations. This method has intra and inter-run coefficients of variations of 5 and 5.5 percent, respectively and a minimum limit of detection of 0.01 μg/ml.

**Detection of cephalothin residues in milk:** The presence of antibiotic residues in milk was detected by means of a standard diffusion method (Delvotest® SP, Gist-Brocades).

**Pharmacokinetic study:** The plasma cephalothin concentration-time data were used to perform a pharmacokinetic analysis following an interactive an weighted-non-linear least-squares regression analysis (Metzler and Tong, 1981). The Akaike Information Criterion (AIC) (Akaike, 1978) was used to determine the compartmental model best adapted to the data set. The concentration-time data of cephalothin obtained in plasma were fitted to a two-compartmental open model, whereas the concentration-time data from milk were analyzed by means of non-compartmental methods (Ritschel, 1986).

Hybrid constant C₁, and C₂ (extrapolations at zero time of the experimental terms), the initial slope (λ₁) and the terminal slope (λ₂) were used to calculate the rate constants from the central to the peripheral compartment (k₁₂) and vice versa (k₂₁), as well as the rate constants of elimination (k₁₀) (Gibaldi and Perrier, 1982). The apparent volume of the central compartment (Vc) was calculated from the following equation:

\[ V_c = \text{Dose (μg/kg)/C}_{(0)} \]

where the concentration at zero time \( C_{(0)} = C_1 + C_2 \)

The distribution volume at steady state (\( V_{ss} \)) was calculated as follows:

\[ V_{ss} = ((k_{12} + k_{21}) / k_{21}) V_c \]

The total plasma clearance (CL) was calculated according to the following equation:

\[ CL = k_{10} \cdot V_c \]

The initial disposition (\( t_{1/2,1} = 0.693 / \lambda_1 \)) and the terminal (\( t_{1/2,2} = 0.693 / \lambda_2 \)) half-lives were calculated by means of equations given by Gibaldi and Perrier (1982).

The area under the curve from time zero to infinity (\( AUC_{0\rightarrow\infty} \)) was estimated by trapezoidal integration as:

\[ AUC_{0\rightarrow\infty} = AUC_{0\rightarrow t} + C_t / k_{el} \]

Where \( AUC_{0\rightarrow t} \) is the AUC from time zero to time \( t \) and \( C_t \) is the concentration of cephalothin in the last plasma (or milk) sample collected at time \( t \) (Gibaldi and Perrier, 1982).

The penetration (P) in milk of cephalothin was calculated by using the following equation:

\[ P = AUC_{(milk)}/AUC_{(plasma)} \]

\[ (Baggot, 1977). \]

**Statistical analysis:** The pharmacokinetic variables of cephalothin were analyzed by one-way analysis of variance by using Statgraphics Plus 4.0.

**RESULTS AND DISCUSSION**

The time-concentration (means ± S.D.) values in plasma and milk of
cephalothin administered by i.v. route to lactating goats fed with restricted diets (E1 and E2) and a balanced diet (E3) are presented in figure 1.

The plasma and milk pharmacokinetic variables of cephalothin administered intravenously to lactating goats during E1, E2 and E3 are shown in table II.

The pharmacokinetic profile of cephalothin administered to lactating goats agrees with what was described for several other cephalosporins using a two-compartmental open model characterized by an initial phase followed by a slower terminal phase (Caprile, 1988, Rule et al., 2003).

The concentrations-time of cephalothin in plasma obtained in Experiments 1, 2 and 3 were lower compared to other cephalosporins administered to animals (Murakawa et al., 1980, Komiya et al., 1981, Matsui et al., 1984, Wilson et al., 1985, Guerrini et al., 1986, Rule et al., 2003). The terminal half-life values for goats fed with restricted diets (t1/2λ (E1)= 0.2 ± 0.1 and (E2)= 0.3 ± 0.1 h) was significantly lower to those observed in goats fed with a balanced diet (t1/2λ (E3)= 0.6 ± 0.3 h). Although they were within the range of the values obtained when cephalothin was administered intramuscularly to avian species (from 16 to 54 min) (Bush et al., 1981) and humans (from 28 to 51 min) (Kirby and...
FEED TYPE AND CEPHALOTHIN ADMINISTERED TO LACTATING GOATS

Regamey, 1973, Nightingale et al., 1975). Oukessou and Toutain (1992) observed that an increase in the protein content of the diet in sheep increased the half-life of gentamicin ($t_{1/2}$; $\lambda_z = 117.0 \pm 67.7 \text{ min}$) compared to the other group, fed with a low protein content ($t_{1/2}$; $\lambda_z = 9.7 \pm 9.4 \text{ min}$).

The volume of distribution at steady state of cephalothin in goats with a balanced diet (E3) ($V_{ss} = 817.8 \pm 219.9 \text{ ml/kg}$) was significantly higher compared to the group fed with a restricted diet (E1) ($V_{ss} = 571.5 \pm 103.5 \text{ ml/kg}$) and a restricted diet plus the addition of energy (E2) ($V_{ss} = 625.6 \pm 128.4 \text{ ml/kg}$) and generally agrees with the work of Oukessou and Toutain (1992) where a high protein content in the portion modifies the volume of distribution of gentamicin in sheep ($V_{ss}$ (high-protein group) = $0.180 \pm 0.109$ and (low-protein group) = $0.132 \pm 0.037 \text{ l/kg}$). Different from what was observed in our work, those authors found higher concentration-time values as well as area under the curve values (1.7 times) and a lower body clearance (CL) of gentamicin in those animals fed with a low protein diet (CL = $0.93 \pm 0.13 \text{ ml/min/kg}$) compared to sheep fed with a high protein diet (CL = $1.64 \pm 0.40 \text{ ml/min/kg}$). In the present investigation the areas under the curves were approximately 1.4 times higher in the group fed with a balanced diet.

### Table II. Pharmacokinetic parameters (means ± 1 D.S.) of cephalothin administered by endovenous route (20 mg/kg BW) to lactating goats fed with a restricted diet (E1), a restricted diet plus an addition of energy (E2) and a balanced diet (E3). (Parámetros farmacocinéticos de la cefalotina administrada por vía endovenosa a cabras lactantes alimentadas con una dieta restringida (E1) una dieta restringida con adición de energía (E2) y una dieta balanceada (E3)).

<table>
<thead>
<tr>
<th>Parameters (units)</th>
<th>E1</th>
<th>E2</th>
<th>E3</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacokinetics (plasma)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_1$ (µg/ml)</td>
<td>$111.2 \pm 25.3$</td>
<td>$121.1 \pm 57.3$</td>
<td>$212.9 \pm 60.3$</td>
<td>0.0176</td>
</tr>
<tr>
<td>$C_z$ (µg/ml)</td>
<td>$26.2 \pm 15.7$</td>
<td>$20.9 \pm 13.8$</td>
<td>$7.2 \pm 2.5$</td>
<td>0.0269</td>
</tr>
<tr>
<td>$\lambda_1$ (h⁻¹)</td>
<td>$16.2 \pm 8.2$</td>
<td>$12.4 \pm 2.5$</td>
<td>$37.4 \pm 21.5$</td>
<td>0.0038</td>
</tr>
<tr>
<td>$\lambda_z$ (h⁻¹)</td>
<td>$3.1 \pm 0.7$</td>
<td>$3.0 \pm 0.9$</td>
<td>$1.7 \pm 1.3$</td>
<td>0.0228</td>
</tr>
<tr>
<td>$t_{1/2}$ (h)</td>
<td>$0.05 \pm 0.02$</td>
<td>$0.06 \pm 0.01$</td>
<td>$0.02 \pm 0.01$</td>
<td>0.0017</td>
</tr>
<tr>
<td>$V_c$ (ml/kg)</td>
<td>$130.6 \pm 60.5$</td>
<td>$164.1 \pm 67.6$</td>
<td>$83.1 \pm 46.1$</td>
<td>0.194</td>
</tr>
<tr>
<td>$CL$ (ml/kg/h)</td>
<td>$2167.7 \pm 511.5$</td>
<td>$2161.5 \pm 331.9$</td>
<td>$1578.4 \pm 236.4$</td>
<td>0.0325</td>
</tr>
<tr>
<td>$V_{ss}$ (ml/kg)</td>
<td>$571.5 \pm 103.5$</td>
<td>$625.6 \pm 128.4$</td>
<td>$817.8 \pm 219.9$</td>
<td>0.0311</td>
</tr>
<tr>
<td>AUC$_{0-t}$ (µg/ml/h)</td>
<td>$9.6 \pm 2.0$</td>
<td>$9.3 \pm 1.5$</td>
<td>$12.8 \pm 1.6$</td>
<td>0.005</td>
</tr>
<tr>
<td>AUC (µg/ml/h)</td>
<td>$9.6 \pm 2.0$</td>
<td>$9.5 \pm 1.4$</td>
<td>$13.0 \pm 1.4$</td>
<td>0.0032</td>
</tr>
<tr>
<td>Pharmacokinetics (milk)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC (µg/ml/h)</td>
<td>$0.2 \pm 0.1$</td>
<td>$3.7 \pm 4.6$</td>
<td>$12.5 \pm 7.0$</td>
<td>0.0007</td>
</tr>
<tr>
<td>Penetration (%)</td>
<td>$2.3 \pm 2.2$</td>
<td>$26.6 \pm 38.1$</td>
<td>$83.2 \pm 27.0$</td>
<td>0.0019</td>
</tr>
</tbody>
</table>

Different numbers in one row correspond to statistically significant differences.
RULE, LACCHINI, GARCÍA ROMÁN, ANTONINI AND BUSCHIAZZO

compared to those observed in restricted diets. The area under the curve and penetration of cephalothin in milk obtained in E3 were significantly higher than those found in E1 and E2. In the three experiments, the presence of cephalothin residues was not found in all animals starting from 48 hours post-administration of the antibiotic. When Storper et al. (1981) used cephalothin together with ampicillin in milking cows by intrammary route three times a day, the milk up to 48 hours post-treatment was discarded.

In general, the administration of cephalothin by intravenous route in lactating goats with restricted diets, showed a pharmacokinetic profile significantly lower compared to those values found in goats in production fed with balanced diets. Such pharmacokinetic differences consisted of a lower diffusion of cephalothin from the central to the peripheral compartment and viceversa this is due to a lower volume of distribution and slower half-life and plasma clearance.

During the present work, we attempted to reproduce the feeding conditions that are generally found in the Argentinian goat flocks (Buenos Aires Province) during the forage scarcity seasons. The aim of this work was to observe the kinetic profile of cephalosporin under those conditions. A restriction on one third of the total nutrient supply and supplementation with highly energetic diets is a tool that many goat producers utilize. Those management practices did not produce clinical signs or alter the normal kidding of the flock during this study. Throughout E1 animals actually tried to compensate their deficient diet by eating more, but this was hindered by restricting the grazing period.

When cephalothin was administered during the postpartum period to the group under nutritional restriction (E1) and energy supplementation (E2), differences were observed in the pharmacokinetic profile of the antibiotic in milk and plasma when compared to the balanced diet group of goats. Those differences are mainly due to the different nutritional planes the animals were under.

In conclusion, although the concentrations-time remained low in the three experiments and taking into account that this antibiotic is time-dependent, the differences found in the kinetic parameters prompt us to evaluate the administration regimes when using cephalothin, in lactating goats under nutritional deficiencies.

ACKNOWLEDGMENTS

This study was supported by a grant, provided by the Commission of Scientific Research of the Province of Buenos Aires, Argentina

REFERENCES


FEED TYPE AND CEPHALOTHIN ADMINISTERED TO LACTATING GOATS


Recibido: 26-4-06. Aceptado: 2-11-06.

Archivos de zootecnia vol. 56, núm. 216, p. 815.