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Ann Rech Vet 1990;21 Suppl 1:67S-71S

[The bioequivalence of two injectable solutions of spiramycin in young cattle]. [Article in French]

Huet AM, Bosc F, Floc'h R, Bayle R

Rhone-Merieux, Toulouse, France.

A bioequivalence study was performed in 12 young cattle in order to compare 2 injectable solutions of spiramycin containing 60 M IU/100 ml (Suanovil 20) and 100 M IU/100 ml, respectively. In a cross-over design, a single dose of 100,000 IU/kg bw was administered intramuscularly, allowing 8 d between the 2 administrations. For each formulation, the following parameters were determined: maximum serum concentration (Cmax) and time to reach peak concentration (Tmax), mean residence time (MRT), area under the time-concentration curve (AUC), half-life (t1/2 beta). Statistical analysis of t1/2 beta, Tmax (Wilcoxon's test) and Cmax, MRT, AUC (ANOVA), indicated no significant differnces between the two formulations (P greater than 0.05). Westlake's confidence intervals calculated for a 95% probability were 23.1% for Cmax, 11.1% for MRT and 13.2% for AUC, respectively, which confirmed the bioequivalence of the 2 formulations. It must be noted that an experimental design using 12 animals is generally insufficient to demonstrate bioequivalence, according to the recommended statistical criteria.

Vet Q 1983 Jul;5(3):122-7

'Pink eye' or 'zere oogjes' or keratoconjunctivitis infectiosa ovis (KIO). Clinical efficacy of a number of antimicrobial therapies.

Konig CD

In a comparative study the clinical efficacy of five different treatments of keratoconjunctivitis infectiosa ovis (KIO) were tested, namely an intramuscular injection of chloramphenicol base (dosage 15 mg/kg), spiramycin base (Suanovil dosages 10 to 25 mg/kg), oxytetracycline (Engemycine Forte, Terramycin LA, dosages respectively 5 and 10 mg/kg), tiamulin (Dynamutulin, dosage 10 mg/kg) and subcutaneous injection of procaine penicillin G, benzathine penicillin G. and dihydrostreptomycin in the lower eyelid. It appeared from these field trials that spiramycin base, oxytetracycline and tiamulin had a clearly positive effect on the clinical course of 'pink eye', although with tiamulin there was only a temporary effect (high percentage of relapses). In view of the field data the following dosage schemes are, for the time being, advised: spiramycin base (Suanovil), and oxytetracycline (formulation with a good biological availability) both 20 to 30 mg/kg and, if necessary, to be repeated on days 5 and 10 after the first intramuscular injection. The dosage scheme advised for tiamulin is 20-30 mg/kg to be repeated on day 3 and if necessary on days 6 and 9 after the intramuscular injection. In mild cases it is sufficient to rub the eyes with for example oxytetracycline eye-ointment, a few times a day.

Vet Pharmacol Ther 1998 Aug;21(4):251-6

Bioavailability of spiramycin and lincomycin after oral administration to fed and fasted pigs.

Nielsen P, Gyrd-Hansen N

Department of Pharmacology and Pathobiology, Royal Veterinary and Agricultural University, Frederiksberg C, Denmark.

The disposition of spiramycin and lincomycin was measured after intravenous (i.v.) and oral (p.o.) administration to pigs. Twelve healthy pigs (six for each compound) weighing 16-43 kg received a dose of 10 mg/kg intravenously, and 55 mg/kg (spiramycin) or 33 mg/kg (lincomycin) orally in both a fasted and a fed condition in a three-way cross-over design. Spiramycin was detectable in plasma up to 30 h after intravenous and oral administration to both fasted and fed

pigs, whereas lincomycin was detected for only 12 h after intravenous administration and up to 15 h after oral administration. The volume of distribution was 5.6 +/- 1.5 and 1.1 +/- 0.2 L/kg body weight for spiramycin and lincomycin, respectively. For both compounds the bioavailability was strongly dependent on the presence of food in the gastrointestinal tract. For spiramycin the bioavailability was determined to be 60% and 24% in fasted and fed pigs, respectively, whereas the corresponding figures for lincomycin were 73% and 41%. The maximum plasma concentration of spiramycin (Cmax) was estimated to be 5 microg/mL in fasted pigs and 1 microg/mL only in fed pigs. It is concluded that an oral dose of 55 mg/kg body weight is not enough to give a therapeutically effective plasma concentration of spiramycin against species of Mycoplasma, Streptococcus, Staphylococcus and Pasteurella multocida. The maximum plasma concentration of lincomycin was estimated to be 8 microg/mL in fasted pigs and 5 microg/mL in fed pigs, but as the minimum inhibitory concentration for lincomycin against Actinobacillus pleuropneumoniae and P. multocida is higher than 32 microg/mL a therapeutically effective plasma concentration could not be obtained following oral administration of the drug. For Mycoplasma the MIC90 is below 1 microg/mL and a therapeutically effective plasma concentration of lincomycin was thus obtained after oral administration to both fed and fasted pigs.

Vet Pharmacol Ther 1996 Apr;19(2):95-103

Pharmacokinetic-pharmacodynamic model for spiramycin in staphylococcal mastitis.

Renard L, Sanders P, Laurentie M, Delmas JM

Unite de Pharmacocinetique, CNEVA-Fougeres, Centre National d'Etudes Veterinaires et Alimentaires, France.

Simultaneous pharmacokinetic-pharmacodynamic (PK/PD) modelling for spiramycin in staphylococcal infections of the mammary gland of cows was used to predict the efficacy of spiramycin. A differential equation derived from the Zhi model was fitted to an in vitro killing curve and post-antibiotic effect determination. A seven-compartment PK model, in which 4 compartments representing each quarter of the mammary gland which was considered

to be the effect compartment, was included. The PD model linked to the PK model was able to describe the in vivo spiramycin effect against Staphylococcus aureus. The parameters calculated from in vitro data predicted a rapid decrease for the first 12-24 h, and regrowth within 72 h following the treatment, whereas in vivo the bacterial effect was much less after 24 h than that predicted by the in vitro data. PK/PD modelling permitted the simulation of various doses to optimize the efficacy of the antibiotic, taking into account such dynamic parameters as bacterial growth rate constant, bacterial killing rate constant and the Michaelis-Menten type saturation constant. An optimal dosage regimen of 20000 IU/kg per day for 3 days was predicted for the treatment of Staphylococcus aureus mastitis.

Am J Vet Res 1994 Mar;55(3):358-62

Pharmacokinetics and tissue residues of spiramycin in cattle after intramuscular administration of multiple doses.

Sanders P, Guillot P, Dagorn M, Moulin G, Delepine B, Mourot D

Laboratoire des Medicament Veterinaires, Centre National d'Etudes Veterinaires et Alimentaires, Ministere de l'Agriculture et de la Foret, La Haute Marche-Javene, Fougeres, France.

Pharmacokinetic variables of spiramycin and its distribution in muscle, liver, kidney, and injection sites were studied in 18 mixed-sex 1-year-old calves to assess drug withdrawal time after 2 IM administrations of 100,000 IU of spiramycin/kg of body weight at 48-hour intervals. Presence of a compound, other than spiramycin I (ie, neospiramycin), was observed in tissues used for withdrawal time determination. High concentrations observed at the injection sites decreased slowly to maximal residue limit with half-life of 109.5 hours for neospiramycin and 77.5 hours for spiramycin. At 14 days, neospiramycin concentrations were higher in kidney than in liver and half-life was different between these 2 tissues. Two methods of withdrawal time determination were used and the part of the samples without residue detected, in the calculation, was discussed.

Withdrawal time of 35 days can be proposed on the basis of average daily intake determined for spiramycin, with concentration at injection sites representing 10% of the whole muscle concentration.

Vet Rec 1992 Jun 6;130(23):510-3

Pharmacokinetics and bioavailability of spiramycin in pigs.

Sutter HM, Engeli J, Muller P, Schneider B, Riond JL, Warner M

Division for Animal Nutrition, Institute of Veterinary Physiology, Zurich, Switzerland.

The pharmacokinetics of spiramycin in pigs were investigated after intravenous and oral administration. The potential therapeutically effective blood level was established after a single administration and examined in a subsidiary five day study. The rapid intravenous injection of 25 mg spiramycin/kg bodyweight produced marked salivation in all the test animals. The elimination half-life (2.3 +/- 1.2 hours) was relatively short, in accordance with the total body clearance rate (27.3 +/- 10.1 ml/minute/kg). The high volume of distribution (5.2 +/- 2.2 litres/kg) was due to the accumulation of the drug in the body tissues. The maximum plasma concentration (4.1 +/- 1.7 micrograms/ml) after oral administration of 85 to 100 mg spiramycin/kg bodyweight was reached after 3.7 +/- 0.8 hours and the half-life of the elimination phase was 6.0 +/- 2.4 hours. The oral bioavailability was 45.4 +/- 23.4 per cent. Ad libitum feeding of a diet containing 2550 mg spiramycin/kg produced a steady state concentration of 0.96 +/- 0.27 micrograms/ml. This plasma concentration would provide a potentially therapeutically effective blood concentration against Mycoplasma species, Streptococcus species and Staphylococcus species.

Aust Vet J 1992 Jun;69(6):126-8

Successful treatment of mycoplasmosis in layer chickens with single dose therapy.

Arzey GG, Arzey KE

New South Wales Agriculture, Windsor.

The efficacy of treatment with single dose administration of 5 drugs at different dosages to layer hens naturally infected with Mycoplasma gallisepticum was studied. The drugs were tiamulin, which was administered orally, tylosin (parenterally and orally), spiramycin (orally), long-acting oxytetracycline (parenterally) and tylosindihydrostreptomycin (parenterally). Cure

was assessed by the absence of nasal discharge. The cure rate was significantly higher (P less than 0.05) in treated hens than in untreated hens, as early as 1 day after treatment. Remission for 33 days was achieved in 60% of hens treated with 100 mg oxytetracycline, in 100% of hens treated with 100 mg or 200 mg spiramycin, in 92% and 85% of hens treated with 100 mg tylosin, parenterally and orally, and in 89% and 88% of birds given 100 mg tiamulin and tylosin-dihydrostreptomycin, respectively.

J Vet Pharmacol Ther 1992 Mar;15(1):53-61

Pharmacokinetics of spiramycin after intravenous, intramuscular and subcutaneous administration in lactating cows.

Sanders P, Moulin G, Guillot P, Dagorn M, Perjant P, Delepine B, Gaudiche C, Mourot D

Ministere de l'Agriculture et de la Foret, Centre National d'Etudes Veterinaires et Alimentaires, Fougeres, France.

Spiramycin is a macrolide antibiotic that is active against most of the microorganisms isolated from the milk of mastitic cows. This work investigated the disposition of spiramycin in plasma and milk after intravenous, intramuscular and subcutaneous administration. Twelve healthy cows were given a single injection of spiramycin at a dose of 30,000 IU/kg by each route. Plasma and milk were collected post injection. Spiramycin concentration in the plasma was determined by a high performance liquid chromatography method, and in the milk by a microbiological method. The mean residence time after intravenous administration was significantly longer (P less than 0.01) in the milk (20.7 +/- 2.7 h) than in plasma (4.0 +/- 1.6 h). An average milk-to-plasma ratio of 36.5 +/- 15 was calculated from the area concentration-time curves. Several pharmacokinetic parameters were examined to determine the bioequivalence of the two extravascular routes. The dose fraction adsorbed after intramuscular or subcutaneous administration was almost 100% and was bioequivalent for the extravascular routes, but the rates of absorption, the maximal concentrations and the time to obtain them differed significantly between the two routes. Spiramycin quantities excreted in milk did not differ between the two extravascular routes but the

latter were not bioequivalent for maximal concentration in the milk. However, the two routes were bio-equivalent for the duration of time the milk concentration exceeded the minimal inhibitory concentration (MIC) of various pathogens causing infections in the mammary gland.

Res Vet Sci 1991 May;50(3):301-7

Distribution of penicillin-G and spiramycin to tissue cages and subcutaneous tissue fluid in calves.

Bengtsson B, Franklin A, Jacobsson S, Luthman J, Horn af Rantzien M

Department of Cattle and Sheep Diseases, Swedish University of Agricultural Sciences, Uppsala.

Antibacterial drug concentrations in serum, tissue cage fluid (TCF) and subcutaneous tissue fluid (SF), sampled either by filter paper discs or by microcapillaries, were measured after single intramuscular injections of potassium penicillin-G (KPG), procaine penicillin-G (PPG) and spiramycin adipate in calves. Concentration-time curves had essentially similar profiles in serum and SF, but peak levels were lower and occurred later in SF. From approximately four hours after drug administration, penicillin-G levels in SF were similar to levels in serum after KPG as well as after PPG administration. Elimination half-life (t1/2) of penicillin-G in serum was similar to t1/2 in SF after PPG administration but was longer in SF than in serum after KPG administration. Spiramycin concentrations were higher in SF than in serum and the t1/2 of spiramycin in SF was longer than in serum. For all three drugs, the t1/2 was longer in TCF than in serum and concentration-time curves in TCF were characterised by a slow rise and decline. The two methods of sampling SF, by filter paper discs and by microcapillaries, gave similar but not identical results. Penetration into SF and TCF, measured as the total area under curve ratio, was better for spiramycin than for penicillin-G, but the latter drug had a higher penetration ratio to TCF in the first 12 hours.

J Vet Pharmacol Ther 1990 Mar;13(1):7-14

Spiramycin concentrations in plasma and genital-tract secretions after intravenous administration in the ewe.

Cester CC, Laurentie MP, Garcia-Villar R, Toutain PL

INRA Pharmacology-Toxicology Station, Toulouse, France.

Uterine infections are associated with reduced fertility in ruminant species. Spiramycin is a macrolide antibiotic potentially active against most of the microorganisms isolated from secretions of infected genital tracts. The present work investigated the ability of systemically administered spiramycin to enter genital secretions, by determining the disposition kinetics of the antibiotic in both plasma and uterine genital secretions. Five healthy ovariectomized ewes were given a single intravenous (i.v.) injection of spiramycin, at a dose of 20 mg/kg. Plasma and genital secretion samples were collected at predetermined intervals for 5 days post-injection. Blood was collected from the jugular vein while mucus was obtained by inserting polyurethane sponges into the vagina. The spiramycin concentration peak in genital-tract secretions was obtained 2.53 +/- 0.63 h after the i.v. administration. The mean residence time was significantly longer (P less than 0.01) in the mucus (18.31 +/- 3.24 h) than in plasma (6.99 +/- 2.53 h). An average mucus to plasma ratio of 7.87 +/- 3.00 was calculated from the area under concentration-time curves covering the period under study. These data indicate that after systemic administration to ewes, spiramycin is rapidly found in genital-tract secretions, at concentrations which are sufficiently high and persistent to suggest its use in the treatment of post-partum uterine infections.

J Antimicrob Chemother 1988 Jul;22 Suppl B:179-82

Efficacy of intravenous spiramycin in the treatment of severe Legionnaires' disease.

Mayaud C, Dournon E, Montagne V, Denis M, Rossert J, Akoun G

Chest Department, Hopital Tenon, Paris, France.

Spiramycin is a 16-membered macrolide that has been shown in cell and animal models to be active against Legionella spp. The activity of the injectable form of spiramycin was evaluated in the treatment of severe Legionnaires' disease in seven immunocompromised and three previously healthy patients. Seven of the ten patients were cured. Three patients died primarily from the

underlying disease or from intercurrent complications. This result and the better tolerance of spiramycin compared with 14-membered macrolides suggest that spiramycin may be a suitable alternative to erythromycin for the treatment of Legionnaires' disease.

Schweiz Arch Tierheilkd 1984 Sep;126(9):479-87

[Efficacy of spiramycin treatment in subclinical and clinically manifested Staphylococcus aureus mastitis in the udder of lactating cows].

[Article in German]

Ziv G, Storper M

Schweiz Arch Tierheilkd 1981 Sep;123(9):443-53

[Therapeutic efficacy of penicillin, ampicillin and spiramycin following parenteral administration in calves].

[Article in French]

Schifferli D, Nicolet J, Wanner M

Ann Rech Vet 1981;12(3):317-20

Enhancement of spiramycin concentration by bromhexin in the bovine nasal secretions.

Escoula L, Larrieu G, Camguilhem R

Intramuscular injection of bromhexin (Quentan) results in increased bioavailability of spiramycin in nasal secretions. In the presence of a mucolytic agent, the area under the curve calculated according to spiramycin concentrations found in nasal secretions increases by 6%, 41% and 32% respectively in the course of three days of treatment. This potentiation reveals the interest involved in administering a combination of bromhexine and antibiotics in the treatment of infectious diseases of the respiratory tract.

J Dairy Sci 1975 Jun;58(6):938-46

Distribution of labeled antibiotics in different components of milk following intramammary and intramuscular administrations.

Ziv G, Rasmussen F

In crossover trials, four lactating goats were given intramammary infusions and intramuscular

injections of radioactivelabeled benzylpenicillin, spiramycin, chloramphenicol, dihydrostreptomycin, and tetracycline. Milk was collected after each treatment and the antibiotic contents in whole milk, skim milk, and whey were determined microbiologically and radiochemically and in cream and casein by radiochemical assay methods. Uptake of antibiotics by cream and casein was highly dependent on drug concentration, increasing with the decrease in antibiotic content in whole milk. Lipophilic chloramphenicol and tetracycline were concentrated in cream to a higher degree than the less lipophilic benzylpenicillin and dihydrostreptomycin. Antibiotic uptake by cream separated from whole milk after intramuscular injection was higher than after intramammary infusion. Antibiotic uptake by casein was independent of the route of administration and was highest for dihydrostreptomycin and tetracycline and lowest for benzylpenicillin.

Minerva Med 1972 Nov 21;63(83):4525-32

[Absorption and urinary elimination of spiramycin following its i.m. administration].

[Article in Italian]

Scalvini A, Del Monte A, Mantovani G, Pollini C, Schioppacassi G, Morvillo E, Curcio L

Minerva Med 1972 Jul 11;63(53):2885-92

[Local tolerance of an intramuscular spiramycin preparation].

[Article in Italian]

Curcio L, Scalvini A, Ferrari-Bravo A

World Health Organ Tech Rep Ser 1998;879:i-vi, 1-73

Evaluation of certain veterinary drug residues in food. Forty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives.

This report presents the conclusions of a Joint FAO/WHO Expert Committee convened to evaluate the safety of residues of certain veterinary drugs in foods and to recommend maximum levels for such residues in food. The first part of the report considers standards for the performance of studies, residues at the injection site, and several initiatives to promote

transparency of the process for setting Maximum Residue Limits (MRLs). A summary follows of the Committee's evaluations of toxicological and residue data on a variety of veterinary drugs: two anthelminthic agents (moxidectin and tiabendazole), eight antimicrobial agents (ceftiofur, danofloxacin, dihydrostreptomycin, streptomycin, enrofloxacin, flumequine, gentamicin and spiramycin), one glucocorticosteroid (dexamethasone), and two insecticides (cyfluthrin and fluazuron). Annexed to the report are a summary of the Committee's recommendations on these drugs, including Acceptable Daily Intakes and MRL's and further toxicological studies and other information required.

Am J Vet Res 1986 Apr;47(4):804-7

Concentrations of penicillin, streptomycin, and spiramycin in bovine udder tissue liquids.

Franklin A, Horn af Rantzien M, Obel N, Ostensson K, Astrom G

Concentrations of benzylpenicillin and spiramycin adipate were determined in bovine plasma and milk and in lymph draining the udder tissue after IM or IV administration. Combined benzylpenicillin and dihydrostreptomycin sulfate concentrations were also determined in the same fluids after intramammary injection. A superficial parenchymal lymph vessel, afferent to the supramammary lymph gland of the left quarters, was cannulated with a polythene catheter from which the lymph was allowed to drain freely. After injections of 9.5 mg of benzylpenicillin/kg of body weight IM, a mean peak concentration (PC) in lymph (3.7 micrograms/ml), constituting 77% of the PC in plasma (4.8 micrograms/ml), was obtained 0.5 to 1 hour after PC in the plasma. The benzylpenicillin lymph concentration was close to that in plasma for about 7 hours after injection. Thereafter, the benzylpenicillin lymph concentration continued to exceed that in plasma, but not that in milk. After IV administration of spiramycin adipate, the lymph concentration was almost identical to that in plasma. After intramammary injection of procaine benzylpenicillin (400 mg), in combination with the same amount of dihydrostreptomycin sulfate, into 2 udder quarters each, mean PC in the lymph of 3.5 micrograms/ml and 8.4 micrograms/ml, respectively, were obtained 6 hours after injection. In plasma, the mean PC of benzylpenicillin (0.07 micrograms/ml) and of dihydrostreptomycin sulfate (0.85 micrograms/ml) were

obtained after 4 and 6 hours, respectively. In milk from the nontreated quarters, a mean concentration of 5 ng of benzylpenicillin/ml was obtained, whereas dihydrostreptomycin sulfate (greater than or equal to 0.3 microgram/ml) was not detected.

Br Poult Sci 1990 Sep;31(3):661-75

Residues of macrolide antibiotics in eggs following medication of laying hens.

Roudaut B, Moretain JP

Ministere de l'Agriculture, Centre National d'Etudes Veterinaires et Alimentaires, Laboratoire des Medicaments Veterinaires Javene, Fougeres, France.

1. The elimination kinetics of four macrolide antibiotics (tylosin, erythromycin, spiramycin and josamycin) in eggs were determined separately for albumen and yolk after oral administration through either drinking water or diet or after intramuscular injection. 2. Residues were assayed by a plate diffusion technique in cylinders with Micrococcus luteus as the test-organism. 3. Drug excretion was usually over a longer time in the yolk. Spiramycin was the most highly excreted in the egg whereas seven to eight times less tylosin and erythromycin was transferred. The conditions for the use of macrolide antibiotics in laying hens are discussed.

Vet Q 1983 Jul;5(3):114-21

Penetration of some antibiotics into the lacrimal fluid of sheep.

Nouws JF, Konig CD

Antibiotic concentrations were determined in the lacrimal fluid of sheep following subcutaneous application of penicillin/dihydrostreptomycin into the lower eyelid, and intramuscular administration of spiramycin base, tiamulin, and oxytetracycline formulations. The penetration of penicillin and dihydrostreptomycin into the lacrimal fluid was poor. The spiramycin and tiamulin concentrations in the lacrimal fluid were 10- and 4-fold higher than in the serum. The peak spiramycin concentration in the lacrimal fluid was 3.4 +/- 0.8 microgram/ml at 8 h post injection (p.i.) and the drug could be detected at least 72 h p.i. For tiamulin and oxytetracycline (OTC) peak concentrations of 1.53 +/- 0.70 and 1.88 +/- 1.9 micrograms/ml, respectively,

were achieved in the lacrimal fluid and these drugs could be detected 25 to 30 h p.i. The OTC and tiamulin concentration-time curves for lacrimal fluid and serum were parallel, whereas for the spiramycin appearance in the lacrimal fluid was delayed.

J Chromatogr 1985 Nov 8;344:275-83

Automated high-performance liquid chromatographic determination of spiramycin by direct injection of plasma, using column-switching for sample clean-up.

Dow J, Lemar M, Frydman A, Gaillot J

A fully automated high-performance liquid chromatographic method is described for the determination of spiramycin 1 in plasma. First, 1 ml of plasma is diluted with 1.5 ml of 4% acetonitrile containing spiramycin 2 as internal standard, and 1 ml is then injected via an automatic sampling unit. A pneumatic valve, which is remote-controlled by the programmable timer of an integrator, switches the sample, initially injected onto a precolumn for sample clean-up, to an analytical column for sample separation. This method was compared with a microbiological assay and has been successfully applied to pharmacokinetic studies on spiramycin in humans.

Vet Res 1996;27(4-5):479-89

The use of an experimental metritis model to study antibiotic distribution in genital tract secretions in the ewe.

Cester CC, Beguin JC, Toutain PL

Unite associee Inra de physiopathologie et toxicologie experimentales, Ecole nationale veterinaire, Toulouse, France.

The influence of experimentally-induced metritis on spiramycin disposition in genital secretions was investigated in six ovariectomized ewes. A crossover study design was selected to compare control with metritis pharmacokinetics. A clinically-relevant metritis was obtained under progestagen priming by inoculation in the uterine lumen of a bacterial suspension of Actinomyces pyogenes and Fusobacterium necrophorum Ewes were given a single iv administration of

spiramycin at a dose of 20 mg.kg-1. Plasma and genital secretions were regularly sampled up to 96 h post-injection and spiramycin activity was measured using a microbiological method.

Experimental metritis did not affect plasma spiramycin disposition and the antibiotic was more concentrated and lasted longer in genital secretions than in plasma regardless of the animal's state of health. The area under the concentration-time curve of spiramycin in genital secretions was twofold higher ($p < 0.05$) in infected than in healthy ewes (3361 +/- 112 micrograms.h.g-1 and 175 +/- 41 micrograms.h.g-1 respectively). The mean residence time of spiramycin in genital secretions was significantly longer in diseased ewes (32 +/- 4 h) than in control ewes (23 +/- 4 h). The maximum concentration of spiramycin in genital secretions was equal for both studies but occurred later in infected ewes (2.7 +/- 1.0 h versus 8.6 +/- 4.5 h). It was concluded that a uterine infection had a marked influence on the disposition of spiramycin in genital tract secretions and that this uterine infection model in the ewe merits consideration for the study of drug treatments of genital tract infection.

J Pharm Sci 1992 Jan;81(1):33-6

Effect of sexual steroid hormones on spiramycin disposition in genital tract secretions of the ewe.

Cester CC, Dubech N, Toutain PL

INRA Station de Pharmacologie-Toxicologie BP 3, Toulouse, France.

The present work investigated the influence of sexual steroid compounds (estradiol 17 beta and fluorogestone) on antibiotic passage across the uterine barrier. Five healthy and mature ewes, with controlled hormonal impregnation, were given a single iv injection of spiramycin, a macrolide antibiotic, at a dose of 64,000 IU/kg. Plasma and uterine secretions were regularly sampled before the injection and for 30 h post-injection. Blood was collected from the jugular vein and uterine secretions were obtained by uterine flushing with a sterile saline solution containing 0.2% inulin. Spiramycin was concentrated in the uterine secretions, whatever the hormonal status; the secretions-to-plasma ratio was 4.68 +/- 1.88 under estrogen priming and 2.68 +/- 0.91 under progestagen priming. The area under the concentration-time curve (AUC) and the

mean residence time (MRT) were significantly higher (p less than 0.001) in uterine secretions than in plasma. The AUC in uterine secretions was significantly higher (p less than 0.05) under estrogen priming (439.07 +/- 241.25 IU.h/mL) than under progestagen priming (141.41 +/- 89.37 IU.h/mL). The spiramycin MRTs in uterine secretions were 11.92 +/- 4.08 and 12.06 +/- 3.35 h for both estrogens and progestagen treatment, respectively. These experiments demonstrate that estrogens increase uterine bioavailability, but not the residence time, of spiramycin when administered by a systemic route.

J Antimicrob Chemother 1988 Jul;22 Suppl B:77-85

Synergy between spiramycin and metronidazole in the treatment of polymicrobial infections.

Brook I

Uniformed Services University for the Health Sciences, Bethesda, Maryland 20814.

The in-vitro and in-vivo activity of metronidazole and spiramycin, singly or in combination, was tested in the eradication of infection caused by Bacteroides spp. alone and in combination with Neisseria gonorrhoea, Staphylococcus aureus, Streptococcus pyogenes or Str. faecalis. The in-vitro tests consisted of determinations of the MICs with or without the addition of a constant amount of the other antimicrobials. The MICs of metronidazole for B. melaninogenicus, B. fragilis and B. bivius were significantly reduced by the addition of 0.125 mg/l spiramycin. The in-vivo tests were carried out in mice and consisted of measurements of the effects of the antimicrobial agents on the bacterial contents of abscesses induced by subcutaneous injection of bacterial suspension. Combined therapy of mixed infections showed further significant reduction of the numbers of Bacteroides spp. in seven of 12 combinations and of the aerobic and facultative bacteria in four of 12 combinations. Furthermore, a reduction in the number of facultative anaerobes was noted in mixed infections with Bacteroides spp. which were treated with metronidazole alone. The synergy in vitro and in vivo between metronidazole and spiramycin may have important clinical implications in the treatment of polymicrobial aerobic-anaerobic infections.

Liquid chromatography of spiramycin on poly(styrene-divinylbenzene).

AU: Liu,-L; Roets,-E; Hoogmartens,-J
AD: Katholieke Univ. Leuven, Lab. Farm. Chem. Anal. Geneesmiddelen, Fac. Farm. Wetenschappen, 3000 Leuven, Belgium
CP: Belgium

SO: **J-Chromatogr,-A. 7 Mar 1997; 764(1): 43-53**
JN: Journal-of-Chromatography,-A
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CO: JCRAEY
PY: 1997
LA: English
PT: Journal

AB: Spiramycin and related compounds were separated on a 8 micro m PLRP-S column (25 cm x 4.6 mm i.d.) operated at 60degreeC, with acetonitrile/0.2M-phosphate buffer of pH 9/H2O (37:5:58) as mobile phase (1 ml/min) and detection at 232 nm. The robustness of the method was evaluated by factorial design. The peak area RSD was 0.8% of the main component, and the limit of detection was 0.04% for an injection of 20 micro g spiramycin.

IA: spiramycin-A: [8025-81-8]. sepn. of, and related compounds, by LC, stationary phases for
IC: chromatography,-liquid-C: stationary phases for, poly(styrene - divinylbenzene) as
SC: G-Pharmaceutical-Analysis
SS: 10300
CR: B3

Symposium on pharmacology, antibacterial spectrum and clinical efficacy.-- **J. Antimicrob. Chemother. 22, Suppl. B, 1-213, 1988**

124:143870
Determination of spiramycin and tylosin in milk by HPLC.
Sorensen, L. K.; Hansen, P. (Steins Laboratorium, Brorup 6650, Den.). Int. Dairy Fed. Spec. Issue, 9505(Symposium on Residues of Antimicrobial Drugs and Other Inhibitors in Milk, 1995), 302-3 (English) 1995.

124:85172
Enzyme immunoassay for the detection of spiramycin in raw milk.
Albrecht, Ute; Hammer, P.; Heeschen, W. (Federal Dairy Research Centre, Institute for Hygiene, Kiel 24103, Germany). Int. Dairy Fed. Spec. Issue, 9505(Symposium on Residues of Antimicrobial Drugs and Other Inhibitors in Milk, 1995), 258-9 (English) 1995.

121:56086
Confirmatory analysis for spiramycin residue in bovine muscle by liquid chromatography/particle beam mass spectrometry.
Sanders, P.; Delepine, B. (Cent. Natl. Etud. Vet. Aliment., Minist. Agicul. Foret, Fougeres 35300, Fr.). Biol. Mass Spectrom., 23(6), 369-75 (English) 1994

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Determination of spiramycin and neospiramycin in plasma and milk of lactating cows by reversed-phase high-performance liquid chromatography.
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