Figure 1. Mean Serum concentrations following the administration of 25 mg/kg ibuprofen in lactating dairy cows (n = 6).

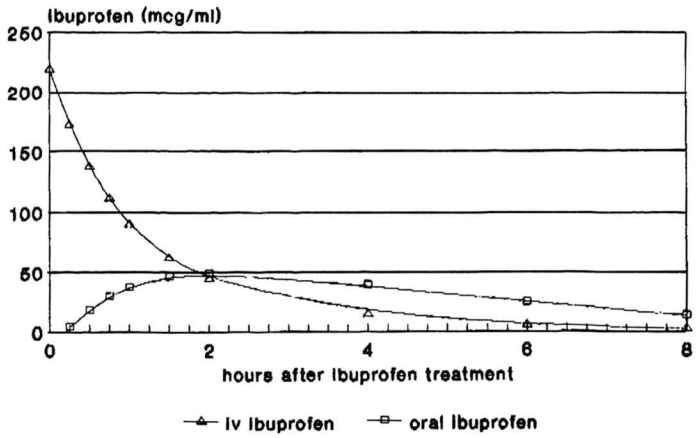

Table 1. Pharmacokinetic parameters of ibuprofen after an intravenous dose of 25 mg/kg in lactating dairy cows (mean ± standard deviation, n = 6).

Ibuprofen dosage, 25 mg/kg			
Intravenous		Per os	
Parameter	Mean ± S.D.	Parameter	Mean ± S.D.
VD (SS), L/kg	0.146 ± 0.018	Lag time, hrs	0.244 ± 0.085
CL (B), ml/kg/hr	87.7 ± 12.5	$t_{½absorp}$, hrs	0.881 ± 0.420
$t_{½(dist)}$, hrs	0.557 ± 0.082	F	0.912 ± 0.107
$t_{½(elim)}$, hrs	1.57 ± 0.14	AUMC, mcg/ml*hr^2	1030 ± 141
AUC, mcg/ml*hr	297 ± 44	AUC, mcg/ml*hr	268 ± 30
MRT, hrs	1.52 ± 0.15	MRT, hrs	3.87 ± 0.60

tration of ibuprofen, but most levels were below the limit of quantification.

Endotoxin studies

Rectal temperature, heart rate, respiratory rate and neutrophilic band cell counts increased significantly ($p < 0.05$) in the saline treated groups as compared to the ibuprofen treated group. Eosinophil numbers, serum phosphorous, sodium, and total carbon dixoide were significantly decreased ($p < 0.05$) in the saline treated group as compared to the ibuprofen group. Indices of renal, hepatic, and red blood cell damage were not increased following ibuprofen administration.

Discussion

Ibuprofen exhibits a pharmacokinetic profile that would be consistent with use in lactating dairy cows. Ibuprofen concentrations in milk were very low. This, in addition to the relatively short half-life of elimination of ibuprofen in dairy cows, would suggest that ibuprofen treated cows would present minimal risk of residue to consumers when used with appropriate caution.

Ibuprofen influenced the clinical course of endotoxin-induced mastitis. Ibuprofen did not appear to influence udder swelling, udder edema, or milk composition following endotoxin-induced mastitis. One 25 mg/kg dose of ibuprofen was well tolerated by lactating Holstein cows and no untoward effects were observed. **Ibuprofen is not currently approved for use in any food animal species.**

Challenge Model for *Escherichia coli* in the Colostrum Deprived Calf

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There is an increasing number of oral immunoglobulin and probiotic preparations commercially available for the bovine neonate. Advertisements for calf immunosupplements may be vague, confusing, or even misleading. Early ingestion of high quality colostrum provides the best defense against calf colisepticemia. Problems associated with modern management practices, the existence of low quality colostrum, and the relative economic significance of certain calves may justify the additional investment of oral immunoglobulins at birth. Objective information needed to evaluate the efficacy and cost effectiveness of these products is currently unavailable. Controlled challenge studies provide one mechanism for evaluation of these products.

In order for challenge studies to provide meaningful information they must produce consistent and reproducible results over time. The model developed by the authors involves three treatment groups: colostrum deprived calves, colostrum fed calves, and colostrum deprived calves fed one of the colostrum supplements to be evaluated. Colostrum deprived calves from attended parturitions are removed from their dam prior to suckling, transported to a

sanitary research facility, processed (identified, weighed, and bled), and fed either the product to be evaluated dissolved in 2 l of water or a non-medicated kid milk replacer within 2-4 hours of age. Colostrum fed calves are allowed to suckle the cow and stay with the cow for 4 hours for the mothering benefit and to encourage maximum absorption of colostral antibody. They are then similarly transported and processed.

Calves are inoculated orally at 15-18 hours of age with an 11 hour culture of 10^9 invasive JL-9 *E. coli* (078:NM:F41). Cultures are grown in N-ZAB broth, a minimal media composed of casein derived amino acids, on a 37°C shaker water bath. Calves receive 20 ml of the culture *per os* with a 2-3 pint feeding of milk replacer. Rectal temperature, heart rate, respiratory rate, fecal consistency, joint and umbilical tenderness, and appetite are monitored twice daily using a modified form of the foal sepsis scoring system developed at the University of Florida. Blood samples collected at 0, 24, and 120 hours. Some groups of calves are not necropsied until 240 hours to allow time for secondary septic arthritis to develop; an additional sample is collected in these calves at 240 hours (pre-necropsy).

Serum samples are used to determine immunoglobulin levels using single radial immunodiffusion plates[1]. Blood samples are submitted to a clinical pathology laboratory for CBC, differential cell count, and fibrinogen. Animals developing signs of septicemia are humanely euthanatized and promptly necropsied.

Necropsies include gross examination of body cavities and serosal surfaces for evidence of sepsis; bacterial cultures from the heart, liver, spleen, and two joints; and histological examination of the adrenal glands. Bacterial isolates are identified using biochemical test strips.[2] Adrenal histological samples are scored by a pathologist on a scale of 0-5 based on tissue congestion, hemorrhage and necrosis.

Trials using this model yield consistent and significant differences in morbidity and mortality between colostrum fed and colostrum deprived calves. Several commercial products evaluated have also been shown to provide substantial protection to the neonate. This model may not simulate the cumulative environmental bacterial challenge the colostrum deprived calf faces daily, but the controlled environment in this model minimizes the extraneous variables present in field studies that make direct comparisons difficult.

[1]*SRID Kits, VMRD Inc., Pullman, Washington 99163.*
[2]*API 20E® System, Analytab Products, Sherwood Medical, Plainview, New York 11803.*

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Protective Effects of a Commercial Cheese Whey Derived Immunoglobulin Product[1] Against Septicemic *Escherichia coli* Challenge in Colostrum Deprived Calves

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A major cause of worldwide calf mortality is coliseptic-emia secondary to failure of passive transfer of colostral antibody. Several new products[1,2,3,4] have been marketed in recent years to combat this problem. These products often consist of immunoglobulins derived from cheese whey or colostral whey. Usefulness of some of these products has been challenged due to low total immunoglobulin (Ig) content. The purpose of this study was to use the JL-9 *Escherichia coli* model (described previously) to evaluate a commercial cheese whey-derived product that has been marketed for calves since 1987[1].

Colostrum fed (N = 7) and colostrum deprived calves (N = 10) were fed and processed as described in the previous abstract. Calves receiving the product (N = 6) to be evaluated (Colostrx™) were colostrum-deprived; between 2 and 4 hours of age they received a 454 gram bag of Colostrx™ (containing no less than 24 grams of total bovine IgG) mixed as per package directions. 10^9 virulent *E. coli* in 20 ml of culture medium were administered orally to all three groups of calves between 15 and 18 hours of age. Blood samples were taken prior to product or control feeding and compared to 24 hour and pre-necropsy samples.