J. Dairy Sci. 91:1347–1360
doi:10.3168/jds.2007-0608

A Meta-Analysis of the Impact of Monensin in Lactating Dairy Cattle. Part 2. Production Effects

T. F. Duffield,*[1] A. R. Rabiee,†‡ and I. J. Lean†‡
*Department of Population Medicine, University of Guelph, Guelph, Ontario, N1G 2W1, Canada
†Strategic Bovine Services, PO 660, Camden, New South Wales, Australia
‡University of Sydney, Camden, New South Wales, Australia

ABSTRACT

A meta-analysis of the impact of monensin on production outcomes in dairy cattle was conducted using the 36 papers and 77 trials that contained eligible data. Statistical analyses were conducted in STATA and included a consideration of fixed or random effects models, assessment of publication bias, and impact of influential studies. Meta-regression was used to investigate sources of heterogeneity of response. There were 71 trials containing data from 255 trial sites and 9,677 cows examining milk production and composition. Monensin use in lactating dairy cattle significantly decreased dry matter intake by 0.3 kg, but increased milk yield by 0.7 kg and improved milk production efficiency by 2.5%. Monensin decreased milk fat percentage 0.13%, but had no effect on milk fat yield; however, there was significant heterogeneity between studies for both of these responses. Milk protein percentage was decreased 0.03%, but protein yield was increased 0.016 kg/d with treatment. Monensin had no effect on milk lactose percentage. Monensin increased body condition score by 0.03 and similarly improved body weight change (0.06 kg/d). Analysis of milk fatty acid profile data indicated that monensin was associated with a reduction of short-chain fatty acids (from 1 to 12% reduction) and stearic acid (–7.8%). The impact of monensin on linoleic and linolenic acids was variable, but monensin significantly increased conjugated linoleic acid (22%). Meta-regression of the effect of monensin on milk component percentages and yields indicated an influence of delivery method, stage of lactation, dose, and diet. Increasing concentrations of C18:1 in the diet enhanced the effect of monensin on decreasing milk fat yield, whereas increasing the rumen peptide balance increased the effect of monensin on milk protein yield. These findings indicate a benefit of monensin for improving milk production efficiency while maintaining body condition. The effect of monensin on milk fat percentage and yield was influenced by diet.
Key words: monensin, dairy cattle, meta-analysis, production

INTRODUCTION

Monensin is a carboxylic polyether ionophore provided to cattle, orally, as a sodium salt. Ionophores modify the transport of ions across bacterial cell walls and selectively inhibit gram-positive bacteria rather than gram-negative bacteria because of differences in bacterial cell wall structure. The resulting shift in rumen bacterial populations results in increased efficiency of energy metabolism and improved nitrogen metabolism, and modifies the risk of bloat (Lowe et al., 1991) and lactic acidosis (Bergen and Bates, 1984).

There have been many papers published on the effects of monensin in lactating dairy cattle. Approvals for use of monensin in lactating dairy cattle were obtained in Canada and the United States and the product has been available for lactating dairy cattle for several years in many other countries including Mexico, Australia, and New Zealand. The effects of monensin on milk production and components have not been consistent. Some studies reported milk yield increases (Hayes et al., 1996; Duffield et al., 1999; Phipps et al., 2000), but others have not (Melendez et al., 2006b; Zahra et al., 2006). Factors that may modify responses to monensin on milk production include herd (Lean et al., 1994), BCS (Duffield et al., 1999), and genetic merit (Van der Werf et al., 1998; Granzin and Dryden, 1999). Similar inconsistencies have been observed for the impact of monensin on DMI. Sauer et al. (1989) reported a decrease in DMI, whereas others reported no effect (Van der Werf et al., 1998; Phipps et al., 2000; Odongo et al., 2007). Perhaps the most variable outcome is the impact of monensin on milk fat percentage. There is both lack of effect (Duffield et al., 1999) and variable magnitude of response (Erasmus et al., 1993; Phipps et al., 2000; Bell et al., 2006) that may be influenced by dietary factors (Bell et al., 2006; Alzahal et al., 2008).

Received August 12, 2007.
Accepted January 10, 2008.
[1]Corresponding author: tduffiel@uoguelph.ca

There have been several excellent, essentially qualitative, literature reviews published on the effects of ionophore use in dairy cattle (McGuffey et al., 2001; Ipharraguerre and Clark, 2003). In both reviews, authors attempted to measure summative responses of ionophores on production. Both considered all studies with equal weight, despite a wide variation in trial size, did not adequately account for measures of dispersion, and did not give analytic consideration to heterogeneity. Meta-analysis can be used to quantitatively summarize effects across studies with appropriate weighting given to study size and investigate factors explaining potential heterogeneity of response.

Given the large body of literature on monensin treatment in lactating dairy cattle, an investigation of monensin by meta-analysis would be helpful in describing its impact and in evaluating differences in response. The objective was to conduct a series of meta-analyses on the effects of monensin on dairy cow metabolism, health, production responses, and reproductive performance.

MATERIALS AND METHODS

Methods of the literature search and screening process were described in the companion paper (Duffield et al., 2008). Briefly, an extensive literature search of scientific electronic search engines and reports of trials was conducted. Following rigorous screening for appropriate subject matter, quality of trial design, and adequate statistical reporting, data were extracted for submission to meta-analysis. For all of the meta-analyses including measurement of effects other than production such as metabolism, health, and reproduction, the screening process yielded 59 papers or reports that met the criteria for inclusion.

There were 36 papers available for evaluating the impact of monensin on production outcomes. A template for data extraction was drafted that included mean, standard error, and number of cows per treatment group. If the standard error was not published, it was either estimated by calculation from reported *P*-values or other measures of variance, or these data were not included. In all cases in which no measure of variance could be extracted or calculated, attempts were made to gather these data from the corresponding authors. These data were utilized if the measures were available. Other factors that might influence an outcome were included in the data extraction process including DIM at treatment start, stage of lactation, treatment dose, duration of treatment, method of delivery of monensin [in-feed, topdress, or controlled release capsule (**CRC**)], breed of cattle, and diet type (pasture, component, or TMR).

Outcomes that were analyzed included DMI, milk yield, milk production efficiency, milk fat percentage, milk fat yield, milk protein percentage, milk protein yield, milk lactose percentage, BCS, BW change, and milk fatty acid profiles. A minimum of 6 trials for any outcome was arbitrarily set as the threshold requirement for assessing the impact of monensin on any production outcome. Sufficient data were available to analyze the effect of monensin on the following fatty acids: C6:0, C8:0, C10:0, C12:0, C14:0, C16:0, C18:0, total C18:1, *trans* C:18:1, total C18:2, conjugated linoleic acid (**CLA**), and total C18:3.

A meta-analysis was conducted on the extracted production outcomes using Stata software (Intercooled Stata V. 9.0, College Station, TX). Guidelines for conducting appropriate meta-analyses were largely based on meta-analytic techniques described by Dohoo et al. (2003). A fixed effect model was first conducted for each production outcome to estimate the effect size (**ES**), 95% confidence intervals (**CI**), and statistical significance of effect size. Heterogeneity was assessed with the Cochran's Q statistic chi-square test (Egger et al., 2001). If this was significant, a random effects model was used. Degree of heterogeneity was assessed by use of the I^2 statistic (Higgins et al., 2003). The statistical procedures used to detect and quantify the level of heterogeneity are described in the companion paper (Duffield et al., 2008). If there was evidence of heterogeneity among trials, a random effects model was used because the presence of heterogeneity violated the fixed-effects model assumption that the effect of monensin was common across studies (Dohoo et al., 2003). The random effects model assumed that the trial effects follow a normal distribution and the variance of the distribution was estimated from the data (DerSimonian and Laird, 1986). A meta-regression analysis was used to explore the sources of heterogeneity of response, using the individual ES for each trial as the outcome and the associated standard error as the measure of variance. Meta-regression was conducted by first screening individual variables such as dose, DIM at treatment start, delivery method, and diet type with a liberal *P*-value of 0.20. All variables meeting the first screening criteria were entered into a backward stepwise regression method until all remaining variables were significant at $P < 0.05$. All significant variables were screened for impacts of outliers and leverage. Forest plots were used to visually display the estimated effect size as measured by the standardized mean difference, 95% CI, and study weights. The study weights were calculated based on the inverse of their variance. This was calculated based on the inverse of the square of the standard error of the effect estimate for each trial (Higgins and Green, 2005). As a result more weight was assigned to larger studies with smaller standard errors than to smaller studies with larger standard errors. Publication bias was investigated both graphically with funnel plots and statistically using Begg's (Begg and Mazumdar, 1994) and Egger's tests (Egger et al., 1997). Finally, the influence of individual studies was assessed with the use of an influence plot to determine the impact of removing individual studies on the effect size estimate (Dohoo et al., 2003). For most significant outcomes, raw weighted mean differences were calculated to assess and report the average magnitude of response.

For studies that reported sufficient dietary information, the potential influence of dietary factors on ES estimates for monensin on milk fat and protein percentage were further analyzed using estimated ration measures derived from CPM-Dairy (Cornell-Penn-Miner Dairy Version 3.08.01; http://www.cpmdairy.com/Index.html), a program to evaluate and formulate dairy cattle rations. Details on the cattle and environment were entered into CPM-Dairy when provided or estimated based on values typical for the region. Amounts of feeds were entered into CPM-Dairy according to the DM details provided in the relevant papers. Feeds were selected from the CPM-Dairy feed library to match details on these provided. The final dietary composition was compared with details where provided in the relevant papers and forage quality was selected or adjusted to match the overall diet analysis. Fatty acid profiles were derived from the feedbank provided in CPM-Dairy, except for ryegrasses (*Lolium* spp.), which were estimated from values tested for this forage (I. J. Lean, unpublished data). Major ration components including ME and protein, peptide balance, NFC, NDF, starch, and estimates of C18:1, C18:2, and C18:3 intakes were extracted from CPM-Dairy, entered into the relational database, and then considered in meta-regression using STATA.

RESULTS

A summary of the 36 papers containing 77 trials with monensin and production outcomes used for the various production meta-analyses is presented in Table 1. Some studies contained a summary of a single trial conducted on multiple trial sites, whereas other studies reported multiple trials conducted at a single trial site. Table 2 summarizes all meta-analysis findings for each measure. Over all the trials analyzed, monensin decreased DMI by 2%, milk fat percentage by 3%, and milk protein percentage by 1%. Monensin treatment increased milk yield by 2%, protein yield by 2%, and improved BCS, BW change, and milk production efficiency. Monensin had no effect on milk fat yield or milk lactose percentage. Monensin had significant effects on milk fatty acid profiles (Table 3). Monensin decreased synthesis of short-chain carbon fatty acids and decreased the presence of stearic acid in milk. Monensin had a variable effect on both linoleic and linolenic acids, but increased CLA.

The impact of monensin on DMI and milk yield is presented in Figures 1 and 2, respectively. No heterogeneity of response or publication bias was noted for these outcomes or for milk production efficiency. The effect size estimates for milk fat percentage, and milk fat yield, milk protein percentage, and milk protein yield are presented in Figures 3 and 4, respectively. All of these models displayed moderate heterogeneity, and random effects models were utilized. Analysis indicated that publication bias was significant for milk fat percentage (data not shown). Smaller studies that reported milk fat percentage reductions from monensin treatment appeared more likely to be published than small studies that reported milk fat percentage increases. The BCS and BW analyses both contained significant heterogeneity (χ^2 = 28.49, df = 17, P = 0.039; χ^2 = 103.60, df = 34, $P < 0.001$, for BCS and BW, respectively). Publication bias was evident for BW change, but not for BCS. Estimates of the number of trials needed with opposite effects to reverse the findings for milk fat percentage and BW were 137 and 58, respectively.

A summary of the findings for meta-regression of variables that influenced ES estimates for monensin on production measures are in Table 4. The milk production response to treatment was increased by topdress delivery of monensin and in pasture-based herds. No variables significantly modified the reduction in DMI caused by monensin treatment. There were too few trials to adequately evaluate the effect of nutrition or herd effects on effect size of monensin on production efficiency. Topdress delivery of monensin increased milk protein yield, but decreased milk protein and fat percentages. The effect of monensin treatment on milk fat yield and percentage was less in early lactation compared with late lactation. Cows that were earlier in lactation at the completion of treatment had more BW change than cows later in lactation at the end of treatment. Pasture-based diets were associated with a greater effect of monensin on increasing milk fat yield. Delivery of monensin using the CRC resulted in a more positive effect of treatment on milk fat percentage (less reduction). Increasing the dose of monensin was associated with increasing BW change (either more gain or less loss).

Models for the impact of monensin on milk fatty acids mostly showed little heterogeneity; thus, fixed effects models were utilized. There was evidence of heterogeneity for the impact of monensin on *trans* C18:1, C18:2,

Table 1. Summary of papers used for meta-analysis of production effects of monensin in lactating dairy cow

Study	Trials, n	Monensin dose (mg/d)	Form of monensin	Total cows, n	Trial sites, n	Diet type	Dietary information?	DIM at treatment start	Outcomes measured
Schuler, 1988	2	200	Topdress	20	1	Component	Yes	Unknown	Milk yield, fat %, protein %, BW change, DMI
Sauer et al., 1989	2	208, 399	TMR	36	1	TMR	Yes	−7	Milk yield, fat %, protein %, lactose %, BW change, DMI
Lowe et al., 1991	1	320	CRC	368	6	Pasture	No	50	Milk yield, fat %, fat yield, protein %, protein yield
Wilson et al., 1992	2	320	CRC	120	1	Pasture	No	−38	Milk yield, fat %, protein %
Erasmus et al., 1993	2	200, 414	TMR	60	1	TMR	No	28	Milk yield, fat %, protein %, DMI
Moate, 1993	1	320	CRC	55	1	Pasture	No	105	Milk yield, fat %, fat yield, protein %, protein yield, lactose %
Abe et al., 1994	1	320	CRC	16	1	Pasture	No	2	Milk yield, BCS
Lean et al., 1994	1	320	CRC	908	6	Pasture, TMR	No	4	Milk yield, fat yield, protein yield
Hayes et al., 1996	1	320	CRC	661	3	Pasture	No	60	Milk yield, fat %, protein %
Beckett et al., 1998	1	320	CRC	1,109	12	Pasture	No	−40	Milk yield, fat %, fat yield, protein %, protein yield
Van der Werf et al., 1998	5	150, 300, 450	Topdress	218[1]	1	TMR	Yes	35	Milk yield, fat %, fat yield, protein %, protein yield, DMI, BW change, efficiency
Dhiman et al., 1999	2	250		48	1	TMR	Yes	66	Milk yield, fat %, fat yield, protein %, DMI, fatty acids
Duffield et al., 1999	3[2]	320	CRC	1,010	25	Component, TMR	No	−21	Milk yield, fat %, fat yield, protein %, Protein Yield
Granzin et al., 1999	4	150, 300, 320	Topdress, CRC	30	1	TMR	Yes	−14, −28	Milk yield, fat %, fat yield, protein %, protein yield, DMI, BW change, BCS
Green et al., 1999	2	320	CRC	52	1	TMR	Yes	−21	DMI
Phipps et al., 2000	5	150, 300, 450	Topdress	265[3]	1	TMR	Yes	56	Milk yield, fat %, fat yield, protein %, protein yield, DMI, BW change, efficiency
Ruiz et al., 2001	1	300	Topdress	30	1	Pasture[4]	Yes	126	Milk yield, fat %, fat yield, protein %, protein yield, DMI
VanderMerwe, 2001	1	300	Topdress	20	1	Pasture	Yes	90	Milk yield, fat %, protein %, BCS
Maas et al., 2002	2	320	CRC	60	1	Pasture	Yes	47	Milk yield, fat %, fat yield, protein %, protein yield
Broderick, 2004	2	237, 252	TMR	48	1	TMR	Yes	53	Milk yield, fat %, fat yield, protein %, protein yield, lactose %, DMI, BW change,
Green and Wilkinson, 2004	6	160, 311, 451, 178, 351, 505	TMR	1,031	9	TMR	No	−21	Milk yield, fat %, fat yield, protein %, Protein yield, lactose %, DMI, BW change, BCS, efficiency
Eifert et al., 2005	2	587, 508	TMR	16	1	TMR	Yes	30	Milk yield, fat %, Fat yield, protein %, protein yield, lactose %, DMI, BCS, efficiency
Erasmus et al., 2005	2	208, 217	TMR	60	1	TMR	Yes	−21	Milk yield, fat %, fat yield, protein %, protein yield, DMI, BW change, BCS
Gallardo et al., 2005	1	320	CRC	58	1	Pasture	Yes	−30	Milk yield, fat %, fat yield, protein %, protein yield, DMI, BCS
Granzin and Dryden, 2005	3	320, 299	CRC, Topdress	96	1		Yes	173, 91	Milk yield, fat %, fat yield, protein %, protein yield, lactose %, DMI, BW change
Bell et al., 2006	3	408, 486	TMR	90	1	TMR	Yes	213	Milk yield, fat %, fat yield, protein %, protein yield, lactose %, DMI, fatty acids
Eifert et al., 2006	2	587, 508	TMR	16	1	TMR	Yes	30	Fatty acids
Erasmus et al., 2006	2	354, 381	TMR	40	1	TMR	No	−21	Milk yield, fat %, protein %, DMI, BW change
Melendez et al., 2006a	1	320	CRC	580	1	TMR	Yes	−60	Milk yield
Zahra, 2006	1	320	CRC	182	1	TMR	Yes	−21	Milk yield, fat %, protein %, DMI
Melendez et al., 2006b	4	320	CRC	1,671	1	TMR	No	−25	Milk yield

Continued

Table 1 (Continued). Summary of papers used for meta-analysis of production effects of monensin in lactating dairy cow

Study	Trials, n	Monensin dose (mg/d)	Form of monensin	Total cows, n	Trial sites, n	Diet type	Dietary information?	DIM at treatment start	Outcomes measured
Odongo et al., 2007	1	458	458	24	1	TMR	Yes	92	Milk yield, fat %, protein %, DMI
Petersson-Wolfe et al., 2007	2	254, 320	TMR, CRC	136	1	TMR	Yes	−21	DMI, BCS
AlZahal et al., 2008	3	453, 466, 469	453	72	1	TMR	Yes	138	Milk yield, fat %, fat yield, protein %, protein yield, DMI, fatty acids
Grainger et al., 2008	2[5]	240	CRC[6]	60	1	Pasture	Yes	46, 176	DMI, milk yield, fat %, fat yield, protein %, protein yield, lactose, BW

[1]80 cows used over 2 lactations considered 2 trials with 80 cows each.

[2]3 trials = 3 BCS classes for milk and component yields, because BCS and treatment found to interact in this trial.

[3]98 cows used over 2 lactations considered 2 trials with 98 cows each.

[4]Fed fresh cut grass to mimic pasture situation.

[5]60 cows receiving a second CRC 130 d following the first considered a separate trial. CRC = monensin delivered in a controlled release capsule.

[6]Payout of CRC in this study measured to be 240 mg/d.

C18:3, and CLA; therefore, a random effect model was used for these outcomes.

The impact of influential studies on all models was examined. Although there were influential studies, especially those with larger sample sizes, inclusion or removal of these studies in any analysis did not change the direction of effect and caused relatively little change in the overall ES estimates.

Twenty-four to 33 trials were available to investigate possible dietary influences on monensin for impact on milk component percentages and yield. A summary of the estimates of the dietary factors derived using CPM-Dairy is in Table 5. Results of meta-regression using CPM-Dairy model outputs are in Table 6. Increasing rumen peptide balance increased the positive effect of monensin on milk protein yield (Table 6). Intake of C18:3 increased milk fat percentage, whereas intake of C18:1 decreased milk fat yield. The control values for milk fat and milk protein percentage affected the magnitude of response to monensin, with greater control values resulting in a greater ES for monensin on these effects. Yet, these effects were not significant with the larger data set that is all trials including those with and without nutritional information.

DISCUSSION

This is the first comprehensive, quantitative evaluation of the effect of monensin on production in lactating dairy cattle. A strength of this analysis was the power derived from the number of trials and cows evaluated. There was variation in responses reported for monensin on milk yield and, especially, on DMI. In one review, the authors found that 8 of 12 studies on ionophores reported no significant difference for DMI (Ipharraguerre and Clark, 2003). Nevertheless, our analysis clearly demonstrated increases in milk yield and decreases in DMI with monensin treatment. Further, these responses were consistent as indicated by the homogeneity test. Thus, the failure to report consistent responses in previous studies most probably reflects inadequate sample size and, consequently, insufficient statistical power to detect an approximate increase of 0.7 L in milk yield and decrease of 0.3 kg in DMI. The estimates of effect obtained in our study are similar to those of Ipharraguerre and Clark (2003) who reported a decrease of 0.3 kg of DMI from 14 ionophore experiments and an increase in milk yield of 0.7 and 1.5 kg/d in low- and high-forage diets, respectively. The approximate 2% decrease in DMI is a consistent response and no variables were identified in meta-regression that influenced the effect of monensin on DMI despite data from 4,000 cows enrolled in 53 trials. The finding that pasture-based herds had a greater produc-

Table 2. Summary of effect size estimates of monensin on production in lactating dairy cows derived from meta-analysis

Outcome measured	Raw weighted mean difference: monensin – control (95% CI)	Change, %	Cows, n		Trials, n	Trial sites, n	Effect size (95% confidence interval)	I^2 (95% uncertainty interval)	Effect size, *P*-value
			Control	Treatment					
DMI (kg/d)	–0.3 (–0.42, –0.18)	–2.3	2,243	2,202	53	152	–0.097 (–0.156, –0.038)	0 (0–32)	0.001
Milk yield (kg/d)	0.7 (0.49, 0.85)	2.3	4,889	4,788	71	255	0.123 (0.083, 0.163)	12 (0–35)	<0.001
Fat (%)	–0.12 (–0.15, –0.08)	–3.1	3,460	3,406	62	193	–0.265 (–0.357, –0.179)	56 (41–67)	<0.001
Fat yield (kg/d)	–0.002 (–0.012, 0.012)	–0.02	2,724	2,751	47	168	–0.0733 (–0.176, 0.029)	55 (38–68)	0.161
Protein (%)	–0.03 (–0.04, –0.02)	–0.9	3,460	3,406	62	193	–0.140 (–0.217, –0.063)	39 (17–55)	<0.001
Protein yield (kg/d)	0.016 (0.011, 0.021)	1.9	2,700	2,727	45	166	0.131 (0.057, 0.205)	23 (0–47)	0.001
Lactose (%)	–0.012 (–0.029, 0.005)	–0.25	1,102	1,110	27	75	–0.027 (–0.460, 0.552)	26 (0–50)	0.540
Production efficiency (% energy yield /energy intake)	2.04 (0.87, 3.13)	2.5	881	875	14	65	0.0879 (–0.0058, 0.182)	0 (0–55)	0.066
BCS (1 to 5)	0.03 (0.014, 0.053)	1.0	1,392	1,385	18	90	0.176 (0.050, 0.301)	40 (0–66)	0.006
BW change (kg/d)	0.06 (0.021, 0.105)	68	1,240	1,231	33	84	0.757 (0.462, 1.053)	67 (53–77)	<0.001

tion response is consistent with the conclusion of Ipharraguerre and Clark (2003) in regard to higher forage diets. We postulate that this effect could be a function of these herds having a greater energy deficit, as opposed to an MP deficit, than TMR-fed herds and, therefore, responding to a greater extent with increased milk yield. This reasoning is consistent with cows higher in BCS precalving having greater milk production re-

Table 3. Effect size estimates of monensin on milk fatty acid (FA) parameters in lactating dairy cows derived from meta-analysis

Milk FA content (g/100 g of FA)	Raw weighted mean difference: monensin – control (95% confidence interval)	Change, %	Cows, n		Trials, n	Trial sites, n	Effect size (95% confidence interval)	I^2 (95% uncertainty interval)	Effect size, *P*-value
			Control	Treatment					
C6:0	–0.182 (–0.295, –0.0687)	–9.7	68	68	8	3	–0.516 (–0.863, –0.179)	0 (0-68)	0.003
C8:0	–0.129 (–0.196, –0.062)	–11.8	68	68	8	3	–0.591 (–0.938, –0.243)	0 (0-68)	0.001
C10:0	–0.183 (–0.288, –0.078)	–7.10	92	92	10	4	–0.359 (–0.652, –0.066)	0 (0-62)	0.016
C12:0	–0.125 (–0.222, –0.028)	–3.9	92	92	10	4	–0.238 (–0.530, –0.0533)	0 (0-62)	0.109
C14:0	–0.105 (–0.364, 0.153)	–0.92	92	92	10	4	–0.077 (–0.373, –0.219)	33 (0-68)	0.145
C16:0	–0.012 (–0.853, 0.829)	–0.04	92	92	10	4	–0.045 (–0.338, 0.248)	9 (0-66)	0.763
C18:0	–0.850 (–1.259, –0.442)	–7.78	92	92	10	4	–0.623 (–0.922, –0.324)	0 (0-62)	<0.001
C18:1	1.03 (–0.252, 2.305)	4.18	68	68	7	3	0.362 (0.0169, 0.707)	18 (0-62)	0.04
Trans C18:1	1.55 (–0.240, 3.342)	22.3	60	60	6	2	1.011 (0.173, 0.850)	77 (49-90)	0.018
C18:2	0.027 (–0.107, 0.160)	1.11	92	92	10	4	0.087 (–0.341, 0.515)	49 (0-75)	0.690
CLA[1]	0.286 (–0.058, 0.629)	22.4	92	92	10	4	0.6337 (0.200, 0.067)	48 (0-75)	0.004
C18:3	–0.002 (–0.0231, 0.0194)	–0.372	92	92	10	4	–0.143 (–0.438, 0.153)	32 (0-68)	0.153

[1]CLA = conjugated linoleic acid.

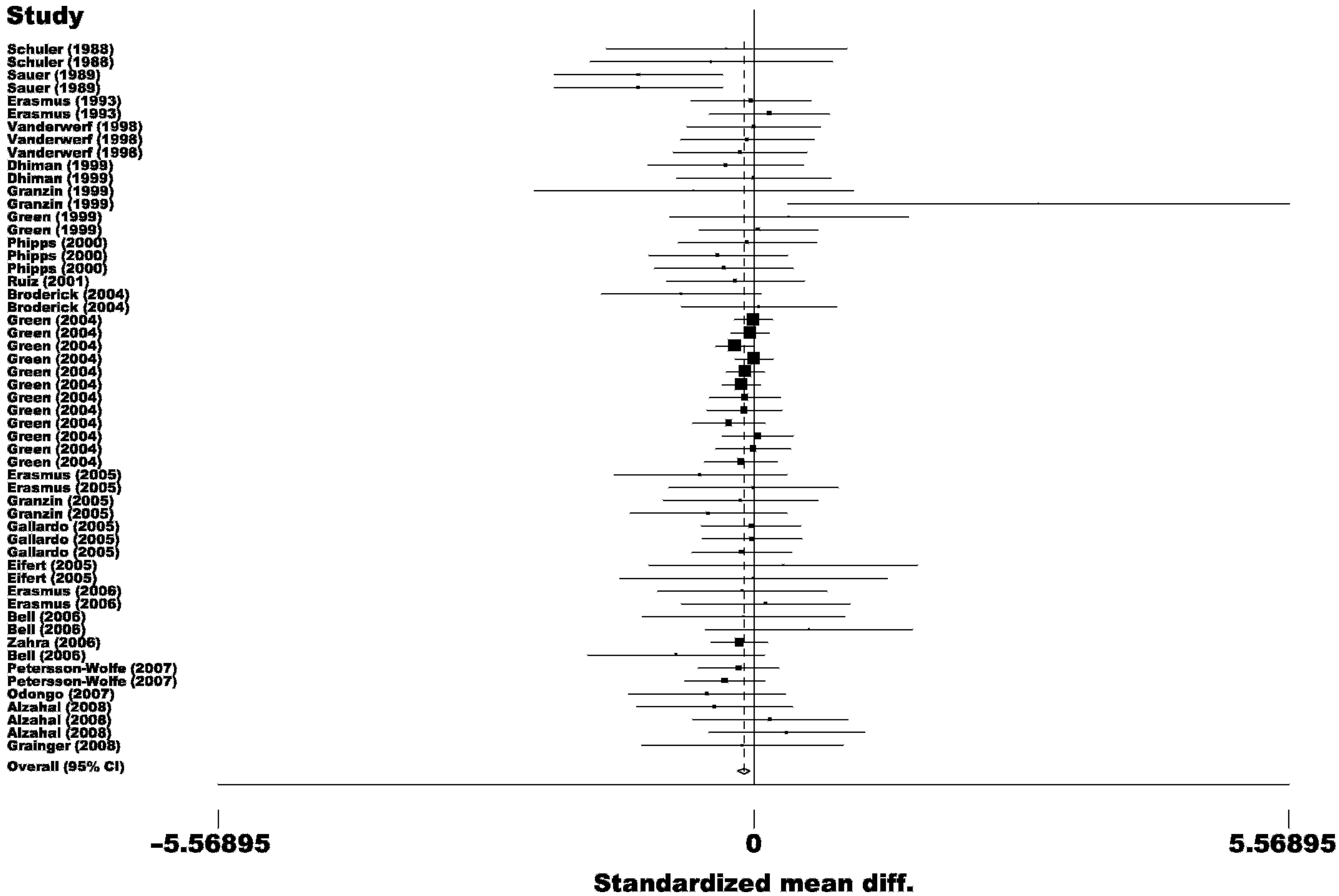

Figure 1. Forest plot of the effect of monensin on DMI in lactating dairy cows. The x-axis shows standardized mean difference (standardized using the z-statistic); thus, points to the left of the line represent a reduction in the trait, whereas points to the right of the line indicate an increase. Each square represents the mean effect size for that study, and the size of the square reflects the relative weighting of the study to the overall effect size estimate with larger squares representing greater weight. The upper and lower limit of the line connected to the square represents the upper and lower 95% confidence interval for the effect size. The dotted vertical line represents the overall effect size estimate. The diamond at the bottom represents the 95% confidence interval for the overall estimate, and the solid vertical line represents a mean difference of zero or no effect. Study refers to the first author and year of publication.

sponses with monensin treatment (Duffield et al., 1999). Further, pasture-based studies had a greater response of monensin to lowering BHBA (Duffield et al., 2008). The combined decrease of DMI and increase of milk yield of about 2% each support the observed increase in milk production efficiency with monensin. This was most likely lower than an expected 4% improvement, given the 2% increase in milk yield and 2% decrease in DMI, because energy efficiency was the variable analyzed. This variable accounts for changes in both milk fat and milk protein yields.

The findings for milk fat and protein demonstrated a reduction in milk fat percentage and protein percentage, but an increase in protein yield and no effect on milk fat yield with monensin treatment. But these responses were heterogeneous. These outcomes were influenced by the stage of lactation, delivery method of monensin, and diet type (Table 4). There were increased fat and protein yields with monensin for pasture-based trials compared with other dietary bases. Topdress delivery enhanced protein yield response with monensin. It is unclear why delivery methods influence responses to treatment. This finding is consistent with delivery method influences found for metabolic outcomes (Duffield et al., 2008). It is possible that sudden concentrated delivery of monensin dose had different rumen bacterial effects compared with a consistent delivery via CRC or with monensin dispersed in a TMR. It can be hypothesized that topdress doses may be delivered with a considerable amount of the daily concentrate fed and this aspect of dietary delivery may influence responses. Differences in delivery of monensin on rumen bacteria and availability of specific substrates such as starches, sugars, and peptides are areas requiring further research.

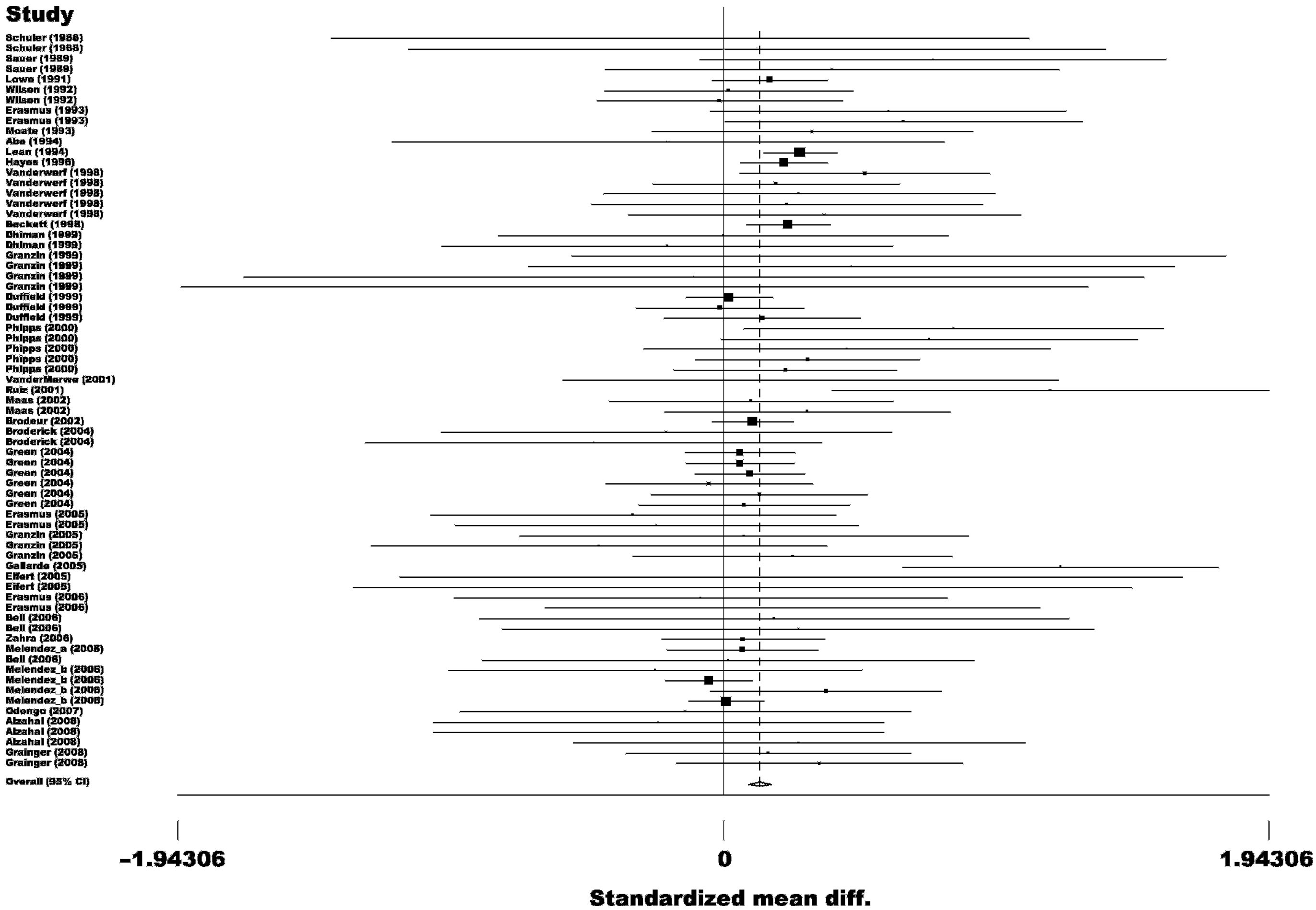

Figure 2. Forest plot of the effect of monensin on milk yield in lactating dairy cows. The x-axis shows standardized mean difference (standardized using the z-statistic); thus, points to the left of the line represent a reduction in the measure, whereas points to the right of the line indicate an increase. Each square represents the mean effect size for that study, and the size of the square reflects the relative weighting of the study to the overall effect size estimate with larger squares representing greater weight. The upper and lower limit of the line connected to the square represents the upper and lower 95% confidence interval for the effect size. The dotted vertical line represents the overall effect size estimate. The diamond at the bottom represents the 95% confidence interval for the overall estimate, and the solid vertical line represents a mean difference of zero or no effect. Study refers to the first author and year of publication.

Starting monensin treatment earlier in lactation or even before calving reduces the negative impact of monensin on milk fat yield compared with commencing treatment later in lactation. This finding suggests a stage of lactation effect, with larger effects on milk fat yield occurring later in lactation.

There were associations between responses in milk components to monensin and diet, and greater observed heterogeneity of response for single-site vs. multi-site trials. These findings indicate that these responses may be influenced by specific environments and diets. Consequently, we evaluated diets using CPM-Dairy to estimate dietary factors, and then conducted sub-analysis of studies in which dietary composition was detailed. Despite limitations of using book values for feeds, there were useful findings for the impact of monensin on milk fat and milk protein yields.

Increasing concentration of C18:1 in the diet was associated with a greater reduction in milk fat yield with monensin treatment (Table 6). These findings are consistent with Moate (P. J. Moate, Univ. Penn, New Bolton Center, Kennett Square, PA; unpublished data) who found a quadratic effect on preformed fats from C4 to C15 of total unsaturated fatty acids in the diet, such that lower concentrations depressed C4 to C15 fat production. It can be postulated that a greater effect on milk fat yield should be expected with C18:2 and C18:3 concentrations. Given that this present finding was based on book values, it may be a marker for the presence of long-chain fatty acids including C18:1 in

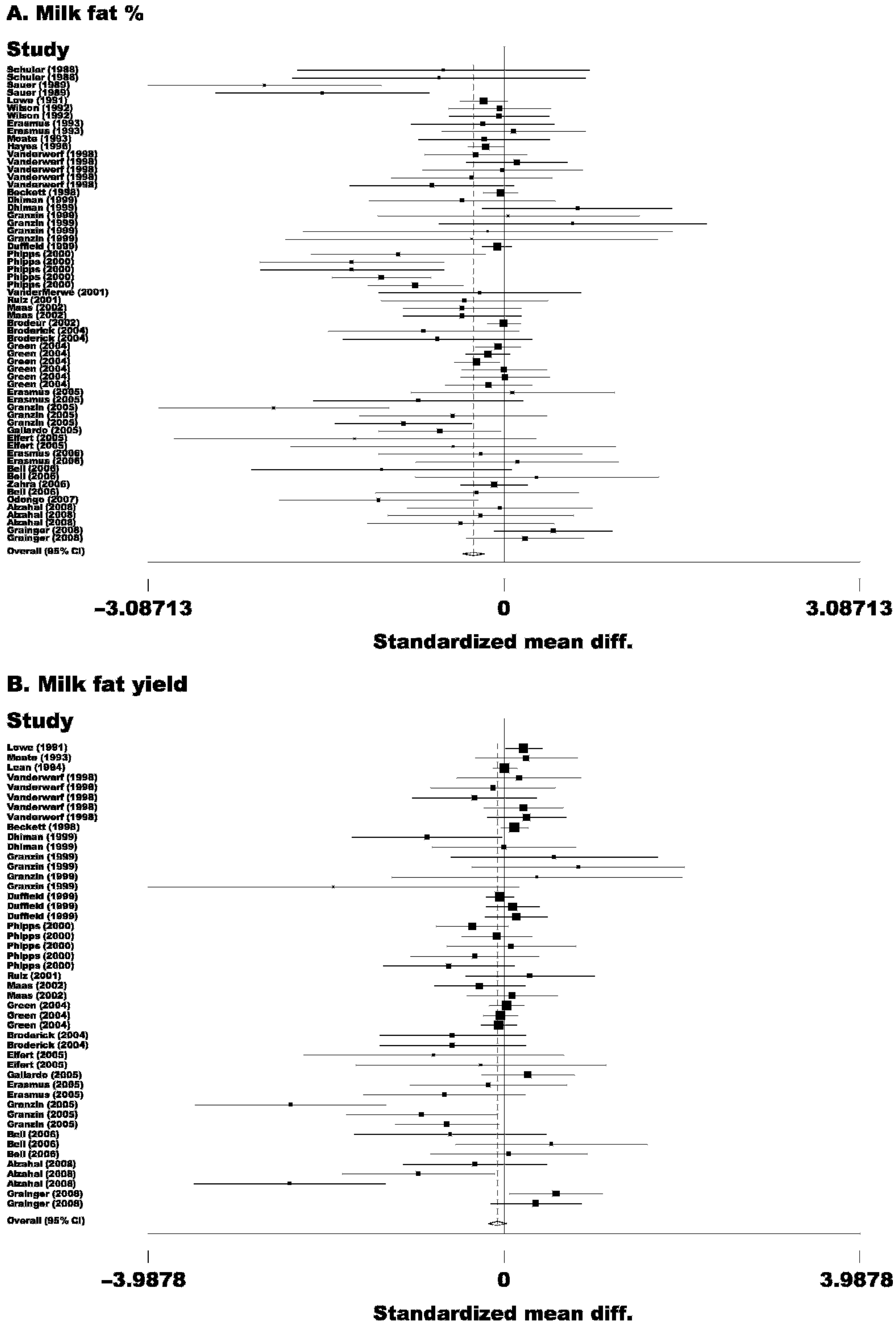

Figure 3. Forest plot of the effect of monensin on A) milk fat (%) in lactating dairy cows, and B) on milk fat yield (kg/d) in lactating dairy cows. The x-axis shows standardized mean difference (standardized using the z-statistic); thus, points to the left of the line represent a reduction in the measure, whereas points to the right of the line indicate an increase. Each square represents the mean effect size for that study, and the size of the square reflects the relative weighting of the study to the overall effect size estimate with larger squares representing greater weight. The upper and lower limit of the line connected to the square represents the upper and lower 95% confidence interval for the effect size. The dotted vertical line represents the overall effect size estimate. The diamond at the bottom represents the 95% confidence interval for the overall estimate, and the solid vertical line represents a mean difference of zero or no effect. Study refers to the first author and year of publication.

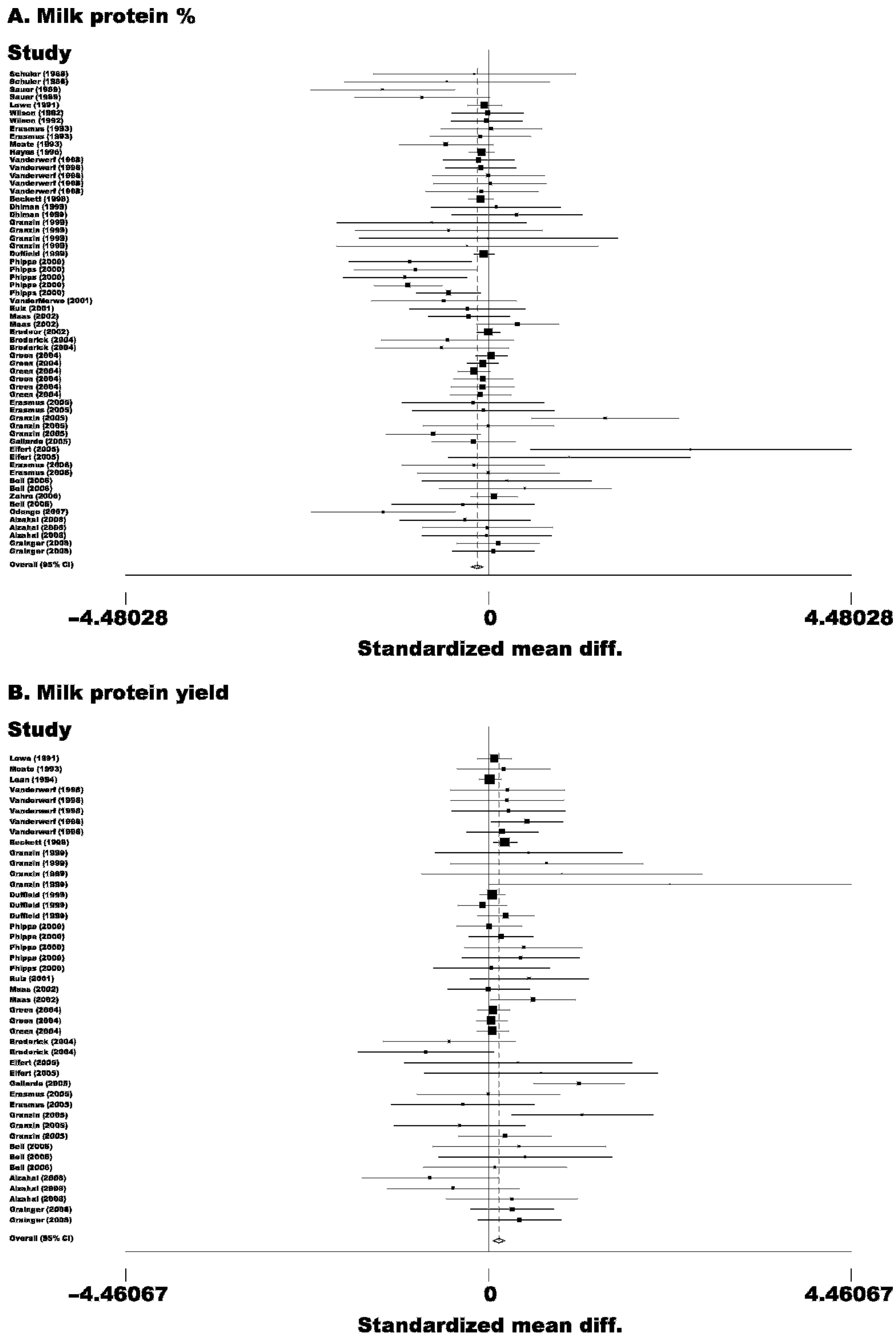

Figure 4. Forest plot of the effect of monensin A) on milk protein (%) in lactating dairy cows, and B) on milk protein yield (kg/d) in lactating dairy cows. The x-axis shows standardized mean difference (standardized using the z-statistic); thus, points to the left of the line represent a reduction in the measure, whereas points to the right of the line indicate an increase. Each square represents the mean effect size for that study, and the size of the square reflects the relative weighting of the study to the overall effect size estimate with larger squares representing greater weight. The upper and lower limit of the line connected to the square represents the upper and lower 95% confidence interval for the effect size. The dotted vertical line represents the overall effect size estimate. The diamond at the bottom represents the 95% confidence interval for the overall estimate, and the solid vertical line represents a mean difference of zero or no effect. Study refers to the first author and year of publication.

Table 4. Summary of meta-regression analysis outputs for the variables that influenced the effect of monensin on milk production, milk components, BW change, and DMI[1]

Variable	Coefficient	Coefficient 95% confidence interval	*P*-value
Milk yield			
Intercept	0.036	(–0.015, 0.088)	0.165
Pasture[2]	0.191	(0.106, 0.276)	<0.001
Topdress monensin[3]	0.308	(0.149, 0.466)	<0.001
Milk fat (%)			
Intercept	–0.197	(–0.286, –0.107)	<0.001
Topdress monensin[3]	–0.280	(–0.467, –0.093)	0.003
DIM at treatment start	–0.002	(–0.003, –0.0007)	0.001
CRC[4]	0.114	(0.005, 0.222)	0.040
Milk fat yield			
Intercept	–0.071	(–0.170, 0.027)	0.156
Pasture[2]	0.212	(0.049, 0.375)	0.011
DIM at treatment start	–0.003	(–0.005, –0.002)	<0.001
Milk protein (%)			
Intercept	–0.056	(–0.110, –0.010)	<0.001
Topdress monensin[3]	–0.340	(–0.558, –0.236)	0.040
Milk protein yield			
Intercept	0.185	(0.066, 0.279)	<0.001
TMR diets[5]	–0.137	(–0.249, –0.001)	0.025
Topdress monensin[3]	0.175	(0.0104, 0.344)	0.039
BW change			
Intercept	0.151	(–0.511, 0.814)	0.654
Monensin dose	0.002	(0.0005, 0.004)	0.011
DIM at treatment end	–0.002	(–0.004, –0.0002)	0.029

[1]No variables influenced effect size estimates for monensin on DMI.

[2]Pasture-fed cows compared with non–pasture-fed cows.

[3]Monensin delivered in a topdress (included in a small amount of supplement) and placed either on feed or fed in the parlor.

[4]Monensin delivered with controlled release capsule (CRC) compared with either topdress or TMR delivery.

[5]TMR diet compared with either pasture-fed or component system (grain and forage fed separately).

the diet, rather than a true effect. Our finding does appear to be consistent with a reported mechanism of monensin disrupting biohydrogenation (Fellner et al., 1997); and thereby potentially increasing the absorbed partially hydrogenated long-chain fatty acids such as *trans*-10 *cis*-12 CLA that may inhibit de novo fat synthesis (Baumgard et al., 2000). We conclude that monensin treatment reduces the presence of short-chain fatty acids in milk based on the meta-regression from 10 trials and 4 studies reporting milk fatty acid profiles with monensin. This hypothesis is further supported by the significant reduction in milk of stearic acid and an increase in both *trans* C18:1 and CLA with monensin treatment. Examination of the forest plot showing the effect of monensin on *trans* C18:1 (data not shown) demonstrated that the greatest effect was observed in diets with the greatest concentrations of unsaturated oils such as soy oil (AlZahal et al., 2008), and safflower oil (Bell et al., 2006). This finding appears to corroborate the dietary association between greater fat yield decreases and diets higher in C18:1.

Table 5. Summary of CPM-Dairy dietary estimates from 34 trials on monensin that included dietary information

Nutrient (DM basis)	Mean ± SE
CP (%)	17.5 ± 0.28
MP balance (g)	–41.4 ± 41.06
Peptide balance (% rqd)[1]	146.7 ± 8.86
Peptide and ammonia balance (% rqd)	141.3 ± 3.78
NDF (%)	34.8 ± 0.89
peNDF[2] (%)	26.4 ± 0.71
NFC (%)	38.4 ± 0.96
Starch (%)	22.8 ± 1.40
Sugar (%)	6.5 ± 0.83
ME balance (MCal)	3.62 ± 0.73
Total fat (% of DM)	4.44 ± 0.29
C18:1 (g/d)	101.1 ± 10.6
C18:2 (g/d)	254.8 ± 29.4
C18:3 (g/d)	80.8 ± 8.22

[1]% of model-estimated requirement.

[2]peNDF% = physically effective NDF%.

The discovery of increased rumen peptide balance enhancing the effect of monensin on milk protein yield is novel (Table 6). The minimum peptide balance estimated from CPM-Dairy for optimal effect was around 140% of requirement. This estimate was based on a scatter graph of peptide balance vs. effect size estimate for monensin (data not shown). These findings are consistent with response to feeds with high concentrations of peptides in increasing microbial protein yields by

Table 6. Summary of meta-regression analysis outputs for variables that influenced the effect of monensin on milk components including CPM-Dairy dietary outputs

Variable	Coefficient	Coefficient 95% confidence interval	*P*-value
Milk fat (%) (n = 32)			
Intercept	0.613	(–0.722, 1.948)	0.368
Control mean milk fat (%)	–0.438	(–0.788, –0.0871)	0.014
C18:3 (g/d)	0.004	(0.001, 0.008)	0.004
Milk fat yield (n = 27)			
Intercept	0.314	(–0.047, 0.674)	0.088
DIM at treatment start	–0.004	(–0.006, –0.001)	0.019
C18:1 (g/d)	–0.005	(–0.008, –0.001)	0.004
Milk protein (%) (n = 33)			
Intercept	2.733	(0.832, 4.634)	0.003
Control mean milk protein (%)	–0.979	(–1.561, –0.398)	0.001
CRC[1]	0.495	(0.169, 0.821)	0.004
Milk protein yield (n = 26)			
Intercept	–0.411	(–0.894, 0.0711)	0.095
Rumen peptide balance	0.0036	(0.0009, 0.0064)	0.010

[1]Monensin delivered with CRC (controlled release capsule) compared with either topdress or TMR delivery.

approximately 15% over isonitrogenous, isoenergetic control diets (Lean et al., 2005). Monensin treatment selectively reduces bacteria that are possibly reducing peptide availability and, consequently, limiting milk protein yield responses. Providing sufficient peptides during monensin treatment should allow both optimal bacterial protein yield and enhanced RUP supply to the small intestine. It should be noted that the peptide balance in this evaluation was derived from estimated ration measures and book values using CPM-Dairy. At this point this finding should be interpreted with caution, and further studies are needed for confirmation and validation.

There was some expectation of finding either NDF or physically effective NDF impacts on the effect of monensin on milk fat. Yet, lack of a significant effect for these variables in the current study may be a function of using book values and because these variables had a fairly small range across the studies (Table 5).

It is interesting to note that in the meta-regression analysis (of herds with dietary information) for factors explaining heterogeneity of response for monensin on milk fat and protein percentage, the control values of both milk fat and milk protein percentage affected the response. These variables (control values) were tested in all other regression analyses and were not significant (including the analysis of milk fat and milk protein percentage with the full data set that included all studies with and without dietary information). This finding suggests that there could be differences in the effect of monensin on milk protein and milk fat percentage depending on the base level of these components before monensin inclusion. Given that this effect was not significant with the full data set, it would appear that the level of the control values for milk fat and protein percentage are of minor importance relative to the other significant explanatory variables contributing to heterogeneity of response.

The observations of improved BCS (Table 2) and improved BW change (Table 6) with monensin are consistent with increased energy and possibly protein supply to the cow. Meta-analysis of metabolic responses found a monensin dose effect for serum glucose (Duffield et al., 2008). The magnitude of response for BCS was 0.014 to 0.053 of a BCS across all study treatment intervals. One BCS is equivalent to approximately 80 kg (Schwager-Suter et al., 2001); thus, the BCS change was approximately equal to 1.2 to 4.2 kg of BW. The BW change data indicated a change of 0.02 to 0.10 kg/d of treatment. Validation analysis of these data; that is, multiplying change in BW by average DIM on treatment, revealed an estimated difference in BW of 2.1 to 10.5 kg for monensin treatment. It appears that the meta-analysis results are internally consistent.

CONCLUSIONS

Inclusion of monensin in lactating cow diets resulted in both increased milk yield and decreased DMI, and improved milk production efficiency. However, effects on milk protein and milk fat yield were heterogeneous and depended on dietary factors. Greater intakes of unsaturated fat in the diet exacerbated milk fat yield decreases with monensin treatment, whereas rumen peptide concentrations exceeding approximately 140% of estimated requirement enhanced effects on increasing milk protein yield. Pasture-based diets and those in which monensin was delivered in topdress had a positive influence on monensin component responses. Monensin elicited small increases in BCS and BW, effects that depend on stage of lactation and dose. Monensin increased the proportion of CLA in milk.

ACKNOWLEDGMENTS

We wish to acknowledge Valetta Taylor-Craig (Strategic Bovine Services, Camden, New South Wales, Australia) for her assistance with the literature search. We wish to thank the authors who provided additional data and Elanco Animal Health (Guelph, Ontario, Canada; Macquarie Park, New South Wales, Australia; Greenfield, IN) for generous funding support for this project.

REFERENCES

Abe, N., I. J. Lean, A. R. Rabiee, J. Porter, and C. Graham. 1994. Effects of sodium monensin on reproductive performance of dairy cattle. II. Effects on metabolites in plasma, resumption of ovarian cyclicity and oestrus in lactating cows. Aust. Vet. J. 71:277–282.

AlZahal, O., N. Odongo, T. Mutsvangwa, M. Or Rashid, T. Duffield, R. Bagg, P. Dick, G. Vessie, and B. McBride. 2008. Effects of monensin and dietary soybean oil on milk fat percentage and milk fatty acid profile in lactating dairy cows. J. Dairy Sci. 91:1166–1174.

Baumgard, L. H., B. A. Corl, D. A. Dwyer, A. Saebo, and D. E. Bauman. 2000. Identification of the conjugated linoleic acid isomer that inhibits milk fat synthesis. Am. J. Physiol. 278:R179–R184.

Beckett, S., I. Lean, R. Dyson, W. Tranter, and L. Wade. 1998. Effects of monensin on the reproduction, health, and milk production of dairy cows. J. Dairy Sci. 81:1563–1573.

Begg, C. B., and M. Mazumdar. 1994. Operating characteristics of a rank correlation test for publication bias. Biometrics 50:1088–1101.

Bell, J. A., J. M. Griinari, and J. J. Kennelly. 2006. Effect of safflower oil, flaxseed oil, monensin, and vitamin E on concentration of conjugated linoleic acid in bovine milk fat. J. Dairy Sci. 89:733–748.

Bergen, W. G., and D. B. Bates. 1984. Ionophores: Their effect on production efficiency and mode of action. J. Anim. Sci. 58:1465–1483.

Broderick, G. A. 2004. Effect of low level monensin supplementation on the production of dairy cows fed alfalfa silage. J. Dairy Sci. 87:359–368.

Brodeur, M. 2002. L'effet du monensin en capsule sur la production et les composantes du lait des vaches Holstein du Québec., Université de Montréal, St. Hyacinthe, Quebec, Canada.

DerSimonian, R., and N. Laird. 1986. Meta-analysis in clinical trials. Control. Clin. Trials 7:177–188.

Dhiman, T. R., G. R. Anand, L. D. Satter, and M. W. Pariza. 1999. Conjugated linoleic acid content of milk from cows fed different diets. J. Dairy Sci. 82:2146–2156.

Dohoo, I., W. Martin, and H. Stryhn. 2003. Meta-analysis. Page 706 in Veterinary Epidemiologic Research. AVC Inc., Charlottetown, Prince Edward Island, Canada.

Duffield, T. F., K. E. Leslie, D. Sandals, K. Lissemore, B. W. McBride, J. H. Lumsden, P. Dick, and R. Bagg. 1999. Effect of prepartum administration of monensin in a controlled-release capsule on milk production and milk components in early lactation. J. Dairy Sci. 82:272–279.

Duffield, T. F., A. R. Rabiee, and I. J. Lean. 2008. A meta-analysis of the impact of monensin in lactating dairy cattle. Part 1. Metabolic effects. J. Dairy Sci. 91:1334–1346.

Egger, M., G. Davey Smith, and D. Altman. 2001. Systematic Reviews in Health Care. Meta-Analysis in Context. BMJ Books, London, UK.

Egger, M., G. Davey Smith, M. Schneider, and C. Minder. 1997. Bias in meta-analysis detected by a simple, graphical test. BMJ 315:629–634.

Eifert, E. d. C., R. d. P. Lana, and D. P. D. Lanna. 2005. Effects of dietary supplementation of monensin and soybean oil on production of early lactating dairy cows. Efeitos do fornecimento de monensina e oeo de soja na dieta sobre o desempenho de vacas leiteiras na fase inicial da lactacao. Rev. Bras. Zootec. 34:2123–2132.

Eifert, E. d. C., R. d. P. Lana, D. P. D. Lanna, W. M. Leopoldino, P. B. Arcuri, M. I. Leao, M. R. Cota, and S. d. C. V. Filho. 2006. Milk fatty acid profile of cows fed monensin and soybean oil in early lactation. Perfil de acidos graxos do leite de vacas alimentadas com oleo de soja e monensina no inicio da lactacao. Rev. Bras. Zootec. 35:219–228.

Erasmus, L. J., P. M. Botha, G. D. Lindsey, J. A. d'Assonville, and M. D. Viljoen. 1993. Effect of monensin supplementation and BST administration on productivity and incidence of ketosis in dairy cows. Pages 413–414 in World Conference on Animal Production. Edmonton, Canada.

Erasmus, L. J., C. Muya, S. Erasmus, and D. G. Catton. 2006. Effect of Virginiamycin and Poulcox, or both, on performance of Holstein cows. J. Dairy Sci. 89(Suppl. 1):234. (Abstr.)

Erasmus, L. J., P. H. Robinson, A. Ahmadi, R. Hinders, and J. E. Garrett. 2005. Influence of prepartum and postpartum supplementation of a yeast culture and monensin, or both, on ruminal fermentation and performance of multiparous dairy cows. Anim. Feed Sci. Technol. 122:219–239.

Fellner, V., F. D. Sauer, and J. K. G. Kramer. 1997. Effect of nigercin, monensin, and tetronasin on biohydrogenation in continuous flow-through ruminal fermenters. J. Dairy Sci. 80:921–928.

Gallardo, M. R., A. R. Castillo, F. Bargo, A. A. Abdala, M. G. Maciel, H. Perez-Monti, H. C. Castro, and M. E. Castelli. 2005. Monensin for lactating dairy cows grazing mixed-alfalfa pasture and supplemented with partial mixed ration. J. Dairy Sci. 88:644–652.

Grainger, C., M. J. Auldist, T. Clarke, K. A. Beauchemin, S. M. McGinn, M. C. Hannah, R. J. Eckard, and L. B. Lowe. 2008. Use of monensin controlled-release capsules to reduce methane emissions and improve milk production of dairy cows offered pasture supplemented with grain. J. Dairy Sci. 91:1159–1165.

Granzin, B., and G. McL. Dryden. 1999. The effects of monensin on milk production and levels of metabolites in blood and rumen fluid of Holstein-Friesian cows in early lactation. Aust. J. Exp. Agric. 39:933–940.

Granzin, B. C., and G. McL. Dryden. 2005. Monensin supplementation of lactating cows fed tropical grasses and cane molasses or grain. Anim. Feed Sci. Technol. 120:1–16.

Green, B. L., B. W. McBride, D. Sandals, K. E. Leslie, R. Bagg, and P. Dick. 1999. The impact of a monensin controlled-release capsule on subclinical ketosis in the transition dairy cow. J. Dairy Sci. 82:333–342.

Green, H., and J. Wilkinson. 2004. The effect of feeding monensin on lactation performance of dairy cows. Report to CVM. Elanco Animal Health, Greenfield, IN.

Hayes, D. P., D. U. Pfeiffer, and N. B. Williamson. 1996. Effect of intraruminal monensin capsules on reproductive performance and milk production of dairy cows fed pasture. J. Dairy Sci. 79:1000–1008.

Higgins, J. P., S. G. Thompson, J. J. Deeks, and D. G. Altman. 2003. Measuring inconsistency in meta-analyses. BMJ 327:557–560.

Higgins, J. P. T., and S. Green, ed. 2005. Cochrane Handbook for Systematic Reviews of Interventions 4.2.5. (updated May 2005). In The Cochrane Library. Issue 3. John Wiley & Sons Ltd., Chichester, UK.

Ipharraguerre, I. R., and J. H. Clark. 2003. Usefulness of ionophores for lactating dairy cows: A review. Anim. Feed Sci. Technol. 106:39–57.

Lean, I. J., M. Curtis, R. Dyson, and B. Lowe. 1994. Effects of sodium monensin on reproductive performance of dairy cattle. I. Effects on conception rates, calving-to-conception intervals, calving-to-heat and milk production in dairy cows. Aust. Vet. J. 71:273–277.

Lean, I. J., T. K. M. Webster, W. Hoover, W. Chalupa, C. J. Sniffen, E. Evans, E. Block, and A. R. Rabiee. 2005. Effects of BioChlor and Fermenten on microbial protein synthesis in continuous culture fermenters. J. Dairy Sci. 88:2524–2536.

Lowe, L. B., G. J. Ball, V. R. Carruthers, R. C. Dobos, G. A. Lynch, P. J. Moate, P. R. Poole, and S. C. Valentine. 1991. Monensin controlled-release intraruminal capsule for control of bloat in pastured dairy cows. Aust. Vet. J. 68:17–20.

Maas, J. A., S. N. McCutcheon, G. F. Wilson, G. A. Lynch, M. E. Hunt, and L. A. Crompton. 2002. The effect of monensin sodium on lactational performance of autumn and spring calving cows. J. Dairy Res. 69:317–323.

McGuffey, R. K., L. F. Richardson, and J. I. D. Wilkinson. 2001. Ionophores for dairy cattle: Current status and future outlook. J. Dairy Sci. 84(E Suppl.):E194–E203.

Melendez, P., J. P. Goff, C. A. Risco, L. F. Archbald, R. C. Littell, and G. A. Donovan. 2006a. Effect of administration of a controlled-release monensin capsule on incidence of calving-related disorders, fertility, and milk yield in dairy cows. Am. J. Vet. Res. 67:537–543.

Melendez, P., G. Gonzalez, M. Benzaquen, C. Risco, and L. Archbald. 2006b. The effect of a monensin controlled-release capsule on the incidence of retained fetal membranes, milk yield and reproductive responses in Holstein cows. Theriogenology 66:234–241.

Moate, P. 1993. Evaluation of anti-bloat capsules. The Dairy Research Institute, Ellinbank Department of Agrictulture, Kyabram, Victoria, Australia.

Odongo, N. E., R. Bagg, G. Vessie, P. Dick, M. M. Or Rashid, S. E. Hook, J. T. Gray, E. Kebreab, J. France, and B. W. McBride. 2007. Long-term effects of feeding monensin on methane production in lactating dairy cows. J. Dairy Sci. 90:1781–1788.

Petersson-Wolfe, C. S., K. E. Leslie, T. Osborne, B. W. McBride, R. Bagg, G. Vessie, P. Dick, and T. F. Duffield. 2007. Effect of delivery method of monensin on dry matter intake, body condition score, and metabolic parameters in transition dairy cows. J. Dairy Sci. 90:1870–1879.

Phipps, R. H., J. I. D. Wilkinson, L. J. Jonker, M. Tarrant, A. K. Jones, and A. Hodge. 2000. Effect of monensin on milk production of Holstein-Friesian dairy cows. J. Dairy Sci. 83:2789–2794.

Ruiz, R., G. L. Albrecht, L. O. Tedeschi, G. Jarvis, J. B. Russell, and D. G. Fox. 2001. Effect of monensin on the performance and nitrogen utilization of lactating dairy cows consuming fresh forage. J. Dairy Sci. 84:1717–1727.

Sauer, F. D., J. K. G. Kramer, and W. J. Cantwell. 1989. Antiketogenic effects of monensin in early lactation. J. Dairy Sci. 72:436–442.

Schuler, D. 1988. The effect of monensin Na on the protein content of cow's milk and further performance criteria. Arch. Tierernahr. 38:947–954.

Schwager-Suter, R., C. Stricker, D. Erdin, and N. Künz. 2001. Quantification of changes in body weight and body condition scores during lactation by modelling individual energy balance and total net energy intake. Anim. Sci. 72:325–334.

van der Merwe, B. J. T. J. D., and K. P. Walsh. 2001. The effect of monensin on milk production, milk urea nitrogen and body condition score of grazing dairy cows. S. Afr. J. Anim. Sci. 31:49–55.

Van der Werf, J. H. J., L. J. Jonker, and J. K. Oldenbroek. 1998. Effect of monensin on milk production by Holstein and Jersey cows. J. Dairy Sci. 81:427–433.

Wilson, G., G. Lynch, and C. van der Wel. 1992. Effects of Rumensin anti-bloat capsules on plasma magnesium concentration and aspects of health and performance of pastured dairy cows. Massey University, Department of Animal Health, Palmerston North, New Zealand.

Zahra, L. C., T. F. Duffield, K. E. Leslie, T. R. Overton, D. Putnam, and S. J. LeBlanc. 2006. Effects of rumen-protected choline and monensin on milk production and metabolism of periparturient dairy cows. J. Dairy Sci. 89:4808–4818.