# Use of a Molasses–based Liquid Feed Supplement to Deliver Ivermectin to Cattle to Control Ectoparasites\*

Kimberly H. Lohmeyer, PhD<sup>1,4</sup>

J. Mathews Pound, PhD<sup>1</sup>

J. Allen Miller, PhD<sup>2</sup>

Jerome A. Klavons, MS<sup>1</sup>

Ronald B. Davey, PhD<sup>3</sup>

 <sup>1</sup>USDA, ARS, Knipling-Bushland U.S. Livestock Insects Research Laboratory, 2700 Fredericksburg Road, Kerrville, Texas 78028
<sup>2</sup>USDA, ARS – Retired
<sup>3</sup>USDA, ARS, Cattle Fever Tick Research Laboratory, 22675 N. Moorefield Rd., Bldg. 6419, Edinburg, Texas 78541
<sup>4</sup>Corresponding author: kim.lohmeyer@ars.usda.gov

This paper reports the results of research only. Mention of a commercial or proprietary product in this paper does not constitute an endorsement by the USDA. In conducting the research described in this report, the investigators adhered to protocol approved by the USDA-ARS Animal Welfare Committee. The protocol is on file at the USDA-ARS, Knipling-Bushland U.S. Livestock Insects Laboratory, Tick Research Unit, Kerrville, TX. 78028. USDA is an equal opportunity provider and employer.

**KEY WORDS:** Feed supplement, freechoice molasses, Rhipicephalus (Boophilus) microplus, Rhipicephalus (Boophilus) annulatus, tick control

## ABSTRACT

Two different dosages of ivermectin (25 ppm and 100ppm) were used to medicate a liquid molasses feed supplement for freechoice consumption by cattle. Calves that fed on supplement medicated at 25 ppm with ivermectin had a 14 day mean consumption of  $0.62 \pm 0.07$  kg supplement/animal/day producing an average dose of 15.5 mg of ivermectin per calf. The mean ivermectin level in serum for the 25 ppm rate was 15.7  $\pm$  2.6 ppb for days 8 - 14 of the study, and the peak average ivermectin blood serum level was 20  $\pm$  8.8 ppb on the fifteenth day, one day after the last day of treatment.

Intern J Appl Res Vet Med • Vol. 10, No. 2, 2012.

Calves that fed on supplement medicated at 100 ppm ivermectin had a 14 day mean consumption of  $0.63 \pm 0.14$  kg supplement/ animal/day, producing an average daily dose of 63 mg of ivermectin per calf. The peak average ivermectin blood serum level for the 100 ppm rate was  $85.6 \pm 23.6$  ppb on the tenth day of treatment; and for days 8 - 14 of the trial the mean ivermectin blood serum level was  $76.7 \pm 6.2$  ppb. Seven days after termination of the study, no ivermectin was detected in the serum of cattle treated at the 25 ppm rate, while cattle treated at the 100 ppm rate still had ivermectin detectable at ~ 14 ppb. Fourteen days after termination of treatment, no ivermectin was detected in the serum of cattle treated at the 100 ppm rate. An ivermectin blood serum level of  $\geq 10$ ppb is known to control biting flies and ticks on cattle, suggesting that use of a molassesbased liquid feed supplement as a delivery method for systemically active drugs could be beneficial to the USDA-APHIS-VS Cattle Fever Tick Eradication Program.

## INTRODUCTION

Efficacy of the avermectins at minute dosages (in the  $\mu$ g/kg range) has proven effective against a variety of livestock arthropod pests.<sup>1-4</sup> Because of the potency and relative safety of this class of control agents, there has been significant interest in the development of novel systems for their delivery including boluses, implants, and injectables for controlling ectoparasites on cattle and other animals. <sup>5-10</sup>

The use of ivermectin-medicated corn as a means of treating free-ranging white-tailed deer has proven effective for controlling lone star ticks, Amblyomma americanum (L.)<sup>11</sup> Because white-tailed deer will limit their consumption of whole kernel corn to approximately 1% of body weight per day, corn can be treated with ivermectin to provide approximately 30 ppb in the serum of the deer without concern of over-treatment.12 Recently the USDA-APHIS-VS Cattle Fever Tick Eradication Program expressed the desire to treat pastured cattle with ivermectin in a similar ad libitum manner. The possibility of using medicated-corn or feed to deliver ivermectin to cattle was not practical because of variable consumption rates, the potential for over-consumption, and the expense of feeding corn to cattle free-choice. Self-limiting molasses-based feed supplements are commonly used by cattle producers and can be implemented with limited labor and operating costs.13 Further, molasses-based liquid supplements can be fed in formulations that allow for safe, yet ad libitum, consumption. For this reason, we elected to determine the potential of a selflimiting molasses-based liquid supplement as a delivery system for passively administering ivermectin to cattle. The objective of the research reported here was to determine the level of ivermectin in a molasses-based liquid supplement that would be needed to

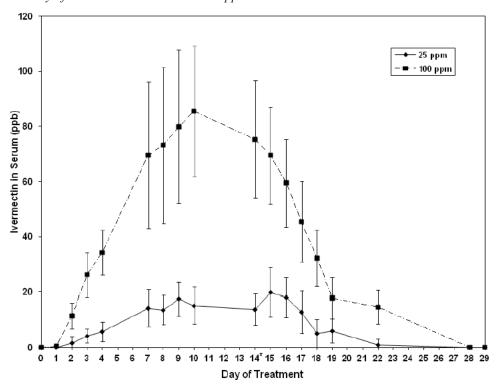
produce adequate drug-serum concentrations for control of ticks and biting flies attempting to feed on treated cattle.

## MATERIALS AND METHODS

A 380 liter (100 gal) lick-wheel feeder was installed in a 1 ha pasture. Smaller (ca. 8 liter) rectangular plastic containers were fitted within the liquid compartment just below each of the two lick-wheels of the feeder. These containers were removable to enable more precise weighing of the amount of molasses supplement added and subsequently consumed. The molasses-based liquid feed supplement used in this study was a product of Cargill Animal Nutrition (CLS 32T 2L #4633, Minneapolis, MN) and had 32 % crude protein with added vitamins and minerals and weighed 1.3 kg /liter. Two trials were conducted with five Black Angus calves weighing ca. 175 kg in each trial. Calves in each trail were allowed to use a lick-wheel feeder filled with untreated molasses supplement for 10 days prior to substitution of the ivermectin-medicated molasses supplement. Cattle were then allowed to feed on the treated supplement for 14 consecutive days. Total daily consumption of the medicated supplement was determined by weighing the amount of supplement remaining in the feeder prior to replenishment.

The molasses supplement was medicated by adding the desired quantity of Ivomec® Pour-on (Merial, Rahway, NJ) to the supplement while it was being stirred with an electric drill fitted with a propeller-like paint stirrer. Batches of 18 kg of supplement were mixed in 20 liter containers and used to replenish the lick-wheel feeder as needed. In the first trial, cattle were given molasses supplement that had been treated with ivermectin at a rate of 25 mg of ivermectin per liter (25 ppm) of molasses supplement. In the second trail, a different set of test calves was given molasses supplement that had been treated with ivermectin at a rate of 100 mg of ivermectin per liter (100 ppm) of molasses supplement.

**Figure 1.** Mean ( $\pm$ SE) concentration of ivermectin in serum of calves as a result of feeding on medicated liquid molasses supplement treated at either 25ppm or 100ppm. \* Last day of access to treated molasses supplement.



Blood samples were collected from the jugular vein of each animal before treatment and at selected times thereafter, including seven time points within the 14 day period after removal of the molasses supplement. Blood for serum analysis of ivermectin levels by HPLC was collected in SST Vacutainers® (Becton Dickinson, Franklin Lakes, NJ). Samples were analyzed using an HPLC method technique that enables quantification of as little as 2 ppb ivermectin in 5 ml of serum.<sup>14</sup> Previous serum concentration data has shown that blood serum levels of >10ppb ivermectin are adequate for control of flies and ticks feeding on cattle, therefore no fly or tick bioassays were necessary in this study. 15-18

#### RESULTS

Calves quickly adapted to the molasses lick-wheel feeder during the 10 day pretreatment period. Within the first day of making the molasses available, the animals were seen visiting the feeder and consuming molasses. Following the adaptation period, the consumption of the medicated molasses remained uniform throughout the treatment period for both treatment rates. In the 25 ppm trial, the daily consumption ranged from 0.51 to 0.65 kg molasses supplement per animal per day. In the 100 ppm trial, daily consumption ranged from 0.45 to 0.77 kg of supplement per animal per day. The trail using 25 ppm ivermectin resulted in a 14 day mean consumption of  $0.62 \pm$ 0.07 kg treated molasses supplement per animal per day producing an average dose of 15.5 mg of ivermectin per calf. The peak average ivermectin serum level was  $20.0 \pm$ 8.8 ppb (range 8 - 30 ppb) on the fifteenth day, one day after the last day of treatment (Fig. 1). For the last seven days of the trial (the equilibrium period), the ivermectin level in serum averaged  $15.7 \pm 2.6$  ppb, and no ivermectin was detected in the serum of

treated cattle at seven days after termination of the treatment (Fig. 1).

The trial using 100 ppm ivermectin resulted in a 14 day mean consumption of  $0.63 \pm 0.14$  kg molasses supplement per animal per day, for an average dose of 63.0 mg of ivermectin per calf. Consumption of the treated molasses resulted in a peak average ivermectin blood serum level of  $85.6 \pm 23.6$ ppb (range 58-114 ppb) on the tenth day of treatment (Fig. 1). During the equilibrium period the mean ivermectin blood serum level was  $76.7 \pm 6.2$  ppb, and no ivermectin was detected in the serum of any animal at 14 days after the treatment was withdrawn.

#### DISCUSSION

From these trials, it was concluded that an ivermectin-medicated molasses feed supplement could be a useful means for passive delivery of the systemically active drug. Levels as low as 25 ppm active ingredient of ivermectin in the supplement produced adequate blood levels for controlling biting flies, ticks, and other hematophagous ectoparasites feeding on cattle. Since supplement consumption can be expected to vary with location, as well as formulation of the molasses mix, treatment protocols should be established by first monitoring supplement consumption for 10 days then dosing according to the consumption rate.

The use of an avermectin-medicated molasses supplement could be of significant benefit to the Cattle Fever Tick Eradication Program in South Texas. According to regulatory protocol, when a pasture is found to contain fever tick-infested cattle, the cattle either must be systematically dipped in coumaphos at two week intervals for six to nine months or be examined and shown to be free of ticks after each of two consecutive dips then vacated from the pasture. The costs of frequently gathering and presenting cattle for treatment make the prescribed six to nine month dipping regimen expensive for producers, therefore many choose to vacate their pastures of cattle rather than comply with the lengthy dipping regimen. In either case, the movement of white-tailed deer

and other wild ungulates among infested and uninfested pastures increases the risk of spreading ticks to adjacent pastures.<sup>19</sup> If cattle are present in these adjacent pastures they are usually gathered and checked for ticks only at the beginning and the end of the dipping program. In some cases, cattle are vacated from these adjacent pastures to avoid potential infestation. The ability to treat the cattle in a predictable manner would enable treatment of cattle in adjacent pastures to limit the spread of fever ticks without the expense of multiple gatherings and treatments and without the need to vacate the pastures. Consequently, way the adjacent pastures would serve to buffer the spread of infestation. The uniformity of consumption of the treated molasses supplement by cattle provides an opportunity for using treated supplements as a predictable methodology for delivering ivermectin to range cattle, thereby substantially reducing the risk of dispersing ticks into uninfested areas

#### ACKNOWLEDGMENTS

The authors thank Gary Earl, Wayne Ryan, and Keith Shelly for their assistance in handling of cattle.

#### REFERENCES

- Campbell WC, Fisher MH, Stapley EO, Ablers-Schonberg A, Jacob TA (1983) Ivermectin: a potent new antiparasitic agent. *Science*. 221: 823-828.
- 2 Drummond RO (1985) Effectiveness of ivermectin for control of arthropod pests of livestock. Southwest. *Entomol. Suppl.* 7: 34-42.
- 3 Campbell WC (1989) Ivermectin and abamectin. Springer Verlag, New York.
- 4 Jackson HC (1989) Ivermectin as a systemic insecticide. *Parasitol. Today.* 5: 146-156.
- 5 Miller JA, Drummond RO, Oehler DD (1983) A sustained release ivermectin implant for livestock pest control. In Roseman TJ, Mansdorf SZ (eds.) *Controlled release delivery systems*. Marcel Dekker, New York, pp 223-236.
- 6 Soll MD, Carmichael IH, Swan GE, Gross SJ (1989). Control of induced infestations of three African multihost tick species with sustained-release ivermectin. *Exp. Appl. Acarol.* 7: 121-130.

- 7 Zingerman JL, Cardinal JR, Chern RT, Holste J, Williams JB, Eckenfoff B, Wright JT (1997) The in vitro and in vivo performance of an osmotically controlled delivery system--Ivomec SR Bolus. J. Control. Rel. 35: 1-11.
- 8 Miller JA, Oehler DD, Pound JM (1998) Delivery of ivermectin by injectable microspheres. J. Econ. Entomol. 91: 655-659.
- 9 Miller J A, Davey RB, Oehler DD, Pound JM, George JE, Ahrens EH (1999) Control of Boophilus annulatus (Acari: Ixodidae) on cattle using injectable microspheres containing ivermectin. J. Econ Entomol. 92: 1142-1146.
- 10 Miller JA, Davey RB, Oehler DD, Pound JM, George JE (2001) The Ivomec SR bolus for control of (Acari: Ixodidae) on cattle in South Texas. J. Econ Entomol. 94: 1622-1627.
- 11 Pound JM, Miller JA, George JE, Oehler DD, Harmel DE (1996) Systemic treatment of whitetailed deer with ivermectin-medicated bait to control free-living populations of lone star ticks (Acari: Ixodidae). J. Med. Entomol. 33: 385-394.
- 12 Pound JM, Miller JA, Oehler DD (2004) Depletion rates of injected and ingested ivermectin from blood serum of penned white-tailed deer, Odocoileus virginianus (Zimmermann) (Artiodactyla: Cervidae). J. Med. Entomol. 41: 65-68.
- 13 Whitlow LH, Marshall SP, Van Horn HH, Flores JR (1976) Liquid feed passage route into stomach compartments, influence of abomasal infusions on plasma glucose, and supplementation of dry rations

with liquid feeds from lick-wheel feeders. J. Dairy Sci. 59:675.

- 14 Oehler DD, Miller JA (1989) Liquid chromatographic determination of ivermectin in bovine serum. J. Assoc. Off. Anal. Chem. 72: 59.
- 15 Miller JA, Garris GL, Oehler DD (1997) Control of lone star ticks on cattle with ivermectin. J. Agric. Urban Entomol. 14: 199-204.
- 16 Miller JA, Davey RB, Oehler DD, Pound JM, George JE (2001) The Ivomec SR Bolus for control of Boophilus annulatus (Acari: Ixodidae) on cattle in South Texas. J. Econ. Entomol. 94: 1622-1627.
- 17 Miller JA, Davey RB, Oehler DD, Pound JM, George JE (2003) Efficacy of the Ivomec SR Bolus for control of horn flies (Diptera: Muscidae) on cattle in South Texas. J. Econ. Entomol. 96: 1608-1611.
- 18 Davey RB, Pound JM, Miller, JA, Klavons JA (2010) Therapeutic and persistent efficacy of a long-acting (LA) formulation of ivermectin against Rhipicephalus (Boophilus) microplus (Acari: Ixodidae) and sera concentration through time in treated cattle.
- 19 Pound JM, George JE, Kammlah DM, Lohmeyer KH, Davey RB (2010) Evidence for role of whitetailed deer (Artiodactyla; Cervidae) in epizootiology of cattle ticks and southern cattle ticks (Acari: Ixodidae) in reinfestations along the Texas/Mexico border in South Texas: A Review and update. *J. Econ. Entomol.* 103: 211-218.