

Compounding Iron Dextran with NSAIDs at processing



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The objective of this project was to evaluate whether the mixing (compounding) of NSAIDs (anti-inflammatory/analgesic agents), such as meloxicam or flunixin meglumine, with iron dextran for administration to piglets at the time of processing has any effects on the availability of the NSAID. In a series of experiments, we evaluated the stability and systemic availability of both NSAIDs when mixed with iron dextran in the same bottle for administration to piglets at the time of processing. We also evaluated the effects of this practice on iron dextran's ability to increase piglet hemoglobin concentrations. We found that the amount of NSAID recovered from the bottle was reduced beginning shortly after mixing. We also found that blood drug levels measured in piglets for each NSAID when compounded with iron dextran was significantly lower than when each NSAID was administered alone to piglets. We did not find any significant effects of mixing NSAIDs with iron dextran on iron dextran's ability to increase hemoglobin following administration to piglets. The overall conclusion from these experiments is that the mixing of NSAIDs with iron dextran in the same bottle for administration to piglets at the time of processing results in a suspected drug interaction that reduces the shelf-life of the formulation and the amount of NSAID available for therapeutic effects.



Introduction

When NSAIDs (anti-inflammatory/analgesic agents) such as meloxicam or flunixin meglumine are administered to piglets at the time of processing, it is tempting to mix or compound the NSAID with iron dextran to be delivered in a single injection, thereby reducing the number of injections to the piglet. Technically the practice of mixing two different products in the same syringe/bottle is not allowed under the Canadian Quality Assurance program, nor is the compounding of drugs for food animal use acceptable to the Canadian Global Food Animal Residue Avoidance Databank, but we are aware that this practice does occur and therefore it seems prudent to evaluate possible drug interactions that could affect the absorption and availability of either the NSAID or iron. The study was carried out using three separate experiments and performed at the University of Guelph, with the following

objectives i) to evaluate the bioavailability of meloxicam (Metacam® 20 mg/mL Solution for Injection, Boehringer Ingelheim Canada LTD) and flunixin meglumine (Banamine®, Merck Animal Health) when compounded with iron dextran (Dexafer-200®, Vetoquinol) and administered to newborn piglets of approximately 5 days of age, ii) to evaluate the effect of compounding these agents on iron dextran's ability to increase piglet hemoglobin concentrations, and iii) to evaluate the storage life by measuring concentrations of the NSAIDs at various times after mixing with iron dextran.

Results and Discussion

Measurement of recoverable flunixin meglumine and meloxicam when compounded in iron dextran was accomplished using high performance liquid chromatography. Our results showed that recoverable levels of either NSAID were reduced,

beginning as early as 2 hours post-mixing, and with over 30% reduction in recoverable flunixin meglumine concentrations and over 10% reduction in meloxicam concentrations by 24 hours post-mixing. These findings suggested a probable drug interaction that could result in reduced NSAID being available for systemic absorption when administered to piglets. In the first of our two live animal experiments, we found no significant effects of compounding either NSAID with iron dextran on measured blood hemoglobin levels, indicating no significant effects on the iron status of the pig. The results of our bioavailability study (n= 8 piglets per group) comparing blood NSAID levels for flunixin meglumine and meloxicam when administered to piglets alone versus compounded in iron dextran did show notable findings. Piglets receiving flunixin meglumine were dosed intramuscularly at 2.2 mg/kg either as the NSAID alone or when compounded with iron dextran. Piglets receiving meloxicam were also dosed intramuscularly at 0.4 mg/kg as the NSAID alone or when compounded with iron dextran. Multiple blood samples collected shortly after dosing to 72 hours post-dosing were analyzed for meloxicam or flunixin meglumine using validated mass spectroscopy methods. Results showed significantly reduced concentrations of both NSAIDs when compounded with iron dextran compared to levels noted when NSAID was given alone rendering the compounding of NSAIDs with iron dextran not bioequivalent to NSAIDs administered alone.

Conclusion

The results of our study show that the mixing of meloxicam or flunixin meglumine with iron dextran likely produces a drug interaction, which does not appear to affect iron dextran's ability to maintain adequate hemoglobin concentrations, but does reduce the availability of the NSAID for absorption into the systemic circulation. The Clinical ramifications of the reduced blood NSAID levels when compounding with iron dextran require additional efficacy studies to evaluate whether adequate analgesia is being provided at the current NSAID concentrations in the compounded formulation. Importantly, if flunixin meglumine or meloxicam is mixed with iron dextran for administration to piglets at the time of castration and processing the compounded product needs to be used right away.



Managing Winter Ventilation



I was asked to write an article on how does Prairie Swine Centre prepare for winter ventilation. In thinking about this, I came to the realization that we really do nothing different than at any other time of the year assuring that proper ventilation parameters are being monitored in all rooms on site and that daily maintenance and repair is performed. One small difference when it comes to winter ventilation, is that for a period of time, in late fall and also in early spring, staff need to be more vigilant on a day to day basis to ensure room temperature fluctuations are kept to a minimum. This usually means daily vigilance monitoring first and second stage ventilation fans and either installing or removing fan covers until the temperature stabilizes late fall and late spring.

I have found that it was very beneficial to set up routing procedures for production technicians in all areas of the operation. Staff work with laminated "daily" work schedules for each day of the week that dictate what they are required to do, depending on that day. We have one work sheet for grow-finish technicians and as well, sheet for breeding/gestation/lactation and nursery staff. There is also room for "other" jobs that we all know comes up and staff or I will add this to the list for that day. Jobs are checked off when completed. Minor maintenance and repairs on grow-finish equipment is daily, by technicians from 10:30-11:00. Major maintenance is scheduled for production technicians to assist our maintenance man, if required, Thursday afternoon from 12:30 to 4:00.

What these sheets do is ensure that every single day staff is reminded of priority job functions that have to be dealt with. If someone is sick, the staff person moving into this position has a record of all job functions completed so far this week and what his priorities are today, with little instruction required.

Daily technician responsibilities:

- Room checks which involve monitoring the controller to see if fan's, heaters, and inlets are doing what the controller is indicating. This is the responsibilities of technicians in all rooms where animals are housed.
- If there are major problems the manager is notified and a request is put into maintenance for immediate repair. Technicians will deal with minor issues that same day.

Weekly technician responsibilities:

- Every Monday morning set point temperatures are changed depending on the room and the average weight of the animal particularly in nursery and grow finish. Set point temperature indicator sheets are kept on a bulletin board by each room. The appropriate time sheet is used in grow-finish vs nursery room set points for fall-winter and spring-summer ventilation.
- Farrowing rooms are set up with a standard curve that is initiated when the majority of sows have farrowed in that particular room.

Seasonal technician and maintenance responsibilities:

- As Manger I will determine temperature room changes in breeding, gestation, and gilt-development and these rooms are changed seasonally.
- As part of our maintenance program all second and third stage fans, louvers and covers in non all-in-all-out rooms are washed late fall so that they are clean when they are shut down for the winter.
- All heaters are blown out in the fall as a regular maintenance procedure.
- Appropriate fresh air inlets to the attics in all barns are closed late fall and again opened in the spring.

