Evaluation of Lidocaine Content and Delivery from Latex Elastrator Bands Using LC-MS, GC-MS and HPLC Techniques

James Saville¹, Tyler Trefz¹, Ori Granot¹, Nick Allan¹, Merle Olson¹, Richard Terry² and Jeremy E. Wulff²

¹ Department of Chemistry, University of Victoria, PO Box 3065 STN CSC, Victoria, British Columbia, Canada V8W 3V6
²Chinook Contract Research Inc., 381 97 East Lake Ramp NE, Airdrie, AB, Canada, T4A 0C3

Abstract
Castration is a necessary management practice in agriculture. The health and safety of cattle and their handlers is improved via castration by reducing aggressiveness of bulls by lowering production of male hormones. Castration allows producers to prevent unwanted mating and poor meat quality has been shown to be consistently higher grade, with more marbling, allowing for beef to be sold at higher prices. Helping manage the animal’s pain during castration is important for the well-being of the animal and for a faster recovery time. The Canadian Code of Practice for the Care and Handling of Beef has recently been updated advising that pain control be used when bulls older than 6 months are castrated, and it is expected pain management will be advised for all castrations in the near future. Lidocaine, a local anesthetic, is often injected during castration procedures to help mitigate pain; however it is relatively short acting and its injected delivery has many practical barriers. Recently, a novel way to administer lidocaine topically has been achieved by loading elastogel bands with the anesthetic. This strategy allows for continuous release of clinically significant doses of anesthetic to the animal upon application of the castration band, providing sustained pain relief. The Wulff lab has worked with Chinook Contract Research (CCR) in a NSERC Engage project to evaluate different sized castration bands loaded with lidocaine (shown below) using GC-MS, LC-MS and HPLC techniques. CCR carried out field studies to compare classical lidocaine injection with the novel castration band delivery method in vivo.

1. Introduction
Castration is a necessary management practice in agriculture. The health and safety of cattle and their handlers is improved via castration by reducing aggressiveness of bulls by lowering production of male hormones. Castration allows producers to prevent unwanted mating and poor meat quality has been shown to be consistently higher grade, with more marbling, allowing for beef to be sold at higher prices. Helping manage the animal’s pain during castration is important for the well-being of the animal and for a faster recovery time. The Canadian Code of Practice for the Care and Handling of Beef has recently been updated advising that pain control be used when bulls older than 6 months are castrated, and it is expected pain management will be advised for all castrations in the near future. Lidocaine, a local anesthetic, is often injected during castration procedures to help mitigate pain; however it is relatively short acting and its injected delivery has many practical barriers. Recently, a novel way to administer lidocaine topically has been achieved by loading elastogel bands with the anesthetic. This strategy allows for continuous release of clinically significant doses of anesthetic to the animal upon application of the castration band, providing sustained pain relief. The Wulff lab has worked with Chinook Contract Research (CCR) in a NSERC Engage project to evaluate different sized castration bands loaded with lidocaine (shown below) using GC-MS, LC-MS and HPLC techniques. CCR carried out field studies to compare classical lidocaine injection with the novel castration band delivery method in vivo.

2. HPLC Quantitation
Effect of Solvent Ratio on Range of Linearity

* The bulk of lidocaine (50-60% of total extract) is extracted in the first 30 minutes, indicating that over half of the lidocaine is loaded near the surface of the bands. This may be important for reduced pain relief.

* Different band extraction variable (such as solution agitation, heating and differing solvent amounts) were examined with no major improvements found compared to the optimal method, whereby the band is soaked in THF (50%) at room temperature.

3. GC-MS Quantitation
Lidocaine Quantitation in Elastrator Bands

- GC (25 m x 0.25 mm, 0.5 µm stationary phase column) resulted in a wider linear range compared to HPLC

- Extracting lidocaine into one extraction (x2) over the same time period, resulted in the same amount of lidocaine recovered (73.9±3.7 mg band and 73.1±2.04 mg band respectively).

Lidocaine Quantitation in Tissue Samples

- The amount of lidocaine remaining in the extraction bands (post-incubation with steak cubes) slowly decreases over time. The relatively high loss of lidocaine in the first 30 minutes suggests an initial high anesthetic release, followed by minimal release.

- The amount of lidocaine recovered from the steak cubes also showed this high initial uptake, however lidocaine recovery plateaued in the first 5 hours, indicating that a portion of the lidocaine being lost from the bands is not accounted for.

4. Field Study Results
Lidocaine Concentration in Bovine Scrotal Tissue

- Under-body temperature is positively correlated with animal health status.

- A 2-fold decrease in temperature between the control and test groups after 7 days (28 ± 2°C and 28 ± 1°C respectively) suggests the Callicrate Bander decreased inflammation

5. Conclusions & Future Directions

- Lidocaine content has been determined using a simplistic extraction method and quantified by HPLC and GC-MS instruments. Bands have been shown to contain significant levels of lidocaine.

- Praval in vitro and in vivo studies indicate the bands are capable of delivering lidocaine over extended periods of time which is advantageous over lidocaine administered by injection.

- Field studies are promising showing the lidocaine loaded bands work as expected eluting lidocaine into tissue. The efficacy of the bands was evaluated by physiological and behavioral techniques indicating the lidocaine loaded bands provide an ongoing numbing effect and pain relief compared to control bands with no lidocaine.

- Future research will help to support the eventual commercial scale up of this novel animal welfare product.

References
3) Lidocaine Volume and Method of Use, PCT/US18/46150.

Acknowledgements

University of Victoria