Coxib inhibitors, or COX-2 selective inhibitors, are nonsteroidal anti-inflammatory drugs (NSAIDs) that selectively inhibit the cyclooxygenase 2 enzyme. This leads to reduced production of inflammatory prostaglandins, thereby decreasing inflammation and providing analgesia.

The NSAID meloxicam, in Healthy Canines – a Pilot Study

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**Background**

Canine osteoarthritis (OA) is an irreversible chronic condition affecting 1 in every 5 adult dogs. It is characterized by inflammation and the gradual breakdown of joint structures, followed by pain and decreased mobility of the affected areas. Treatment strategies aim to slow the progression of disease and decrease pain and inflammation. The cyclooxygenase (COX) enzyme, specifically the COX-2 isoform, is inhibited by the COX inhibitors, thereby decreasing inflammation and providing analgesia.

The NSAID meloxicam, a COX-2 selective inhibitor, is commonly used to treat OA cases, and is associated with fewer adverse effects relative to other NSAIDs. Frequently administered as an oral suspension, this mode of delivery poses various challenges including decreased owner compliance and reduced tolerance in some dogs. Recently, transdermal delivery systems have been suggested with advantages such as: better patient compliance, consistent and controllable drug levels, and localized drug delivery with reduced systemic levels of drug.

In 2009, Yuan et al. demonstrated that higher levels of meloxicam were achieved in synovial fluid compared to the plasma of beagles dogs when treated with a gel form of meloxicam that was topically applied to the stifle joint. They also showed that this ratio was higher than that achieved with an oral meloxicam pill.

In this study, meloxicam compounded in deriVra® is being investigated for use in veterinary medicine as an alternative to currently available meloxicam dosage forms. Meloxicam is administered to healthy research dogs as a clinically approved oral suspension (Metacam®) or compounded in a transdermal delivery system (deriVra®). Levels of meloxicam in plasma and synovial fluid are compared between the two delivery systems. Additionally, any adverse systemic or local effects on the skin tissue are compared.

**Objectives**

Objective 1: Compare meloxicam levels in the synovial fluid of the stifle joint of healthy research dogs following topically applied deriVra® to orally administered Metacam®

Objective 2: Evaluate systemic and local adverse effects following topical application of deriVra® or oral administration with Metacam®

**Hypothesis**

It is expected that:

i) Topically applied meloxicam using deriVra® will achieve equal or higher synovial fluid drug levels in the stifle compared to orally administered Metacam®

ii) Topically applied meloxicam using deriVra® will achieve lower plasma drug levels compared to orally administered Metacam®

iii) Topically applied meloxicam using deriVra® will result in fewer adverse effects compared to orally administered Metacam®

**Methods**

**Phase 1**

Eligibility criteria samples:
- Plasma - biochemical profile – complete blood cell count
- Urine – Weight – Subjective clinical assessment

Sample collection:
- Baseline samples:
  - Plasma – meloxicam concentration
  - Synovial fluid – cytological profile – meloxicam concentration
  - 2 stifle skin biopsies – Histological analysis

Post-treatment samples:
- Plasma – meloxicam concentration
- Synovial fluid – cytological profile
- 2 stifle skin biopsies – Histological analysis

**Phase 2**

Dogs were randomized to either oral or topical meloxicam groups in phase 1, then crossed over in phase 2 after a 21-day washout period. As shown above, dogs were also randomized to either left or right stifle joint for sample collection in phase 1, with the remaining stifle joint used for sample collection in phase 2.

Meloxicam and deriVra® were given once daily for 8 days, as shown below. After treatment assignment, dogs were randomized to group 1 or 2. Group 1 dogs began treatment on day 1, Group 2 dogs began treatment on day 2. A loading dose of meloxicam was administered on day 1 in the Metacam® treatment group.

Daily assessments were performed on temperature, weight, respiration rate, pulse and behavior of every dog.

**Results**

**Phase 1**

- Baseline samples:
  - Plasma – meloxicam concentration
  - Synovial fluid – cytological profile – meloxicam concentration
  - 2 stifle skin biopsies – Histological analysis

**Phase 2**

- Baseline samples:
  - Plasma – meloxicam concentration
  - Synovial fluid – cytological profile – meloxicam concentration
  - 2 stifle skin biopsies – Histological analysis

**Future Directions**

Drug stability study
- Investigate the effects of various storage conditions on the shelf life and distribution of meloxicam compounded in the deriVra® carrier system. Conditions include varying:
  - Temperatures
  - Light sources
  - Freeze-thaw cycles

Relaxation study
- Investigate the effects of topically applied meloxicam in deriVra® on the carrageenan-induced paw edema model of inflammation in rats

**References**


**Acknowledgements**

Dr. Saad Enouri
Amanda Hathway
Dr. Joseph Gabriele (Faculty Advisor)
Dr. Ron Johnson (Faculty Advisor)
Dr. Thomas Gibson (Faculty Advisor)

PET trust fund

University of Guelph Ontario Veterinary College
Dogs from U of G Central Animal Facility (Hunter, Janev, Baron, Major, Ruby, Baby)