

## Intra-articular Treatment Combining Sustained Release Colchicine Encapsulated in Microspheres, and Ropivacaine, Is Effective in Inflammatory Arthritis in Rats



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## BACKGROUND

- Gout is a common type of arthritis, causing excruciatingly painful and disabling flares.
- Gout flares are poorly managed by existing treatments: slow and limited efficacy against pain, combined with safety risks.
- Oral Colchicine (COL) is approved for treating gout flares, but its use and dose levels are limited due to its toxicity.
- We aimed to evaluate the efficacy of a novel intra-articular (IA) combination of sustained release (SR) COL and Ropivacaine (ROPI) (PKM-01)

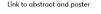
destruction (D) scores after SR COL + ROPI in knee joint.

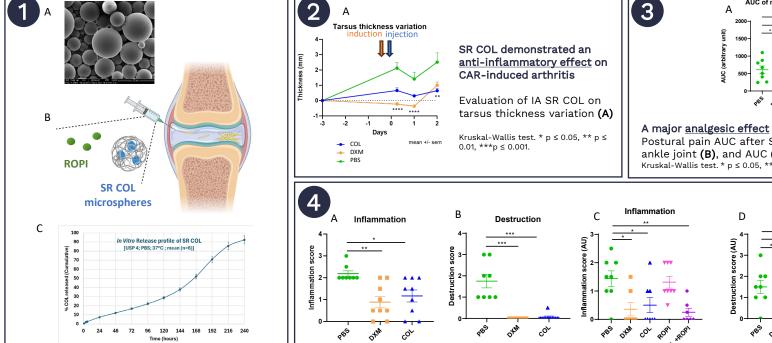
Kruskal-Wallis test. \*  $p \le 0.05$ , \*\*  $p \le 0.01$ , \*\*\* $p \le 0.001$ .

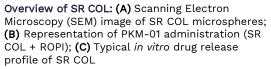
shown).

## **METHODS**

- SR COL microspheres are made of already approved biodegradable poly(lactic-co-glycolic acid) (PLGA) polymer
- Carrageenan (CAR) (50 µL CAR 3% injected IA in Sprague Dawley rats) was used to induce ankle or knee hyper acute and severe arthritis
- Controls were PBS or Dexamethasone (DXM) injected in rat joints

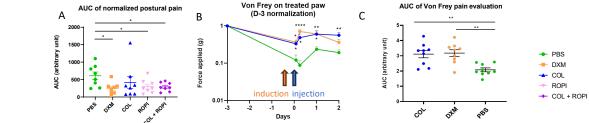






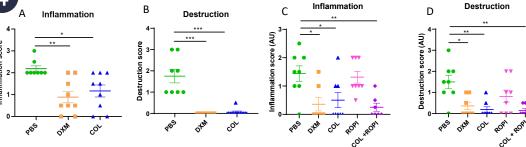
SR COL is designed to maximize local concentration and lead to negligible systemic levels preventing DDI and safety concerns

## RESULTS



A major analgesic effect was demonstrated in CAR-induced arthritis (ankle and knee) Postural pain AUC after SR COL + ROPI in knee joint (A), and Von Frey pain evaluation scores after SR COL in the ankle joint (B), and AUC (C).

Kruskal-Wallis test. \* p ≤ 0.05, \*\* p ≤ 0.01, \*\*\*p ≤ 0.001.

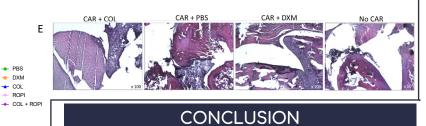


Significant protection against joint inflammation and destruction in CAR-induced arthritis. Histological

inflammation (A) and destruction (B) scores after SR COL in ankle joint. Histological inflammation (C) and

(E) Histological characterization of ankles from representative rats in the different conditions of treatment.

Nota: Addition of ROPI to SR COL had no effect on histological pattern compared to COL alone (data not



SR COL + ROPI (PKM-01) demonstrates efficacy in the CAR-induced arthritis model, showing a rapid analgesic effect and significantly preventing joint inflammation and destruction. A Phase II clinical study is planned in gout flares. These results may also highlight potential applications in pseudo-gout and osteoarthritis (OA), where SR COL could be beneficial.

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