Background

- Osteoarthritis (OA) is a degenerative joint disease that affects over 32 million U.S. adults
- OA causes painful cartilage breakdown in joints and currently has no cure
- The gene MMP13 plays a key role in cartilage degradation
- Small interfering RNA (siRNA) against MMP13 silences the gene by cleavage of mRNAs, reducing cartilage breakdown and inhibiting disease progression
- siRNA delivery is limited in vivo due to endosomal escape issues and kidney clearance
- Encapsulating siRNA in polymeric nanoparticles (si-NPs) can help overcome delivery challenges

Objective

To develop a polymeric nanoparticle formulation to optimize siRNA delivery

Nanoparticle Composition

- si-NP Components:
  1. Poly(lactic-co-glycolic acid) (PLGA) for stability
  2. 50:50 DP 100 DMAEMA-co-BMA (DB) for endosomal escape
  3. Surfactant-DSPE-PEG (Lipid-PEG) for biocompatibility
  4. siRNA for gene silencing

Formulation Optimization Parameters:

1. PLGA + DB concentration: 1-6 mg/mL
2. Percent DB: 25, 50, and 75%
3. Amines to Phosphates (N/P) Ratio 5 and 10

Nanoparticle Preparation

- PLGA + DB + siRNA in ACN
- Lipid-PEG in DI water

Results - In Vitro Luciferase Knockdown/Cell Viability

- Luciferase knockdown in si-NP containing MDA-MB-231 cells 48 hours after treatment with luciferin. Top three rows contain luc-NP, bottom rows contain si-NP.
- Luciferase knockdown in si-NP with a core composition of 50% DB and an N/P ratio of 5 were most uniform, viable, and effective at luciferase knockdown.

Future Work

- Test more si-NP formulations
- Vary si-NP dose in vitro
- Quantify siRNA loading
- Test novel DMA surfactants

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- Figures created with BioRender.com

References

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