

## Liposomal formulation promising for managing osteoarthritis-induced pain

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Osteoarthritis (OA), one of the most common forms of arthritis, is a chronic condition marked by the gradual breakdown of cartilage in the joints, causing pain and physical limitations. It involves various changes, such as the degradation of the cartilage and its mechanical properties, as well as the development of fissures. At the same time, it increases bone turnover, resulting in thickening of the bone around the joints. Osteophytes are also formed on the joint edges, indicating abnormal bone remodelling.

The signs of osteoarthritis include pain, swelling, reduced mobility and joint deformity. In severe cases, it can lead to muscle loss, decreased proprioception and even disability. Studies say that, by 2050, 130 million people worldwide will have osteoarthritis, with 40 million experiencing severe disability due to the condition. The prevalence of osteoarthritis is rising due to factors like an ageing population and increasing obesity rates.

## **Therapy for Osteoarthritis**

Despite extensive research on osteoarthritis, its complex pathophysiology has yet to be understood completely. As of now, there is no universally accepted treatment standard. Currently, a "step therapy" approach is commonly employed, and it involves non-pharmacological, pharmacological, and surgical treatments aimed at alleviating pain symptoms and restoring joint function.

Pharmacological treatments are often used in the early stages of osteoarthritis to manage symptoms effectively and are widely practised in clinical settings. One such treatment methodology for osteoarthritis is using Hyaluronic Acid supplements. Hyaluronic Acid (HA) is a gel-like substance that naturally occurs in the human body.

It aids in joint cartilage and bone growth and development. Hyaluronic Acid reduces joint inflammation and pain resulting from injury or tissue degeneration. This is why intra-articular Hyaluronic Acid injection has emerged as an effective therapy for osteoarthritis pain relief. Hyaluronic Acid also exhibits excellent gelling properties due to its strong water-binding capacity.

However, some cases have shown a lack of effectiveness of the Hyaluronic Acid injection treatment, possibly due to its brief retention duration in the joint cavity. This often requires repeated intra-articular injections to showcase its therapeutic benefits.

Apart from its brief retention post-injection, another factor contributing to the perceived inefficacy of Hyaluronic Acid injection into the synovial joint is its failure to localize to the joint surface when administered. Studies have shown that while Hyaluronic Acid supplementation improves the viscoelasticity of synovial fluid, it does not achieve lubrication of the cartilage surface unless localized there. However, emerging technologies like encapsulation in liposomes are overcoming these barriers.

## **Role of Liposomes as Effective Drug Carriers**

In general, liposomal nanoparticles have been known to enhance the effectiveness of many formulations and have been in clinical use for years. They have also been thoroughly explored as drug carriers for treating Rheumatoid Arthritis, another type of arthritis. However, many drugs used for rheumatoid arthritis treatment suffer from low bioavailability, rapid clearance and lack of selectivity, which means they need frequent, high dosing for effective therapy. Unfortunately, these high doses also raise the likelihood of systemic side effects.

Using liposomes as drug carriers enhances the therapeutic potential of these antirheumatic drugs. By adjusting liposomal properties, such as size and surface charge, it is possible to optimize their ability to penetrate biological barriers. This also increases the likelihood of them remaining at the administration site, reducing premature degradation and toxicity to unintended tissues.

The ideal properties of liposomes vary depending on the administration route. Larger liposomes are adequate for local injection, while smaller ones are better for passive targeting. Moreover, liposomal surfaces can also be tailored for selective drug delivery to specific cells in arthritis.

## **Why Liposomal Hyaluronic Acid Can Be an Effective Treatment Arthritis**

Hyaluronic Acid hydrogel can be combined with additional molecules and particles that function as lubricants. Liposomes, for instance, are a class of molecules known to decrease the friction typical of biological surfaces through boundary lubrication. Researchers have investigated the combined lubricating effects of liposomes with hyaluronic acid hydrogel as a possible treatment approach for joints affected by arthritis.

This approach involves encapsulated liposomes offering improved boundary lubrication to Hyaluronic Acid hydrogel by creating a hydration shell on the gel surface. This shell prevents water molecule loss from the gel bulk. Research has shown this synergistic effect of Hyaluronic Acid hydrogel-mediated liposome delivery using a tendon explant model. In this model, the combined delivery method significantly decreased the tissue surface friction coefficient compared to delivering Hyaluronic Acid or liposomes alone.

In another research, a combination of Hyaluronic Acid and liposomal nanoparticles was developed and evaluated as a potential treatment for osteoarthritis inflammation and pain relief. The optimal liposomal nanoparticle maintained stability, efficient drug delivery and encapsulation without losing efficacy until reaching the target organ.

### **Key Takeaways**

Studies and research into the efficacy of liposomal formulation for reducing inflammation show promise for managing osteoarthritis-induced pain. Similar strategies have shown beneficial effects in rheumatoid arthritis therapy.

Administering biodegradable liposomal Hyaluronic Acid-based analgesics directly into the joint cavity has emerged as a viable option. These formulations aim to minimize adverse reactions while providing effective pain relief.

However, several challenges remain in translating this treatment to human clinical use. Determining the optimal dose, frequency and timing of treatment based on disease severity and location is crucial. This calls for further research to advance the application of this treatment approach in the future. More government- and academia-based research could be a way to enhance the uptake of such treatments.

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