

TN HYDROGELS AS A POTENTIAL ANTI-INFLAMMATORY DRUG DELIVERY SYSTEM TARGETED TO OSTEOARTHRITIC KNEES

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ABSTRACT

Arthritis affects 26.3% of adults and approximately 50,000 children in the United States [1]. Hydrogel drug-delivery systems have been considered as a viable option for drug delivery to arthritic articular cartilage in the knee. To determine physiologically relevant loading, a Qualisys motion capture system was used to analyze the gait of college-aged females as they took several steps on a flat surface, then stepped onto a force plate. The motion capture and force plate data was used to determine maximum force exerted on the knee during normal gait. Three different alginate-based hydrogels, where the superior one had a triple interpenetrating graphene oxide network (TN hydrogels), were investigated for use as an anti-inflammatory drug delivery system in a human knee joint. Physiologically relevant cyclic loading was performed to ensure that the TN hydrogel could withstand the force exerted in the knee. The TN hydrogel experienced a change in energy of 50% after cyclic loading (10.6 ± 15.0 Pa) and survived high stresses of 4 kPa, which is 80 magnitudes larger than observable gait forces as measured in this study. From a mechanical perspective, TN hydrogel appears to be mechanically viable for arthritis drug delivery. In addition, based on calculations and Flory-Rehner equations, the pore size of the TN hydrogel is adequate for encapsulating most NSAIDs, which have a molecule size ≤ 5μm.

Keywords: Hydrogel, drug-delivery system, gait analysis, knee joint, cartilage

INTRODUCTION

Arthritis affected approximately 26.3% of United States adults as of 2014 [1]. Osteoarthritis (OA), which is the most common form of arthritis, is characterized by the loss of physiological function in the joints of the body due to the degradation of articular cartilage [2]. As the articular cartilage degrades, bone-on-bone articulation occurs, leading to irritation of the surrounding tissue. Symptoms of this condition include joint stiffness and inflammation, joint dysfunction, and pain. The amount of pain experienced can range from minor irritation to debilitating pain for those affected by OA. Inflammation, especially that which is caused by a knee injury, can be traced to the progression of the disease [3]. Early and multimodal conservative treatment is also vital to slow this progression [4]. Included in conservative treatment is the use of anti-inflammatory drugs, such as acetaminophen, aspirin, ibuprofen, and intra-articular corticosteroids [5]. Controlling inflammation is therefore vital not only to slowing the progression of the disease but also to managing pain.

Non-steroidal anti -inflammatory drugs (NSAIDS), in particular ibuprofen, are often used as a short-term (~4 weeks) solutions for combating pain associated with osteoarthritis in the knee joint [6]. Systemic administration of drug is limited by dosing requirements; and systemic drug administration, direct bolus injections, corticosteroid injections, and viscosupplementation all fail over time due to drug loss to systemic circulation [7]. As a way to overcome pharmacokinetic limitations and