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Intraarticular drug delivery in osteoarthritis☆

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Abstract

Osteoarthritis (OA) is a primarily non-inflammatory, degenerative joint disease characterized by progressive loss of articular cartilage, subchondral bone sclerosis, osteophyte formation, changes in the synovial membrane, and an increased volume of synovial fluid with reduced viscosity and hence changed lubrication properties. As OA is the most common type of arthritis and a leading cause of disability, there is a largely unmet medical need for disease-modifying and symptomatic treatment. Due to the localized nature of the disease, intraarticular (IA) drug injection is an attractive treatment approach for OA. The various glucocorticoid and hyaluronic acid (HA) formulations, which are currently available on the market for IA treatment, provide only short-term pain relief or/and often do not provide adequate pain relief. The available oral drugs for symptomatic treatment also have shortcomings, most notably side effects. Therefore, there is still a large unmet need for novel OA drugs, which provide effective long-term pain relief and/or have disease-modifying properties. To achieve long-term drug exposure, different established formulations such as suspensions and hydrogels, and also novel approaches such as lipid based formulations and nano- or microparticles are currently in development. The development of novel drugs in combination with new formulations for IA treatment of OA, represents a promising approach in this challenging area of research.
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Keywords: Osteoarthritis; Intraarticular; Sustained release; Hyaluronic acid; Glucocorticoid

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Contents

1. Introduction

Osteoarthritis (OA) is the most common form of arthritis, with a prevalence after the age of 65 years of about 60% in men and 70% in women [1]. Current treatment options for OA are limited. They include symptomatic treatment with simple analgesics, non-steroidal anti-inflammatory drugs (NSAIDs) or intra-articular (IA) injected glucocorticoids and hyaluronic acid (HA) preparations. Non-pharmacological measures range from physical exercise and weight loss to joint lavage, and eventually surgical joint replacement.

There are major unmet needs in OA treatment, for disease-modifying OA drugs (DMOADs), which are not available yet, and also for efficacious pain treatments with long-lasting effects. Furthermore, there is a significant unmet need for OA treatments which do not have any major side effects, due to the chronic nature of the disease often requiring treatment of extended duration. The currently available systemic drugs for relief of OA pain, e.g., the non-selective NSAIDs and selective cyclooxygenase 2 (COX-2) inhibitors, are effective in the early-mid stages of OA, but often fail to provide adequate pain relief as the joint deteriorates. In addition, NSAIDs cause gastrointestinal complications in a significant number of patients, and the COX-2 inhibitors have recently raised concerns regarding cardiovascular side effects/risks, resulting in the with-

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