NEW DRUGS AND NUTRACEUTICALS IN THE TREATMENT OF OSTEOARTHRITIS

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1 INTRODUCTION

Osteoarthritis (OA) is one of the most prevalent and chronic diseases affecting the elderly. Its most prominent feature is the progressive destruction of articular cartilage that results in impaired joint motion, severe pain, and, ultimately, disability. Its prevalence and its moderate to severe impact on daily life pose a significant public health problem [1].

Today, a cure for OA remains elusive and the management of OA is largely palliative focusing on the alleviation of symptoms. Current recommendations for the management of OA include a combination of nonpharmacological interventions and pharmacological treatments (Table 1) [2, 3]. Until now, the pharmacological management of OA is dominated by nonsteroidal anti-inflammatory drugs (NSAIDs) and analgesics (mainly paracetamol). Beside these conventional drugs, some new compounds classified as symptomatic slow-acting disease-modifying drugs (SYSADOA) have shown symptomatic efficacy in treating human hip and knee OA. The term SYSADOA covers a range of agents, including glucosamine sulfate (GS), chondroitin sulfate (CS), diacerhein, hyaluronic acid (HA, intra-articularly), and avocado soybean unsaponifiables (ASU). This group of compounds is mainly composed by nutraceuticals, which have been investigated in clinical trials but commonly used as a health food supplement rather than prescribed drugs in Europe and United States. This chapter reviews the available scientific evidence supporting the efficacy, and explaining the mechanism of action, of drugs and nutraceuticals targeting OA.

2 OA PATHOPHYSIOLOGY: IDENTIFICATION OF NEW BIOCHEMICAL TARGETS

Osteoarthritis is a heterogeneous group of skeletal disorders characterized by common structural and functional changes in overall joint tissues, including cartilage loss, synovium inflammation, bone sclerosis, cysts, and osteophytes.

The chondrocytes play a critical role in the structural changes in OA cartilage. When chondrocytes experience modification of their environment, they undergo different "phenotype modulations" that result in the expression of a different pattern of genes. The main phenotypic modulations, comprise "dedifferentiation" (characterized by the overexpression of type I collagen), hypertrophy (with the expression of type X collagen, tidemark doubling, and apoptosis as a consequence), recapitulation of development (with the re-expression of type IIa and III collagens), as well as regeneration of mature cartilage (with an overproduction of cartilage-specific matrix macromolecules and cell proliferation) (see a review in [4]). It is unclear if the same chondrocyte may express successively different phenotypes or if chondrocytes from different areas of cartilage express different phenotypes. Nevertheless, it is clear that depending on

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